

DOCUMENT SOURCE University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE School of Medicine - Department of History and Health Sciences	
ACCESSION NO. AR 87-46	<b>COPY</b>
FILE CODE NO.	
CARTON NO. Box 5 of 8	
FOLDER NAME Laboratory of Experimental Oncology	
NOTES	
FOUND BY Perry Hall 10/21/94	

721817

## Lost Colony: Laboratory of Experimental Oncology, San Francisco, 1947-54: Historical Note<sup>1, 2</sup>

Michael B. Shimkin<sup>3</sup>

"In the light between you and the world, back the world."  
—Franz Kafka  
from *The Great Wall of China*

Four volumes bound in Government-green are arrayed at my left. They record a 7-year period of cancer research, my life, and the lives of several hundred patients and other people. This is the visible residue of the Laboratory of Experimental Oncology (LEO), a collaborative activity between the National Cancer Institute (NCI) and the University of California School of Medicine in San Francisco; I headed this activity between 1947 and 1954. The volumes consist of annual reports, a collection of published reprints, a scrapbook, an album of pictures—and some memories.

This collection of four volumes probably is unique. I may be the only one who had read every word herein contained. Dr. Nicholas Petrakis, a legacy from the LEO who remained at the medical school, retained the brass plate from the front door—a relic that undoubtedly will outlast the papers. Yet the experience, as an early example of a regional cancer center, retains heuristic values, perhaps mostly negative ones.

### THE LAUNCHING

A constellation of occasions and circumstances differentiated into the LEO. After 8 years at the NCI and war service with a parade of acronymic agencies (OSRD, UNRRA, SHAEF, and WHO), I wanted to settle down in an academic environment and contribute to the solution of the cancer problem. Surgeon General Thomas Parran agreed to such an arrangement and even edited an exploratory letter that I drafted to Dr. Francis Scott Smyth, dean of the University of California School of Medicine in San Francisco, my alma mater. Dr. Roscoe R. Spencer, director of NCI, was favorable to the concept of colonies and also encouraged me.

One of the members of the National Advisory Cancer Council in 1946 was Dr. Robert S. Stone, professor of radiology at the University of California Medical School in San Francisco and a medical director in the Manhattan Project. He heard about me from his academic associates and from my involvement with an extension of the Manhattan Project at the NCI. Dr. Egon Lorenz, who was studying the lifetime effects of low levels of radiation on several species of rodents, was having difficulties with the pathologist assigned to him for the hematology work. I was asked to take over; in the process, I learned some hematology.

One day I was asked to meet Stone. We chatted, and I expounded my ideas on a well-supported combined clinical-laboratory unit on cancer research in an academic environment. I wanted to demonstrate that biomedical research programs of the National Institutes of Health (NIH) could develop as colonies of full partnership with universities and that such research should be pursued by full-time research teams. Stone was interested, and careful. The dean and his cancer committee were in favor, he said, but no money, no space, no academic positions were available.

Despite these discouraging words, an exchange of letters between the president of the University of California and the Surgeon General of the Public Health Service formalized an agreement. A sum of \$40,000 was allocated from the budget of the NCI, and negotiations for space were on the way in San Francisco. Dr. Howard R. Bierman, about to leave the Navy, appeared on the scene via an introduction by Spencer. He was a graduate of Washington University in St. Louis and an enthusiastic physiologist who was taking out a patent on a new strain gauge (1). He appeared to be a good man around whom to develop clinical investigations, and a civil service position was obtained for him. He proceeded ahead of me to San Francisco, where I arrived in January 1947.

Space for LEO was found at the Laguna Honda Home, a facility for the aged poor of the city's Department of Health. It was a castle housing some 1,500 souls, whose average age was over 85. The name, meaning "deep lake" in Spanish, was derived from its proximity to a water reservoir about 3 miles south of the medical school campus on Parnassus Hill. San Francisco's director of Public Health, Dr. Jacob Geiger, was an old Public Health Service officer from the plague days in California, a big, pleasant diplomat with a hobby of gathering medals. He, the dean, and the director of the Public Health Service district compiled the necessary documents of agreement, and for the rent of \$10 per year we acquired two floors of one wing of the building. The upper floor was to house the clinical beds and facilities; the lower floor was for the

<sup>1</sup> Received June 30, 1977; accepted September 8, 1977.

<sup>2</sup> Supported by Public Health Service contract NIH 263-76-C-0419 from the National Cancer Institute.

<sup>3</sup> Department of Community Medicine, School of Medicine, University of California at San Diego, La Jolla, Calif. 92093.

No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder.

DOCUMENT SOURCE University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE School of Medicine - Department of History and Health Sciences	
ACCESSION NO. AR 87-46	<b>COPY</b>
FILE CODE NO.	
CARTON NO. Box 5 of 8	
FOLDER NAME Laboratory of Experimental Oncology	
NOTES	
FOUND BY Perry Hall 10/21/94	

basic laboratories, physiology equipment, and animals. Immediately, we ran into long discussions with the administrator of the home, who was not at all sure that rats and mice were included in the agreement. The administrator was a dedicated man with much time on his hands, and discussions with him were interminate.

Contracts were let via the medical school for construction in our area, and reimbursement from the NCI was arranged by one telephone call. Surplus laboratory and office equipment accumulating from demobilization was easily procured, and we were soon munificently equipped. By summer we were in place. Surgeon General Parran dropped in to give his blessing.

No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder.



FIGURE 1.—Surgeon General Thomas Parran (left) inspects the LEO, May 27, 1947; Dr. M. B. Shimkin (center) and Dr. H. R. Bierman (right).

The basic staff was quickly assembled. Among the earlier additions were a biochemist, Dr. Bernard Shacter; an M.D.-Ph. D. immunologist, Dr. Leo Melcher; and a physicist, Mr. Bruce Shumway. But most important were two indispensable women who really ran the place: Miss Dorothy Messee, chief administrative assistant; and Miss Marjorie Brown, chief nurse. By the time the facilities were completed in June 1947, 15 people were on the staff.

Meanwhile, Bierman and I were making clinical and academic contact in the area, including seeing a few patients on consultation. One was a man with a disseminated lymphosarcoma, with external nodules covering his whole body. We had ampuls of nitrogen mustard and gave the patient one course. Every nodule disappeared and the terminal patient sat up and demanded food. News of the miracle, which unfortunately lasted but a short time, spread through the city.

We had meetings with the cancer committee, a consultative cancer board was reorganized, and Bierman was put in charge of the NCI cancer teaching grant to the medical school. With a statistician hired for the purpose, plans were started to devise a national test of cancer knowledge among medical students.

The laboratory reported to the medical school and to the NCI. Good as well as bad consequences came from having more than one bureaucracy to work with. Printing of forms and announcements, for example, was proscribed by Government regulations but simply achieved via the university. Travel to meetings was difficult to finance by the university, but at that time easily arranged with the NCI. Such alternate arrangements were made possible by our several sources of funds. The basic allocation was from the direct operations budget of the NCI; we were, in turn, a "branch" of their structure, loosely placed in the office of the director. The experimental ward was financed by an NCI grant, one of the largest at the time, to the medical school; I expended this money by university rules. A small budget was set up for us by the medical school; this was later derived from the all-university cancer appropriation from the State.

The three sources of funds were reflected in three personnel systems for employment. With the exception of Bierman, members of the scientific professional staff were officers in the Public Health Service. Others on the direct NCI funds were on Federal civil service. The clinical help were hired through the university system. The salaries and emoluments differed and had to be reconciled, a reasonable problem for all but the clinical professionals.

The last item was an Achilles' heel of the activity. I had a fixed idea that clinical investigations should involve no financial arrangements between the patients and the investigators. Thirty years later, I believe this more strongly than ever. The world of the real, even in 1947, however, was out of focus with my beliefs. The medical school faculty derived much of their income from private practice—open, or hidden, or rationalized. I soon found that even seeing patients on consultation and not charging for such consultation embarrassed the physician and the patient.

All services were free to patients admitted to the laboratory ward, and we had no accounting or billing system. Inasmuch as officers of the Public Health Service were "on duty" 24 hours a day, I had control over their activities and allowed no outside practice except for one who supplemented his resources by emergency room attendance on weekends. Such restriction was not applied to civil service employees, whose time after work was their own.

## IN FLIGHT

By the end of the first year, the LEO was a fully developed mini-experimental hospital of 15 beds in addition to laboratories for physiologic, biochemical, and immunologic work. The total budget was now \$212,000. The staff comprised 9 professional investigators, 12 administrative and technical assistants, 8 nurses, and others for a total of 49 people. Residents in medicine and in pathology were rotated through the facility. I was secretary of the statewide Cancer Research Coordinating Committee of the university, on the cancer

DOCUMENT SOURCE University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE School of Medicine - Department of History and Health Sciences	
ACCESSION NO. AR 87-48	<b>COPY</b>
FILE CODE NO.	
CARTON NO. Box 5 of 8	
FOLDER NAME Laboratory of Experimental Oncology	
NOTES	
FOUND BY Perry Hall 10/21/94	

board, and chairman of the planning committee for a research floor of the new medical school buildings. Bierman was chairman of the consultative tumor board and of the cancer teaching program for the medical school.

The clinical work was oriented around two internists and required collaboration and participation by many other specialists. Pathology needs were met by setting up a service extension from the medical school, with a full-time technician and resident, thus expanding the Laguna Honda Home pathology services. Radiology needs were initially met by Laguna Honda Home, but required the purchase of a new fluoroscope. For minor surgical procedures, consulting surgeons provided free services; for major surgery, patients had to be transferred to the University Hospital.

We hoped to develop isotopic radiotherapy and assembled the necessary equipment, including a hood with a collecting device on the roof four stories above. Three research fellows in radiobiology served with us, but later changed careers to pathology and pediatrics.

The professional staff had clinical appointments at the medical school in experimental oncology, and for administrative purposes they were under the Division of Medicine. We were listed separately in the catalog of the medical school. Our main relation, however, was to the interdepartmental cancer board of the medical school, initially chaired by the professor of pathology but soon replaced by Stone, the professor of radiology. He was a capable radiologist and a pioneer of the atomic age (2).

Stone was the *eminence grise* of the cancer situation at the medical school. He enjoyed complete control in his department and volunteered his participation in budgetary and administrative matters of the laboratory. Not having attained this goal, he began to draw up a "constitution" for a Cancer Research Institute (CRI) at the medical school. The rules became increasingly more restrictive and formal, with long hours of acrimonious discussion about specific provisions that seemed trivially detailed.

I finally recognized that the planned institute was being set up for Stone as its director, and that I was seen as a competitor for the position. I announced that my role would continue to remain in the Public Health Service and to head the LEO and that, although the LEO would be within the proposed CRI, I intended to retain control over it whether at Laguna Honda Home or in the new facilities in the medical school. The CRI constitution was soon patched up, and my relations with Stone became formal. The medical school obtained a building grant of \$1 million for an extra floor to house the LEO. Stone decided not to become the director, and instead a pathologist from Stanford University, Dr. David A. Wood, was appointed in 1951. Wood, a stolid, patient man, headed the CRI for over 2 decades.

By the third year of operations, the LEO was too busy to get involved in institutional politics. In retrospect, that was one of the troubles: I should have made frequent trips back to Bethesda to solidify personal

relationships, especially since the leadership there was changing rapidly, with Dr. Leonard A. Scheele and Dr. Harry Eagle now in top positions and with little background or sympathy about our arrangements and goals.

The annual report for 1948-49 proudly proclaimed: "The objective of the Laboratory is clinical research in cancer. With the cancer patient as the focal point of investigations, the work is oriented along four broad approaches: (1) experimental therapy, providing clinical material for other studies as well as permitting evaluation of such procedures on neoplastic disease; (2) physiology, particularly cardiovascular and respiratory physiology of the cancer patient, and the study of neoplastic tissue, *in vitro* and *in vivo*; (3) biochemistry, including metabolic studies on the cancer patient and investigation of specific biochemical reactions; and (4) the study of protein fractions of cancer and normal tissue of human origin, utilizing immunochemical techniques for their identification and differentiation."

This was not wishful thinking. Already 19 publications were printed or in press, and 88 patients had been studied on the ward; this comprised over 3,000 patient-days, explored 10 therapeutic chemicals or procedures, and expanded our pre-LEO experiences. The pathology unit had performed 82 autopsies (18 on our patients) and examinations of 162 biopsy specimens. Even the isotope unit had performed 57 determinations.

The experimental chemotherapy program depended upon clinical observations for the determinations of effect (3). Biometric design, random assignment, and double-blinding were features of the future. Our case numbers were insufficient, and the approaches were foreign to our clinical setting. Frankly, we did not miss them at this early phenomenologic period.

It did not take much astuteness to recognize that nitrogen mustard and amethopterin were active against leukemias and lymphomas, whereas pteropterin and stilbamidine were devoid of useful activity. We soon found that nitrogen mustard did not have to be spaced over several days but could be given in a single dose and that the induction of fever did not enhance the therapeutic response (4). Chymotrypsin was a local cancer nostrum; we tried it on 10 patients, and the only effect was severe anaphylactoid reactions (5). Chymotrypsin was not further advocated.

Hydroquinone monobenzyl ether, used in depigmentation of rubber, was described to block melanin formation. We obtained a commercial product, purified it, and treated patients having disseminated melanoma (6). No beneficial effects were noted, and the trial was completed without the subsequent interminable regulations of "investigational new drug" provisions of the Food and Drug Administration.

