Radiumtherapy / by Louis Wickham [and] Degrais; Tr. by S. Ernest Dore.

RADIUMTHERAPY

Ouvrage Couronné par l'Académie de Médecine de Paris

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BY

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ILLUSTRATED WITH 20 COLOURED PLATES AND 72 FIGURES IN THE TEXT

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INTRODUCTION TO THE ENGLISH EDITION

BY SIR MALCOLM MORRIS, K.C.V.O.

It has been well said that a fair face is the best letter of introduction. Still more true is it that the good reputation of a writer makes any recommendation of his book superfluous. But I have been asked to write a few words of introduction to the English translation of Dr. Louis Wickham's work on Radiumtherapy, and, considering it an honour that my name should appear in association with his, I have gladly consented. He is the true pioneer in the new region, now gradually being opened up, of the therapeutic application of the wonderful substance the discovery of which by Mme. Curie and her late husband has already changed our concepts of physics and chemistry, and may have results of the most far-reaching character in the sphere of applied science.

Among the most striking and important of these results is the application of radium to the treatment of disease. The medical profession is as eager as were the Athenians of old to hear of any new thing; and it is somewhat prone to welcome a therapeutic novelty with excessive enthusiasm, and, when the inevitable reaction occurs, to dismiss it with perhaps undeserved depreciation. To this general rule of the formation of medical opinion radium has been no exception. On the strength of some exaggerated statements it has been hailed as the long-expected cure for cancer; and the notion of radioactivity has inflamed some minds to a degree far beyond anything for which the facts so far ascertained afford justification. It is scarcely too much to say that but for the judicial temper brought by Dr. Wickham to the study of the problem, radium, whatever potency of healing it

holds in itself, would have been relegated, as other remedies have been, to the limbo of charlatanism. As I remarked at the meeting of the British Medical Association held at Belfast in 1909, in the application of radium to medicine there are two great epochs, " before Wickham " and " after Wickham." To Dr. Wickham and to his collaborator, Dr. Degrais, the profession owes a deep debt of gratitude for the time and care they have given to a most difficult investigation, and for the frankness with which they have made known their results. Their book is written in a truly scientific spirit. The methods of radiumtherapy are fully described, and the evidence for its efficacy is in each instance impartially discussed. Throughout their work the authors, as they rightly claim, have held fast by the principle, so often, and with such disastrous results, neglected in therapeutic experiment, that statements must be guarded, and must be based on a sufficiently wide experience and controlled by that final test of remedial action—*time*.

Whether the theory of the mode of action of radium set forth by the authors will be accepted as final is a question that need not detain us. What practitioners of medicine are particularly interested in is the therapeutic efficacy of radium, and the permanence of the results. Drs. Wickham and Degrais have used this agent in various ways in the treatment of cancer, cheloids, and troublesome scars, angiomata, pigmentary nævi, muco-cutaneous tuberculosis, pruritus and chronic itching affections of the skin, and neuralgia, as well as in the treatment of women's diseases. In regard to cancer, which from the first has occupied a large place in Dr. Wickham's researches, the authors claim to have shown that radium is suitable not only for small, slowly developing growths, but for large, rapidly spreading, malignant ulcers, many of them cases of recurrence ; and, while frankly confessing their failures, they hold that their results are much better than those obtained by previous workers with radium. In cases in which the treatment failed to effect a cure, it stopped bleeding and discharge, did away with fœtor, and abolished pain. Although, as might be expected, the treatment is most successful in cases where the lesions are superficial and easily accessible, the authors speak hopefully of the usefulness of radium in deep-seated regions, such as the prostate, the rectum, the œsophagus and the abdomen.

The authors have been particularly successful in the treatment of cheloid, on which they hold that radium has a selective action ; but

cicatricial bands do not, in their experience, yield readily to its influence. In the treatment of nævi and inoperable vascular tumours, radium has in their hands almost invariably given good results; there is still, however, a large place left for electrolysis, X-rays, and surgical procedures. It is in the case of young children that radium is most useful in the treatment of these growths. In lupus and other forms of cutaneous tuberculosis, it appears to have no selective action. Considerable improvement has in certain cases occurred, but the authors speak very cautiously of their results. An experience of one hundred and fifty cases has led them to the conclusion that radium may be serviceable in varying degree in all forms of skin tuberculosis, but that it especially deserves a place in the treatment of lupous nodules, ulcerations, lupus of the conjunctiva, erythematous lupus, warty tuberculosis, and certain infiltrations and prominent scars following suppurating glands.

In the treatment of pruritus—anal, vulvar, etc., and in various forms of neuralgia, the results of treatment with radium have been satisfactory; its analgesic effect has also been proved in inflammatory pains in joints. In chronic lichenoid forms of eczema, psoriasis, and various other pruriginous affections of the skin which have proved refractory to other treatment, radium has stopped the itching, and the consequent scratching with its attendant evils has been suppressed. As to syphilides, Drs. Wickham and Degrais speak with some reserve, but they are able to cite certain cases in which radium has "seemed to hasten and favour a cure." In gynæcology they believe that it has a great future before it.

From what has been said, it will be seen that Drs. Wickham and Degrais have proved that radium has a wide field of therapeutic usefulness. They have the advantage of a laboratory, together with an abundant supply of cases, and are thus in a position to study under the most favourable conditions the methods of applying radium, its mode of action, the nature of the morbid conditions in which its properties are likely to be serviceable, and its limitations.

It cannot be too strongly impressed on the mind of the profession that, brilliant as is the work of which the present book contains the record, the exploration of this new region has only just begun. Our knowledge of the subject is still in its infancy. A British Radium Institute, which

owes its establishment to the initiative of our gracious Sovereign King Edward, will, it is hoped, before long have begun its appointed work of testing in the fullest possible manner the therapeutic properties of radium. But whatever may be accomplished by the workers in our own Institute, nothing can deprive Dr. Wickham of the glory of having laid the foundation-stone of scientific radiumtherapy.

PREFACE TO THE ENGLISH EDITION

BY DR. WICKHAM

The MS. of the French edition of this work was finished in March, 1909. Since that time, with the assistance of Dr. Degrais, I have collected a large number of new observations dealing with the technique and therapeutic results. During this period of ten months a great advance has been made in our work. As the science is entirely new, and therefore in constant progress, the favourable conclusions put forward in the French edition might have been completely changed, and even contradicted. Nothing of the kind, however, has occurred, and the statements then made remain true, at any rate in their main features. The new facts recorded have, for the most part, amplified and corroborated those first indicated in this work.

It was important to bring these new facts to the notice of the medical profession, and I have done this by means of additional notes, which bring the subject of radiumtherapy up to date in the English edition.

These additions chiefly concern the development of radiumtherapy as applied to malignant tumours, and the unquestionable value of the method devised by us for the treatment of most forms of vascular nævi, even when flat and superficial, a method which we had previously put forward with some reservations.

I have also laid stress on the importance of combining different methods of treatment, for radium plays a more extensive and effective part when it assists other methods, or is assisted by them. This is especially true of cancer, in the treatment of which the use of surgical and other methods of exploration allows radium to be introduced at the very centre of the mischief.

*

In conclusion, I wished to remind the younger radium workers who are in touch with our investigations of the necessity of avoiding exaggeration, particularly in connection with cancer, and of moderating their enthusiasm by a spirit of scientific criticism.

Radiumtherapy is indeed a very complex and delicate weapon to handle. Long and thorough personal experience is necessary, in order to turn it to the best account, to learn to distinguish accurately the cases for which it is most suitable, and to avoid injuring patients, either by badly proportioned doses or by depriving them of other therapeutic measures, which might prove more successful.

I desire to thank the translator and the English publishers for their courtesy in accepting these notes, and for the care which they have bestowed on the execution of their work.

PARIS, *January*, 1910.

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AUTHORS' PREFACE TO THE FRENCH EDITION

We dedicate this book to the memory of Professor Curie and to Mme. Curie.

Soon after the discovery of radium, numerous experiments made on plants and the lower animals clearly demonstrated its biological properties; but it was only by accident that, in 1901, its action on the human tissues became known. Becquerel happened to be using a tube containing pure radium, and put it into his waistcoat pocket. M. Matout, his assistant, drew his attention to the imprudence of doing this. Becquerel, however, took no notice, and carried the tube about with him for several hours. A fortnight afterwards, severe inflammation appeared on the skin beneath, which was attributed by Besnier to the action of the radium. Such was the famous "Becquerel burn," the remembrance of which is still so vivid that, in the minds of many physicians, radium is only a synonym for burn.

Professor Curie then made a conclusive experiment on himself, and, thinking that the properties of radium might be useful for medical purposes, at Besnier's suggestion he entrusted a specimen to M. Danlos, of the St. Louis Hospital. This was the starting point of a new branch of physiotherapy. The properties of radium as a therapeutic agent have now become recognised, and great progress has been made in its study. We now possess fairly accurate methods of measurement, and the results obtained have fulfilled our highest expectations. A large number of patients suffering from diseases which had hitherto proved refractory have already been greatly benefited by the discovery made by the Curies. It is therefore with much pleasure that we place at the head of this work, as a testimony of the gratitude felt by us all, the names of these great authorities, to whom doctors and patients are alike indebted for the discovery of so valuable a remedial agent.

Some points in the history of radiumtherapy will be touched on in different portions of our work, but we shall not devote a special chapter to it. As to the part we have ourselves taken in these studies,

we prefer to leave this to be indicated by others. As we were in possession of new apparatus, which gave us unusual facilities for investigation, we have been obliged to go back to the very beginning of the subject. In the Introduction we shall put on record the first stage of the investigations pursued by one of us since March, 1905, in his own practice and in his clinics at St. Lazare and elsewhere. This preliminary work formed a basis for the establishment of the Laboratoire Biologique du Radium, which could not have been instituted without it, and the recent progress in radiumtherapy is due to the improved organisation of this new centre. It then became possible for us to develop our first researches, and to extend them to a more systematic study of those refractory diseases which seemed amenable to the influence of radium, and to arrive by degrees at the conclusions which have suggested the compilation of this book. We were guided by the principle that, in the study of radiumtherapy, perhaps more than in any other subject, *assertions must be made with great caution, and always based on a sufficient length of time and number of cases.* The effect of radium on the tissues continues for many months, and it is necessary to allow time for the final development of any possible changes before pronouncing on the success of a course of treatment. Our observations have now extended over four years, and included about nine hundred patients. *We have always devoted special attention to the study of measurements, filtration, and dosage.* So fascinating is the magic effect of radium, and so great the danger of being carried away by imagination, that we are always careful to bring to our clinical observations a spirit of scientific criticism and analysis. Any new and complex science is liable to frequent alteration, and it is therefore with some diffidence that we have ventured to formulate our conclusions, and offer this work to the public. We cannot, however, expect to escape a considerable amount of criticism. The primary object of this book is to set forth, in a field where almost everything is new, the facts which have come under our own observation, so that other members of the profession may be able to use radium for the benefit of their patients, without the long and minute investigations which we have been obliged to undertake.

As regards physics, we owe much to the advice of MM. Razet, Danne, Matout, Sagnac, and Debierne, but we must also mention the important part taken by our physics laboratory at the Laboratoire Biologique du Radium. The work carried out there by M. Beaudoin, of the Chemistry and Physics Department, has largely contributed to the study of the therapeutic application of radium. We are also

indebted to our colleagues, MM. Dominici and Jaboin, for their valuable collaboration.

It will be noticed how often the names of MM. Balzer, de Beurmann, Brocq, Ertzbischoff, Gaucher, Gastou, Hallopeau, Jeanselme, Magnin, Robinson, Triboulet, and others occur in this book. Our colleagues at the hospitals—among whom M. de Beurmann, physician at the St. Louis Hospital, was the first to take any personal part in our work—have been of great assistance by entrusting to us many of their patients. Nor must we forget that poor patients have also had the advantage of radium treatment—(Professor Gaucher alluded to this fact in the course of a lecture which has set an official seal on radiumtherapy)—owing to the readiness with which M. Armet de Lisle and M. Farjas have lent us radium for this purpose, and also to the good feeling which has prevailed in the organisation of our new institute. We must also acknowledge the help afforded by earlier works on the subject, amongst which those of MM. Danlos, Béclère, Abbé, Williams, Davidson, Lassar, and Blaschko may be specially mentioned ; and by the eloquent words of Sir Frederick Treves in a lecture recently delivered at the London Hospital. Special interest has also been taken in our researches by Professor Bayet, Sir Malcolm Morris, and others, who, having had free access to our laboratory, have been able to follow the treatment of our patients. It is impossible for us to mention them all here by name. We desire likewise to express our gratitude to Messrs. Baillière for the care they have bestowed on the publication of this work. To all these collaborators our most cordial thanks are offered.* Our revered teacher, Professor Fournier, well knows what gratitude we feel for his constant interest and kindness. It is to the great weight of his authority that we owe the interest in radiumtherapy shown by the Académie de Médecine.

