Reviews


There has just appeared a special number of the Acta of the International Union Against Cancer, comprising 645 pages, devoted to “The International Cancer Week and the Commemoration of the Discovery of Radium, Electrons, X-Rays, and Hertzian Waves,” observed in Paris, Nov. 23 to 30, 1938. The meeting was under the presidency of Senator Justin Godart, President of the International Union Against Cancer, with Professor Jean Perrin, Nobel prize winner, presiding at the scientific sessions, aided by M. Tomarkin, at that time Executive Secretary of the International Union Against Cancer.

The opening session was held in the grand amphitheatre of the Sorbonne on the evening of Nov. 23. M. Albert Lebrun, President of France, presided and delivered an address of welcome to the delegates from the various countries, and a message from President Moscicki of Poland was received by radio from Warsaw. The program included, in addition to speeches by Senator Godart, Professor Roussy, Rector of the University of Paris, M. Rucort, Minister of Public Health, and M. Zay, Minister of Education, a number of short general addresses by eminent scientists, including Perrin on electrons, de Broglie on x-rays, Gendreau of Montreal on the life and work of Pierre and Marie Curie, Langevin on Hertzian waves, Béclère on the medical applications of radiation, and Gutton on the technical applications of Hertzian waves. Ambassadors from many countries presented their greetings and messages were received from universities and scientific societies in all parts of the world.

The scientific sessions were held during the week in the Palais de la Découverte, which had been equipped for this purpose. In the section on Physics the first paper presented was that by Professor W. Bjerknes, of the Institute of Physics, Oslo, whose wide teaching experience includes courses in the University of Leipzig and a series of lectures in Columbia University, New York. Bjerknes’ subject was The Work of Hertz in the Domain of Electromagnetic Waves. He paid a moving tribute to Hertz, whose first pupil he had been, and as he spoke held in his hand the original manuscript of his master’s paper on the electromagnetic waves. It was the great German physicist, Helmholtz, who suggested to Hertz the experimental investigation of the famous Maxwellian equations, which suggested that there existed electrical waves comparable to those of light but of vastly greater wavelength. Four years of concentrated labor were required to complete the experimental proof of Maxwell’s theory, and lay the basis for the spectacular achievements in radio engineering subsequently attained by Marconi and others. Professor de Broglie spoke on the wave properties of electrons and G. P. Thomson on the diffraction of electrons.

The biological applications of radiation were discussed by another group. Professor Bernal, of the University of London, spoke on the structure of the virus as revealed by x-rays; Dr. Francis C. Wood, Director of the Institute of Cancer Research of Columbia University, presented a paper on the utilization of biological tests in the estimation of the intensity and distribution of radiation; Professor Hevesy of Copenhagen reported experimental studies on the use of artificial radioactive substances to trace the circulation of phosphorus about the body, and Holweck of the Radium Institute, Paris, spoke on the effect of the irradiation of bacteria and yeasts, while others discussed historadiography, and the electron microscope.

A third section dealt with the technical applications of radiations, Hertzian waves, and electrons. Bouwers of Eindhoven, in a paper on the production of high voltages and the results to be expected, pointed out that there is no advantage in the construction of apparatus furnishing energy of over 5,000,000 volts since this is not of interest from a practical point of view, but solely for the study of atomic structure. Since the wavelength in radiations produced at 3,000,000 volts has been found to be greater than that at 2,000,000, there seems to
be no practical need for going higher. In fact there is much evidence that 600–700 kv. is ample for therapy. Another interesting paper in this section was that by Clavier on the development of the radio-telephone system using a wavelength as short as 2 inches. At present communication on this wavelength takes place between England and France and is entirely secret, for it is impossible to tap the circuit unless from an aeroplane equipped with an apparatus to receive 5 cm. waves. These very short waves go directly from spot to spot and in the receiving station are focussed by wooden mirrors, exactly as if they were light.

The fourth session included various communications, among which those by Rowntree of London, on the "Anti-Cancer Effort of Great Britain," and by Schinz of Zurich, on "The Possibilities and Limitations of the Treatment of Cancer by Radiation," were of special importance.