Therapeutic approaches also included cautious exploration of virus infections, a trend popular at the time and of hypophysectomy for advanced breast cancer and melanoma. In the animal room, mice with tumors were used to test fungicides, tetrazoliums, and esters (2,4-dichlorophenoxy)acetic acid (2,4-D) for antineoplastic effects.

Studies on the physiology of patients with cancer

No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder.

1159114

DOCUMENT SOURCE	
University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE	
School of Medicine - Department of History and Health Sciences	
ACCESSION NO.	COPY
AR 87-46	
FILE CODE NO.	
CARTON NO.	
Box 5 of 8	
FOLDER NAME	
Laboratory of Experimental Oncology	
NOTES	
FOUND BY	
Perry Hall 10/21/94	



FIGURE 2.—After a complete work-up of the patient, he is discussed at staff rounds for possible therapeutic approaches and for physiologic determinations that would assist in the management of the case. The young patient has a retro-orbital neurofibroma. Left to right: Dr. N. L. Petrakis, Miss F. Cordes, Dr. H. R. Bierman, Mrs. G. Singer, Mrs. O. Mitchell, Dr. M. Goldfarb, Dr. R. L. Byron, Jr., Mrs. A. Knight, Miss L. Lance, and Dr. K. R. Kelly.

involved the development of methods to measure intracardiac and intracardiac blood pressures by means of strain gauges, and circulation times by means of oxime-  
 These measurements, as could have been anticipated, were more useful for patients with cardiovascular problems than for those with neoplastic diseases (7).  
 More specific investigations of the fate of transfused leukemia cells indicated the prodigious capacity of the lungs to remove such cells from the circulation. Experience with various intravascular catheterization procedures was leading to observations on the vascularization of tumors and intra-arterial drug therapy.  
 Biochemical approaches included determinations of serum catecholase (8) and urinary coproporphyrin (9); neither seemed useful indicators in neoplastic disease. As another indication of the need for specificity in neoplastic diseases, blood histamine values in patients with myelocytic leukemia were of interest (10). The rise in gastric lactic acid after iv administration of glucose in patients with gastric carcinoma, as investigated by Shacter et al. (11), seemed to demonstrate the anaerobic glycolytic activity of the tumor.

Melcher proceeded with fractionation of tumor and normal tissues for the protein components as the first step toward the demonstration of tumor-specific antigens. The indicator system was to be the sensitized intestine of the guinea pig, which would be exposed to proteins of normal tissues to ascertain residual reaction

to subsequent exposure to tumor proteins. In vitro precipitin reactions on antitumor rabbit serum absorbed with a pool of normal organ extracts also were being explored. These attempts to demonstrate tumor antigens received no support from the scientific director of the NCI, who believed that tumors elicit no immunologic response.

#### AT APOGEE

By mid-1951 the research program of the LEO was in full swing, with the staff and budget at a steady state. Publications numbered 61, with 10 more in press. The clinical group, under Bierman, used increasingly more sophisticated arteriographic methods that allowed observations on the increased abnormal vascular supply of tumors in man (12, 13). The tumor vessels responded poorly to epinephrine. The ability to approach visceral tumors, such as metastases to the liver, by the arterial route also enabled the exploration of therapeutic effects of chemicals introduced via the arterial supply.

Studies on the physiologic dynamics of leukocytes in man (14) showed the importance of leukocyte removal mechanisms in patients with leukemia and suggested that longer survival of leukemia leukocytes was a factor in the disease. Cross-transfusions between patients with leukemia and patients with disseminated neoplasms (15) showed that the lung was more active in removing

DOCUMENT SOURCE	
University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE	
School of Medicine - Department of History and Health Sciences	
ACCESSION NO.	<b>COPY</b>
AR 87-46	
FILE CODE NO.	
CARTON NO.	
Box 5 of 8	
FOLDER NAME	
Laboratory of Experimental Oncology	
NOTES	
FOUND BY	
Perry Hall 10/21/94	

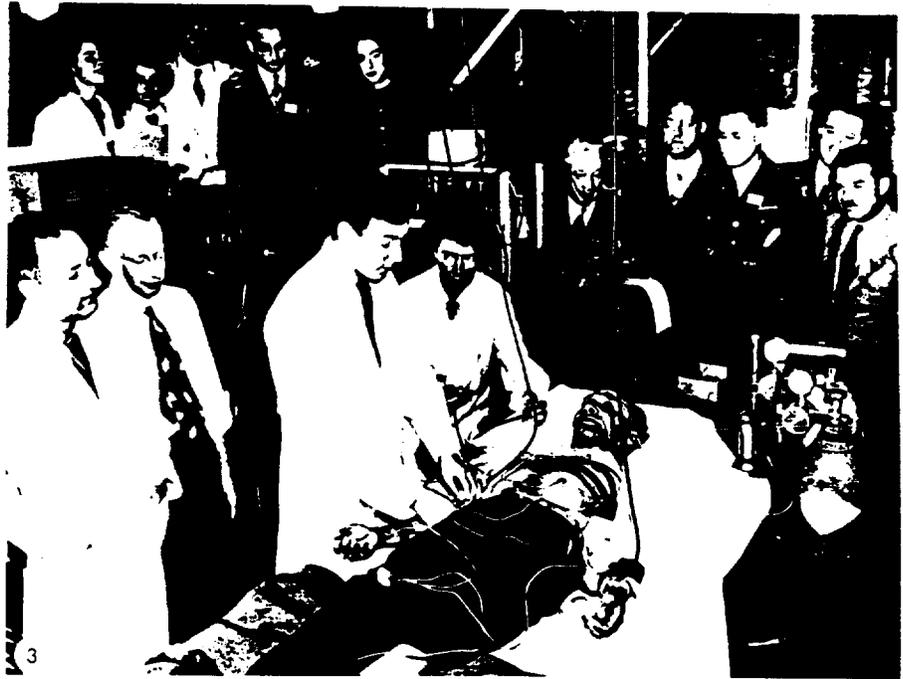


FIGURE 3.—Dr. Elliott Rapaport demonstrates multilead electrocardiography at a meeting of the American College of Physicians, April 20, 1948. *Left to right, foreground:* Dr. B. Shacter, Dr. L. Melcher, Dr. E. Rapaport, and Miss M. Brown.



FIGURE 4.—Dr. L. R. Melcher and Mr. R. R. Reed immunize a guinea pig with radioactive antibodies against tissue proteins. The metabolism of this radioactive-tagged material was then studied by determination of the radioactivity in the tissues and excreta of the animal.

No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder.

leukocytes than was the spleen or liver. Lungs of leukemia patients were relatively ineffective in the removal of white blood cells. Since two-thirds of the lymphocytes

enter the circulation through the thoracic duct, this duct was catheterized (16). Regardless of the peripheral lymphocyte or granulocyte count, the lymphocyte count in the thoracic duct lymph remained stubbornly the same. Drainage of lymph fluid up to 10 days did not alter the peripheral lymphocyte count. The resulting information showed that lymphocytes in lymphatic leukemia do not gain access to the blood in increased numbers through the thoracic duct.

Experimental chemotherapy was attempted with about a dozen compounds (17-19). Activity was limited to alkylating agents, antifolic acids, and hormones. Triethylenemelamine was an interesting addition to nitrogen mustard, but less predictable in its effects (20). Cortisone and adrenocorticotropin became available in small amounts and were used in children with acute leukemia. It soon became apparent that, although remissions were induced, their duration was brief and did not add to the survival period (21).

In the absence of formal controls or contrasts, we began in 1948 to analyze historical experiences in the survival of patients with malignant diseases; these experiences were culled from the records maintained by the tumor registry of the University Hospital. The late Dr. Eschsholzia Lucia, a trained statistician who was with the registry at that time, not only facilitated the analyses but provided for me an intense postgraduate course in statistics, a topic to which I had not been exposed

DOCUMENT SOURCE	
University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE	
School of Medicine - Department of History and Health Sciences	
ACCESSION NO.	COPY
APR 87-46	
FILE CODE NO.	
CARTON NO.	
Box 5 of 8	
FOLDER NAME	
Laboratory of Experimental Oncology	
NOTES	
FOUND BY:	
Perry Hall 10/21/94	

SHIMKIN



Transfusion of blood between 2 patients. By means of an artery-to-artery cross connection through polyethylene tubes and a pump, with the aid of anticoagulants, up to 150 liters of blood were exchanged between 2 patients on 12 occasions. Fundamental to the dynamic physiology of blood cells, as well as some clinical therapeutic benefits in patients with marked blood stasis were made possible by this technique.

...nal education.  
... analyses of survival and the effects of  
... and therapeutic factors on survival were  
... the leukemias (22, 23), lymphomas (24,  
... cancer (26). For the leukemias and  
... no increase in survival could be demon-  
... the 30-year period from 1918 to 1948, nor  
... be related to therapy (27). Earlier reports  
... failure also indicated that the survival had  
... ble, thus reinforcing the possibility that  
... that was a palliative for symptoms.  
... the early 1950's a mounting debate arose  
...ponents of the classic Halsted radical mas-  
... cancer of the breast, proponents of ex-  
... tations, and critics who could elicit no statis-  
... for operative removal beyond simple mas-  
... the surgeons at the University Hospital had a  
... record of their breast cancer material, main-  
... a devoted secretary who would eventually  
... own breast cancer and die therefrom. Life  
... lysis of the material failed to reveal improve-  
... survival, but the radical operation had been  
... therapeutic approach over the 3 decades of  
... ce. The similarity of the results with those  
... l from other centers and with the use of some-  
... ferent approaches did cast doubt on the inviol-  
... the classic concepts.  
... 51 the first rumblings of criticism also came.  
... ofessor of medicine had a long, friendly chat  
... e, informing me that we were being accused of

performing drastic, deleterious procedures on patients and that the release form we had devised for admission to the research ward was "psychologically harmful." The sources of the criticisms were not identified, but we were in the middle of the sticky area of experimentation on human beings.  
On a trip to the NCI, I was asked to see the director of the NIH and was accused of experimenting on man. The procedure particularly condemned was hypophysectomy for malignant melanoma (28). I pointed out that the procedure was not being done by us at LEO because none of us would know how to do one, but it was being done by the respected, nationally known neurosurgeon Dr. Howard Naffziger. Moreover, hypophysectomy for advanced neoplasms was also being investigated in Sweden.  
Whatever may have been the injustices or lack of communication, remedial steps obviously had to be taken. We instituted written protocols for all new departures in our clinical research, which we asked the cancer board of the medical school to review. A symposium arranged with Dr. Otto Guttentag on the subject of human experimentation was held in October 1951 and was well received. An almost visible thawing of attitude was felt by the airing of the problem. We gathered the four presentations for publication but were stopped by the NIH. They, too, were grappling with this sticky problem and formulating their guidelines for the Clinical Center that was being built in Bethesda. In some way, an enunciation from California was considered

contrary to possi  
exchanged, with  
academic freedo  
structions that I  
proceedings fina  
issue of Science I  
papers, in which  
view and Guttent  
view, have becom  
many subsequen

DESCENT

Although I th  
had served a use  
we also drew atte  
or sources of in  
Francisco and B  
our demise 2  
our certainly must h  
Our type of w  
patients, of cour  
tic disease with  
of our procedur  
mycosis fungoi  
arterial infusio  
ries cleared re  
however, cause  
lingered for n  
ning, a termin  
rette in his ox  
for the most  
transfusions of  
everything we  
in our attempt  
with acute leu-  
remission in c  
pox without or  
We eventua  
experimental  
concerns and  
patients were s  
had to unde  
work, and ev  
them; the init  
to an autopsy  
negligence ne  
actions, but  
relationships.  
single threat  
voiced. Two  
attempts at th  
Inasmuch  
patients, we  
sidered a con  
were termin  
cial condit  
our admis  
fully at th  
some of ou  
A few p

DOCUMENT SOURCE	University of California at San Francisco Special Collections Library, San Francisco CA
RECORDS SERIES TITLE	School of Medicine - Department of History and Health Sciences
ACCESSION NO.	AR 87-46
FILE CODE NO.	
CARTON NO.	Box 5 of 8
FOLDER NAME	Laboratory of Experimental Oncology
NOTES	
FOUND BY	Perry Hall 10/21/94

COPY

contrary to possible policy. Letters and telegrams were exchanged, with the dean emerging as a champion of academic freedom. Approval finally arrived, with instructions that I not be identified with the NIH. The proceedings finally appeared in the February 27, 1953, issue of *Science* 16 months after the meeting (29). The papers, in which I took the research worker's point of view and Guttentag spoke on the physician's point of view, have become classics and have been included in many subsequent compilations on the subject.

**DESCENT**

Although I thought we had met the challenges and had served a useful purpose in confronting the issues, we also drew attention as real or possible troublemakers or sources of institutional embarrassment, both in San Francisco and Bethesda. How much this contributed to our demise 2 years later remains unknown, but it certainly must have been an influencing factor.

Our type of work was not free of complications. Our patients, of course, had advanced disseminated neoplastic disease with fatal prognosis, and they were informed of our procedures. There was a 210-pound Texan with mucosis fungoides, who looked like a raw steak. By arterial infusions of nitrogen mustard (30), his extremities cleared remarkably. Attempts to clear his face, however, caused development of a hemiplegia, and he lingered for months as a nursing problem. One evening, a terminal patient with lymphosarcoma lit a cigarette in his oxygen tent and sustained fatal burns. But for the most dramatic investigations, such as cross-transfusions of blood or drainage of the thoracic duct, everything went smoothly. Neither were we criticized in our attempts to induce virus infections in children with acute leukemia, after we observed a remarkable remission in one little patient who developed chicken pox without our help (31).