The arrangement adopted in this work is simple, and explains itself. It was necessary to describe the nature, origin, and available energy of radium. The first Part is therefore concerned with Physics.

In order to describe the instruments, the methods of treatment, and the conditions of measurement and dosage, the second Part deals with Instruments and Technique.

Lastly, to show what results we have obtained by the use of these various methods, there is a third Part—namely, Clinical Therapeutics.

* Our hearty thanks are due to M. Combres, Dr. Wickham's house physician in his St. Lazare clinic, for the help he has given us in drawing up the alphabetical index, and in preparing the chapters on pigmentary nævi and tuberculosis.

This section includes general considerations on reaction, together with chapters on carcinoma, cheloids and disfiguring cicatrices, angiomata, pigmentary nævi, tuberculosis, chronic refractory affections of the skin (inflammatory and pruriginous), and various other diseases; and a chapter on the use of radium in gynæcology.

INTRODUCTORY LETTER TO THE FRENCH EDITION

My dear Wickham

You ask me to introduce to the notice of the scientific world the work which you have written in collaboration with M. Degrais. Do you think there is really any need for an introduction from me? I feel sure that the public will not agree with you on this point.

Your researches have long been known and appreciated by us all, and I cannot do better than repeat here what I said at the Academy when presenting your first memoir. Your work is excellent, and has produced the most fruitful results, on which I congratulate you.

My only regret is that syphilis has not had a larger share in these results. I am confident, however, that before long you will be able to give us some hope from this quarter.

No one knows better than I do the conscientious and scientific work of which you are capable. You have been associated with me for twenty years, and the sentiments of esteem and affection with which I regard the former chief of my clinic at the St. Louis Hospital have only grown stronger with the lapse of time.

Yours most sincerely

Alfred Fournier.

RADIUMTHERAPY

INTRODUCTION

By LOUIS WICKHAM

I. SCIENTIFIC PRINCIPLES

If certain facts are established, and certain hypotheses justified, a momentous revolution in the sciences of physics and chemistry will take place during the early part of this century. The very foundations of these sciences are being shaken by new theories, and some of the laws hitherto regarded as unassailable are seriously threatened.

Two distinct worlds were formerly recognised in the universe; the world of "ponderable" things (matter which could be weighed), and the "imponderable" world (ether and all the phenomena of energy produced in its wake, such as light, heat, electricity, etc.). A clearly defined and impassable barrier existed between the ponderable and the imponderable. Energy and matter were considered indestructible. The latter could, indeed, assume new forms; a solid could become a liquid or a gas, but the aggregate of the newly formed elements always reproduced the exact weight of the original matter. Matter, again, was inert, and possessed in itself no force except that which had been previously transmitted to it. It could not *create* energy. Electrical energy, for instance, could only be manifested by matter in so far as it was the subject of physical impulses or chemical reactions, and the transmutation of elementary bodies appeared to be an impossibility. The sciences of physics and chemistry seemed solidly and permanently established on these bases. After centuries of investigation and experiment, we believed ourselves to be at last in possession of fixed laws and fundamental principles. It is true that certain discordant notes made themselves heard towards the end of the last century. Doubts were raised by experiments that gave contradictory results, but did not shake convictions, for the arguments they suggested were too weak and easily refuted. Observations and experiments of

a much clearer and more decisive character were necessary in order to undermine foundations which had been so firmly established.

The discovery of radioactivity, and especially of the activity of radium, by M. and Mme. Curie supplied the necessary lever, and shed on the subject a much-needed ray of light. Owing to the clearly defined properties of radium, its discovery has given solid grounds for many new beliefs, about which there had previously been much hesitation. It has enabled experiments of a more conclusive nature to be successfully performed, and suggested hypotheses which would formerly have been considered highly improbable. It is, indeed, the central point around which a scientific revolution appears to be taking place.

Sir William Ramsay had previously shown that a certain quantity of helium, analogous to the helium of the solar spectrum, existed in the air, and, on isolating in a tube the gas or "emanation" produced by the disintegration of radium, he ascertained that this gas, as it gradually disappeared, was transformed into helium. This phenomenon led to the supposition that the helium of the air was the final result of the emanation, slowly produced by a natural process of transformation which had been going on since the most remote ages. It furnished an example of one element—the radium emanation—giving rise to another, namely, helium. M. Debierne has also found that the emanation of actinium is transformed into helium. The production of helium, therefore, appears to be a result of the disintegration of radioactive substances in general. But Sir William Ramsay would seem to have provided, by means of this emanation of radium, an even more definite instance of the transmutation of elements. If this should be the case —the fact is disputed by Mme. Curie—it would invalidate the fundamental laws of chemistry. Having brought the emanation into contact with nitrate of copper, he obtained products of various kinds, amongst which, under spectroscopic examination, he found lithium rays.

When considered in relation to physics, the facts are no less astonishing. The gaseous emanation produces the extremely curious phenomenon of *induced* radioactivity; that is to say, other substances, when brought into contact with it, themselves become for a time radioactive, and acquire new properties derived from the radium. Thus water, vaseline, etc., may become radioactive *without containing any radium*, merely through being subjected to the influence of the emanation.

As radium disintegrates, it gives off energy in the form of infinitely attenuated material and semi-material particles, *spontaneously* charged with electricity. These are known as α particles and β electrons, their size varying from that of the hydrogen atom, the smallest known, down

to dimensions 2,000 times less. Radium emits them with an extraordinary velocity, more or less akin to that of light (300,000 kilometres per second). A disturbance of the ether results from this outflow of energy, which is shown in the form of the so-called γ rays. The stream of particles, and the accompanying perturbation of the ether, together make up the radium rays, which possess a considerable amount of energy, manifesting itself in the domains of physics, chemistry, and biology. These rays can penetrate bodies, produce images on photographic plates, affect the condition of the air, and modify organic cells. Radium produces not only electricity, but heat in abundance, and light; it is also phosphorescent. Now all these different forms of energy come into existence, and manifest themselves, *spontaneously*. Radium seems to receive no stimulation from any source whatever. It therefore appears to re-generate spontaneously the energy that it is constantly giving out. Up to the present time it has not been possible to discover any source from which it can be replenished and sustained. It ought, therefore, to lose weight rapidly. But nothing of the kind takes place; fragments weighed after an interval of several years have been found to retain their exact weight. Some recent calculations, however, seem to indicate that there is some loss, although it occurs under such conditions that we cannot estimate it. It would take hundreds of years to exhaust the energy of a single grain of radium.

These are the remarkable and disquieting facts which have led eminent physicists to indulge in speculations, somewhat fanciful it may be, but not without plausibility, and in any case of the greatest interest.

When we consider that other substances, though of an entirely different nature, when under the influence of well-known physical and chemical reactions, liberate elements analogous to those produced by radium (products of the electric discharge in a Crookes tube—anode and cathode rays—and, outside the Crookes tube, X-rays), may we not ask ourselves whether all these phenomena have not a common point of origin, and whether matter—whatever be its nature—is not that which, in the ultimate analysis of its atoms, always contains the same constituent elements? The rays would thus be the product of the disintegration of matter in general, such disintegration taking place in certain rare substances in a rapid and spontaneous manner, while in others it is only brought about by some external stimulus.

In order to explain the mechanism of the process, one may suppose that the constituent elements of the atoms of all substances are animated by gyratory movements, and revolve at so great a speed that they are the subject of attraction and repulsion, as in a planetary system. Rotation at such high speed would produce a condition of equilibrium

which would account for the apparent stability of matter. The faster a top spins, the steadier it is. Now it is in this very rapidity of the rotation of its elements that the incalculable energy latent in matter resides. If anything should occur to diminish the speed of rotation essential for stability, the equilibrium would be disturbed and the immediate consequence would be the setting free of a part of the force held in reserve. Some particles would escape with considerable velocity, and the more complete and accentuated the disturbance of equilibrium, the more violent would be the force thus liberated. Now we may suppose that the stability of the atoms can never be absolutely perfect. Disturbance of equilibrium always occurs in some of them, so that a certain amount of energy is constantly being set free. In other words, all matter is in process of dissolution and decomposition. It is throwing off atomic particles, and is therefore in a permanent state of disintegration, a process which manifests itself in the output of various forms of energy: heat, light, electricity, radioactivity, etc. The forces resulting from the liberation of the energy latent in the atoms are in a state of transition between the material and the immaterial. Some of them are hardly more than semi-material (such as the gas emanating from radium and the electrons); others are no longer material at all. These forces vanish, and we cannot follow them beyond a certain limit. Perhaps they return to ether, to the imponderable world; perhaps they form a transition stage, destroying the barrier that was supposed to exist between the ponderable and imponderable worlds. Some of them are already in our possession, and the subject of our investigations; such are heat, electricity, light and radioactivity. We think ourselves rich in possessing these, but it may well be that they form only a small, and even an infinitesimal part of the energy which is apparently latent in the matter from which they proceed. This disintegration of matter—so pregnant in consequences, if it is indeed the source whence all the forces of nature are derived—arises spontaneously and is continuous in its action; but it proceeds at so slow a rate that it escaped all previous methods of investigation and remained unknown until the present time. We did, indeed, control and utilise some of its effects, but without the slightest suspicion of their real origin. Our method of obtaining heat, electricity, light and phosphorescence consisted, although we were not conscious of it, in stimulating and hastening this disintegration.

We have so far been dealing with processes which are still extremely slow, and of which we know only the bare outlines. But should investigators find some means of hastening them, energy of incalculable power will be set free, increasing the forces already known to us and reveal-

ing new ones. It is not long since Galvani had only enough electricity at his disposal to excite movement in the legs of a frog. No one, therefore, can deny that we may be able in the near future to utilise the enormous forces contained in matter. Various methods of increasing the intensity of the radiation of certain spontaneously radioactive bodies are now being investigated. If the liberation of the forces latent in matter could be accomplished easily and economically, we should possess the means of applying unlimited force. The following figures are of interest, being derived from the calculations of eminent physicists. They are based chiefly on the formula $\frac{M V^2}{2}$ (half the product of the mass of particles multiplied by the square of the velocity). According to Sir J. J. Thomson, the energy contained in one gramme of matter would represent 100,000,000,000 kilogrammetres. Max Abraham calculates that one gramme of electrons (particles set free in the disintegration of matter) represents the energy of a horse-power of 80,000,000,000 per second.

And here we cannot resist the pleasure of quoting the following passage from the "Éloge de Curie" delivered at the "Académie des Sciences" by M. H. Poincarré :—

"When the Curies had collected and isolated radium, it was found that this new metal was endowed with astonishing properties. There issue continually from it radiations which may be compared to a flow of electrified corpuscles, extraordinarily minute, with a velocity almost equal to that of light. It is believed that these corpuscles are so light that radium could emit them for thousands of millions of years without appreciably diminishing in weight. When they come in contact with an electroscope, they discharge it; when they strike certain bodies, they illuminate them, and one's first impression is that their light must be eternal, for its source seems inexhaustible. These corpuscles attain a velocity hitherto unknown, and the study of their movements reveals to us a new science of mechanics, which, in the eyes of some enthusiasts, promises soon to supplant the old one, good enough at best for miserable machines that can only do twelve miles an hour, or for lazy planets going barely a thousand times faster. And this new science is sweeping all before it. Already we are told that no such thing as matter exists, and that what we have called matter is only an electrical illusion.

"Radium, which gives out light, should also produce heat, and Curie has shown that it produces it in abundance. This was a fresh surprise. Was this perpetual motion? Perhaps undue haste was shown in asserting that it was, for we now know that radium exhausts itself in twelve hundred years. At any rate, it would still contain a hundred thousand times more heat than the same weight of coal. The idea was thus suggested that the internal heat of the globe, and even the heat of the sun, might be due to hidden stores of radium.

