THE EARLY WORKERS IN CLINICAL RADIOTHERAPY OF CANCER AT THE RADIUM INSTITUTE OF THE CURIE FOUNDATION, PARIS, FRANCE

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THE FIFTIETH ANNIVERSARY OF THE RADIUM Institute of the Curie Foundation was celebrated at the UNESCO Palace, Paris, France, on April 27, 1971, with Robert Boulin, Minister of Health, presiding. Other distinguished participants were: The President of the Administrative Council of the Curie Foundation, J. Roche; Professor A. Lacassagne, Honorary Director of the Radium Institute; C. Chavanne and R. Latarjet, Directors, respectively, of the Clinical and Biological Sections of the Institute, and J. Regaud and Mercier. Also attending were several former foreign trainees or alternates; among them were Sir Brian Windeyer of Great Britain (1929), J. Jovin of Rumania (1924), and the present author, Maurice Lenz of the United States (1923–1924). The speakers traced the history of the growth and development of the Radium Institute from its modest beginning in 1921 to its prominent position in 1971.

EMILE ROUX

The Radium Institute was established primarily through the efforts of Emile Roux, Director of the Pasteur Institute. He understood the significance of the discovery of radium in 1898, and believed this element should be studied further in a special Radium Institute. He thought these studies should include physics, biology, and the clinical application of radium for the treatment of cancer.

He appointed Marie Curie, pupil, collaborator, and widow of Pierre Curie, as the Provisional Director of the Radium Institute and head of the Division of Physics. The subjects to be investigated in the physics section were general physics, radiation physics, and radioactive substances, with a special department for measuring the latter.

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CLAUDIUS REGAUD

Roux chose Claudius Regaud as head of the Biological Division. Regaud was Professor of Histology at the University of Lyons, and had published some studies of x-ray effects on normal tissues. He believed that the Radium Institute was especially suited for close collaboration between physics and chemistry, and radiophysiology and radiotherapy. He felt such combined studies would be more valuable for the progress of clinical radiotherapy of cancer than studies limited solely to the practical experience in treating patients with irradiation.

In 1912, Roux invited Regaud to join him in planning the organization of the future Radium Institute. In 1913, Regaud resigned as Professor of Histology in Lyons to join Roux in Paris. World War I interrupted their plans until 1919 when Regaud returned from military service. Then he, Marie Curie, Emile Roux, and Paul Appel, Director of the Academy of Paris, set out once more to plan the Radium Institute.

CLAUDIUS REGAUD AND ANTOINE LACASSAGNE

Regaud's chief assistant in the histology laboratory in Lyons had been Antoine Lacassagne. In November 1913, Regaud invited Lacassagne to help him develop the organization of the Radium Institute. Lacassagne moved to Paris and joined his former chief in the capacity of Associate Director. They continued their histologic studies and other research. The results of these efforts and other work done at the Radium Institute appeared in a number of volumes of a new publication, *The Archives of Radiophysiology and Radiotherapy*. They decided to finance this undertaking from funds of the Curie Foundation and the French League Against Cancer. The articles in these volumes dealt primarily with microscopic changes in irradiated cancers of various organs. Thus, these two scientists founded and

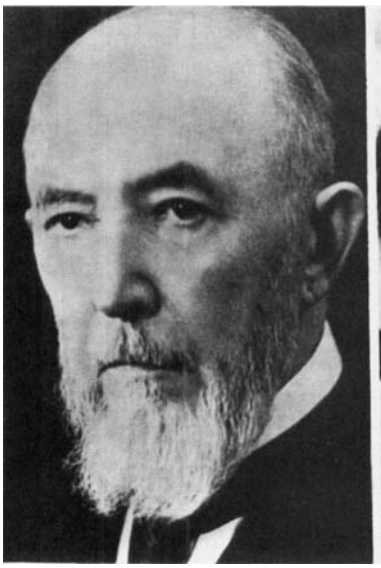

FIG. 1. *(left)*. Claudius Regaud (1870–1940).
FIG. 2. *(right)*. Antoine Lacassagne (1884–1971).

guided not only the laboratory research at the Radium Institute, but also the clinical application of radiotherapy to cancer. The general principles of radiotherapy of cancer, as postulated by Regaud and Lacassagne, were that a single course of treatment should be given—never to be repeated—with the maximum amount of radiation tolerated by normal tissues. The clinicians who later developed the specific application of radiotherapy to individual cancers bore these principles in mind when they worked out the details of the treatment of various cancers. The work by Regaud and Lacassagne in their later years was in laboratory research rather than the clinic. In 1945 and 1946, Lacassagne published laboratory research on the production of experimental cancer by the use of electromagnetic radiation, corpuscular radiation, the exogenous chemical substances.

Regaud was a serious, austere chief who was not readily approachable. He protected himself from intrusion by a cold exterior. Actually, however, he was a kind and considerate person, always willing to help young people. Lacassagne was just as serious, wellinformed, scientifically reliable, and intellectually honest as Regaud. He was more amenable and, consequently, was consulted more often than Regaud; thus, he helped a greater number of individual workers. For instance, when he realized that my knowledge of tumor pathology was limited, he daily spent time teaching me this subject.