The program included many more papers too numerous to summarize here. Most of these are reproduced in the Acta.

Simultaneously with the Paris meeting a large number of celebrations of the occasion were held in other parts of the world—in the Argentine, under the capable direction of Professor A. H. Rofio of Buenos Aires, in Australia, Cuba, Egypt, Afghanistan, Turkey, Japan, Lithuania, Mexico, Poland, to mention a few. Records of these celebrations are included in this double number of the Acta. Special series of postage stamps were issued by many governments and the occasion was marked by meetings of the various societies whose function it is to attack cancer through education and research.


The first number of Volume III of Radiophysiologie et Radiotherapie, from the Radium Institute of Paris, has been reviewed previously. Numbers 2–4, which complete the volume, contain publications from the Institute appearing during the years 1933 to 1937 inclusive. In addition to the more important papers, which are given in full, each number contains a group of abstracts and references to publications by the members of the staff appearing in other journals.

Fascicule 2: The first paper in this number is a survey by Gosset, Monod, and Regaud of the results obtained by irradiation of gastric carcinoma with radium. A 4-gram pack was used with a skin focus, distance of 10 cm. Of 30 patients, all of whom were inoperable, 17 were not benefitted by the treatment and there was no evidence that life was prolonged. In 7 patients the treatment produced an appreciable amelioration of the condition without prolonging life to any extent, and in 7 others not only was amelioration obtained but the existence of the patient was notably lengthened. One was cured for six and a half years, one for four years and nine months, while another is living at the end of nearly three years. Patients in poor general condition and with highly resistant tumors should not be treated. The gastric cancers studied showed widely varying sensitivity to radiation and while it is hoped that histologic investigation of the fixed tissues of the patients who were explored will give some clue to the cause for this difference, the authors regard their material as too limited to offer any definite opinion on the subject.

The second paper, by Regaud, which appeared also in Volume II of the Fourth International Radiological Congress at Zurich, concerns the details of irradiation of uterine cancer as carried on in the Radium Institute. Regaud believes that many early failures were due to the difficulty of determining the degree of distribution of the tumor. Because of this difficulty it is necessary, especially in cases of Groups II, III, and IV, not only to insert radium in the cervico-uterine cavity, but to supplement this radiation with subsequent roentgen therapy in order, if possible, to destroy parametrial and pelvic deposits. An attempt is made to submit the whole pelvic interior to an evenly distributed dosage, which may be quite impossible with radium alone. The amount of radium used at the Institute is less than is employed by the majority of operators. Three tubes of 5, 10 and 15 mgm. are convenient, the tendency being to give long exposures, usually for about a week. Every care is taken to avoid infection: the tubes are removed daily and the uterus is flushed with a mild antiseptic. The total dose is usually 8000 milligram hours but the writer points out that the

error is still too frequently made of considering that any given dose of radiation will produce a definite effect. The dose considered from a purely physical point of view, that is the quantity of radiation absorbed in a certain volume of tissue during a determined time, can be calculated or measured with reasonable accuracy, but with two exactly similar physical doses remarkable differences may be noted from a biological point of view even though other factors, the most important of which are the quality of the radiation and the length of the treatment, are equally constant. At the Radium Institute much more consideration is given to the biological effects than to the mere physical measurements, care being taken that all the complex factors, physical, geometric and radiophysical receive due attention.

The next paper in this number is by Lacassagne and is a more general survey of methods of irradiation of uterine cancer, including those employed in different clinics. At the Radium Institute the tendency is to use smaller quantities interstitially for a longer time in the attempt to achieve about 8000 mg. hours, or 60 mc. destroyed, according to the French nomenclature. The external treatment with the radium pack lasts about twenty days and at least six fields are used. To each is given about 2000 mc. destroyed. Others use x-ray in an attempt to give about 4000 r in the tumor. There is some tendency observed to employ a combination of radiation and surgery, but this has not made much headway. In badly infected cases many prefer to begin with roentgen irradiation so as to shrink the tumor and diminish the amount of infection, radium to be applied later, followed by a second, long course of x-ray. A good bibliography gives references to all the writers mentioned in the text and covers the whole field of radiation extremely well.