"The more the new substance was studied, the more new facts were discovered, which seemed to contradict everything we imagined we knew about matter. We saw mysterious emanations issuing from it, the successive transformations of which appeared to be the cause of the heat produced, their final result being helium, an extremely light gas, discovered in the sun long before it was met with on the earth. Had the dream of the old alchemists come true at last? Were we face to face with transmutation of the elements? Those who distrust novelties need not as yet feel uneasy on this score. It is probable that chemists will ultimately succeed in placing these strange phenomena in a familiar setting; for, after all, things have a way of righting themselves, and if, as their definition implies, the elements are bodies which remain unchanged in the midst of change, it follows that they are immutable. However this may be, we are confronted with reactions of a totally different kind from any we knew before—reactions which bring into play incredible amounts of energy. We may perhaps have been over-hasty in forming conclusions, but, apart from our dreams, enough will remain to revolutionise the whole science of physics."

These lines give an admirable summary of the various hypotheses that have been advanced in connection with radium. It is easy to understand how fascinating and engrossing the study of so powerful and mysterious a force must be, when applied to the treatment of intractable and chronic diseases, especially those of the skin and mucous membranes; and if, passing from conjecture to reality, we confine our attention to facts observed in the field of medicine—such as those which, in collaboration with Dr. Degrais, I shall set forth in the course of this work—we cannot fail to recognise the extent and variety of the resources which radium has already placed at the disposal of the medical practitioner.

II. FOUNDATION AND ORGANISATION OF A LABORATORY FOR RADIUMTHERAPY

My first studies in the therapeutic action of radium in dermatology, especially in cases of epithelial cancers of the skin, having resulted in the foundation of the Laboratoire Biologique du Radium, it seems desirable that I should preface the following chapters with a few lines dealing with the origin and organisation of this first centre for the study of radiumtherapy.

At the beginning of the year 1905, some radium obtained from the Armet de Lisle works, and incorporated in newly constructed apparatus, was placed at my disposal. M. Danlos had just published an extremely interesting account of the work he had done at the St. Louis Hospital, with radium supplied to him by M. Curie. His experiments satisfied

him as to its value within very restricted limits, and at the same time showed that, if an adequate supply of improved apparatus in good working order could be procured for therapeutic purposes, most important results might be obtained. The appliances handed over to me were eight in number,* and gave out a considerable amount of external radioactivity. They were of a new and improved type, and had not yet been tried in dermatological practice. From a scientific point of view they possessed great advantages, and made it possible to undertake the serious study of therapeutic dosage. It should be added that the physics laboratory at the works from which they were supplied was under the direction of M. Danne, assistant to the Curies at the Sorbonne. The manufactory itself had been placed at the disposal of the Curie Laboratory for the researches carried on there, and therefore possessed every guarantee for good scientific work. In view of these advantages, strongly impressed as I was with the great future in store for the study of radioactive substances, I agreed to experiment with these specimens of radium, the scientific value of which was, to some extent, vouched for officially.

After several months of study, I was able to form an idea of the therapeutic value of the appliances, and the great variety of uses to which they could be put. The resolution of certain neoplasms was easily obtained, without the slightest surface irritation, by the interposition of screens serving to diminish the total available radioactivity of the apparatus, and allowing the more penetrating rays to pass through in small quantities. It seemed evident that radium might become a valuable resource in dermatology, and in the treatment of various diseases in the field of surgical pathology (tumours, gynæcological affections, etc.), and might also be useful in medical pathology, owing to the properties of the gaseous emanation (induced radioactivity communicated to various substances), the solubility of certain radium salts, and lastly, the possibility of incorporating radium in many products of the pharmacopœia (as demonstrated by the earlier researches of M. Jaboin). But this was not all. I also felt convinced that no really permanent system of therapeutics could be formulated, no practical results, apart from mere empiricism, obtained, and no investigations of sufficient value to medical practitioners carried out, without the close

				Available External Radiation.
*1.	Round, flat, varnished,	500,000 ; 0·04	50,000	(0 α ; 85 % β ; 15 % γ)
2.	Round, flat, varnished,	500,000 ; 0·03	64,000	(2 % α ; 84 % β ; 14 % γ)
3.	Round, flat, varnished,	500,000 ; 0·01	10,000	(5 % α ; 80 to 85 % β ; 10 to 15 % γ)
4.	Apparatus with screen	500,000 ; 0·05	48,000	(0 % α ; 89 % β ; 11 % γ)
5.	Square, varnished	pure ; 0·01	50,000	(10 % α ; 75 % β ; 15 % γ)
6.	Cylindrical	500,000 ; 0·02		
7. 8.	Two radioactive "toiles" 4 centimetres square (activity 8,000 and 15,000).			

collaboration of physics, chemistry and experimental medicine, and the help of an ample, well-devised, and powerfully acting armamentarium.

Fortunately, these ideas were shared by others, and at the beginning of 1906 the results I had so far obtained justified the organisation of a centre for the study of radiumtherapy, under the name of the Laboratoire Biologique du Radium.

The large extent and variety of the field thus opened to investigation necessitated a division of the work. The laboratory for chemical research was entrusted to M. Jaboin. The physics laboratory, furnished with the most sensitive instruments of measurement (Curie's electrometer, special electroscopes, etc.) was to be under the supervision of M. Danne ; it was afterwards directed by M. Beaudoin, of the École de Physique et de Chimie. Dr. Dominici, who had not worked with radium before, was appointed director of the physiological laboratory, and of therapeutic studies as applied to medical pathology. The direction of research work in surgical pathology was naturally reserved for me, on account of my former work in dermatology and gynæcology, and I asked my friend Dr. Degrais to assist me in the arduous task with which I was entrusted.

On July 1st, 1906, the Institute began its work, having been supplied with a considerable quantity of radium. But up to that date, during the time required for the fitting up of the laboratories, I had been carrying on with the first instruments, eight in number, the researches already begun ; and the outcome of these preliminary labours, dating from March, 1905, was recorded in a paper which appeared in the *Annales de Dermatologie* (October, 1906).

The following is a summary of the principal conclusions drawn from these early studies :—

1. **Measurements. Systematic use of radium.**—Up to this time, workers in radium had been content to indicate the radioactivity of the salt incorporated in the apparatus ; they would say, *e.g.*, that an apparatus contained 0·05 of radium bromide, with an activity of 500,000. Now, as radium must necessarily be enclosed in some substance or other, the radiations which filter through this substance are subject to alteration in quantity and quality. For a scientifically conducted investigation in therapeutics, the only thing one need know is—not what is in the apparatus, but what comes out of it. It is not sufficient, then, to state that an apparatus contains 0·05 of salt with an activity of 500,000. We must show that what issues from it is a radioactivity of 45,000, composed, let us say, of 10 per cent. of α rays, 85 per cent. of β rays, and 5 per cent. of γ rays. In short,

what it concerns us to know is the strength—as regards both quantity and quality—which penetrates the tissues, and can be utilised.

We give here some examples of experiments in therapeutic dosage:

Resolution of a vegetating epithelioma after thirteen applications, each lasting an hour, in twenty-two days, with an apparatus whose available external radiation had an activity of 50,000, and was composed of 0 α rays, 85 to 90 per cent. of β rays, and 10 to 15 per cent. of γ rays.

Healing of an ulcerating epithelioma of the nose with the same available radioactive force, by means of eight applications lasting one hour, every other day.

Complete removal of two cheloids, by three applications of thirty minutes each, at intervals of three days, with an apparatus having an external radioactivity of 48,000, composed of 0 α rays, 89 per cent. of β rays, and 11 per cent. of γ rays.

Disappearance of a neurodermatitis after four applications of twenty minutes each, with an apparatus giving out an external radioactivity of 20,000, composed of 15 per cent. of α rays, 73 per cent. of β rays, and 12 per cent. of γ rays.

2. **Screens and filtering.**—Filtration had not been previously used in therapeutic work, but since radium could not be brought into direct contact with the tissues, and had to be enclosed in some substance, and as the apparatus had to be protected, the radiation would necessarily be filtered by passing through this substance. But the idea had not yet been suggested of interposing screens between the completed appliances and the tissues to be treated, with a view to modifying the amount of radiation emitted by the apparatus. In my first applications, I began by interposing screens made of compressed pads of absorbent cotton-wool, about 1 cm. thick, enclosed in two sheets of Hamilton's gold-beater's skin and in layers of aluminium, in order to moderate the radioactive power of my apparatus; and in the course of the work already mentioned, I pointed out the importance of ascertaining the nature of any substance that might be thus interposed.

3. **Reaction and destructive effect produced.**—I have shown the possibility of curing epitheliomata, cheloids, and neurodermatitis, even with direct applications and massive doses of radioactivity, without causing surface inflammation and resulting irritation.

"Radioactivity can effect the cure of diseased tissues either by destroying them by the production of a sore, which later on will behave like a simple ulcer, or by merely modifying the cell structure without ulceration, restoring the tissues to their normal condition, or producing cicatrisation. Between these two phenomena of ulcerative

destruction and simple modification, all degrees of intermediate effect are met with.

"In certain cases we see a real absorption of diseased tissues, and a renewal of pathologically ulcerated tissues, followed by cicatrisation, without a secondary ulcerative stage, even when very strong doses are employed. In two cases of small cheloids . . . . the tumours were effaced without any alteration of the skin."

4. **Production of analgesia without surface reaction.**—"The rays certainly have an effect upon pain and superficial pruritus. In a case of intense cutaneous hyperæsthesia following a zoster of the cervical region, almost complete analgesia was obtained after one application. After eight applications, it appeared to be cured without resulting erythema. . . . In several cases of neurodermatitis, analgesia was obtained. . . . It is worth noting that, in the whole course of our experiments, we have hardly ever produced cutaneous erythema, in spite of the intensity and great penetration of the doses, this result being due to the operative method we devised. We have repeated the applications over an entire series of neighbouring points in succession, with the object of making the rays converge towards the deep-seated painful parts, without subjecting the skin to too much radiation at any one spot. It is sufficient that the length of each exposure should be less than that required to produce a slight erythema."

From this period, therefore, I was able to use very penetrating rays even when applying the apparatus direct, without producing any surface irritation. It was from this technique that Dr. Degrais and I were afterwards led to devise the method of "cross-fire."

5. **Difference in resistance of tissues.**—The resistance of healthy and diseased tissues varies greatly, according to their position and structure. A vegetating epithelioma is much more easily influenced than an ulcerating epithelioma or lupous tissue.

"Pathological cutaneous tissues generally offer more resistance than healthy skin. Three applications have resulted in the complete removal of a small seborrhœic papilloma of the scalp, without producing the least erosion; but the same applications on ourselves (anterior surface of the forearm) have produced a quite severe ulcer. In the same way the mucous membranes appear to be specially refractory, as we have had occasion to observe in gynæcological applications. A case of chronic catarrhal metritis of the cervix with considerable ectropion has been treated and healed in our practice at St. Lazaire, without marked destruction, and with an amount of radioactivity which would certainly have caused ulceration of the healthy skin."

6. **Action of rays by diffusion beyond the points of application of apparatus.**—The rays can act at a distance, without causing ulceration of the tissues. "Radium was applied in destructive doses to the centre of a large plaque of cutaneous tuberculosis, which was the only part ulcerated. Deeper and more extensive ulceration was produced at this point, followed by slow cicatrisation; but, strange to say, the part surrounding the ulceration (which was diseased, but not ulcerated, and which had not been treated by radium) was modified without any ulcerative reaction, and, three months later, a beautifully fine and smooth cicatrix appeared over the whole of the tuberculous part."

7. **Early results in epitheliomata, etc.**—The following is a list of the diseases which I had treated and cured up to this period, some of them with the assistance of Dr. Degrais:—

Epitheliomata, 12 cases. Ulcerative epitheliomata of nose, 3 cases; of back of hand, 3 cases; of cheek, 3 cases; fungating epithelioma of pubic region, 2 cases; of temporal region, 1 case.

Papillomata of scalp, 2 cases; of tongue, 1 case.

Cheloids, 2 cases.

Lupus vulgaris, 5 cases.

Verrucous and ulcerative tuberculous affections, 3 cases.

Scrofulo-tuberculous gummata, 3 cases.

Vascular nævi, 2 cases.

Refractory syphilitic ulcers, 4 cases.

Gonorrhœal ulceration of anus, 1 case.

Psoriasiform parakeratosis, 1 case.

Severe hyperæsthesia, following cervical zoster, 1 case.

Chronic catarrhal metritis, 2 cases.

8. **Injections of radiferous and radioactivated water.**—In a case of lupus of the neck which was sent us by my chief, Dr. Hallopeau, injections into the lupous tissue of one to two cubic centimetres of radioactive water (one litre to 0·001 of pure radium sulphate) and of radiferous water (one litre to 0·001 of pure radium bromide) were used, and were very well borne by the patient. This opens up quite a new channel for investigation. The possibility of bringing radioactive energy to bear on any part of the system would seem to point to a valuable resource in therapeutics.