We eventually admitted almost 500 patients to the experimental ward. These were our main professional concerns and where our duties and devotions lay. The patients were screened carefully before admission. They had to understand the experimental nature of our work, and every procedure was again explained to them; the initial release form even included agreement to an autopsy. The understanding did not absolve us of negligence nor deprive patients of recourse to legal actions, but it did set the tone and nature of our relationships. In all our 5 years of operations, not a single threat or implied threat of action against us was voiced. Two patients did instruct us to terminate our attempts at therapy.

Inasmuch as we had no fiscal arrangements with the patients, we had to guard ourselves against being considered a convenient dumping ground for patients who were terminal in regard to their physical or their financial condition. By insisting upon complete control over our admissions, we avoided the problem quite successfully at the cost of being considered uncooperative by some of our conferees.

A few patients insisted on making contributions, the

largest one being a pickup truck that was used to accelerate the delivery of supplies from the university storehouses. The process of getting the truck accepted by the Government was ludicrously complex and lengthy. We set up a petty cash fund for the other contributions; from this a television set for the ward was purchased.

I remain convinced that investigations on man should be pursued in absence of financial relationships between the subject and the investigator. Evidence was ample in our experiences to indicate how little reality was contained in the demand for complete informed consent by the subject, which is now accepted dogma and a stringent requirement. A much more realistic safeguard is the independent doctor-counselor suggested by Guttentag (29). Even there, the ethical problems do not adequately encompass children, mental incompetents, and the trusting and ignorant.

We dealt with people with fatal afflictions predicted to be of rather short duration, for whom standard treatments were ineffective or unavailable. The bravery and fortitude of the patients and their families were a constant wonder. Who can forget the brave young wife of a man whose face was being eaten away by a mixed tumor? She nursed him at home and one night he mercifully died, an emaciated Quasimodo without a recognizable face. Who can forget the beautiful children with acute leukemia, in whom remissions were induced with methotrexate or cortisone, and who then would relapse and die before one's eyes? It was always the young father who would collapse, and the mother who would bear up under the tragedy. My advice to such families was to conceive another child, and often the mother was already pregnant.

All the drugs and procedures we had were so limited, so temporary in their effects. Yet despite all cautions, the placebo effect was evident in many of our patients. In anticipation of a miracle, they would eat better, sleep better, require less narcotics, and even gain some weight. Such improvements were ephemeral, and we learned to anticipate them and not to confuse them with therapeutic effects of our drugs.

The patients had to know they had cancer before admission, and almost all of them did. A woman with disseminated breast cancer, however, would ask us not to tell her husband; her husband had just previously asked us not to tell her. Cancer was seldom mentioned after that—an unwelcome intrusion known to all but recognized by none.

How important is body contact! The dying woman whose face you stroke and whose hair you rearrange, and the smile that passes between you. The hand of the father of the leukemic child that you grasp and feel its flutter, its sweat, and the almost electrical transmission of his woes to you. We, too, wept.

The whole staff—physicians, nurses, dieticians, and attendants—was immersed by the activities. After several deaths, in rapid succession, of patients who had become their friends as well, one wanted to send the staff for a vacation to assuage their grief. No, it was not a detached, cold experience. It was a very warm, human

No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder.

DOCUMENT SOURCE	University of California at San Francisco Special Collections Library, San Francisco CA
RECORDS SERIES TITLE	School of Medicine - Department of History and Health Sciences
ACCESSION NO.	AR 87-46
FILE CODE NO.	
CARTON NO.	Box 5 of 8
FOLDER NAME	Laboratory of Experimental Oncology
NOTES	
FOUND BY	Perry Hall 10/21/94

COPY

experience that could not be communicated to those who had not had such an enrichment in their lives.

The staff was young, but we did have one death. Dr. Nellie Halliday, a biochemist who supervised our clinical laboratory, had chronic ulcerative colitis. Her last few weeks were as heartrending as any of the deaths from cancer.

LEO was involved in two major extracurricular activities. I was for 7 years the executive secretary for an all-university cancer research program, which allocated some \$300,000 per year for projects on three campuses (32). Bierman continued with the annual national examination of medical and dental students (33), which eventually was found to be the only evaluative attempt of the cancer teaching program of the NCI. The clinical staff participated in various consultative cancer boards at the university and other hospitals in the area, and residents and research fellows in medicine, pathology, and radiology rotated through our clinical facilities.

One of the original purposes of LEO was to have highly integrated work at the clinical and laboratory level. This aim floundered on that most human of all reasons: personality clashes. Clinicians considered the laboratory workers to be available for their projects. The laboratory workers were of a different mind, and force collaboration was hopeless. Instead, the staff went their separate ways, with collaboration evolving spontaneously between individuals as they found problems of mutual interest. I retain a great amount of skepticism about programs in research based upon collaborative interactions between mature investigators, especially in programs designed for others by administrative supervisors. Things simply don't work that way. To force the issue results in rebellion, noncompliance, a staff of complaisant technicians rather than independent investigators and sources of original ideas.

**THE CRASH**

The apogee and the nadir of LEO were only a year apart. We continued to report progress in the studies of physiologic dynamics of leukocytes in man. Thoracic lymph fluid had been analyzed in 10 patients. The effect of sympathetic and parasympathetic drugs on leukocyte dynamics continued to show the importance of the lungs in the sequestration and release of leukocytes into the circulation (34). Additional studies reiterated that leukemia cells often had a longer life-span than normal leukocytes. Petrakis (35) measured bone marrow temperatures and pressures, which were elevated in leukemia patients. He and Dr. Serafeim Masouredis also determined the blood flow in human bone marrow by clearance of radioiodide and found it increased in leukemia patients.

Bierman et al. (36) performed percutaneous portal vein puncture on 45 patients, measuring glucose and oxygen consumption and blood flow. Portal venograms were obtained by this technique, and a dispute over priority immediately occurred with the radiology department.



FIGURE 6.—Miss P. Miller, Dr. S. P. Masouredis, and Mr. B. S. Shumway studying the clearance rate of radioiodinated albumin from the bone marrow of a patient with Hodgkin's disease. Such clearance rates, probably a manifestation of increased blood flow, markedly increase in some patients with leukemia, particularly those with acute disease.

In experimental chemotherapy, 10 chemicals were tried, the most interesting being the new GT-41, discovered by Dr. George Timmis of London and eventually to be known as busulfan or Myleran (37). Satisfactory responses were achieved in 16 patients with myelocytic leukemia. The news that we had an interesting new agent for myelocytic leukemia spread rapidly, and a small flood of patients with the disease appeared by referrals.

Nitrogen mustard and its analogs continued to be the mainstay, along with methotrexate and cortisone. Colchicine, alloxan, azaguanine, Nile blue, the *Serratia marcescens* polysaccharide, and a soluble methylcholanthrene were tried without therapeutic effect.

The University Hospital experience with leukemias, lymphomas, and breast cancer was analyzed. Our comparisons with historical controls, such as acute leukemia in children, demonstrated no significant improvements in survival. We concluded that our therapeutic manipulations, including those with objective effects on tumor mass, were palliative of symptoms but did not arrest the neoplastic process and progression.

Laboratory investigations in immunology and biochemistry were also progressing satisfactorily. Melcher and Masouredis prepared radioiodine-tagged antibody to ovalbumin as a simplified model for extension to more complex proteins. The fate of the antigen and the antibody in guinea pigs was determined, with the conclusion that iodine-labeled antibodies could be used as indicators for the presence or absence of antigenic proteins in vivo (38). The techniques were then applied to anti-virus antibodies, first to ectromelia and finally to the mammary tumor agent in mice (39). These, in turn, were preliminary to the planned return to human tumors and possible identification of specific antigenic components.

Shacter, with Dr. Cecelia Entenman (40), studied

DOCUMENT SOURCE	University of California at San Francisco Special Collections Library, San Francisco CA
RECORDS SERIES TITLE	School of Medicine - Department of History and Health Sciences
ACCESSION NO.	AR 87-46
FILE CODE NO.	
CARTON NO.	Box 5 of 8
FOLDER NAME	Laboratory of Experimental Oncology
NOTES	
FOUND BY	Perry Hall 10/21/94

COPY

LOST COLONY

487

plasma sulfhydryl, including its measurement during the growth and regression of a rat lymphosarcoma. Decreases in sulfhydryl levels seemed to reflect increases in sulfhydryl utilization by proliferating tissues.

Dr. Joseph Shack, who was transferred to LEO from the NCI, worked with others (41) on nucleic acids and nucleoproteins from calf thymus and mouse lymphoma. Drs. Francis Crick and James Watson announced their resolution of the structure of the DNA molecule in 1953. Postulations in that field were being made by others; the blackboard in Shack's laboratory was filled with odd diagrams of possible structures that perhaps could be tested by studies with depolymerases. Meanwhile, he was finding some distinct differences in depolymerases extracted from mouse serum and from a mouse lymphoma.

Our isotope unit, under Masouredis, also showed clinical productivity (42), and the material in the pathology unit allowed some reports on unusual metastases (43, 44).

I was unaware of the fact that our fate already was sealed. Visits came from the director of the NCI and from the Surgeon General; both were taciturn, uncommunicative, and obviously pessimistic. The Clinical Center was about to open, and I was told that 15 beds in San Francisco could in no way be justified when they were concerned about filling 500 research beds in Bethesda. Further concerns about the staffing continued, inasmuch as clinicians were a new addition to NIH and the salaries that could be paid were not competitive. Thus clinicians deployed elsewhere were being pulled back to Bethesda, and Bierman and his associates were among such candidates. Dr. Jesse Steinfeld was transferred to NCI to develop isotope studies. He eventually became Surgeon General of the Public Health Service, after two tours at NCI and a period at the University of Southern California.

I was not privy to the high-level discussions about the fate of the LEO that may have taken place at NCI or the university. In April 1953, I received official notification that our clinical activities would not be supported after June 30. This decision, the notification stated, "... is based on budgetary considerations and should not be interpreted as a reflection on the quality of the work." The director of the CRI offered sympathy; the dean became unavailable; the local press was indignant; but the decision was final. Places for the professional staff were made available at the NCI in Bethesda, each on an individual basis. The research floor that had been added to the new medical school building for our use, and was to be completed some months later, quickly acquired other occupants on the plans.

The last year was a sad one, spent with the remnants of the basement laboratories and the animal room. I returned to my old interest, research on the adenomatous lung tumor in mice, and developed some quantitative studies with Dr. Milton Polissar (45). Bierman became scientific director of the City of Hope Hospital in Duarte, California, taking Drs. Keith Kelly and Ralph Bryon with him. Shack, Shacter, and Dr. Laurens White transferred to Bethesda, but Melcher went into private

practice in allergy and Petrakis found a spot on the faculty of the medical school. Brown, our invaluable head nurse, was already at the Clinical Center, and Messee accompanied me East.

Thus after 7 years, 500 patients, 1.6 million 1950-vintage dollars (plus another \$1 million for construction we never occupied), and over 130 publications, the LEO was closed (46). My wife and I were guests at a medical school faculty dinner at which I was presented a parchment scroll. An administrative officer came from Bethesda to take charge of the Government property.

The real farewell was on June 4, 1954. The Tin Angel night club on the Embarcadero, opposite the ship piers of San Francisco, was rented for the occasion. Only the LEO staff was invited and they all came. Alcohol flowed and the atmosphere became heavy with sentiment, loud singing, and a camaraderie described among survivors of sinking ships.

## REFERENCES

- (1) BIERMAN HR: A device for measuring physiologic pressure phenomena using the bonded electrical wire resistance strain gauge. *Rev Sci Instrum* 19:707-710, 1948
- (2) STONE RS: Neutron therapy and specific ionization. *Am J Roentgenol* 59:771-785, 1947
- (3) SHIMKIN MB, BIERMAN HR: Experimental chemotherapy of neoplastic diseases. *Radiology* 55:518-529, 1949
- (4) BIERMAN HR, SHIMKIN MB, MATTIER SR, et al: Methyl-bis(beta-chloroethyl)amine in large doses in the treatment of neoplastic diseases. *Calif Med* 71:117-125, 1949
- (5) SHIMKIN MB, BIERMAN HR: Chymotrypsin in cancer. *Proc Soc Exp Biol Med* 71:250-252, 1949
- (6) KELLY KH, BIERMAN HR, SHIMKIN MB: Negative effects of oral monobenzyl ether of hydroquinone in malignant melanoma in man. *Proc Soc Exp Biol Med* 79:589-590, 1952
- (7) KERR WJ, HARP VC, RAPAPORT E, et al: The propagation of murmurs and the local production of vascular murmurs in relation to the pulse waves. *Trans Assoc Am Physicians* 61:308-312, 1948
- (8) SHACTER B, SHIMKIN MB: Catecholase and catecholase-inhibitor activity of human blood sera. *J Natl Cancer Inst* 10:637-645, 1949
- (9) BIERMAN HR, STRAIT LA, HRENOFF K: Excretion of urinary coproporphyrin in patients with neoplastic diseases treated with methyl-bis(beta-chloroethyl)amine hydrochloride (HN2). *J Natl Cancer Inst* 10:93-103, 1949
- (10) SHIMKIN MB, SAPIRSTEIN I, GOETZL FR, et al: Blood histamine in leukemia and erythremia. *J Natl Cancer Inst* 9:379-387, 1949
- (11) SHACTER B, BYRON RL JR, SHIMKIN MB: Effect of intravenous glucose on gastric lactic acid in gastric carcinoma. *J Natl Cancer Inst* 10:331-336, 1949
- (12) BIERMAN HR, BYRON RL JR, KELLY KH, et al: Studies on the blood supply of tumors in man. III. Vascular patterns of the liver by hepatic arteriography in vivo. *J Natl Cancer Inst* 12:107-117, 1951
- (13) BIERMAN HR, MILLER ER, BYRON RL JR, et al: Intra-arterial catheterization of ulcers in man. *Am J Roentgenol Radium Ther* 66:555-568, 1951
- (14) BIERMAN HR, KELLY KH, KING FW, et al: The pulmonary circulation as a source of leukocytes and platelets in man. *Science* 114:276-277, 1951
- (15) BIERMAN HR, BYRON RL JR, KELLY KH, et al: Studies on cross circulation in man. I. Methods and clinical changes. *Blood* 6:487-503, 1951
- (16) BIERMAN HR, BYRON RL JR, KELLY KH, et al: The characteris-

Reproduction from Special Collections, the Library, University of California, San Francisco. No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder.