In the next paper Coutard analyzes 89 cases of carcinoma of the hypopharynx. Five-year cures were obtained in 12 per cent; seven-year cures in 9 per cent. The tendency is to increase the length of time over which these patients are rayed. Instead of 25 days Coutard now believes that 40 days is a minimum and if the muscular infiltration is extensive he increases treatment to 50 or 60 days. Where the tumor is localized it is possible to give large doses on the skin, even up to 600 r at a time, obviously with different portals, completing the treatment rapidly, but where invasion has occurred prolonged dosage is necessary.

The two final papers in this number concern the problem of the action of quanta. Lacassagne discusses this from the point of view of biology. He is still inclined to hold to the older view that the wavelength has some effect on the biological reaction, his arguments being based upon results obtained with irradiation of the yeast, Saccharomyces ellipsoideus. Holweck, who takes up the problem from the physical point of view, believes that the effect is a target one and that when only one quantum is sufficient to produce a definite lesion, the appearance of the effects of this lesion follows simple exponential law. When a threshold value of 2, 3 or more quanta is necessary to produce a lesion in the cell, the appearance of this can be calculated from the exponential series of Poisson and the experimental results fit very well with the calculated curves.

Fascicule 3: The first paper in the third number of the volume is by Ferroux, Regaud, and Samssonow, on the increase of the radioresistance of the seminal epithelium following the administration of repeated small, spaced doses of x-ray. The writers find that the administration of a massive dose, 1180 r, to the testicle of the rat produces a serious lesion of the seminal epithelium, consisting in the disappearance of the seminal cells with the exception of certain spermatogonial groups. When, however, such a massive dose has been preceded by 10 fractions of 75 r each, at intervals of a month, the lesions are much less striking, and the testicles, as a rule, are found to contain numerous spermatic cells, among which are some that are completely normal. The treatment of the testicle by 7, 9 or 10 fractions of 75 r each at monthly intervals does not produce any lesion of great importance, causing only slight damage to the seminal epithelium. The writers consider that they have experimentally established a diminution in the radiosensitivity of seminal epithelium by preliminary prolonged and fractional irradiation and believe that this is an important suggestion as regards the type of therapy to be employed in human carcinoma.

The following paper is by Lacassagne on irradiation of the hypophysis. In the rabbit this gland is completely destroyed by the introduction into it of a glass tube of radon, about 1 mc. affording sufficient radiation for this effect. The insertion can be done without anesthesia and requires only about five minutes. Only a few animals die from the treatment. Sections show that the destruction in most cases is complete. The result in the female is
complete loss of ovarian function. Since the conservation of as little as one third of the anterior lobe insures the maintenance of normal genital function, it appears doubtful that any influence can be exerted on the function of the ovary by therapeutic irradiation of the hypophysis.

A paper by Ferroux and Folichon concerns the loss of radon from radium tubes containing a large amount of element. The phenomenon is presumably due to the fact that the walls of tubes which have a 0.5 mm. thickness of platinum containing 10 per cent iridium are slightly porous. The pressure of the helium which accumulates in such tubes may possibly assist in the issue of the radon from the tube. After considerable study it was found, however, that the amount of radon escaping is entirely unimportant either to the patient or the personnel handling large radium packs containing 8 grams of radium.

A short paper by Loiseleur concerns the effect of radon in a thin glass tube on proteins. The amino-acids undergo hydrolysis with formation of ammonia and there is also a flocculation of the serum which, however, requires the presence of electrolytes. The quantity of radiation necessary to produce these actions is of the same order of magnitude as the lethal dose for unicellular organisms, which is far higher than for mammalian tumors.

Regaud and Hermet report on an investigation of a group of patients with cancer of the cervix who were irradiated but not cured. The material comprised 559 persons. Nearly 50 per cent of these died in the first year after the treatment was finished. Only 5 per cent died after the fifth year. The clinical course in such cases is described. The lesions are variable. For example, the cancerous process in the cervix and vagina may not be influenced; there may be a reinvasion and late ulceration of the walls of the vagina; the neoplasm may develop into the depths of the uterus or in the pelvic nodes or there may be distant metastatic localization. The writers also describe a persistent thickening of the pelvic connective tissue surrounding the uterus, rectum and bladder, which is due to chronic inflammation or late chronic radiation lesions. It is impossible to prove by examination that these changes are not due to a recurrence of the cancer, but certain patients have remained cured despite this condition. The detailed records of 28 patients who survived beyond the fifth year are included.