9. **Bactericidal action.**—The external radiation of apparatus in which the salts are embedded in varnish has, in some cases, arrested staphylococcal and gonococcal suppurations; clinically, therefore, it appears to be endowed with bactericidal properties. But this bactericidal action is only apparent, for our laboratory experiments

have shown that the result was really due to a modification of the culture medium.

In fact, the rays emitted by the apparatus do not affect vigorous cultures of staphylococci or gonococci in the incubator, at least in the length of exposure possible in clinical practice (experiments made at the Leysin Laboratory on cultures of *Staphylococcus aureus* and of the gonococcus). On the other hand, water containing even a millionth part of pure radium seems to act on the cultures. The α corpuscles would, therefore, play a special part in bactericidal action, since they are to a great extent absorbed by the varnish of the apparatus, whilst they exist in abundance in all solutions of radium bromide, and are emitted from them.

It would, therefore, seem probable that substances which are directly or indirectly radioactive, and allow the α rays to pass, should be employed when bactericidal action is desired.

Such were the conclusions, many of them original, to which my first investigations led me. Since then, with the help of Dr. Degrais, further progress has been made in my clinic in the technique, method of dosage, and clinical results of radium treatment.

Great improvement has taken place in other departments since the opening of the Laboratoire Biologique du Radium. The chemical laboratory has largely contributed by supplying a number of radium products for experiments in medical pathology. The physics laboratory has likewise been of great service to us. The advance made at the Laboratory in dosage and the study of filtration, from the standpoint of physics, is due to the researches and suggestions of M. Beaudoin. Contributions from the physiological department and that of medical pathology have also been numerous and extremely interesting.

Briefly, the work so far accomplished has given radiumtherapy an impetus sufficiently strong to free it from the obstacles which beset its initial progress, and has thereby justified its claim to a scientific position in therapeutics.

But the Laboratory had another object. It was intended to be open both to patients and to the medical profession for study; and in this way many practitioners from our own and other countries have been enabled to profit by our work, and have become firm believers in the therapeutic effects of radium. Similar centres of study, based on the results obtained by us, are now being officially established in various foreign countries, including one in London, which is under the patronage of King Edward the Seventh.

The Laboratory was also willing to put its means of investigation

at the disposal of some of the hospital clinics, and in this connection I especially wish to thank our professors and friends at the St. Louis and other hospitals, for having entrusted to us a number of their own patients. We also desire to express our gratitude to M. Armet de Lisle, who enabled us to employ our methods in hospital practice by kindly sending us a supply of radium.

My own results, and those obtained in collaboration with Dr. Degrais, have been made known, from time to time, through papers communicated to the learned societies, and our friends have now asked us to collect these in one volume.

In spite of the difficulties inseparable from the execution of a work in which many of the subjects are new and personal, we present it to the public, our sole object being to set forth the results we have been able to achieve.

PART I

PHYSICS

As this work is intended for physicians rather than scientists, and as we wish to avoid obscurity in this new and complex subject, we shall treat only of elementary principles in the present chapter.

I. DISCOVERY OF RADIOACTIVITY AND RADIO-ACTIVE SUBSTANCES

Becquerel rays and uranium.—When studying the phosphorescence of uranium salts, H. Becquerel discovered, in 1896, that the invisible spontaneous radiations emitted by phosphorescent uranic salts were also emitted by salts of uranium oxide and uranium protoxide, and by the metal uranium itself, all of which are non-phosphorescent substances. From this he concluded that spontaneous radiation was independent of phosphorescent properties, and was only produced by the uranium atom. He afterwards found that this invisible radiation not only acted on photographic plates, after passing through opaque bodies, but was capable of discharging electrified bodies, *e.g.* the electroscope. It was to this new phenomenon, which differs from phosphorescence and fluorescence, that the name of "Becquerel rays" was given.

Thorium.—In 1898, Mme. Curie and M. Schmidt discovered, independently of each other, similar rays in thorium, a metal which, like uranium, had long been known. Continuing her investigations, Mme, Curie succeeded in ascertaining and formulating the degree of activity possessed by the rays of metallic uranium, and on studying the different uranium compounds, such as pitch-blende (uranium oxide ore), she was surprised to observe that they emitted rays which were evidently more active than those of uranium itself. She concluded from this that those compounds must contain radioactive substances other than uranium.

Radium and polonium.—Such were the experiments which, in 1900, after long and skilfully conducted researches, led Professor P. and Mme. Curie to the discovery of two new bodies. One of these, which they named radium, was extremely active. To the other, which was different and much weaker, they gave the name of polonium, in memory of Mme. Curie's native country.

Actinium.—In the same year, 1900, M. Debierne, a professor at the École Alsacienne, whilst studying the residues left by the chemical process for the extraction of these bodies, discovered a new radioactive substance, viz. actinium.

Radiothorium.—Finally, in 1904, Ramsay and Hahn discovered radiothorium.

These are the principal radioactive bodies known at present. It was natural that attention should be specially directed to radium, on account of the interest aroused by its immense activity, which is 2,000,000 times greater than that of uranium, taken as the unit of measurement. In this work we shall deal with radium alone, because this metal is, so far, the only radioactive body used for therapeutic purposes. But since each of the above-mentioned bodies has special physical properties, and possesses certain material advantages over radium, it is possible that a time will come when the particular qualities of their radiant energy will be turned to account in therapeutics. Thus polonium emits only α rays, and radioactive lead only β rays. The comparative abundance of uranium renders it less costly, and it is easily extracted.

The chief obstacle to the therapeutic use of these substances is the weakness of their radioactivity, but a method of concentrating it has been found in some cases. The activity of uranium, for instance, can be concentrated by precipitating barium sulphate in a solution of uranium chloride. There is every probability, therefore, that it will be possible, in future, to utilise other radioactive bodies besides radium.

II. NATURE AND ORIGIN OF RADIUM

To judge from the chemical properties peculiar to it, radium appears to be a metal of the alkaline earths, akin to barium and strontium. Its existence as an element has now been exactly ascertained by spectroscopic analysis, which has revealed a new and characteristic spectrum, and also by its atomic weight of 226·45, these figures having been obtained by Mme. Curie. The limited quantities of radium as yet at our disposal, and the difficulty of isolating metals of this class, have hitherto prevented any attempt to obtain it in the metallic state. Such an experiment could not be made without risk of losing a certain amount, and has therefore never yet been tried. For the same reasons it has hitherto only been possible to study it in the form of its salts (chloride, bromide, sulphate, carbonate, etc.).*

The radium used in our therapeutic work comes from the Armet de Lisle works, where most of the French and foreign ores are treated.

* Matout, "Propriétés du radium" (*Presse médicale*, April 8th, 1908).

Professor P. and Mme. Curie extracted radium in the first instance from pitch-blende residues, which came from St. Joachimsthal. Its presence has been subsequently discovered, not only in all pitch-blende beds, but also in all the minerals which contain uranium. A connection has even been traced between uranium and radium.

Radium ore.—Radium ore exists in all the uranium compounds, viz.:—

Pitch-blende and *pitch-uranium* (uranium oxide).

Uranite or *autunite* (double phosphate of uranium and calcium).

Chalcolite (double phosphate of uranium and copper).

Carnotite (vanadate of uranium).

Thorianite (uranium and thorium oxide).

Pyromorphite, a phosphate of lead which contains radium without uranium, has, however, been worked for some time. This is the only instance of a radium ore free from uranium.

The principal pitch-blende workings are those at St. Joachimsthal in Bohemia, in a mountainous region, 16 kilometres from Carlsbad, as the crow flies. There are many other pitch-blende mines in existence, the most important being in Bohemia, Hungary, Saxony, Turkey, Sweden, Canada, Colorado, and Cornwall.

Autunite takes its name from the locality of Autun, in the neighbourhood of which it is present in considerable quantities ; it has also been found in Auvergne, Portugal, and Tonquin.

Chalcolite, mixed with autunite, has been met with in France, Saxony, and Portugal.

Carnotite has been found in the plains of Utah, U.S.A.

Thorianite comes from Ceylon, where it occurs in the form of crystallised cubes, which are sometimes quite regular.

Pyromorphite has been met with in France, at Issy l'Évêque (Saône-et-Loire).

III. PREPARATION OF RADIUM *

Although the general process is always the same, the treatment of ores for the purpose of extracting radium differs in each case according to their chemical composition. The operations necessary for such treatment are invariably long, numerous, and difficult of execution. They include :—

1. Mechanical preparation.
2. Chemical treatment.
3. Fractionisation.

* The methods described in this paragraph are those in use at the Armet de Lisle works. We give them from information very kindly furnished by M. de Razet, engineer of the École de Physique et de Chimie, and curator of the laboratory.

1. **Mechanical preparation.**—This consists of a series of different operations: grinding, pulverisation, and mechanical enrichment by dressing. Crushing is effected by means of an American grinder with jaws, which reduces the lumps of ore to about the size of a nut. Pulverisation is done with a hammer crusher, by which the ore is ground to a fine powder. When very thorough reduction is required, a shot-grinder is used. Enrichment by dressing is obtained in the way most suitable for each substance, by means of percussion tables, or by washing, followed by separation according to varying degrees of density.

2. **Chemical treatment.**—The simplest chemical treatment is that employed for pitch-blende dross; we will therefore take it as a type.

Radium exists in pitch-blende residue in an insoluble state. It is

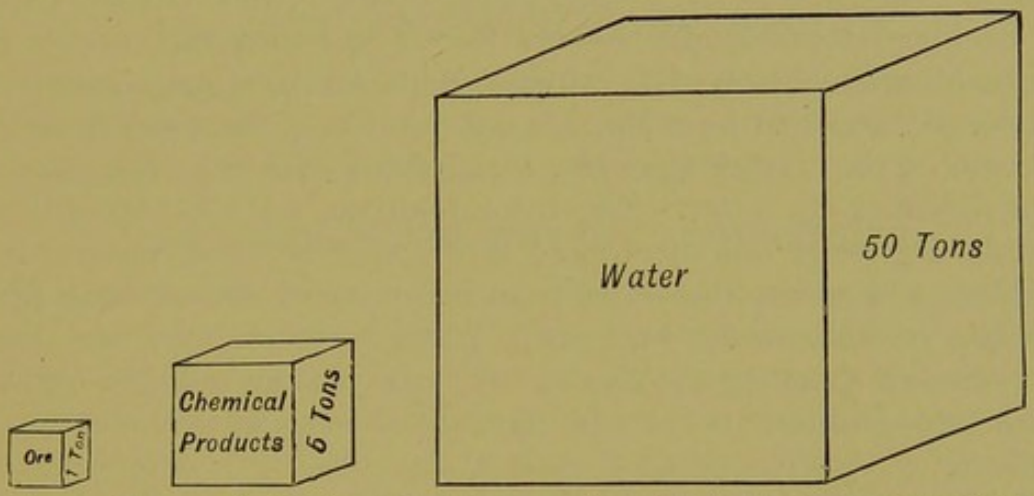


Fig. 1.—Diagram by M. Razet showing proportion of materials necessary to obtain 2 to 5 cg. of pure radium bromide from 1 ton of ore.

blended or combined with earthy silicates, alkaline earth and alkalis, etc., and acids do not affect it. Repeated washings with hydrochloric acid and water free these remains from a considerable quantity of inactive material. The insoluble part contains the radium; it is subjected to prolonged boiling with carbonate of soda, which brings about the transformation of the insoluble radium salts, unchangeable by acids, into salts equally insoluble, but capable of being affected by acids. The washings with water are necessary in order to eliminate substances that would transform the radium into compounds which acids could not alter. When they are finished, the slime is treated with hydrochloric acid, which dissolves the radium, together with a large quantity of impurities. The radium is then in solution, and is afterwards carefully purified by precipitation of sulphides in the acidified liquid, and oxides in the same liquid rendered alkaline. Finally, after using 56 tons of material (1 ton of ore, 5 tons of chemical products, 50 tons of

water) a solution is obtained from 1 ton of ore weighing about 25 kilogrammes. This is already very active, and contains only barium and radium. (Fig. 1.)

3. **Fractionisation.**—The solution is now ready for fractionisation, which includes several stages: fractionisation on a large scale, fractionisation on a small scale, and fractionisation of the bromides. When a solution of radiferous barium chloride is crystallised, the crystals are seen to contain more radium than the water which remains; and this circumstance is turned to account in the process which we will now describe.