DOCUMENT SOURCE	
University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE	
School of Medicine - Department of History and Health Sciences	
ACCESSION NO.	<b>COPY</b>
AR 87-46	
FILE CODE NO.	
CARTON NO.	
Box 5 of 8	
FOLDER NAME	
Laboratory of Experimental Oncology	
NOTES	
FOUND BY	
Perry Hall 10/21/94	

- tics of thoracic duct lymph in man. *J Clin Invest* 32:637-649, 1953
- (17) PETRAKIS NL, BIERMAN HR, SHIMKIN MB: Substituted malononitriles in neoplastic diseases in man. *Cancer Res* 12:573, 1952
- (18) STEINFELD JL, WHITE LP, PETRAKIS NL, et al: Negative effects of some metabolite analogs in human neoplasms. *Cancer Res* 14:315-318, 1954
- (19) WHITE LP, SHIMKIN MB: Effects of DL-ethionine in six patients with neoplastic diseases. *Cancer* 7:867-872, 1954
- (20) SHIMKIN MB, BIERMAN HR, KELLY KH, et al: Trisethylamine-imino-z-triazine (triethylene melamine or TEM) in the treatment of neoplastic diseases. *Calif Med* 75:26-34, 1951
- (21) BIERMAN HR, KELLY KH, PETRAKIS NL, et al: Duration of life in children with leukemia treated with corticotrophin and cortisone. *Calif Med* 77:238-241, 1952
- (22) SHIMKIN MB, METTIER SR, BIERMAN HR: Myelocytic leukemia: An analysis of incidence, distribution and fatality, 1910-1948. *Ann Intern Med* 35:194-212, 1951
- (23) SHIMKIN MB, LUCIA EL, OPPERMANN KC, et al: Lymphocytic leukemia: An analysis of frequency, distribution, and fatality at the University of California Hospital, 1913-1947. *Ann Intern Med* 39:1254-1266, 1953
- (24) SHIMKIN MB, OPPERMANN KC, LOW-BEER BV, et al: Lymphosarcoma: An analysis of frequency, distribution, and mortality at the University of California Hospital, 1913-1948. *Ann Intern Med* 40:1095-1107, 1954
- (25) SHIMKIN MB, OPPERMANN KC, BOSTICK WL, et al: Hodgkin's disease. An analysis of frequency, distribution and mortality at the University of California Hospital, 1914-1951. *Ann Intern Med* 42:136-153, 1955
- (26) SHIMKIN MB, LUCIA EL, STONE RS, et al: Cancer of the breast. Analysis of frequency, distribution and mortality at the University of California Hospital, 1918-1947. *Surg Gynecol Obstet* 94:645-661, 1952
- (27) SHIMKIN MB: Chemotherapeutic management of lymphomas: effect upon survival. *Acta Un Int Contra Cancrum* 11:318-328, 1955
- (28) SHIMKIN MB, BOLDREY EB, KELLY KH, et al: Effects of surgical hypophysectomy in a man with malignant melanoma. *J Clin Endocrinol Metab* 12:439-453, 1952
- (29) SHIMKIN MB, GUTTENTAG OE, KIDD AM, et al: The problem of experimentation on human beings. *Science* 117:205-210, 1953
- (30) BIERMAN HR, KELLY KH, BYRON RL JR, et al: Studies on the blood supply of tumors in man. II. Intra-arterial nitrogen mustard therapy of cutaneous lesions. *J Natl Cancer Inst* 11:811-905, 1951
- (31) BIERMAN HR, CRILE DM, DOD KS, et al: Remission of leukemia in children following acute infectious disease. *Staphylococcus, Streptococcus, varicella, and feline panleukopenia. Cancer* 6:591-605, 1955
- (32) SHIMKIN MB: The University of California program in cancer research. *Calif Med* 73:297-300, 1950
- (33) BIERMAN HR, McCLELLAND JN, GALLOWAY DW: Three years' progress in the assessment of knowledge of the medical student on the subject of cancer. *J Med Educ* 27:272-277, 1952
- (34) BIERMAN HR, KELLY KH, CORDES FL, et al: The release of leukocytes and platelets from the pulmonary circulation by epinephrine. *Blood* 7:683-692, 1952
- (35) PETRAKIS NL: The temperature of human bone marrow. *J Appl Physiol* 4:549-553, 1952
- (36) BIERMAN HR, STEINBACH HL, WHITE LP, et al: Portal venipuncture. A percutaneous, trans-hepatic approach. *Proc Soc Exp Biol Med* 79:550-552, 1952
- (37) PETRAKIS NL, BIERMAN HR, KELLY KH, et al: The effect of 1,4-dimethanesulfonxybutane (GT-41 or Myletan) upon leukemia. *Cancer* 7:383-390, 1954
- (38) MELCHER LR, MASOUREDIS SP: The in vivo stability of the <sup>125</sup>I protein label of rabbit antibody in guinea pigs as determined by the quantitative precipitin reaction. *J Immunol* 67:393-402, 1951
- (39) MASOUREDIS SP, MELCHER LR, SHIMKIN MB: Behavior of <sup>125</sup>I anti-mammary tumor microsome fraction in mice. *Cancer Res* 12:281, 1952
- (40) SHACTER B, ENTENMAN C: Effect of cortisone, corticotropin and adrenalectomy on plasma sulfhydryl and protein levels. *Am J Physiol* 170:442-447, 1952
- (41) SHACK J, JENKINS RJ, THOMPSETT JM: Desoxypentose nucleic acids and nucleoproteins of malignant tissues. II. Physicochemical studies of the desoxypentose nucleic acid of a transplantable mouse lymphoma. *J Natl Cancer Inst* 13:1435-1446, 1953
- (42) MASOUREDIS SP, LOW-BEER BV, BIERMAN HR, et al: The partition of radiophosphorus (<sup>32</sup>P) in blood, urine, and tumor tissue in patients with Hodgkin's disease and lymphosarcoma before and after treatment with nitrogen mustard [methyl bis(beta-chlorethyl)amine]. *J Natl Cancer Inst* 11:289-300, 1950
- (43) ORTEGA P, LI IV, SHIMKIN MB: Metastasis of neoplasms to other neoplasms. *Ann West Med Surg* 5:601-609, 1951
- (44) ORTEGA P, MALAMUD N, SHIMKIN MB: Metastasis to the pineal body. *Arch Pathol* 52:518-528, 1951
- (45) SHIMKIN MB, POLISSAR MJ: Some quantitative observations on the induction and growth of primary pulmonary tumors in strain A mice receiving urethan. *J Natl Cancer Inst* 16:75-97, 1955
- (46) SHIMKIN MB: Upon man and beast—adventures in cancer epidemiology: Presidential address, American Association for Cancer Research, Houston, 1974. *Cancer Res* 34:1525-1535, 1974

No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder.

DOCUMENT SOURCE University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE School of Medicine - Department of History and Health Sciences	
ACCESSION NO. AR 87-46	<b>COPY</b>
FILE CODE NO.	
CARTON NO. Box 5 of 8	
FOLDER NAME Report of the Prospectus Committee	
NOTES 4-7-48/ Section II, Appendix 3, page 3.	
FOUND BY Perry Hall 10/21/94	

APPENDIX 3

Pharmacy is ideally situated to develop a sound educational program in this specialty and to do so will require the addition of a qualified staff member of professional rank to develop and administer the program. The area of Pharmacy Administration must also be expanded at the graduate level but this should present no special problem other than office space for one or more members of the staff. In order to develop this area of instruction, it will be necessary to develop a collaborative program with the School of Business Administration on the Berkeley Campus. Negotiations for such a collaborative program are now in progress.

METROLOGY

Several members of the faculty on the San Francisco Campus have suggested that there is need for the development of a Division of Metrology and if this should be agreed upon at some time in the future, the School of Pharmacy is the most logical school to develop and nourish the several disciplines involved in this area of physical science. This is certainly true unless the San Francisco Campus is expanded into a general campus. The school already offers instruction at both the undergraduate and graduate levels in physical measurements which embraces a number of disciplines that would be strengthened by integration both at the academic and administrative levels. Mathematics may be regarded as the basic discipline to Metrology, and there is clearly need for one or more able mathematicians on the San Francisco Campus. Metrology represents a broad area which includes such special activities as the Spectrographic Laboratory (UV, IR, X-ray, etc.) which is a part of the School of Pharmacy, the Radioactivity Center, and the Research and Development Laboratory. By closer integration of staff members in the above areas and by additional staff, the general area of Metrology could be properly supported.

In summary, the School of Pharmacy is presently short four offices and three research laboratories to house and accommodate the number of faculty for instruction of 80 students in Metrology. There is need to expand the physical plant to accommodate up to 100 students in a class. There is also need to strengthen and expand instruction in Metrology, Pharmacy and Pharmacy Administration. If some additional space will be required for this purpose. Should it be decided that the School of Pharmacy should develop a Division of Metrology, some additional allocation of space will be necessary.

Troy C. Daniels,  
Dean, School of Pharmacy

UCSF Archives  
Box 5 of 8  
AR 87-46

DOCUMENT SOURCE	University of California at San Francisco Special Collections Library, San Francisco CA
RECORDS SERIES TITLE	School of Medicine - Department of History and Health Sciences
ACCESSION NO.	AR 87-46
FILE CODE NO.	
CARTON NO.	Box 5 of 8
FOLDER NAME	1963 - Departmental Projections for Future Development (10 year plan)
NOTES	
FOUND BY	Perry Hall 10/21/94

COPY

Vice President James H. Corley  
January 29, 1964  
Page 5

course of treatment that fits one of those patients for normal social existence and a productive life. The management of cleft palate patients demands the combined skills of many specialists: plastic surgeons, pediatricians, orthodontists, prosthodontists, radiologists, speech therapists, and others. To help meet the need for this coordinated care, our Cleft Palate Panel was established in 1953 under auspices of the School of Dentistry. It has been supported almost entirely by private funds, and over the years has assisted in the treatment of more than 900 children. In some cases, treatment is undertaken at the Medical Center; in others, the panel provides expert evaluation and recommendations to guide referring physicians and dentists in home communities. Besides rendering a service of inestimable value, this program has resulted in important advances in the evaluation and treatment of cleft palate. The highly successful approach used in the cleft palate program is now serving as a guide to the establishment of a similar referral center for rehabilitation of patients who have been treated for cancers of the face and mouth.

Research in radiology: The AEC-supported Radiological Laboratory now has nearly eight years of experience in the treatment of cancer with the 70-million-volt synchrotron, the world's most powerful x-ray machine. In certain types of patients, this means of therapy achieves results that would be impossible with more conventional treatment, because the extremely high energy of the radiation beam permits the delivery of an effective dose deep in the body with a minimum of damage to intervening healthy tissue. Among tumors that have been treated with the synchrotron are those of the head and neck, uterus, lung, and urinary bladder. The Radiological Research Laboratory has made important contributions to x-ray diagnosis. The use of image intensifiers and special television circuits, for example, has made it possible to visualize internal structures exceptionally well while markedly reducing the exposure of patient and staff to radiation; x-ray motion pictures of such complex processes as swallowing and speech require no more radiation exposure than a conventional chest x-ray. The Radioactivity Research Center is recognized as an outstanding laboratory for work with radioactive isotopes. It provides facilities for research programs of many departments, and has made important contributions of its own -- particularly in the study of thyroid function and the evolution of chemical techniques for destroying thyroid tissue in patients with goiter.

Mental retardation programs: When public interest is newly focussed on a major medical problem, the feeling that "something must be done" tends to be translated into an assumption: "nothing is being done." There is also a tendency to overlook the prolonged effort required to develop new programs. Actually, the San Francisco Medical Center is doing highly significant work in the field of mental retardation and in the cluster of neurological handicaps, sensory disorders and emotional problems from which retardation cannot be segregated. Our Department of Pediatrics has what is recognized by national authorities as an outstanding clinic for children with cerebral palsy, retardation, and related problems. Working closely with this clinic is the Pediatric Mental Health Unit, which does

1159123

DOCUMENT SOURCE University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE School of Medicine - Department of History and Health Sciences	
ACCESSION NO. AR 87-46	<b>COPY</b>
FILE CODE NO.	
CARTON NO. Box 5 of 8	
FOLDER NAME Laboratory of Experimental Oncology	
NOTES	
FOUND BY Perry Hall 10/21/94	

721817

## Lost Colony: Laboratory of Experimental Oncology, San Francisco, 1947-54: Historical Note<sup>1,2</sup>

Michael B. Shimkin<sup>3</sup>

"In the fight between you and the world, back the world."