A paper by Baclesse discusses the treatment of uterine cancers, mostly fairly advanced cases, by x-ray alone. Nine patients are considered as cured out of 63 treated. The doses given were very large, amounting to 16,000 r on the skin. Treatment was given rather rapidly, with portals up to 20 x 20 cm., though these dimensions were reduced in the later cases. Serious damage to the skin occurred in a certain number of the patients and on the whole Baclesse considers the treatment unsatisfactory, as it is difficult to avoid these unfavorable effects and requires a great deal of courage on the part of the patient to withstand the discomforts entailed. He thinks, however, that with the higher voltages now available better results can be obtained. This has been confirmed by the observations of those who have been able to use 700 or 800 kv., with which the penetration is much greater and the skin lesions, owing to low back-scatter, are less serious than with 200 kv.

Tailhefer reports on the results obtained in 83 cases of cancer of the tongue. Histologic examination of the nodes showed that they were invaded in 69 cases. The number of cures, most of which are for more than five years, is 19. Tailhefer believes that the results might be improved if bilateral cervical excision of the nodes were carried out in all cases, promptly after the treatment of the lesion in the tongue by the insertion of radium needles. It is evident from his study, also, that even with small lesions it is necessary to make a complete resection of the nodes on both sides if the primary growth has reached or passed the midline of the tongue.

Regaud discusses the treatment of carcinomata of the rectum and anus with radiation. Owing to the great radio-insensitivity of the tumors, few cases are cured. Among the histologic varieties treated were adenocarcinoma, which is the least sensitive, and wholly undifferentiated carcinoma, which though rare is relatively radiosensitive.

Fascicule 4: This number contains eight papers. The first, by Lacassagne, concerns the result of irradiation of the Shope rabbit papilloma. A single dose of 3000 r will kill the tumor, regression being complete in about eighteen days. The histologic changes are similar to the alterations in cancer of the skin, which have been described in many publications, including that of Lacassagne and Monod in Arch. franç. de path. gén. et exper. 1: 1,
1922. The same amount of x-ray, or often less, will cure many of the tar papillomas produced in rabbits' ears. A good deal of confusion exists in the literature concerning the nature of the papillomatous tumors produced by tar painting. While they have been described as carcinoma, the majority of such tumors of a non-metastasizing type can be so easily cured by radiation that it is obvious that they are, instead, merely papillomas.

The second paper, by Baclesse and Dulac, concerns the technic of studying the nasopharyngeal region by radiographs. Two views are necessary: one a lateral view centered at 1 cm. below the zygomatic arch and just in front of the temporal maxillary joint, and the other in the standard chin vertex angle. The article is illustrated by typical radiographs.

The third paper, by Baclesse and Leroux-Robert, discusses the importance of radiographic examination in the diagnosis of subglottic cancers. It is illustrated by 38 figures and a full bibliography is appended.

Lacassagne contributes a general survey of the place of radium in the treatment of cancer, the original text of which was published in English, in the Journal of the Canadian Medical Association (38: 9, 1938). He points out that the development of radium therapy and x-ray therapy have made parallel progress. With radium the first step was the perfection by Dominici of heavy screening so that only the gamma rays reached the tissues. The further development has passed through three phases: (1) study of the mechanism of the action of radiation on living material; (2) determination of the radiosensitivity of human tumors; and (3) practical adaptation of radiation to tumor therapy.