The liquid obtained after the last purification is concentrated by heat in a receiver, No. 1. It is then left to cool, when crystals are deposited along the walls and at the bottom of the vessel. After complete cooling, the liquid is emptied into receiver No. 2, and then the crystals from No. 1 are again dissolved in water. Both solutions are concentrated. When cool, the water from No. 2 is put into No. 3, the water from No. 1 is poured on the crystals from No. 2, and the crystals from No. 1 are once more dissolved in water. The three solutions are now brought to a suitable degree of concentration. When they are cold, receiver No. 4 is added, and so on, the water from one receiver always being poured over the crystals of the next one. When a certain time has elapsed, only a small quantity of very active salt remains at the beginning of the series, whilst at the end there is a large quantity of inactive products.

Fractionisation on a large scale is performed at the works. It is begun in large vats, and finished in earthen pans, the material being reduced from 25 to 4 (or at most 5) kilogrammes.

Fractionisation on a small scale is carried out at the laboratory of the factory, in porcelain capsules. When only 400 to 500 grammes of chloride remain, the process is stopped, and a final purification very carefully made. The chlorides are transformed into bromides, which are fractionised in the same way as the chlorides, in porcelain capsules. Fractionisation at length produces several centigrammes of pure radium bromide. The purity of the salt is ascertained either by the spectroscope or the Curie electrometer.

Radioactivity of pure radium: 2,000,000.—The strength of pure radium salt is determined by its power of ionisation. Taking uranium as the unit of measurement, this salt is considered to possess an activity of about 2,000,000. In other words, a given quantity of it renders a column of air an almost 2,000,000 times better conductor of electricity; it ionises it 2,000,000 times more strongly than an equal quantity of pure uranium would do. Radium bromide is a perfectly

well-defined salt, from which all the other salts, such as the carbonate, sulphate, nitrate, stearate, etc., are prepared, according to the uses for which the radium is intended. The bromide, chloride and nitrate are soluble, the sulphate and carbonate insoluble. It is the sulphates that are contained in the applicators with the salts in varnish (either those with "toile" or with metal) which have been constructed for therapeutic purposes.

The various processes described above show how delicate and laborious a task is the extraction of radium. The quantity of materials necessary to treat 1 ton of ore, and extract a small amount of pure radium bromide, is very large, as is well shown by Fig. 1, for which we are indebted to M. Razet.

IV. THE PROPERTIES OF RADIUM

In this section we shall only mention the chief physical, chemical, and biological properties of radium, those, in fact, which are essential for a knowledge of its application to therapeutics.

1. CHEMICAL AND PHYSICAL PROPERTIES

Liberation of heat.—Radium liberates heat in a spontaneous, regular and continuous manner. It has been calculated that 1 gramme liberates one small calorie in an hour, and can melt nearly its own weight of ice in the same time. Radium is capable of adding this amount to any temperature. This is a particularly interesting property, for such a quantity of heat, which at first sight seems small, becomes colossal when one considers what the possible life of radium may be, and what is implied by energy stored up for a period far beyond our conception. *It may some day be recognised that this property plays the principal rôle in the processes leading to the modification of diseased cells.*

Liberation of light.—When a certain quantity of very active radium salt is put into a glass tube, it will become luminous in the dark.

Colorisation of bodies.—If a grain of radium salt is placed on a Sabouraud-Noiré pastille of barium platino-cyanide, the latter will lose its green colour after a certain time. It turns yellow, and then becomes orange. It was at first thought that this property would serve as a measure for therapeutic applications, but, as a matter of fact, it has not been of any practical use up to the present time.* Radium has also

* Wickham, "Note sur l'emploi du radium en thérapeutique" (*Ann. de derm.*, October, 1906, p. 7): "An apparatus containing 0.006 of pure radium produces erythema on the anterior surface of the forearm after an application of five minutes, but instead of the pastille being changed in five minutes, as it should be according to the laws of Röntgentherapy, in the case of radium four or five hours are required to produce erythema and reach the standard tint."

the power of colouring glass violet, brown, or black. It gives a yellow-orange tone to uncoloured topaz, and colours the diamond rose, green, blue, or yellow. But these changes are for the most part transitory, and disappear soon after contact, either of themselves, or under the influence of time or of physical agents, such as heat.

Impression on photographic plates.—Radium rays act on substances commonly employed in photography, and so permit radium-graphs to be obtained. The phenomenon of the passage of the rays through substances—which is more or less easy according to the degree of opacity of the latter—easily explains the formation of lights and shadows on the photographic plate. This property can be utilised for comparison of the respective values of the instruments at our disposal. Dr. Abbé makes great use of it. We ourselves think that ionisation gives a more rapid, useful and accurate basis for calculation.

Ionisation.—Radium renders air a good conductor of electricity, that is to say, it has the property of separating the particles of air into elements called *ions*, which it charges with electricity. If, therefore, a charged electroscope be placed in a room, it will be discharged as soon as radium is introduced into the room. The velocity of this discharge can be readily calculated, and is in exact relation to the power of activity possessed by the salt. This property, which is common to all radio-active bodies, has been utilised for the measurement and comparison of the various radioactivities. In this way it has been possible to fix the standard of 2,000,000 attributed to pure radium, by comparison with uranium, taken as the unit of measurement. This quality of ionisation still remains the only one by which radioactive strength can be accurately estimated, and it enables us to measure the activity emitted by our apparatus.

Production of phosphorescence in certain bodies.—Radium excites phosphorescence in certain bodies, *e.g.* in barium platino-cyanide. The radium is placed in the dark at some distance from a screen of this substance, which is then lighted up. When the apparatus is brought nearer, the light becomes limited in extent, and of greater intensity. If a book or some other object be interposed, the screen will still be illuminated, but in inverse ratio to the opacity of the intervening substance.

Passage through opaque bodies.—The foregoing experiment proves that the rays can penetrate bodies, for, if radium lights up a screen placed at some distance, it is obvious that the rays can traverse a layer of air, and the same kind of experiment can be used to show the passage of radiation through solid opaque substances, and also through liquids, since the screen is illuminated when such bodies are interposed in the same way between it and the radium.

But the screen will have more or less light thrown on it, according to their nature; the more opaque they are, the more difficult being the passage of the rays. This is especially the case with lead and platinum. Some bodies, such as aluminium, mica, and certain varnishes, are very easily traversed, as is shown by electrometric analysis, and the vivid light which illuminates the screen when these substances alone are interposed between it and the radium. This is the reason they were used in the construction of the first instruments; the facility with which they are penetrated reducing to a great extent the loss which the radiations would suffer if they were to pass through denser substances.

2. BIOLOGICAL PROPERTIES

The biological properties of radium have been ascertained by numerous experiments. Matout has shown that seeds which are exposed to radium rays for a week, and are afterwards planted, lose their power of germination. M. Giesel, when subjecting the leaves of plants to the action of radium, saw them become yellow and shrivel up. M. J. Reverdin has studied its effects on chrysalides. M. Bohn has shown that it modifies the tissues of the lower animals in their growth. M. Danysz and other physicists have also recorded experiments of the greatest interest.* With regard to human tissues, with which we are concerned, we saw in the preface how the action of radium was discovered. The portion of our work devoted to clinical therapeutics is a progressive demonstration of its biological properties.

V. COMPOSITION OF THE RAYS

We have now briefly considered the chief properties of radium. Their uniformity and diversity alike prove that this metal liberates energy of a highly complex and active nature, which it is essential to analyse and explain. Radium may be split up, and this process produces a gas called the emanation, setting free energy that is manifested in the form of invisible rays. We must therefore study (1) the rays; (2) the emanation.

1. α, β, AND γ INVISIBLE RAYS

We have already stated that the radiation from radium is not homogeneous. MM. H. Becquerel, Rutherford, P. Curie, and P. Villard have been able to distinguish three distinct kinds of rays, known as α, β, and

* The reaction of vegetable tissues and those of the lower animals is very interesting, and we regret that it is impossible to mention here the numerous works dealing with these questions. They have formed the subject of communications to the learned societies, principally to the Académie des Sciences. We strongly recommend a perusal of them.

γ rays. They are invisible, but manifest themselves by certain reactions.

α **Rays.**—Rays of this class are attributed to atoms, that is to say, to particles in the order of their chemical size. These particles are material, and extremely small, resembling the hydrogen atom in size. They are of the same nature as the anode rays of a Crookes tube, but possess greater penetration. Like real projectiles, these radioactive atoms are animated by a velocity measuring about a tenth or twentieth part of the velocity of light. They are charged with positive electricity, and form a group which varies in homogeneity, according to the date of preparation of the radium.* They are deviated to the left by a magnet, but only very slightly. Their proportion of the radiation emitted from naked radium is considerable, amounting to about 90 per cent. (Fig. 2). They are very easily absorbed, and only slightly penetrating, a thin layer of metal or rubber being sufficient to intercept them.

β **Rays.**—These are similar to cathode rays, but about 500 times more penetrating; they are attributed by some physicists to material atoms. But, for the most part, according to M. Kaufmann, the β particles or "electrons" are of electro-magnetic nature, not absolutely material, and holding a position midway between matter and ether. The β particle has considerable interest for students of physics, as it is supposed to be the primordial atom of electricity. The existence of the electron, which is believed to be the origin of all thermal, electrical, and luminous phenomena, is the basis on which all the theories of modern physics rest. These β particles are charged with negative electricity, and are strongly deviated to the right by a magnet. They exist in the proportion of about 9 per cent. in the radiation from naked radium (Fig. 2), forming a heterogeneous group; that is to say, they vary among themselves in size and velocity of movement, and consequently in their power of penetration. As regards the latter property, the less rapid and less attenuated β rays are comparable to α rays. These are soft β rays. Others, known as hard β, are composed of particles of extreme tenuity (2,000 times less than that of the hydrogen atom), and are animated by great velocity, akin to that of light (200,000 to 300,000 kilometres to the second). Between these two extremes, soft β and hard β, come the intermediate rays, called medium β. By reason of their tenuity and velocity, they have great powers of penetration, and easily traverse

* The rays from newly prepared radium are homogeneous; their course through the air at 760 mm. being 3 m. 25 cm. α rays emitted by old radium or by the apparatus are not homogeneous. The following are the distances traversed by the five kinds of α rays from old naked radium:—3 m. 5 cm.; 3 m. 9 cm.; 4 m. 3 cm.; 4 m. 8 cm.; 7 m. 1 cm. (Note by M. Razet.)

substances, but they do so unequally, and with more and more ease, in an ascending scale from soft to hard β. Soft β are quickly absorbed; hard β, on the contrary, travel through several metres of air. According to M. Debierne, it cannot be exactly stated where the rays stop between 5 mm. and 1 cm. of lead, when a very intense source of pure radium is used. Sir William Ramsay thinks that minute quantities of β rays will still be found, after radiation through 5 mm. of lead. It must be understood that we are only concerned here with the original rays, known as primary, which have penetrated the lead, and not with secondary β rays, which are produced afterwards. This is a fact upon which we cannot too strongly insist. It is always more prudent, in questions of radiumtherapy, to avoid a too methodical, cut-and-dried distinction between the action of the different groups of rays. Besides the primary β, it seems that we must reckon with the secondary β rays. The latter, indeed, result from the action of γ rays, which, on encountering matter, produce the secondary rays described by M. Sagnac. Probably these secondary β rays are formed in appreciable quantities all along the path of the γ rays through matter. Even when γ rays are isolated by an intense magnetic field, new β rays will be formed as soon as the γ rays encounter matter.

γ Rays.—These rays are a pulsation of the ether, and are similar to X-rays. The undulations most likely originate in the disturbance produced by the disintegration of radium into α and β atoms. It is also probable that they have a velocity equal to that of light. They are never deviated by a magnet. Their frequency and wave-length have not yet been determined, for they are not subject to optical laws. γ rays possess the property of extreme penetration, being able to traverse as much as 10 cm. of lead, and indeed, in the laboratory, it is very difficult to get rid of them. Their power greatly exceeds that of X-rays, which is limited to 1 or 2 mm. of lead. For instance, with a sufficient quantity of pure radium (about 5 cg.), M. Matout considers it possible—owing to the property possessed by radium of lighting up a radioscopic screen—to observe the prodigious penetration of the γ rays, passing through the body of a man at the level of the thorax. They traverse it without revealing the least trace of the skeleton, and with as much facility as when penetrating the fleshy parts of the body. It is not even possible, by varying the degrees of intensity, to indicate the moment at which the object comes between the radium and the screen. In this experiment, the radium can be placed at 4 m. 20 cm. from the screen. γ rays form 1 per cent. of the radiation from uncovered radium. (Fig. 2.)