—Franz Kafka

from *The Great Wall of China*

Four volumes bound in Government-green are arrayed at my left. They record a 7-year period of cancer research, my life, and the lives of several hundred patients and other people. This is the visible residue of the Laboratory of Experimental Oncology (LEO), a collaborative activity between the National Cancer Institute (NCI) and the University of California School of Medicine in San Francisco; I headed this activity between 1947 and 1954. The volumes consist of annual reports, a collection of published reprints, a scrapbook, an album of pictures—and some memories.

This collection of four volumes probably is unique. I may be the only one who had read every word herein contained. Dr. Nicholas Petrakis, a legacy from the LEO who remained at the medical school, retained the brass plate from the front door—a relic that undoubtedly will outlast the papers. Yet the experience, as an early example of a regional cancer center, retains heuristic values, perhaps mostly negative ones.

### THE LAUNCHING

A constellation of occasions and circumstances differentiated into the LEO. After 8 years at the NCI and war service with a parade of acronymic agencies (OSRD, UNRRA, SHAEF, and WHO), I wanted to settle down in an academic environment and contribute to the solution of the cancer problem. Surgeon General Thomas Parran agreed to such an arrangement and even edited an exploratory letter that I drafted to Dr. Francis Scott Smyth, dean of the University of California School of Medicine in San Francisco, my alma mater. Dr. Roscoe R. Spencer, director of NCI, was favorable to the concept of colonies and also encouraged me.

One of the members of the National Advisory Cancer Council in 1946 was Dr. Robert S. Stone, professor of radiology at the University of California Medical School in San Francisco and a medical director in the Manhattan Project. He heard about me from his academic associates and from my involvement with an extension of the Manhattan Project at the NCI. Dr. Egon Lorenz, who was studying the lifetime effects of low levels of radiation on several species of rodents, was having difficulties with the pathologist assigned to him for the hematology work. I was asked to take over; in the process, I learned some hematology.

One day I was asked to meet Stone. We chatted, and I expounded my ideas on a well-supported combined clinical-laboratory unit on cancer research in an academic environment. I wanted to demonstrate that biomedical research programs of the National Institutes of Health (NIH) could develop as colonies of full partnership with universities and that such research should be pursued by full-time research teams. Stone was interested, and careful. The dean and his cancer committee were in favor, he said, but no money, no space, no academic positions were available.

Despite these discouraging words, an exchange of letters between the president of the University of California and the Surgeon General of the Public Health Service formalized an agreement. A sum of \$40,000 was allocated from the budget of the NCI, and negotiations for space were on the way in San Francisco. Dr. Howard R. Bierman, about to leave the Navy, appeared on the scene via an introduction by Spencer. He was a graduate of Washington University in St. Louis and an enthusiastic physiologist who was taking out a patent on a new strain gauge (1). He appeared to be a good man around whom to develop clinical investigations, and a civil service position was obtained for him. He proceeded ahead of me to San Francisco, where I arrived in January 1947.

Space for LEO was found at the Laguna Honda Home, a facility for the aged poor of the city's Department of Health. It was a castle housing some 1,500 souls, whose average age was over 85. The name, meaning "deep lake" in Spanish, was derived from its proximity to a water reservoir about 3 miles south of the medical school campus on Parnassus Hill. San Francisco's director of Public Health, Dr. Jacob Geiger, was an old Public Health Service officer from the plague days in California, a big, pleasant diplomat with a hobby of gathering medals. He, the dean, and the director of the Public Health Service district compiled the necessary documents of agreement, and for the rent of \$10 per year we acquired two floors of one wing of the building. The upper floor was to house the clinical beds and facilities; the lower floor was for the

<sup>1</sup> Received June 30, 1977; accepted September 8, 1977.

<sup>2</sup> Supported by Public Health Service contract NIH 263-76-C-0419 from the National Cancer Institute.

<sup>3</sup> Department of Community Medicine, School of Medicine, University of California at San Diego, La Jolla, Calif. 92093.

No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder.

DOCUMENT SOURCE	University of California at San Francisco Special Collections Library, San Francisco CA
RECORDS SERIES TITLE	School of Medicine - Department of History and Health Sciences
ACCESSION NO.	AR 87-46
FILE CODE NO.	
CARTON NO.	Box 5 of 8
FOLDER NAME	Laboratory of Experimental Oncology
NOTES	
FOUND BY	Perry Hall 10/21/94

COPY

basic laboratories, physiology equipment, and animals. Immediately, we ran into long discussions with the administrator of the home, who was not at all sure that rats and mice were included in the agreement. The administrator was a dedicated man with much time on his hands, and discussions with him were interminate.

Contracts were let via the medical school for construction in our area, and reimbursement from the NCI was arranged by one telephone call. Surplus laboratory and office equipment accumulating from demobilization was easily procured, and we were soon munificently equipped. By summer we were in place. Surgeon General Parran dropped in to give his blessing.



FIGURE 1—Surgeon General Thomas Parran (left) inspects the LEO, May 27, 1947; Dr. M. B. Shimkin (center) and Dr. H. R. Bierman (right).

The basic staff was quickly assembled. Among the earlier additions were a biochemist, Dr. Bernard Shacter; an M.D.-Ph. D. immunologist, Dr. Leo Melcher; and a physicist, Mr. Bruce Shumway. But most important were two indispensable women who really ran the place: Miss Dorothy Messee, chief administrative assistant; and Miss Marjorie Brown, chief nurse. By the time the facilities were completed in June 1947, 15 people were on the staff.

Meanwhile, Bierman and I were making clinical and academic contact in the area, including seeing a few patients on consultation. One was a man with a disseminated lymphosarcoma, with external nodules covering his whole body. We had ampuls of nitrogen mustard and gave the patient one course. Every nodule disappeared and the terminal patient sat up and demanded food. News of the miracle, which unfortunately lasted but a short time, spread through the city.

We had meetings with the cancer committee, a consultative cancer board was reorganized, and Bierman was put in charge of the NCI cancer teaching grant to the medical school. With a statistician hired for the purpose, plans were started to devise a national test of cancer knowledge among medical students.

The laboratory reported to the medical school and to the NCI. Good as well as bad consequences came from having more than one bureaucracy to work with. Printing of forms and announcements, for example, was proscribed by Government regulations but simply achieved via the university. Travel to meetings was difficult to finance by the university, but at that time easily arranged with the NCI. Such alternate arrangements were made possible by our several sources of funds. The basic allocation was from the direct operations budget of the NCI; we were, in turn, a "branch" of their structure, loosely placed in the office of the director. The experimental ward was financed by an NCI grant, one of the largest at the time, to the medical school; I expended this money by university rules. A small budget was set up for us by the medical school; this was later derived from the all-university cancer appropriation from the State.

The three sources of funds were reflected in three personnel systems for employment. With the exception of Bierman, members of the scientific professional staff were officers in the Public Health Service. Others on the direct NCI funds were on Federal civil service. The clinical help were hired through the university system. The salaries and emoluments differed and had to be reconciled, a reasonable problem for all but the clinical professionals.

The last item was an Achilles' heel of the activity. I had a fixed idea that clinical investigations should involve no financial arrangements between the patients and the investigators. Thirty years later, I believe this more strongly than ever. The world of the real, even in 1947, however, was out of focus with my beliefs. The medical school faculty derived much of their income from private practice—open, or hidden, or rationalized. I soon found that even seeing patients on consultation and not charging for such consultation embarrassed the physician and the patient.

All services were free to patients admitted to the laboratory ward, and we had no accounting or billing system. Inasmuch as officers of the Public Health Service were "on duty" 24 hours a day, I had control over their activities and allowed no outside practice except for one who supplemented his resources by emergency room attendance on weekends. Such restriction was not applied to civil service employees, whose time after work was their own.

#### IN FLIGHT

By the end of the first year, the LEO was a fully developed mini-experimental hospital of 15 beds in addition to laboratories for physiologic, biochemical, and immunologic work. The total budget was now \$212,000. The staff comprised 9 professional investigators, 12 administrative and technical assistants, 8 nurses, and others for a total of 49 people. Residents in medicine and in pathology were rotated through the facility. I was secretary of the statewide Cancer Research Coordinating Committee of the university, on the cancer

No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder.

1

DOCUMENT SOURCE	University of California at San Francisco Special Collections Library, San Francisco CA
RECORDS SERIES TITLE	School of Medicine - Department of History and Health Sciences
ACCESSION NO.	AR 87-46
FILE CODE NO.	
CARTON NO.	Box 5 of 8
FOLDER NAME	Laboratory of Experimental Oncology
NOTES	
FOUND BY	Perry Hall 10/21/94

COPY

board, and chairman of the planning committee for a research floor of the new medical school buildings. Bierman was chairman of the consultative tumor board and of the cancer teaching program for the medical school.

The clinical work was oriented around two internists and required collaboration and participation by many other specialists. Pathology needs were met by setting up a service extension from the medical school, with a full-time technician and resident, thus expanding the Laguna Honda Home pathology services. Radiology needs were initially met by Laguna Honda Home, but required the purchase of a new fluoroscope. For minor surgical procedures, consulting surgeons provided free services; for major surgery, patients had to be transferred to the University Hospital.

We hoped to develop isotopic radiotherapy and assembled the necessary equipment, including a hood with a collecting device on the roof four stories above. Three research fellows in radiobiology served with us, but later changed careers to pathology and pediatrics.

The professional staff had clinical appointments at the medical school in experimental oncology, and for administrative purposes they were under the Division of Medicine. We were listed separately in the catalog of the medical school. Our main relation, however, was to the interdepartmental cancer board of the medical school, initially chaired by the professor of pathology but soon replaced by Stone, the professor of radiology. He was a capable radiologist and a pioneer of the atomic age (2).

Stone was the *éminence grise* of the cancer situation at the medical school. He enjoyed complete control in his department and volunteered his participation in budgetary and administrative matters of the laboratory. Not having attained this goal, he began to draw up a "constitution" for a Cancer Research Institute (CRI) at the medical school. The rules became increasingly more restrictive and formal, with long hours of acrimonious discussion about specific provisions that seemed trivially detailed.

I finally recognized that the planned institute was being set up for Stone as its director, and that I was seen as a competitor for the position. I announced that my role would continue to remain in the Public Health Service and to head the LEO and that, although the LEO would be within the proposed CRI, I intended to retain control over it whether at Laguna Honda Home or in the new facilities in the medical school. The CRI constitution was soon patched up, and my relations with Stone became formal. The medical school obtained a building grant of \$1 million for an extra floor to house the LEO. Stone decided not to become the director, and instead a pathologist from Stanford University, Dr. David A. Wood, was appointed in 1951. Wood, a stolid, patient man, headed the CRI for over 2 decades.

By the third year of operations, the LEO was too busy to get involved in institutional politics. In retrospect, that was one of the troubles: I should have made frequent trips back to Berkeley to solidify personal

relationships, especially since the leadership there was changing rapidly, with Dr. Leonard A. Scheele and Dr. Harry Eagle now in top positions and with little background or sympathy about our arrangements and goals.

The annual report for 1948-49 proudly proclaimed: "The objective of the Laboratory is clinical research in cancer. With the cancer patient as the focal point of investigations, the work is oriented along four broad approaches: (1) experimental therapy, providing clinical material for other studies as well as permitting evaluation of such procedures on neoplastic disease; (2) physiology, particularly cardiovascular and respiratory physiology of the cancer patient, and the study of neoplastic tissue, *in vitro* and *in vivo*; (3) biochemistry, including metabolic studies on the cancer patient and investigation of specific biochemical reactions; and (4) the study of protein fractions of cancer and normal tissue of human origin, utilizing immunochemical techniques for their identification and differentiation."

This was not wishful thinking. Already 19 publications were printed or in press, and 88 patients had been studied on the ward; this comprised over 3,000 patient-days, explored 10 therapeutic chemicals or procedures, and expanded our pre-LEO experiences. The pathology unit had performed 82 autopsies (18 on our patients) and examinations of 162 biopsy specimens. Even the isotope unit had performed 57 determinations.

The experimental chemotherapy program depended upon clinical observations for the determinations of effect (3). Biometric design, random assignment, and double-blinding were features of the future. Our case numbers were insufficient, and the approaches were foreign to our clinical setting. Frankly, we did not miss them at this early phenomenologic period.

It did not take much astuteness to recognize that nitrogen mustard and amethopterin were active against leukemias and lymphomas, whereas pteropterin and stilbamidine were devoid of useful activity. We soon found that nitrogen mustard did not have to be spaced over several days but could be given in a single dose, and that the induction of fever did not enhance the therapeutic response (4). Chymotrypsin was a local cancer nostrum; we tried it on 10 patients, and the only effect was severe anaphylactoid reactions (5). Chymotrypsin was not further advocated.

Hydroquinone monobenzyl ether, used in depigmentation of rubber, was described to block melanin formation. We obtained a commercial product, purified it, and treated patients having disseminated melanoma (6). No beneficial effects were noted, and the trial was completed without the subsequent interminate regulations of "investigational new drug" provisions of the Food and Drug Administration.