Regaud, in order to gain clinical experience with the use of radium in cancer, convinced a number of his surgeon friends to permit him to treat some of their cancer patients with this new and untried agent. Once a week, Regaud, riding his bicycle, carried radium to these patients, applying it personally. Lacassagne participated in this work soon after it began. Within 6 months, Regaud was able to inform Roux about improvement in some of the cancer patients he was treating. Later, because of his heavy work load and the danger from the radium transported by Regaud, the Administration of the Curie Foundation granted him the use of an automobile.

BUILDINGS AND EQUIPMENT

When the Radium Institute was first officially dedicated as a public utility in 1921, it had only two functioning pavilions. Additional growth and development was irregular, depending on availability of space and funds. Practically all radiotherapy in 1921 was done in the dispensary building at 26 Rue D'Ulm. Here, most patients were treated on an ambulatory basis. Those who required inpatient care were hospitalized in one of two small hospital departments: one at the Pasteur Institute and the other at the Antoine Ghantin Hospital.

The dispensary building had small rooms for physical examinations and larger rooms for conferences. Special rooms were used for the preparation of radium or radon applicators. There was also an entire wing for x-ray

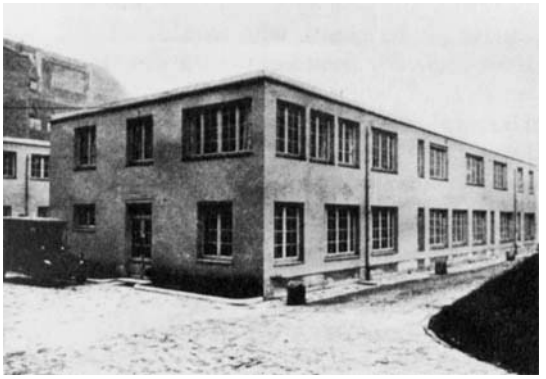

FIG. 3. Dispensary at 26 Rue D'Ulm, Paris (1921).

therapy containing six machines, which were operated from 100 to 200 kv and 4 ma.

NEW EQUIPMENT

New x-ray and Co^{60} equipment became available as follows:

Year	*Kilovoltage used*	
1921–1938	100–200 kv	
1939	600 kv	
1936–1942	200 kv	Co^{60}
1942	45 kv	
1956		Co^{60}
1962	35 Mev.	Betatron Electron Beam

The old dispensary was eventually replaced by a new building containing a modern outpatient clinic and various offices. Diagonally across from this building, a 183-bed Curie Hospital was built with complete facilities for major surgery and radiotherapy, and officially dedicated by Jean Courtial in 1956. In 1970, the Curie Institute had 50 attending physicians and 550 paramedical personnel.

RADIUM THERAPY: OCTAVE MONOD AND JULIETTE BAUD

When I arrived at the Institute in April 1923, most radium and radon treatments were applied either by Octave Monod, who was in charge of the Radium Service, or by his assistant, Juliette Baud. Three methods of application were employed: external, intracavity, and interstitial.

External radiation: The lesion and a clinically uninvolved border were first covered by a wax mold, and radium or radon tubes were fastened to the outer surface of the mold corresponding to the lesion. The radiation from these unprotected tubes was not limited to the lesion but also irradiated the adjacent tissues and, to a lesser degree, the rest of the patient's body, neighboring patients, and personnel attending the patient. Well-protected larger radium containers, like the one developed by R. Ferroux and M. Brouzau, were as yet not perfected.

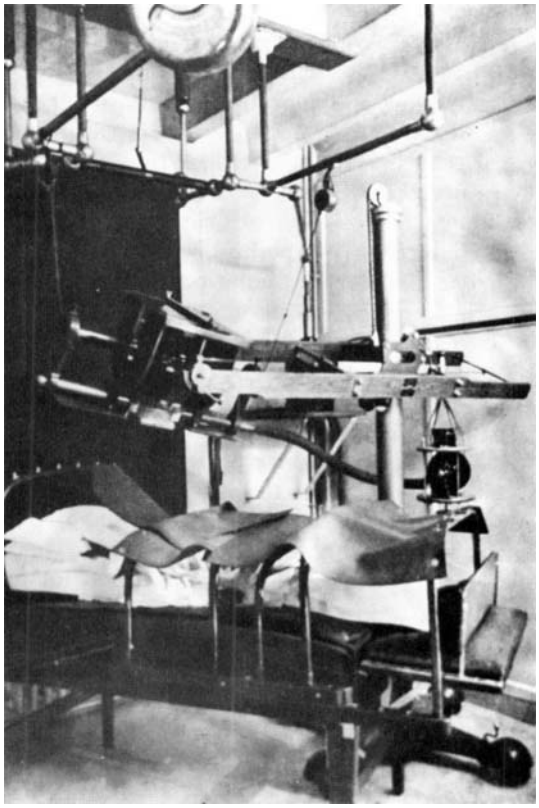

FIG. 4. X-ray therapy room (1921).

Intracavity method: One-half millimeter platinum tubes containing radium or radon

FIG. 5. Octave Monod. Radium therapy (1922).

were inserted into the natural cavities of the body, e.g., the uterus.