Mechanism and explanation of passage of rays through bodies.—It will be easily understood that projectiles so swift and slender

as α and β rays must possess some power of penetration in relation to matter. It is further obvious that the larger and less rapid α atoms do not penetrate so far as β rays, and that the latter, by reason of their heterogeneous character, have different degrees of penetration, according to whether they are soft or hard. It now remains to explain the mechanism of this penetration. All bodies reduced to their ultimate expression appear in the form of an aggregation of atoms, separated by what are called inter-atomic spaces. Now, since α and β particles are infinitely smaller than the atoms of the bodies they strike, their velocity causes them to slip into the inter-atomic spaces of these bodies. As to γ undulations, it is sufficient to know that ether bathes and permeates every substance, in order to understand how easily they are propagated. The respective degrees of penetration possessed by the three kinds of rays will now be easily understood.

γ vibrations lose very little energy in their passage, and for this reason can only be finally intercepted by a sheet of lead about 10 cm. in thickness. For α and β particles the loss is greater, since there is friction of one mass against another, and the greater the friction, the more difficult is the passage rendered; α rays, however, lose their energy more quickly than β rays. This is expressed by the qualification "easily absorbed," applied to α in relation to β rays.

Filtration.—These facts explain the operation which, under the name of filtering, allows of selection of the different rays. Since the various constituent elements of the radiation are more or less liable to absorption, every object placed in front of the source of emission will not only diminish the total amount of radiation, but will select these constituent elements according to their power of penetration. Such an intervening substance will intercept one or more kinds of the most easily absorbed rays, and only allow the other kinds to filter through. A radiation placed in contact with cutaneous tissues will permeate them throughout their thickness and even go beyond it, α rays being arrested by the superficial layers, β rays, from soft to hard β, going considerably further, and γ rays passing through without difficulty. In this way the tissues themselves act as a filter. We have utilised these different degrees of penetration from the time of our first experiments, in order to modify the radiation for therapeutic purposes.

When a screen of cotton-wool, or aluminium, of a thickness sufficient to intercept the α rays, is placed before radium apparatus, only β and γ rays are allowed to filter through. With screens of increasing density, only hard β rays and γ rays, which constitute "surpénétrant" radiations, will escape; and lastly, only γ rays, which can

scarcely be secured alone, unless there is a lead screen at least 5 to 6 mm. in thickness.

Proportion of α, β, and γ rays.—As the power of penetration differs for each kind of ray, so does the relative quantity of rays contained in a given radiation.

When radium is examined in the free state, α rays are by far the most numerous, including, as they do, nine-tenths of the total radiation; the proportion of β and γ rays is very small; 9 per cent. of β and 1 per cent. of γ. (Fig. 2.) But when it is a question of application to the surface of the skin, the varnish or other substance required to fix the radium salt, which acts of necessity as a screen, causes the absorption

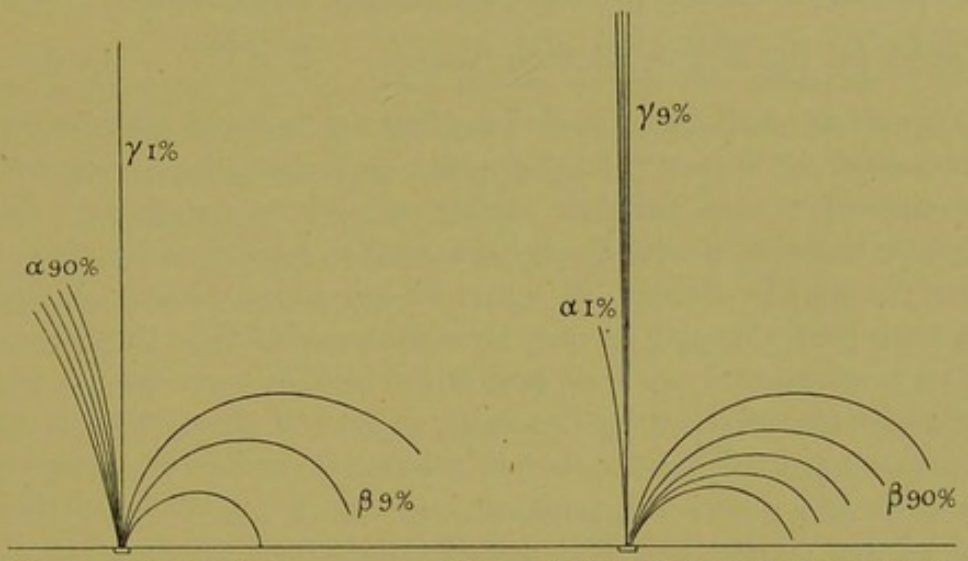


Fig. 2.—Naked radium. Fig. 3.—Radium in varnish of apparatus.
Diagram by M. Razet showing separation of radium rays by magnetic field.

of a large number of α, the proportion of the various rays among themselves being therefore to some extent disturbed. α rays then only exist in very small proportions (1 to 10 per cent.); β predominate in the proportion of 80 to 90 per cent., and γ have a percentage of 1 to 10, so that, in practice, the principal quantitative value of the activity emitted by radium resides in the β rays (Fig. 3).

Action of magnet on rays (Fig. 3).—The action of a magnet on the rays should be borne in mind, for a time may come when it will be useful for therapeutic purposes. α and β rays can be deviated by a magnet, but γ rays are not affected by it at all. It follows that a very intense magnetic field, placed behind the source of the rays, would allow γ rays only to penetrate the tissues, without the necessity of interposing a screen; from which we may deduce the possibility of also employing β rays alone. By means of special appliances, one might, indeed, be able to do so; making them describe a curve which would pass through

the tissues to be treated. But this would involve the use of a powerful, and consequently very heavy and unwieldy electro-magnet.

How can action of rays be explained?—Many explanations have been suggested, but none of them is quite satisfactory. Perhaps the heat liberated by the radiation may have something to do with it. It is generally considered sufficient to say that the rays yield energy to the tissues which they penetrate, but this vague statement is only a cloak for our ignorance. With regard to α and β rays, the phenomena of their energy hitherto ascertained may correspond to a law in physics closely uniting the three terms of velocity, heat, and force. In proportion as projectiles lose their velocity when traversing bodies, they are deprived of an amount of energy proportional to half the product of their mass multiplied by the square of their velocity: $E = \frac{M V^2}{2}$. As for γ rays, no explanation of the way in which they act has yet been found. The production of secondary rays composed of β electrons during the whole progression of γ rays through matter should be noted, and this may perhaps be the reason why these rays seem to have a real action even on the surface of the tissues, in spite of the extraordinary facility with which they pass through them. It is conceivable that these forces may make an impression upon and modify the cells in their normal biological or pathological evolution, by becoming gradually absorbed in the tissues, in proportion to their depth ; but this does not explain the actual method of their working, and the problem, one of the most fascinating with which we are confronted, still awaits solution.

2. EMANATION

Radium in process of disintegration not only sets free energy in the form of α, β, and γ rays, but also gives off continuously a radioactive gas called the emanation, which radiates α rays, and is itself transformed in turn, so as to give rise to induced radioactivity. We shall only say a few words about this gas, confining ourselves to essential points, for as yet it has been little used in radiumtherapy. We have, however, made trials and experiments which have shown its employment to be possible. This force, which possesses bactericidal properties, should not be neglected, for when the technique is perfected, it is likely to take an important place in therapeutics. The emanation given off by radium is subject, like other gases, to the laws of Mariotte and of Gay-Lussac. This material and radioactive gas has been carefully studied by Rutherford and Sir W. Ramsay. It can be collected and condensed in liquid air, and is diffused through bodies, but so feebly that its diffusion need not be taken into account in therapeutics. It

will therefore be understood that the emanation cannot be given off and utilised in the apparatus at present employed for therapeutic purposes, upon which the radium is fixed by a varnish. On the other hand, it is emitted in solutions in which radium is present in the free state, and can be used in injections of radiferous water, or some other radiferous solution. Its production by radium is proportional to the time of emission, but once produced, it is transformed and lost according to a definite law, of which we shall speak again when treating of induced radioactivity.

Induced radioactivity.—The emanation has the curious property of conferring radioactive power on all bodies and elements which it touches. This is an acquired property, the duration of which is longer or shorter, and the strength greater or less, according to the nature of the body influenced, and the time during which the emanation remains in contact with it. If, for instance, the emanation is brought into contact with vaseline for some time, the latter will become luminous and emit rays, but only for a few days. This is the phenomenon known as induced radioactivity. Thus water, oil, or any other substance, made radioactive by the emanation, can be introduced into the tissues, and can act as a radioactive body and give out rays, without containing the slightest trace of radium. Radioactive mineral waters furnish an example of the action of this property. When a subterranean stream of running water meets with radiferous earth in its course, it will be influenced by the emanation, and on emerging from the ground will possess a certain induced radioactivity. This, however, seldom exists except at the source, and the water will soon lose its borrowed properties. The entirely different therapeutic effects obtained, according to whether certain mineral waters are taken on the spot, or after transport, may well be due to this rapid loss. Radioactive mineral springs are numerous, those which are among the richest in radioactivity being Bad-Gastein (Austria), Source Vauquelin, in Plombières (Vosges), Cadellas (Portugal), Bussang (Vosges), Bains-les-Bains (Vosges), Aix-les-Bains (Savoy), Dax (Landes).

Law of decrease of induced radioactivity.—The loss of induced radioactivity leads to some interesting considerations. It takes place in accordance with an invariable law of diminution, of the kind known as "exponential." The loss is one-half for each half-hour, when the substance impregnated with radioactivity is not shut in. When, on the contrary, the body containing the emanation is carefully enclosed, measurement of its radiation through the walls shows a loss corresponding to only half the activity in four days. The active matter deposited by the gas is therefore of a different nature from the gas itself, and

consists of the products of disintegration of the radium. These have been carefully studied by Rutherford, who has given them a whole series of names, such as radium emanation, A, B, C radium, etc. These products, continually in a state of transformation, impregnate the radium, and impart to it complex radiations according to an absolutely invariable rule. For example, if, by the action of a high temperature, we drive off these products, and separate them from the radium, the latter partly loses its activity, but afterwards recovers it spontaneously, in accordance with a law complementary to that of destruction of the emanation. Thus, however much activity radium may lose, this activity will always be reproduced. We need not again refer (*see* Introduction) to the property possessed by the emanation of transforming itself slowly into helium, nor to the experiments made by Sir W. Ramsay for producing lithium out of substances which do not contain it, such as nitrate of copper, by means of the emanation. As we have already pointed out, if all these facts should be confirmed, the possibility of the transmutation of elements will be demonstrated, and the fundamental principles of chemistry and energy, which have appeared to be so firmly established for many centuries, will be overthrown.

PART II

USE OF INSTRUMENTS

CHAPTER I

EMANATION

We have just seen that radium is a powerful source of energy, manifested in the form of emanation and rays. In what way can such energy be made available for medical practice? How can it be utilised, varied, and measured? These are the questions which we shall try to answer. Emanation gives promise of much interest in the future, and in the present chapter we shall briefly sum up the essential points concerned in its use. At present the practice of radiumtherapy almost entirely consists of the use of rays without the emanation. This subject of radiation will be specially dealt with in the next chapter of this Part.

The operative methods involved in the use of the **emanation** relate, for the most part, to medical pathology. Indeed, in order that the emanation, which cannot itself penetrate any substance, may have a direct action, it must be employed either in the form of inhalations in the state of gas, or by ingestion, injection, etc., in substances which act as a vehicle for it or its properties, setting its energy free after their own absorption has taken place. It is clear that external applications which require the incorporation of radium in apparatus cannot be utilised for the emanation in any way; at any rate, directly. Although it is not yet employed in any systematic or definite manner in surgical pathology, we must not neglect to mention the principal methods of using it, for a future is certainly in store for it, when radium becomes less scarce. We are firmly convinced of this, from the encouraging and definite results which we have obtained on various occasions. We think, for instance, that the action of certain lotions and ointments, by means of which the emanation may be conveyed, as well as of solutions of soluble or insoluble salts injected into tumours, the deeper parts of diseased cutaneous tissue, etc., may either be successfully combined with that of

the external applications with apparatus, or may be used alone. Unfortunately medical pathology can afford very little help in the study of this question. Physics and chemistry long ago put a number of useful products, perfectly combined and measured, at the disposal of experimenters, but progress has been slower in medical therapeutics than in surgical pathology, in which the employment of radium apparatus speedily gave many authentic results.