Therapeutic approaches also included cautious exploration of virus infections, a trend popular at the time and of hypophysectomy for advanced breast cancer and melanoma. In the animal room, mice with tumor were used to test fungicides, tetrazoliums, and esters of (2,4-dichlorophenoxy)acetic acid (2,4-D) for antineoplastic effects.

Studies on the physiology of patients with cancer

No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder.

4116511

DOCUMENT SOURCE University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE School of Medicine - Department of History and Health Sciences	
ACCESSION NO. AR 87-46	COPY
FILE CODE NO.	
CARTON NO. Box 5 of 8	
FOLDER NAME Laboratory of Experimental Oncology	
NOTES	
FOUND BY Perry Hall 10/21/94	



2

FIGURE 2—After a complete work-up of the patient, he is discussed at staff rounds for possible therapeutic approaches and for physiologic determinations that would assist in the management of the case. The young patient has a retro-orbital neurofibroma. Left to right: Dr. N. L. Petrakis, Miss F. Cordes, Dr. H. R. Bierman, Mrs. G. Singer, Mrs. O. Mitchell, Dr. M. Goldfarb, Dr. R. L. Byron, Jr., Mrs. A. Knight, Miss Lance, and Dr. K. R. Kelly.

involved the development of methods to measure intracranial and intracardiac blood pressures by means of strain gauges, and circulation times by means of oxime-  
 These measurements, as could have been anticipated, were more useful for patients with cardiovascular problems than for those with neoplastic diseases (7).  
 More specific investigations of the fate of transfused leukemia cells indicated the prodigious capacity of the lungs to remove such cells from the circulation. Experience with various intravascular catheterization procedures was leading to observations on the vascularization of tumors and intra-arterial drug therapy.  
 Biochemical approaches included determinations of tumor catecholase (8) and urinary coproporphyrin (9); neither seemed useful indicators in neoplastic disease. As another indication of the need for specificity in neoplastic diseases, blood histamine values in patients with myelocytic leukemia were of interest (10). The rise in gastric lactic acid after iv administration of glucose in patients with gastric carcinoma, as investigated by Shacter et al. (11), seemed to demonstrate the anaerobic glycolytic activity of the tumor.

Melcher proceeded with fractionation of tumor and normal tissues for the protein components as the first step toward the demonstration of tumor-specific antigens. The indicator system was to be the sensitized intestine of the guinea pig, which would be exposed to proteins of normal tissues to ascertain residual reaction

to subsequent exposure to tumor proteins. In vitro precipitin reactions on antitumor rabbit serum absorbed with a pool of normal organ extracts also were being explored. These attempts to demonstrate tumor antigens received no support from the scientific director of the NCI, who believed that tumors elicit no immunologic response.

#### AT APOGEE

By mid-1951 the research program of the LEO was in full swing, with the staff and budget at a steady state. Publications numbered 61, with 10 more in press. The clinical group, under Bierman, used increasingly more new sophisticated arteriographic methods that allowed observations on the increased abnormal vascular supply of tumors in man (12, 13). The tumor vessels responded poorly to epinephrine. The ability to approach visceral tumors, such as metastases to the liver, by the arterial route also enabled the exploration of therapeutic effects of chemicals introduced via the arterial supply.

Studies on the physiologic dynamics of leukocytes in man (14) showed the importance of leukocyte removal mechanisms in patients with leukemia and suggested that longer survival of leukemia leukocytes was a factor in the disease. Cross-transfusions between patients with leukemia and patients with disseminated neoplasms (15) showed that the lung was more active in removing

DOCUMENT SOURCE	University of California at San Francisco Special Collections Library, San Francisco CA
RECORDS SERIES TITLE	School of Medicine - Department of History and Health Sciences
ACCESSION NO.	AR 87-46
FILE CODE NO.	
CARTON NO.	Box 5 of 8
FOLDER NAME	Laboratory of Experimental Oncology
NOTES	
FOUND BY	Perry Hall 10/21/94

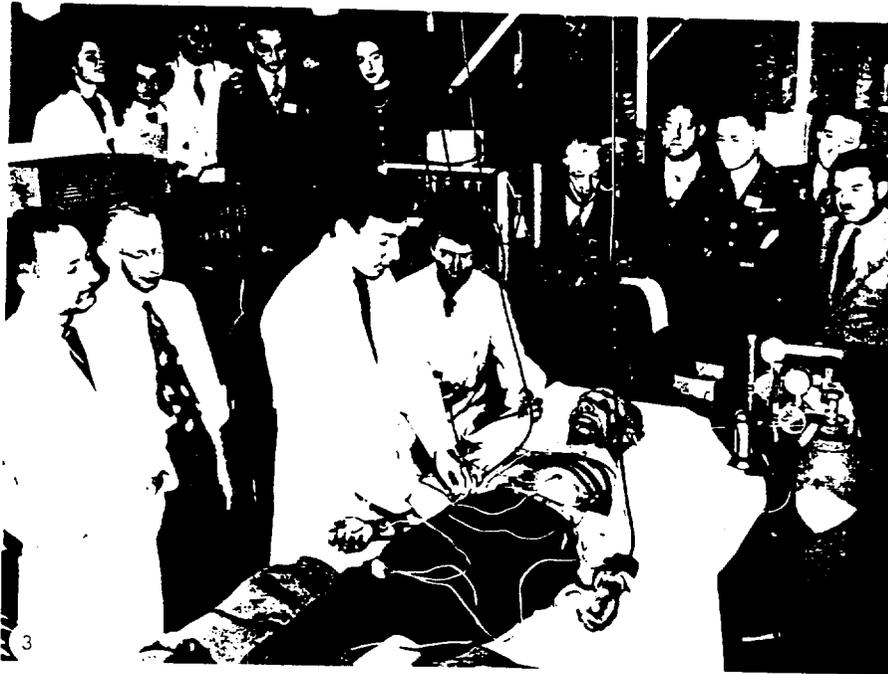


FIGURE 3.—Dr. Elliott Rapaport demonstrates multilead electrocardiography at a meeting of the American College of Physicians, April 20, 1948. Left to right, foreground: Dr. B. Shacter, Dr. L. Melcher, Dr. E. Rapaport, and Miss M. Brown.



FIGURE 4.—Dr. L. R. Melcher and Mr. R. R. Reed immunize a guinea pig with radioactive antibodies against tissue proteins. The metabolism of this radioactive-tagged material was then studied by determination of the radioactivity in the tissues and excreta of the animal.

enter the circulation through the thoracic duct, this duct was catheterized (16). Regardless of the peripheral lymphocyte or granulocyte count, the lymphocyte count in the thoracic duct lymph remained stubbornly the same. Drainage of lymph fluid up to 10 days did not alter the peripheral lymphocyte count. The resulting information showed that lymphocytes in lymphatic leukemia do not gain access to the blood in increased numbers through the thoracic duct.

Experimental chemotherapy was attempted with about a dozen compounds (17-19). Activity was limited to alkylating agents, antifolic acids, and hormones. Triethylenemelamine was an interesting addition to nitrogen mustard, but less predictable in its effects (20). Cortisone and adrenocorticotropin became available in small amounts and were used in children with acute leukemia. It soon became apparent that, although remissions were induced, their duration was brief and did not add to the survival period (21).

In the absence of formal controls or contrastests, we began in 1948 to analyze historical experiences in the survival of patients with malignant diseases; these experiences were culled from the records maintained by the tumor registry of the University Hospital. The late Dr. Eschsholzia Lucia, a trained statistician who was with the registry at that time, not only facilitated the analyses but provided for me an intense postgraduate course in statistics, a topic to which I had not been exposed

leukocytes than was the spleen or liver. Lungs of leukemia patients were relatively ineffective in the removal of white blood cells. Since two-thirds of the lymphocytes

No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder.

Reproduction from special collections, the Library, University of California, San Francisco

DOCUMENT SOURCE	
University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE	
School of Medicine - Department of History and Health Sciences	
ACCESSION NO.	COPY
AR 87-46	
FILE CODE NO.	
CARTON NO.	
Box 5 of 8	
FOLDER NAME	
Laboratory of Experimental Oncology	
NOTES	
FOUND BY	
Perry Hall 10/21/94	

SHIMKIN



transfusion of blood between 2 patients. By means of an artery-to-artery cross connection through polyethylene tubes and a with the aid of anticoagulants, up to 150 liters of blood were exchanged between 2 patients on 12 occasions. Fundamental the dynamic physiology of blood cells, as well as some clinical therapeutic benefits in patients with marked blood are made possible by this technique.

...al education.  
... analyses of survival and the effects of  
... and therapeutic factors on survival were  
... the leukemias (22, 23), lymphomas (24,  
... cancer (26). For the leukemias and  
... increase in survival could be demon-  
... the 30-year period from 1918 to 1948, nor  
... be related to therapy (27). Earlier reports  
... also indicated that the survival had  
... ble, thus reinforcing the possibility that  
... was a palliative for symptoms.  
... the early 1950's a mounting debate arose  
...ponents of the classic Halsted radical mas-  
... cancer of the breast, proponents of ex-  
... operations, and critics who could elicit no satisfac-  
... for operative removal beyond simple mas-  
... surgeons at the University Hospital had a  
... record of their breast cancer material, main-  
... a devoted secretary who would eventually  
... own breast cancer and die therefrom. Life  
... lysis of the material failed to reveal improve-  
... survival, but the radical operation had been  
... therapeutic approach over the 3 decades of  
... ce. The similarity of the results with those  
... from other centers and with the use of some-  
... ferent approaches did cast doubt on the inviol-  
... the classic concepts.  
... the first rumblings of criticism also came.  
... fessor of medicine had a long, friendly chat  
... e, informing me that we were being accused of

performing drastic, deleterious procedures on patients and that the release form we had devised for admission to the research ward was "psychologically harmful." The sources of the criticisms were not identified, but we were in the middle of the sticky area of experimentation on human beings.

On a trip to the NCI, I was asked to see the director of the NIH and was accused of experimenting on man. The procedure particularly condemned was hypophysectomy for malignant melanoma (28). I pointed out that the procedure was not being done by us at LEO because none of us would know how to do one, but it was being done by the respected, nationally known neurosurgeon Dr. Howard Naffziger. Moreover, hypophysectomy for advanced neoplasms was also being investigated in Sweden.

Whatever may have been the injustices or lack of communication, remedial steps obviously had to be taken. We instituted written protocols for all new departures in our clinical research, which we asked the cancer board of the medical school to review. A symposium arranged with Dr. Otto Guttentag on the subject of human experimentation was held in October 1951 and was well received. An almost visible thawing of attitude was felt by the airing of the problem. We gathered the four presentations for publication but were stopped by the NIH. They, too, were grappling with this sticky problem and formulating their guidelines for the Clinical Center that was being built in Bethesda. In some way, an enunciation from California was considered

contrary to possibl  
exchanged, with t  
academic freedom  
structions that I r  
proceedings final  
issue of *Science* 16  
papers, in which  
view and Guttent  
view, have becom  
many subsequent

#### DESCENT

Although I the  
had served a use  
we also drew atte  
or sources of ins  
Francisco and Be  
our demise 2 y  
certainly must ha

Our type of wi  
patients, of cour  
tic disease with f  
of our procedur  
mycosis fungoic  
arterial infusio  
ties cleared rer  
however, cause  
lingered for n  
ning, a termin.  
rette in his ox  
for the most  
transfusions of  
everything we  
in our attemp-  
with acute leu-  
remission in c  
pox without or

We eventua  
experimental  
concerns and  
patients were s-  
had to under  
work, and ev  
them; the initi  
to an autopsy-  
negligence ne  
actions, but  
relationships.  
single threat  
voiced. Two  
attempts at th

Inasmuch  
patients, we  
sidered a cor  
were termin  
cial condit  
our admis  
fully at th  
some of o

A few p

DOCUMENT SOURCE	University of California at San Francisco Special Collections Library, San Francisco CA
RECORDS SERIES TITLE	School of Medicine - Department of History and Health Sciences
ACCESSION NO.	AR 87-46
FILE CODE NO.	
CARTON NO.	Box 5 of 8
FOLDER NAME	Laboratory of Experimental Oncology
NOTES	
FOUND BY	Perry Hall 10/21/94

COPY

contrary to possible policy. Letters and telegrams were exchanged, with the dean emerging as a champion of academic freedom. Approval finally arrived, with instructions that I not be identified with the NIH. The proceedings finally appeared in the February 27, 1953, issue of *Science* 16 months after the meeting (29). The papers, in which I took the research worker's point of view and Guttentag spoke on the physician's point of view, have become classics and have been included in many subsequent compilations on the subject.

**DESCENT**

Although I thought we had met the challenges and had served a useful purpose in confronting the issues, we also drew attention as real or possible troublemakers or sources of institutional embarrassment, both in San Francisco and Bethesda. How much this contributed to our demise 2 years later remains unknown, but it certainly must have been an influencing factor.

Our type of work was not free of complications. Our patients, of course, had advanced disseminated neoplastic disease with fatal prognosis, and they were informed of our procedures. There was a 210-pound Texan with mycosis fungoides, who looked like a raw steak. By arterial infusions of nitrogen mustard (30), his extremities cleared remarkably. Attempts to clear his face, however, caused development of a hemiplegia, and he lingered for months as a nursing problem. One evening, a terminal patient with lymphosarcoma lit a cigarette in his oxygen tent and sustained fatal burns. But for the most dramatic investigations, such as cross-transfusions of blood or drainage of the thoracic duct, everything went smoothly. Neither were we criticized in our attempts to induce virus infections in children with acute leukemia, after we observed a remarkable remission in one little patient who developed chicken pox without our help (31).