It is generally accepted today that radiation acts for the most part directly on the cells, and that the average quantity necessary for the destruction of the cells varies with the cell type. To cure cancer it is necessary to administer to all the cells of the tumor an amount of radiation in correspondence with their radiosensitivity. As an essential for such treatment the physician must know the type of the tumor, its seat, and its extent. Sufficient knowledge is now available concerning the ordinary types of tumor to furnish a rough approximation to the radiosensitivity. The radiotherapist must arrange that the deepest part of the tumor receives the necessary sterilizing dose, which implies a determination of the quality of the radiation administered and the number, area, and direction of the ports of entry. The extent of tissue involved by the tumor also influences the type of treatment, which must avoid too severe reactions in normal tissues. In many cases this compels fractionation and extension of the doses in order that such tissues may escape destructive action. Two technics remain: one, the caustic destruction of the cancer tissues; and the other, selective sterilization. The first can be used only for superficial tumors of limited extent. It not only destroys the tumor cells but also produces severe damage of surrounding tissues. The radiation employed must obviously be of long wavelength in order that destructive action on the internal organs does not occur; hence it is largely limited to tumors of the epidermis. Selective action is obtained only with multiple doses instead of a large single dose as in the first instance, and in general with higher voltages in order to obtain penetration, and a highly screened beam in order to remove rays which are absorbed in the upper layer of tissues. As concerns radium, the great penetrability of short wavelength gamma rays is counterbalanced by the small quantities of material which are available, necessitating close approximation to the skin and therefore a small depth dose. Radium possesses an incalculable advantage in the possibility of the insertion of highly filtered radiation in the tumor itself, though the recent development of high-voltage x-ray tubes has permitted the use of roentgen radiation of a comparable wavelength, at considerably less cost.

The work of exploring the action of the two types of radiation on cancer may be considered as provisionally finished unless some entirely new factors are discovered. The results have shown that tumors can be divided into three groups, the radiosensitive, the fairly resistant, and the wholly resistant types. The second class includes the adenocarcinomas of the breast, viscera, and mucous membranes of the gastro-intestinal tract, and the sarcomas of the connective tissues. In general, the tumors of this group are not favorable for palliative treatment. In the third group lie a few tumors which it is not possible to cure by radiation. These are the neurosarcomas, nevus carcinomas, and many of the tumors derived from nerve tissue.

There are two localities in which radium still plays an important part in cure. One is the buccal cavity and the other the uterus. Most of the cancers of the mouth were in-
curable until the technic of radium insertion was highly developed, and even now the number of cures is small. Neither penetrating x-radiation nor radium packs are as efficacious in this region as properly inserted radium needles. If we except certain tumors of high radiosensitivity, such as are found in the tonsillar region, the tongue furnishes a very excellent example. Cancers of the anterior dorsal portion of the organ are almost always epidermal, hence moderately radiosensitive, and a considerable proportion may be cured by the interstitial introduction of radio-active material. On the other hand, irradiation of the cervical metastases from a tumor in this region is almost always futile. It is necessary therefore to associate with the radium treatment of the primary lesion the surgical removal of the involved lymph nodes.

Carcinoma of the cervix is equally instructive. More and more it is being realized that this type of neoplasm should be treated by radiation. Not only is a high proportion of cervical cancers in the early stages cured, but an important percentage of five-year survivals is now seen following the radiation treatment of inoperable carcinoma of this region. Also it is being recognized that the local application of radium is far more valuable in the production of permanent results than any amount of exposure by a radium pack or million-volt x-rays.

For other types of neoplasms, roentgen therapy is at the moment preferable. This is especially true of rapidly extending and highly radiosensitive neoplasms such as the lymphosarcomas, seminomas, and germinal carcinomas of the ovary. With such growths it is possible to cover a much larger field than can be covered with radium and to attack distant extensions. The same is true of the carcinomas of the pharynx and larynx. The prolonged and careful studies made by Coutard of the Curie Institute have developed this treatment to a point where it is more satisfactory than radium.

A question frequently asked is whether, with the use of very large quantities of radium at a considerable distance from the body, the results would be more effective and malignant growths hitherto refractory could be satisfactorily handled. This it is impossible to predict. The original hopes that radium and x-ray would cure large numbers of patients with cancer have failed to be realized, and there is no evidence at present to suggest any great improvement in the results. Large quantities of radium are extremely dangerous to those handling the material because of the great penetration of the rays, and from this aspect x-ray is preferable. It is a delusion to think that by increasing the quantity of radiation or even obtaining radiation of a shorter wavelength any great increase in effectiveness will be found.