There are two different methods of employing the emanation :

1. It may be collected and used by itself ;
2. It may be used simultaneously with the rays.

I. EMANATION USED ALONE

We have seen that radium salts continuously produce the emanation, a gas which gives off radiation and becomes transformed in its turn, so as to induce radioactivity in other substances. We know that the production of the emanation by radium is in proportion to its time of emission, and also that its loss by transformation is brought about in accordance with a fixed law, so that radium salt in a closed vessel produces only a limited quantity of emanation. The amount will be constant from the moment at which its formation and disappearance become equal. This is known as the law of radioactive equilibrium. In order to collect the emanation, it is allowed to accumulate in special apparatus, from which it is drawn out, by aspiration, into tubes or receivers from which the air has been exhausted. The appliance which we use consists of a horizontal reservoir containing the radium solution (Fig. 4), which is provided with two vertical tubes, having a stop-cock at each end. One of these is connected with a retort, through which the air passes, driving out the emanation accumulated above the solution. The other serves for the aspiration of the gas. In order to perform the experiment, the producing apparatus is connected with an exhausted receiver by rubber tubing, the stop-cocks being then manipulated in such a way as to draw up the accumulated gas and drive it out with the external air.

Manner of using the emanation.—Produced and collected in this way, the emanation can be employed—

1. In the form of a gas.
2. For the production of induced radioactivity.

1. **Emanation in the state of gas. Inhalation.**—Strictly speaking, the emanation is used for inhalation, not in the state of pure gas, but always more or less mixed with air, or with some other gas. This can be accomplished in two ways. (1) By placing the patient at the free tube-opening of the apparatus described above, and making him directly breathe the emanation produced by the solution of radium

bromide. (2) A second method consists in putting a mixture of air and emanation into the apparatus used by M. Bournigaux for his investigations into respiratory changes. For this purpose it will be sufficient to pass a current of air into the apparatus containing the emanation, by means of a force-pump. It may perhaps be possible, by the use of special apparatus, to put the emanation in direct contact with the cutaneous tissue.

2. **Emanation producing induced radioactivity.** — The emanation has the power of making all substances radioactive, whether they are liquid or solid, organic or inorganic. Water alone, or containing

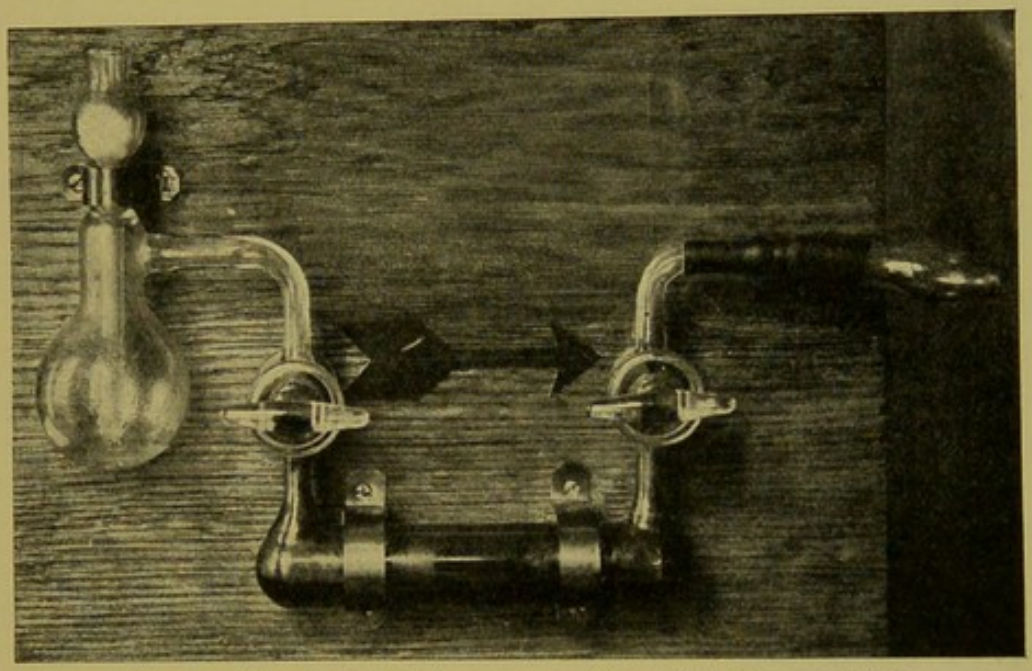


Fig. 4.—Armet de Lisle's apparatus for collecting emanation.

different kinds of chemical products, all pharmaceutical substances, and even tissue cells, acquire, by contact with this gas, the property of giving out radioactivity. There are many products capable of becoming radioactive, and conveying to the depths of the tissues increased energy, in addition to the properties of the products themselves. Radioactive mineral waters, of which we have spoken on page 27, furnish an excellent example of natural radioactivation.

An interesting experiment was made as follows. A quantity of radium was introduced into the waters, and measured in such a way that they retained for an indefinite period a radioactivity equal to that found at the source. MM. Jaboin and Beaudoin, working from the data of the late Professor P. Curie and M. Laborde, carried out this experiment successfully with the mineral waters of Bussang, conferring on them permanent

radioactivity by the introduction of minute and accurately measured quantities of radium. The memoir which they presented on this subject to the Pharmaceutical Society * was reported on by a Commission, which decided that the work performed had given well-founded conclusions. Thus waters which are radioactive at their source, but lose this special property in transport, may henceforth be rendered permanently radioactive, and their natural condition may be preserved at a distance.

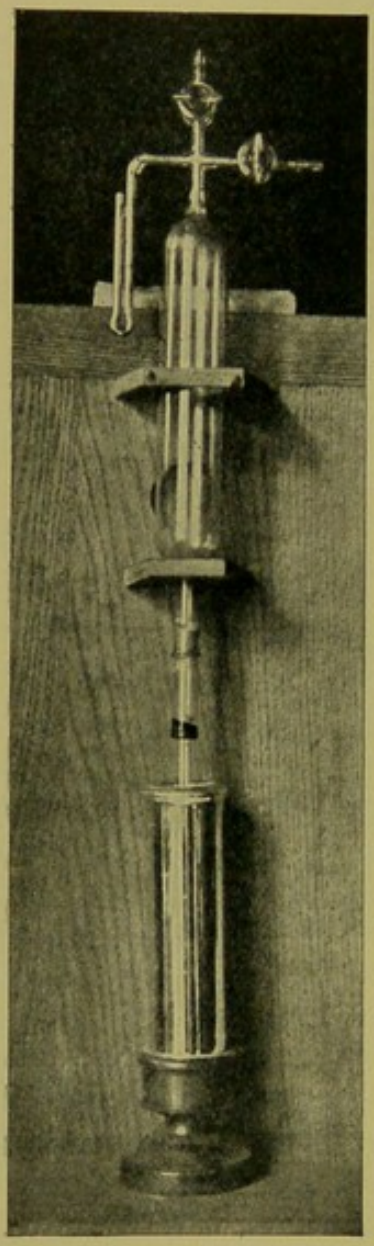


Fig. 5. — Emanation condenser (Danne's apparatus).

Concentration of the emanation.— Induced radioactivity, as we have said, is rapidly dissipated, and diminishes according to the law of decrease ; a loss of one-half the radioactivity in thirty minutes, and so on. The rapidity of this decrease is a drawback in practice, but it may be remedied by condensing the emanation in the vehicle which it renders radioactive, and by employing products of more intense activity, for which this law acts with less rapidity. Concentration of the emanation is obtained by a very simple process, with the apparatus represented in Fig. 5.

Apparatus for concentration of emanation by condensation in liquid air (Fig. 5).—Two reservoirs are placed in communication by a joint carefully ground with emery. The lower one contains the substance for retaining the emanation. After a vacuum has been produced in both, the emanation is introduced in the usual way, and the lower reservoir is then immersed in liquid air. In a few moments, the whole emanation becomes condensed in the reservoir above the substance, which has become highly radioactive. This method possesses numerous advantages, amongst which the following should be borne in mind :—

1. The radioactivity of the new media is rendered much more intense by this process than by the ordinary methods.

2. By means of electrical apparatus, the intensity in radioactivity of the media can be measured, and the quantity of emanation enclosed

* Jaboin and Beaudoin, "Sur la radio-activation artificielle des eaux minérales et l'élimination du bromure de radium soluble," Société de Pharmacie de Paris, July 29th, 1908, and *Journal de Pharmacie et de Chimie*, January 7th, 1909.

in the apparatus and in the radioactive substances estimated in gramme-hours. A gramme-hour is the total quantity of emanation furnished by 1 gramme of pure radium bromide in one hour, if the emanation is not spontaneously destroyed. In the same way, a milligramme-minute is the quantity of emanation produced by 1 milligramme of pure radium bromide in one minute, without taking into account spontaneous destruction.

Method of using emanation.—The emanation thus described may be employed in two ways—

1. Conveyed by an inert substance with the object of allowing the radioactive properties to act alone.

2. Conveyed by active substances with the object of reinforcing them, and combining their action with that of the radioactivity.

1. **Emanation conveyed by inert substances.** — In this case the vehicles are generally water, vaseline, oil, or glycerine. Any of these may be used, according to their several properties, by ingestion, or by injection into cavities, sinuses, the various passages of cutaneous, conjunctival, and muscular tissue, and into tumours. They can also be applied to different parts of the surface of the skin. These pharmaceutical and other products, being endowed with radioactivity by the emanation which they contain, act on the tissues. Part of the emanation is given off and permeates with induced radioactivity the tissues which it reaches.

2. **Emanation conveyed by therapeutically active substances.**— Quinine, mercury, arsenic, subnitrate of bismuth, carbon, and many other drugs have been rendered radioactive by induced radioactivity. But this method of utilising such energy is very restricted and of little value, because the energy is rapidly lost. In the following section we shall try to indicate the possibility of continuous action for the emanation by making use of the soluble properties of certain radium salts, and more particularly by the incorporation in pharmaceutical substances of the insoluble salts in suspension.

II. EMANATION AND RADIATION EMPLOYED SIMULTANEOUSLY

The emanation and radiation are used simultaneously, either in the case of an insoluble radium salt in suspension in a substance capable of being absorbed or injected, or in that of a soluble radium salt dissolved in some such substance. Radium salts may be mixed with many different products, the object being—

1. To restore to them their lost radioactivity. (We have seen an example of this in the permanent radioactivation of mineral waters.)

2. To augment a power already belonging to them. That radioactivity increases the power of ferments has been proved by many

experiments. Acting on this principle, M. Jaboin has prepared radiferous ferments, and a whole series of radiferous pharmaceutical products, such as quinine, grey oil, and colloidal metals, with the aim of increasing their special properties.

3. To confer on them a new power, or to make use of them as vehicles for transmitting radioactivity to certain parts of the economy.*

Substances used with radium appear, then, in the form either of radiferous products, or simply of radioactive products.

Radiferous substances are those containing radium in a state which may be soluble or insoluble (in suspension). They are, as a matter of fact, radioactive from induced radioactivity, since the emanation is present, and continuously emitted by the radium. Their radioactivity is therefore permanent.

Simple radioactive products are those which have merely been brought within reach of insoluble radium in the free state, and put in contact with the emanation alone. The radium salt having been removed after a given time, the products are only temporarily radioactive, and this activity diminishes very quickly, in accordance with the law to which it is subject. This is certainly a drawback ; but on the other hand, such products possess a practical interest from being radioactive without containing radium, and from being moderate in price, since the smallest particle of the metal which has served on one occasion for radioactivity can be used again any number of times.

For instance, we have experimented with both radioactive and radiferous substances, such as various kinds of water, and solutions of biniodide of mercury and grey oil. The waters have been chiefly used for subcutaneous and hypodermic injections, in the treatment of lupous nodules and tumours. Radiferous grey oil and biniodide of mercury have been employed in syphilis. Interesting results have been obtained by injecting into the tissues solutions holding in suspension some grains of insoluble radium salt. Dr. Dominici and Dr. Barcat have shown at the Académie des Sciences that radium can be conveyed into certain tissues, by injections of insoluble salts. In such cases the liquid part is eliminated, and the solid particles of radium sulphate, which can act for a long time by means of their rays, remain fixed. But this method has not yet become common in ordinary medical practice, on account of the high price of radium. In any case, the experiments which we have personally carried out with grey oil and radiferous

* When introduced into the organism, the emanation becomes rapidly diffused, and can thus reach the deeper regions. It is localised in the glands of internal secretion, especially the suprarenal capsules, and eliminated by the skin and lungs, and to a small extent by the kidneys. ("Recherches de Bouchard, Curie et Balthazar," International Congress, Lisbon, April, 1906.)

waters show that the organism easily tolerates this process. The liquids with which we worked were prepared by M. Jaboin.