We eventually admitted almost 500 patients to the experimental ward. These were our main professional concerns and where our duties and devotions lay. The patients were screened carefully before admission. They had to understand the experimental nature of our work, and every procedure was again explained to them; the initial release form even included agreement to an autopsy. The understanding did not absolve us of negligence nor deprive patients of recourse to legal actions, but it did set the tone and nature of our relationships. In all our 5 years of operations, not a single threat or implied threat of action against us was voiced. Two patients did instruct us to terminate our attempts at therapy.

Inasmuch as we had no fiscal arrangements with the patients, we had to guard ourselves against being considered a convenient dumping ground for patients who were terminal in regard to their physical or their financial condition. By insisting upon complete control over our admissions, we avoided the problem quite successfully at the cost of being considered uncooperative by some of our conferees.

A few patients insisted on making contributions, the

largest one being a pickup truck that was used to accelerate the delivery of supplies from the university storehouses. The process of getting the truck accepted by the Government was ludicrously complex and lengthy. We set up a petty cash fund for the other contributions; from this a television set for the ward was purchased.

I remain convinced that investigations on man should be pursued in absence of financial relationships between the subject and the investigator. Evidence was ample in our experiences to indicate how little reality was contained in the demand for complete informed consent by the subject, which is now accepted dogma and a stringent requirement. A much more realistic safeguard is the independent doctor-counselor suggested by Guttentag (29). Even there, the ethical problems do not adequately encompass children, mental incompetents, and the trusting and ignorant.

We dealt with people with fatal afflictions predicted to be of rather short duration, for whom standard treatments were ineffective or unavailable. The bravery and fortitude of the patients and their families were a constant wonder. Who can forget the brave young wife of a man whose face was being eaten away by a mixed tumor? She nursed him at home and one night he mercifully died, an emaciated Quasimodo without a recognizable face. Who can forget the beautiful children with acute leukemia, in whom remissions were induced with methotrexate or cortisone, and who then would relapse and die before one's eyes? It was always the young father who would collapse, and the mother who would bear up under the tragedy. My advice to such families was to conceive another child, and often the mother was already pregnant.

All the drugs and procedures we had were so limited, so temporary in their effects. Yet despite all cautions, the placebo effect was evident in many of our patients. In anticipation of a miracle, they would eat better, sleep better, require less narcotics, and even gain some weight. Such improvements were ephemeral, and we learned to anticipate them and not to confuse them with therapeutic effects of our drugs.

The patients had to know they had cancer before admission, and almost all of them did. A woman with disseminated breast cancer, however, would ask us not to tell her husband; her husband had just previously asked us not to tell her. Cancer was seldom mentioned after that—an unwelcome intrusion known to all but recognized by none.

How important is body contact! The dying woman whose face you stroke and whose hair you rearrange, and the smile that passes between you. The hand of the father of the leukemic child that you grasp and feel its flutter, its sweat, and the almost electrical transmission of his woes to you. We, too, wept.

The whole staff—physicians, nurses, dieticians, and attendants—was immersed by the activities. After several deaths, in rapid succession, of patients who had become their friends as well, one wanted to send the staff for a vacation to assuage their grief. No, it was not a detached, cold experience. It was a very warm, human

Reproduction from Special Collections, The Library, University of California, San Francisco  
 No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder

DOCUMENT SOURCE	University of California at San Francisco Special Collections Library, San Francisco CA
RECORDS SERIES TITLE	School of Medicine - Department of History and Health Sciences
ACCESSION NO.	AR 87-46
FILE CODE NO.	
CARTON NO.	Box 5 of 8
FOLDER NAME	Laboratory of Experimental Oncology
NOTES	
FOUND BY	Perry Hall 10/21/94

COPY

experience that could not be communicated to those who had not had such an enrichment in their lives.

The staff was young, but we did have one death. Dr. Nellie Halliday, a biochemist who supervised our clinical laboratory, had chronic ulcerative colitis. Her last few weeks were as heartrending as any of the deaths from cancer.

LEO was involved in two major extracurricular activities. I was for 7 years the executive secretary for an all-university cancer research program, which allocated some \$300,000 per year for projects on three campuses (32). Bierman continued with the annual national examination of medical and dental students (33), which eventually was found to be the only evaluative attempt of the cancer teaching program of the NCI. The clinical staff participated in various consultative cancer boards at the university and other hospitals in the area, and residents and research fellows in medicine, pathology, and radiology rotated through our clinical facilities.

One of the original purposes of LEO was to have highly integrated work at the clinical and laboratory level. This aim floundered on that most human of all reasons: personality clashes. Clinicians considered the laboratory workers to be available for their projects, the laboratory workers were of a different mind, and no force collaboration was hopeless. Instead, the staff went their separate ways, with collaboration evolving spontaneously between individuals as they found problems of mutual interest. I retain a great amount of skepticism about programs in research based upon collaborative interactions between mature investigators, especially in programs designed for others by administrative supervisors. Things simply don't work that way. To force the issue results in rebellion, noncompliance, a staff of complaisant technicians rather than independent investigators and sources of original ideas.

THE CRASH

The apogee and the nadir of LEO were only a year apart. We continued to report progress in the studies of physiologic dynamics of leukocytes in man. Thoracic lymphatic fluid had been analyzed in 10 patients. The effect of sympathetic and parasympathetic drugs on leukocyte dynamics continued to show the importance of the lungs in the sequestration and release of leukocytes into the circulation (34). Additional studies reiterated that leukemia cells often had a longer life-span than normal leukocytes. Petrakis (35) measured bone marrow temperatures and pressures, which were elevated in leukemia patients. He and Dr. Serafeim Masouredis also determined the blood flow in human bone marrow by clearance of radioiodide and found it increased in leukemia patients.

Bierman et al. (36) performed percutaneous portal vein puncture on 45 patients, measuring glucose and oxygen consumption and blood flow. Portal venograms were obtained by this technique, and a dispute over priority immediately occurred with the radiology department.



FIGURE 6.—Miss P. Miller, Dr. S. P. Masouredis, and Mr. B. S. Shumway studying the clearance rate of radioiodinated albumin from the bone marrow of a patient with Hodgkin's disease. Such clearance rates, probably a manifestation of increased blood flow, markedly increase in some patients with leukemia, particularly those with acute disease.

In experimental chemotherapy, 10 chemicals were tried, the most interesting being the new GT-41, discovered by Dr. George Timmis of London and eventually to be known as busulfan or Myleran (37). Satisfactory responses were achieved in 16 patients with myelocytic leukemia. The news that we had an interesting new agent for myelocytic leukemia spread rapidly, and a small flood of patients with the disease appeared by referrals.

Nitrogen mustard and its analogs continued to be the mainstay, along with methotrexate and cortisone. Colchicine, alloxan, azaguanine, Nile blue, the *Serratia marcescens* polysaccharide, and a soluble methylcholanthrene were tried without therapeutic effect.

The University Hospital experience with leukemias, lymphomas, and breast cancer was analyzed. Our comparisons with historical controls, such as acute leukemia in children, demonstrated no significant improvements in survival. We concluded that our therapeutic manipulations, including those with objective effects on tumor mass, were palliative of symptoms but did not arrest the neoplastic process and progression.

Laboratory investigations in immunology and biochemistry were also progressing satisfactorily. Melcher and Masouredis prepared radioiodine-tagged antibody to ovalbumin as a simplified model for extension to more complex proteins. The fate of the antigen and the antibody in guinea pigs was determined, with the conclusion that iodine-labeled antibodies could be used as indicators for the presence or absence of antigenic proteins in vivo (38). The techniques were then applied to anti-virus antibodies, first to ectromelia and finally to the mammary tumor agent in mice (39). These, in turn, were preliminary to the planned return to human tumors and possible identification of specific antigenic components.

Shacter, with Dr. Cecil Entenman (40), studied

DOCUMENT SOURCE	University of California at San Francisco Special Collections Library, San Francisco CA
RECORDS SERIES TITLE	School of Medicine - Department of History and Health Sciences
ACCESSION NO.	AR 87-46
FILE CODE NO.	
CARTON NO.	Box 5 of 8
FOLDER NAME	Laboratory of Experimental Oncology
NOTES	
FOUND BY	Perry Hall 10/21/94

COPY

No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder. Reproduction from Special Collections, the Library, University of California, San Francisco

plasma sulfhydryl, including its measurement during the growth and regression of a rat lymphosarcoma. Decreases in sulfhydryl levels seemed to reflect increases in sulfhydryl utilization by proliferating tissues.

Dr. Joseph Shack, who was transferred to LEO from the NCI, worked with others (41) on nucleic acids and nucleoproteins from calf thymus and mouse lymphoma. Drs. Francis Crick and James Watson announced their resolution of the structure of the DNA molecule in 1953. Postulations in that field were being made by others; the blackboard in Shack's laboratory was filled with odd diagrams of possible structures that perhaps could be tested by studies with depolymerases. Meanwhile, he was finding some distinct differences in depolymerases extracted from mouse serum and from a mouse lymphoma.

Our isotope unit, under Masouredis, also showed clinical productivity (42), and the material in the pathology unit allowed some reports on unusual metastases (43, 44).

I was unaware of the fact that our fate already was sealed. Visits came from the director of the NCI and from the Surgeon General; both were taciturn, uncommunicative, and obviously pessimistic. The Clinical Center was about to open, and I was told that 15 beds in San Francisco could in no way be justified when they were concerned about filling 500 research beds in Bethesda. Further concerns about the staffing continued, inasmuch as clinicians were a new addition to NIH and the salaries that could be paid were not competitive. Thus clinicians deployed elsewhere were being pulled back to Bethesda, and Bierman and his associates were among such candidates. Dr. Jesse Steinfeld was transferred to NCI to develop isotope studies. He eventually became Surgeon General of the Public Health Service, after two tours at NCI and a period at the University of Southern California.

I was not privy to the high-level discussions about the fate of the LEO that may have taken place at NCI or the university. In April 1953, I received official notification that our clinical activities would not be supported after June 30. This decision, the notification stated, "... is based on budgetary considerations and should not be interpreted as a reflection on the quality of the work." The director of the CRI offered sympathy; the dean became unavailable; the local press was indignant; but the decision was final. Places for the professional staff were made available at the NCI in Bethesda, each on an individual basis. The research floor that had been added to the new medical school building for our use, and was to be completed some months later, quickly acquired other occupants on the plans.

The last year was a sad one, spent with the remnants of the basement laboratories and the animal room. I returned to my old interest, research on the adenomatous lung tumor in mice, and developed some quantitative studies with Dr. Milton Polissar (45). Bierman became scientific director of the City of Hope Hospital in Duarte, California, taking Drs. Keith Kelly and Ralph Byron with him. Shack, Shacter, and Dr. Laurens White transferred to Bethesda, but Melcher went into private

practice in allergy and Petrakis found a spot on the faculty of the medical school. Brown, our invaluable head nurse, was already at the Clinical Center, and Messee accompanied me East.

Thus after 7 years, 500 patients, 1.6 million 1950-vintage dollars (plus another \$1 million for construction we never occupied), and over 130 publications, the LEO was closed (46). My wife and I were guests at a medical school faculty dinner at which I was presented a parchment scroll. An administrative officer came from Bethesda to take charge of the Government property.

The real farewell was on June 4, 1954. The Tin Angel night club on the Embarcadero, opposite the ship piers of San Francisco, was rented for the occasion. Only the LEO staff was invited and they all came. Alcohol flowed and the atmosphere became heavy with sentiment, loud singing, and a camaraderie described among survivors of sinking ships.