The application of the recently discovered neutrons is an example of the possibility of advances in therapy by the use of other destructive materials. In conclusion, it is certain that radium will retain a prominent place in the treatment of certain types of cancer because of the possibility of insertion of small amounts in the tumor, amounts insufficient to cause serious damage at a distance; but x-ray will probably ultimately replace radium packs.

The fifth paper in this number, also by Lacassagne, is a study of the indications for various methods of treatment of cancers of the skin. These tumors present a diversity of problems to the therapist because of the multiplicity of their histologic types and considerations due to the situation, extent, and state of evolution in each case. The difficult problem is to make the proper choice of the three applicable methods: electrocoagulation, surgery both scalp and electric, and radiation. The advantages of diathermic destruction are: (1) the immediate effect, thus shortening the treatment, and (2) the diffuse destructive action due to coagulation of all the living structures to a certain distance beyond the heating electrode. The method therefore can be applied to all sorts of malignant tumors without risk of spreading the neoplastic cells; on the other hand, the normal tissues in the tumor and in the neighborhood of the neoplasm are severely damaged. Repair is slow and cicatrix from an esthetic point of view, is unsatisfactory, considerations which limit the method to small, circumscribed lesions. Surgery is equally radical. With proper technic the lesions heal quickly and the effect is excellent from a cosmetic point of view. Radiation therapy possesses, on the other hand, certain qualities which are both advantageous and disadvantageous. The selective action of the rays permits the destruction of tumor cells at considerable depth without inflicting irreparable damage on the normal cells. But this advantage is limited to neoplasms of considerable radiosensitivity. Nevertheless, it is possible to employ it in situations where access is difficult for surgery and the freedom from risk of dissemination is important.
The author continues with a discussion of the indications for the treatment of different types of skin tumors and offers suggestions as to the proper therapeutic technic. Treatment of the regional nodes is discussed in general. As the basal-cell tumors do not invade the nodes, excision of the latter is not necessary. The squamous-cell tumors of the lip, on the other hand, do metastasize, and here the question of excision of the regional nodes depends to a considerable extent on the size of the tumor. It has been found that of cases in which the growth does not invade the mucous membrane, the muscular planes are not involved, and the size does not exceed 2 cm. in diameter, only 3 per cent show invasion of the cervical nodes. Larger and infiltrating growths imply excision of the nodes, even if no clinical evidence is available to show that they are involved. The situation is entirely different with the epitheliomas of the ano-genital region, where the nodes are involved in from 50 to 70 per cent of the cases. When the involved nodes are attached to the bone and where the lesions are extensive, it is useless to dissect, as a prompt recurrence is almost certain. Palliative irradiation is therefore preferable. Nevocarcinomas, whether pigmented or not, are radioresistant and should be destroyed by extensive electrocoagulation or by wide surgery preferably with the electric cutting current followed by excision of the regional nodes. Only a few cases, however, are cured by any method.

The sixth paper, by Regato, concerns the roentgen therapy of the carcinomas of the maxillary sinus. These tumors are chiefly squamous-cell epitheliomas, but may be partially or entirely glandular in type. They are, as a rule, sensitive to x-ray. Of 10 inoperable patients treated at the Curie Institute, 4 are still living after at least five years, the best results having been obtained from divided dose x-ray treatment extending over four to five weeks. Good results have been obtained in the operable tumors, when not too extensive, either by radical excision of the maxilla or by exposure of the tumor and its destruction by cautery and subsequent irradiation with inserted radium.

The final paper, by Courtial, concerns the radiotherapy of the primary squamous-cell carcinomas of the vagina. Treatment consists of direct irradiation by radium followed by external x-ray therapy through the pelvis. Two out of a series of 32 patients were treated by radium alone and 3 by x-ray alone. Of the total number, 15 are still living and apparently free from recurrence.

This short summary touches only on the main points discussed in this valuable volume. It should be read in detail by all who are interested in the radium and x-ray treatment of the various types of cancer which have been considered.