Interstitial method: In this, 0.5-mm hollow platinum needles containing radium or radon were inserted in and around the cancer, according to a method developed by Monod.

Monod knew little physics and his radium dosimetry was mainly empiric, based on a clinical trial-and-error method with various radium dosages. His explanation of the method was that "this was a matter of clinical experience." It was not until Ralston Paterson and his physicist colleague, Herbert Parker, had spent some time with Monod in Paris and with Mlle. Simon at the Radiotherapy Department of the University of Brussels, Belgium, and had worked on the physics of these empiric methods, that Monod's original experiences and those of Mlle. Simon were scientifically interpreted and then published for use in practice. Thereafter, they were known as the Paterson-Parker dosage tables.

HENRI COUTARD

Roentgen therapy at the Curie Foundation was first used primarily for palliation of advanced cancer. In 1919, Henri Coutard arrived and decided to devote himself to the improvement of x-ray therapy and attempted to use it for curative purposes in cases of cancer. The x-ray machines at that time could not deliver more than 4 ma. Coutard developed the theory that roentgen treatment of cancer with higher milliamperes, i.e., faster treatment, might be injurious. He even convinced other radiotherapists of this, e.g., Professor Schinz of Zurich, Switzerland, who would not use more than 3 ma for treatment of cancer. It was not until 1934, when Coutard visited Montefiore Hospital in New York City, that he changed his mind. There, I showed him cancer patients whom I had treated with cancerocidal x-ray dosage given with 30 ma and 250 kv. The skins, mucosae, and other tissues of these patients did not show any worse injury than those receiving similar dosages with 4 ma. In order to administer adequate cancerocidal dosage, Coutard had to treat his patients 2 hours a day, an hour in the forenoon and another in the afternoon. Therefore, he could treat only a few patients a day. The use of 30 ma changed this completely, making it possible for him to give cancerocidal dosage radiation for only a few minutes daily, thereby enabling him to increase his patient load.

Coutard believed that the original site of the cancer, i.e., its oldest area, was more radioresistant than the rest of the tumor, requiring a higher dosage. In order to obtain higher dosage in this tumor area, the radiation field was constricted daily during the course of radiotherapy until at the end only the *oldest* site was being treated.

Coutard was an excellent clinican and observer. He made careful drawings of the daily clinical changes in the irradiated skin, mucosa, and cancer. He used these progressive changes in appearance of the irradiated tissues to guide his daily tumor dose. In addition, he also compared the daily changes in appearance of a barium cyanide plaque which he ex-

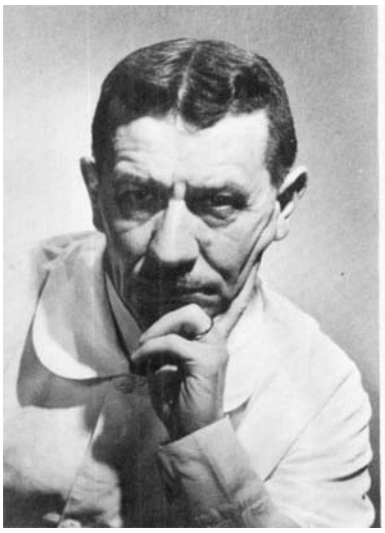

FIG. 6 *(left)*. Henri Coutard. Radium therapy (1922).
FIG. 7 *(right)*. Francois Baclesse (1896–1967).

posed to the x-ray beam during the treatment. These changes, perhaps, also influenced him in the selection of the daily dose he applied. Yet this observation always followed the clinical comparison of the irradiated area so that, apparently, his main guide to dosage was the observed daily clinical changes and not the change in appearance of the cyanide capsule. At the end of his treatment series, Coutard had made a collection of over 50 drawings which gave him a clear picture of the daily changes in the treated areas, enabling him to set up his radiotherapy schedule which he described as the "Coutard method."

The principle of a single course of treatment with a maximum total amount of radiation, fractionated over a number of days and never repeated, had been established by Regaud and Lacassagne. The actual number of days which should be used in an individual case, however, had not been decided upon. Coutard, therefore, experimented with the length of the total period of treatment and individual fractions. Treatment was given either every day or with interruptions of several days or weeks. The usual duration of a continuous course varied from 1 to 6 weeks; it was longer if the course was interrupted, as is often done today.

FIG. 8. Curie Foundation (1970).

FRANCOIS BACLESSE

Coutard's chief associate and successor in x-ray therapy was Francois Baclesse. He, too, was an excellent clinician, but thought that he could produce cancerocidal radiation without simultaneously causing skin radioepidermitis or mucosal radioepithelitis. In order to avoid these unwanted radiation reactions, he subdivided the total radiation into smaller daily fractions.

CONCLUSIONS

The early radiotherapists left a legacy of intellectual honesty, knowledge, and dedication which has been transmitted to cancer centers throughout the world.

We all owe these founders of radiotherapy a debt of gratitude. My own medical career has been greatly influenced by my experience at the Curie Foundation, and I deeply appreciate the privilege of having worked there.