REFERENCES

- (1) BIERMAN HR: A device for measuring physiologic pressure phenomena using the bonded electrical wire resistance strain gauge. *Rev Sci Instrum* 19:707-710, 1948
- (2) STONE RS: Neutron therapy and specific ionization. *Am J Roentgenol* 59:771-785, 1947
- (3) SHIMKIN MB, BIERMAN HR: Experimental chemotherapy of neoplastic diseases. *Radiology* 55:518-529, 1949
- (4) BIERMAN HR, SHIMKIN MB, MATTIER SR, et al: Methyl-bis(beta-chloroethyl)amine in large doses in the treatment of neoplastic diseases. *Calif Med* 71:117-125, 1949
- (5) SHIMKIN MB, BIERMAN HR: Chymotrypsin in cancer. *Proc Soc Exp Biol Med* 71:250-252, 1949
- (6) KELLY KH, BIERMAN HR, SHIMKIN MB: Negative effects of oral monobenzyl ether of hydroquinone in malignant melanoma in man. *Proc Soc Exp Biol Med* 79:589-590, 1952
- (7) KERR WJ, HARP VC, RAPAPORT E, et al: The propagation of murmurs and the local production of vascular murmurs in relation to the pulse waves. *Trans Assoc Am Physicians* 61:308-312, 1948
- (8) SHACTER B, SHIMKIN MB: Catecholase and catecholase-inhibitor activity of human blood sera. *J Natl Cancer Inst* 10:637-645, 1949
- (9) BIERMAN HR, STRAIT LA, HRENOFF K: Excretion of urinary coproporphyrin in patients with neoplastic diseases treated with methyl-bis(beta-chloroethyl)amine hydrochloride (HN2). *J Natl Cancer Inst* 10:93-103, 1949
- (10) SHIMKIN MB, SAPIRSTEIN L, GOETZL FR, et al: Blood histamine in leukemia and erythremia. *J Natl Cancer Inst* 9:379-387, 1949
- (11) SHACTER B, BYRON RL JR, SHIMKIN MB: Effect of intravenous glucose on gastric lactic acid in gastric carcinoma. *J Natl Cancer Inst* 10:331-336, 1949
- (12) BIERMAN HR, BYRON RL JR, KELLY KH, et al: Studies on the blood supply of tumors in man. III. Vascular patterns of the liver by hepatic arteriography in vivo. *J Natl Cancer Inst* 12:107-117, 1951
- (13) BIERMAN HR, MILLER ER, BYRON RL JR, et al: Intra-arterial catheterization of viscera in man. *Am J Roentgenol Radium Ther* 66:555-568, 1951
- (14) BIERMAN HR, KELLY KH, KING FW, et al: The pulmonary circulation as a source of leukocytes and platelets in man. *Science* 114:276-277, 1951
- (15) BIERMAN HR, BYRON RL JR, KELLY KH, et al: Studies on cross circulation in man. 4. Methods and clinical changes. *Blood* 6:487-503, 1951
- (16) BIERMAN HR, BYRON RL JR, KELLY KH, et al: The characteris-

DOCUMENT SOURCE University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE School of Medicine - Department of History and Health Sciences	
ACCESSION NO. AR 87-46	<b>COPY</b>
FILE CODE NO.	
CARTON NO. Box 5 of 8	
FOLDER NAME Laboratory of Experimental Oncology	
NOTES	
FOUND BY Perry Hall 10/21/94	

488

SHIMKIN

- tics of thoracic duct lymph in man. *J Clin Invest* 32:637-649, 1953
- (17) PETRAKIS NL, BIERMAN HR, SHIMKIN MB: Substituted malononitriles in neoplastic diseases in man. *Cancer Res* 12:573, 1952
- (18) STEINFELD JL, WHITE LP, PETRAKIS NL, et al: Negative effects of some metabolite analogs in human neoplasms. *Cancer Res* 14:315-318, 1954
- (19) WHITE LP, SHIMKIN MB: Effects of DL-ethionine in six patients with neoplastic diseases. *Cancer* 7:867-872, 1954
- (20) SHIMKIN MB, BIERMAN HR, KELLY KH, et al: Trisethylane-imino-2-triazine (triethylene melamine or TEM) in the treatment of neoplastic diseases. *Calif Med* 75:26-34, 1951
- (21) BIERMAN HR, KELLY KH, PETRAKIS NL, et al: Duration of life in children with leukemia treated with corticotrophin and cortisone. *Calif Med* 77:238-241, 1952
- (22) SHIMKIN MB, METTIER SR, BIERMAN HR: Myelocytic leukemia: An analysis of incidence, distribution and fatality, 1910-1948. *Ann Intern Med* 35:194-212, 1951
- (23) SHIMKIN MB, LUCIA EL, OPPERMANN KC, et al: Lymphocytic leukemia: An analysis of frequency, distribution, and fatality at the University of California Hospital, 1913-1947. *Ann Intern Med* 39:1254-1266, 1953
- (24) SHIMKIN MB, OPPERMANN KC, LOW-BEER BV, et al: Lymphosarcoma: An analysis of frequency, distribution, and mortality at the University of California Hospital, 1913-1948. *Ann Intern Med* 40:1095-1107, 1954
- (25) SHIMKIN MB, OPPERMANN KC, BOSTICK WL, et al: Hodgkin's disease. An analysis of frequency, distribution and mortality at the University of California Hospital, 1914-1951. *Ann Intern Med* 42:136-153, 1955
- (26) SHIMKIN MB, LUCIA EL, STONE RS, et al: Cancer of the breast. Analysis of frequency, distribution and mortality at the University of California Hospital, 1918-1947. *Surg Gynecol Obstet* 94:645-661, 1952
- (27) SHIMKIN MB: Chemotherapeutic management of lymphomas: effect upon survival. *Acta Un Int Contra Cancrum* 11:318-328, 1955
- (28) SHIMKIN MB, BOLDREY EB, KELLY KH, et al: Effects of surgical hypophysectomy in a man with malignant melanoma. *J Clin Endocrinol Metab* 12:439-453, 1952
- (29) SHIMKIN MB, GUTTENTAG OE, KIDD AM, et al: The problem of experimentation on human beings. *Science* 117:205-210, 1953
- (30) BIERMAN HR, KELLY KH, BYRON RL JR, et al: Studies on the blood supply of tumors in man. II. Intra-arterial nitrogen mustard therapy of cutaneous lesions. *J Natl Cancer Inst* 11:811-905, 1951
- (31) BIERMAN HR, CRILE DM, DOD KS, et al: Remission of leukemia in children following acute infectious disease. *Staphylococcus, Streptococcus, varicella, and feline panleukopenia. Cancer* 6:591-605, 1953
- (32) SHIMKIN MB: The University of California program in cancer research. *Calif Med* 73:297-300, 1950
- (33) BIERMAN HR, MCCLELLAND JN, GALLOWAY DW: Three years progress in the assessment of knowledge of the medical student on the subject of cancer. *J Med Educ* 27:272-277, 1952
- (34) BIERMAN HR, KELLY KH, GORDS FL, et al: The release of leukocytes and platelets from the pulmonary circulation by epinephrine. *Blood* 7:683-692, 1952
- (35) PETRAKIS NL: The temperature of human bone marrow. *J Appl Physiol* 4:549-553, 1952
- (36) BIERMAN HR, STEINBACH HL, WHITE LP, et al: Portal venipuncture. A percutaneous, trans-hepatic approach. *Proc Soc Exp Biol Med* 79:550-552, 1952
- (37) PETRAKIS NL, BIERMAN HR, KELLY KH, et al: The effect of 1,4-dimethanesulfonoxylbutane (GT-41 or Myleran) upon leukemia. *Cancer* 7:383-390, 1954
- (38) MELCHER LR, MASOUREDIS SP: The in vivo stability of the <sup>125</sup>I protein label of rabbit antibody in guinea pigs as determined by the quantitative precipitin reaction. *J Immunol* 67:393-402, 1951
- (39) MASOUREDIS SP, MELCHER LR, SHIMKIN MB: Behavior of <sup>125</sup>I anti-mammary tumor microsome fraction in mice. *Cancer Res* 12:281, 1952
- (40) SHACTER B, ENTENMAN C: Effect of cortisone, corticotropin and adrenalectomy on plasma sulfhydryl and protein levels. *Am J Physiol* 170:442-447, 1952
- (41) SHACK J, JENKINS RJ, THOMPSETT JM: Desoxyribose nucleic acids and nucleoproteins of malignant tissues. II. Physicochemical studies of the desoxyribose nucleic acid of a transplantable mouse lymphoma. *J Natl Cancer Inst* 13:1435-1446, 1953
- (42) MASOUREDIS SP, LOW-BEER BV, BIERMAN HR, et al: The partition of radiophosphorus (<sup>32</sup>P) in blood, urine, and tumor tissue in patients with Hodgkin's disease and lymphosarcoma before and after treatment with nitrogen mustard [methyl bis(beta-chlorethyl)amine]. *J Natl Cancer Inst* 11:289-300, 1950
- (43) ORTEGA P, LI Y, SHIMKIN MB: Metastasis of neoplasms to other neoplasms. *Ann West Med Surg* 5:601-609, 1951
- (44) ORTEGA P, MALAMUD N, SHIMKIN MB: Metastasis to the pineal body. *Arch Pathol* 52:518-528, 1951
- (45) SHIMKIN MB, POLISSAR MJ: Some quantitative observations on the induction and growth of primary pulmonary tumors in strain A mice receiving urethan. *J Natl Cancer Inst* 16:75-97, 1955
- (46) SHIMKIN MB: Upon man and beast—adventures in cancer epidemiology: Presidential address, American Association for Cancer Research, Houston, 1974. *Cancer Res* 34:1525-1535, 1974

No portion of this material may be quoted, copied, or reproduced in any fashion without written permission from the copyright holder.

DOCUMENT SOURCE University of California at San Francisco Special Collections Library, San Francisco CA	
RECORDS SERIES TITLE School of Medicine - Department of History and Health Sciences	
ACCESSION NO. AR 87-46	<b>COPY</b>
FILE CODE NO.	
CARTON NO. Box 5 of 8	
FOLDER NAME Report of the Prospectus Committee	
NOTES 4-7-48/ Section II, Appendix 3, page 3.	
FOUND BY Perry Hall 10/21/94	

APPENDIX 3

Pharmacy is ideally situated to develop a sound educational program in this specialty and to do so will require the addition of a qualified staff member of professional rank to develop and administer the program. The area of Pharmacy Administration must also be expanded at the graduate level but this should present no special problem other than office space for one or more members of the staff. In order to develop this area of instruction, it will be necessary to develop a collaborative program with the School of Business Administration on the Berkeley Campus. Negotiations for such a collaborative program are now in progress.

METROLOGY

Several members of the faculty on the San Francisco Campus have suggested that there is need for the development of a Division of Metrology and if this should be agreed upon at some time in the future, the School of Pharmacy is the most logical school to develop and nourish the several disciplines involved in this area of physical science. This is certainly true unless the San Francisco Campus is expanded into a general campus. The school already offers instruction at both the undergraduate and graduate levels in physical measurements which embrace a number of disciplines that would be strengthened by integration both at the academic and administrative levels. Mathematics may be regarded as the basic discipline to Metrology, and there is clearly need for one or more able mathematicians on the San Francisco Campus. Metrology represents a broad area which includes such special activities as the Spectrographic Laboratory (UV, IR, X-ray, etc.) which is a part of the School of Pharmacy, the Radioactivity Center for Research and Development Laboratory. By closer integration of staff members in the above areas and by additional staff, the general area of Metrology can be properly supported.

In summary, the School of Pharmacy is presently short four offices and three research laboratories to house and accommodate the number of faculty required for instruction of 80 students in this field. There is need to expand the physical plant to accommodate up to 100 students in this class. There is also need to strengthen and expand instruction in Pharmacy and Pharmacy Administration. If some additional space will be required for this purpose. Should it be decided that the School of Pharmacy should develop a Division of Metrology, some additional allocation of space will be necessary.

Troy C. Daniels,  
Dean, School of Pharmacy

The University of California, San Francisco Special Collections Library

1159122

UCSF Arch  
Box 5 of 8  
School of Med

mm: hce

DOCUMENT SOURCE	University of California at San Francisco Special Collections Library, San Francisco CA
RECORDS SERIES TITLE	School of Medicine - Department of History and Health Sciences
ACCESSION NO.	AR 87-46
FILE CODE NO.	
CARTON NO.	Box 5 of 8
FOLDER NAME	1983 - Departmental Projections for Future Development (10 year plan)
NOTES	
FOUND BY	Perry Hall 10/21/94

COPY

Vice President James H. Corley  
January 29, 1964  
Page 5

course of treatment that fits one of these patients for normal social existence and a productive life. The management of cleft palate patients demands the combined skills of many specialists: plastic surgeons, pediatricians, orthodontists, prosthodontists, radiologists, speech therapists, and others. To help meet the need for this coordinated care, our Cleft Palate Panel was established in 1953 under auspices of the School of Dentistry. It has been supported almost entirely by private funds, and over the years has assisted in the treatment of more than 900 children. In some cases, treatment is undertaken at the Medical Center; in others, the panel provides expert evaluation and recommendations to guide referring physicians and dentists in home communities. Besides rendering a service of inestimable value, this program has resulted in important advances in the evaluation and treatment of cleft palate. The highly successful approach used in the cleft palate program is now serving as a guide to the establishment of a similar referral center for rehabilitation of patients who have been treated for cancers of the face and mouth.

Research in radiology: The AEC-supported Radiological Laboratory now has nearly eight years of experience in the treatment of cancer with the 70-million-volt synchrotron, the world's most powerful x-ray machine. In certain types of patients, this means of therapy achieves results that would be impossible with more conventional treatment, because the extremely high energy of the radiation beam permits the delivery of an effective dose deep in the body with a minimum of damage to intervening healthy tissue. Among tumors that have been treated with the synchrotron are those of the head and neck, uterus, lung, and urinary bladder. The Radiological Research Laboratory has made important contributions to x-ray diagnosis. The use of image intensifiers and special television circuits, for example, has made it possible to visualize internal structures exceptionally well while markedly reducing the exposure of patient and staff to radiation; x-ray motion pictures of such complex processes as swallowing and speech require no more radiation exposure than a conventional chest x-ray. The Radioactivity Research Center is recognized as an outstanding laboratory for work with radioactive isotopes. It provides facilities for research programs of many departments, and has made important contributions of its own -- particularly in the study of thyroid function and the evolution of chemical techniques for destroying thyroid tissue in patients with goiter.

Mental retardation programs: When public interest is newly focussed on a major medical problem, the feeling that "something must be done" tends to be translated into an assumption: "nothing is being done." There is also a tendency to overlook the prolonged effort required to develop new programs. Actually, the San Francisco Medical Center is doing highly significant work in the field of mental retardation and in the cluster of neurological handicaps, sensory disorders and emotional problems from which retardation cannot be segregated. Our Department of Pediatrics has what is recognized by national authorities as an outstanding clinic for children with cerebral palsy, retardation, and related problems. Working closely with this clinic is the Pediatric Mental Health Unit, which does