Radioactive waters.—Proportion : 1 milligramme of radium sulphate added to 1 litre of distilled water. Several patients have had a series of injections, each containing about 30 drops, into the cutaneous and subcutaneous tissue fifteen or twenty times, with an interval of one day. No harmful effect worth mentioning has been produced on the general state of health.

Radiferous waters.—Two solutions : (1) 1 microgramme, *i.e.* a millionth of a gramme, to 1 c.c. of distilled water ; (2) 10 microgrammes to 1 c.c. The maximum injections have been a total of about 100 drops of the strong solution, spread over a period of ten days.

Radiferous grey oil containing 20 per cent. of mercury.—Proportion : half a microgramme to 1 c.c. Thirty patients had a series of injections, administered in the way usual for mercurial treatment, without feeling the least inconvenience. The series was composed of six injections of 7 drops each, every five days, each dose therefore containing one-sixth of a microgramme. Analysis of the urine led to the following conclusions : The urine is radioactive for three or four days after the injection of radiferous grey oil, and its activity diminishes almost regularly during this period, thus conforming approximately to the law of decrease of induced radioactivity. When, after the lapse of several days, mercury begins to make its appearance in the urine, the latter no longer shows radioactivity. It would seem, therefore, that the injected radium is eliminated, as a rule, by organs other than the kidneys. Other solutions or vehicles of soluble or insoluble radium salts have for some time been prepared from pharmaceutical and other substances, and employed in experiments of a therapeutic nature.

CHAPTER II

RADIATION

I. RADIUM APPARATUS

We now come to the most important part of our study, in which we shall consider the radiations used alone, without the emanation. This will deal with the application of apparatus to the surface of the skin and the accessible mucous membranes. The gradual but rapid and effective advance in the construction of the instruments has placed radium-therapy, in the course of the last few years, on a really scientific and practical basis. In this and the next two chapters we shall only describe the technique, operative methods and analytical measurement of the available radiation. The value of the various modes of operation will be dealt with in the clinical section.

We must first inquire what radium apparatus consists of. The scarcity of radium and its very high price necessarily led the first makers to devise instruments in the shape of protective boxes intended to prevent any loss of the original material. Two stages may be traced in the construction of these appliances: the primitive stage, in which the salt was poured into tubes or boxes, like grains of corn into a sack, and the present one, in which an ideal apparatus is striven after. What are the qualities indispensable for such appliances? They are very numerous, but some are so important as to outweigh all the rest. They are:

1. *Homogeneity of the radioactive output.*—This means that any portion of the surface of the apparatus, considered separately, ought to have the same radioactive strength as any other part. In this way the therapeutic effects will be uniform and identical at every point. In order to obtain such a result, the radium particles must be of the same size and distributed in such a manner that they do not overlap, and are equidistant from each other and from the surface of application of the apparatus.

2. *Maximum quantity of output,* or liberation of the largest possible total of rays. The thinner the substance required to contain and enclose the particles, and the more easily it is permeable by rays of weak penetration, the more valuable will be the apparatus. If this fact

is borne in mind, it will be possible to utilise, not only all the γ and β rays, but also a certain quantity of α rays.

3. *Possibility of measuring the radioactivity with ease and accuracy.*—To obtain this result, it is necessary not only that the output shall be homogeneous, but also that the radium particles shall be kept permanently in place by the containing and fixing substance. Movable grains in a tube represent the reverse of these conditions.

4. *Resistance to wear and tear of the surface of application.*—All these conditions depend on the nature of the substance in which the radium salt is contained. This substance therefore is a matter of great importance in the construction of the apparatus. It should combine the following qualities :

(1) Extremely strong fixative power, effectually preventing any loss.

(2) Very great permeability by the most easily absorbed rays.

(3) Perfect resistance, not only to all the operations necessary for cleaning and sterilisation, and to injury, however slight, but also to the solvent action of the radioactivity itself.

(4) A perfectly smooth and even surface.

An apparatus thus constructed will present a minimum of uncertainty with regard to the measurement of radioactivity, and any doubt felt by the operator on this point can only arise from the reaction peculiar to the individual patient. This, however, is a drawback which no drug or method of treatment can entirely overcome. Radium apparatus intended for application to the skin should possess all these different qualities, but the old-fashioned kinds, which are still occasionally used, do not conform to the requirements which we have laid down. Indeed, radiumtherapy has emerged from the pure empiricism with which it started precisely because these advantages are found combined in the newer instruments, and because calculations have been made which render systematic dosage more practicable.

We shall therefore explain—

1. What the old apparatus consisted of.
2. How the appliances now in use are constructed.

But before attempting the analysis of these subjects, which seem to us of the first importance, it should be mentioned that the perfection to which the extraction and manipulation of radium and the construction of the appliances have been brought, making radioactivity of practical use, rendering the study of radiumtherapy more scientific, and producing many valuable results in the course of the last few years,

is due to the chemical and physical researches carried out in France. This is equally true of the new studies now being pursued, with the object of placing, not only the properties of radium, but also those of other radioactive substances, such as polonium and uranium, at the disposal of the medical profession. From inquiries which we have made on this subject, it seems evident that the old-fashioned methods with tubes and lens-shaped apparatus are still in vogue in other countries, and that centres of study devoted to the elucidation of these subjects are rare and of very recent date.

I. ORIGINAL APPARATUS

The first appliances manufactured for the use of the profession were little more than containers, in which the radium salt was enclosed. They included rubber bags, ebonite boxes, and glass tubes and capsules. The rubber bags were easily perforated, and open to the same objection as the boxes or capsules, owing to the free condition of the radium salt. The particles were movable, the small mass being carried from one side to the other, according to the direction in which the apparatus was inclined. There was great inequality of action, and much difference in the quantity of radiation, according to whether the grains were massed together, or spread out over a more or less extensive surface. The action, moreover, was always considerably diminished, on account of the absorption of a large proportion of the rays by the substance through which they had to travel, and also from the fact that this substance was too thick. It is true that the glass tubes, which are still used, give excellent therapeutic results in certain cases; when introduced, for instance, into tumours. The homogeneity of the radioactive output over the whole surface of the apparatus is not absolutely necessary in this case, as it always is in the treatment of surface lesions, with regard to which æsthetic considerations naturally predominate. Nevertheless, these tubes are faulty from a scientific point of view, on account of the difficulty of measuring their external radioactivity. For surface action, and to obtain more regularity in the output of energy, the grains used to be fixed by sticking them on, or firmly pressing them down in a cup with a slight depression. Most appliances of foreign manufacture are constructed in this way. Such are the little ebonite boxes, covered with a sheet of mica, in the shape of a small naturalist's lens. The salt is fixed on a cup-shaped plate, and immediately covered by the mica sheet, so that the rays have to pass through a thin layer of air, and then through the mica. The radium particles being compressed, and forming several layers, the output is less than it should be. We have observed much more acute reaction,

in patients treated with this form of apparatus, at the centre of the lesions than at their periphery, and this want of uniformity in action might have been foreseen.

In France an aluminium sheet one-tenth of a millimetre in thickness was at first substituted for the mica, and the radium particles were better distributed in the little cup. In this way an attempt was made to arrive at an ideal form of apparatus, but the compression of the particles, the excessive absorption of the total radiation, and the difficulty of determining the limits of the surface covered by the radium, still prevented experimenters from ascertaining and dealing with the energy at their disposal in a sufficiently accurate manner. We could only calculate the original activity of radium with this primitive apparatus. We contented ourselves with indicating the weight and value of the contained salt, and did not take into consideration the amount of the total radioactive energy, or the percentage of α, β, and γ rays emitted outside the instruments. The only thing which could affect therapeutic reaction, namely, a knowledge of how much of the radiation really penetrated and acted upon the tissues, was neglected. From the medical point of view, it is of little importance to know that a certain salt, enclosed in a particular apparatus, originally had a given radioactive strength dating from the moment when it was enclosed, and that it must traverse some substance before reaching the skin. The only point of scientific importance is the value of the radiations which have passed through the enclosing substance, and the exact amount of energy which is available. We were enabled to ascertain these points at the beginning of our studies, owing to the improved instruments placed at our disposal.

II. APPARATUS NOW IN USE

We employ apparatus of two different kinds. Those of one variety are used for external application, with the radium on the outer surface. They are covered with a special varnish, by means of which the salts are stuck on. For the most part, they fulfil the conditions we have laid down, and put radiumtherapy on a sufficiently accurate posological basis for medical practice. The other variety consists of tubes containing radium salts, which are specially useful for insertion into tumours or passages. The following chapter will be devoted to the discussion of these instruments, and we shall not again refer to the other means we possess of using radium, namely, ingestion, injection, and the application of ointments and other substances.

A. APPARATUS IN THE FORM OF TUBES

We shall have little to say about radium in tubes, a form of apparatus which has been in use from the first. It is true that we can now, as we could not then, measure their external radioactivity, but this measurement, by the method at present employed, does not give the stability and accuracy claimed for the apparatus with salts varnished on. These types are, however, worth retaining, because there is an indication for their therapeutic use. The tube is made of glass and sealed, and the radium particles are seen moving inside according to the inclination at which the tube is held. It is difficult to arrange them in such a way that they shall occupy the whole interior space of the tube. The latter is enclosed in a second tube of gold, silver, or platinum, of a thickness depending upon the intensity of radioactivity desired. This tube acts as a filter. Constructed in this way, this form of apparatus, which is very small, can be introduced with advantage into the substance of tumours,* and allowed to remain there for a sufficient length of time. It may also be introduced into fistulas, cavities, and fissures. The radiation will have to pass through the wall of the glass, and afterwards through that of the gold or silver tube.

There is another way of constructing this kind of applicator. A very small cylindrical apparatus with the salts adhering, and a radiferous "toile" rolled up, can be enclosed in a gold or silver tube, and introduced into a tumour. In this case the radiation will have to pass first through the varnish and then through the wall of gold or silver. On the whole, this second apparatus provides a homogeneity which is lacking in the first, but uniformity is not necessary in this particular case, and the glass tube possesses the great advantage of making recovery of the radium easy, without risk of the slightest loss.

B. APPARATUS WITH RADIUM SALTS APPLIED IN VARNISH

There are two kinds of apparatus in which the salts are stuck on with varnish :

1. Those with a metallic base.
2. Those with a linen base ("toile" applicators).

1. Apparatus with Salts in Varnish and Metallic Base

These appliances consist of two parts :

(1) A metallic base :

(2) The radium varnish which covers it.

* Methods of Morton and Robert Abbé.

(1) METAL BASE

Its nature and thickness.—The base is usually made of copper, sufficiently thick to be rigid. Formerly the edge was turned in at the circumference, in order to hold the varnish, but we suggested that this rim should be done away with, so as to facilitate application.

Its surface.—The surface, instead of being flat, is roughened with small projections, which grip the lower part of the varnish. A fine metal plate is fixed to the surface in such a way that the varnish when poured on completely covers the plate. The apparatus now possesses a certain stability; it will stand shocks without much injury to the varnish, and without loss of the radioactive substance.

Its form.—The form of this support can be varied to any extent, and the best armamentarium will undoubtedly be that which has a sufficient number of appliances of different forms to correspond in shape and size to the lesion to be treated. But the number of instruments must of necessity be limited, and we therefore have to content ourselves with those patterns which can be adapted to the greatest number of cases. Some of the appliances which we use are shown on p. 42 (Fig. 6). Their shape principally depends on whether the applications are to be made (1) externally, on even surfaces, or (2) in cavities, passages, and folds. In special cases, the apparatus for external use can also be employed for cavities, and vice versâ.

Form of apparatus best adapted for plain surfaces.—**Flat apparatus** (Fig. 6).—These applicators are made in two distinct shapes, either round, in the shape of a disc, or rectangular, both being useful and adaptable to various conditions. By placing the latter in juxtaposition large areas may be covered. These instruments, which vary considerably in size, are most useful from 1 to 25 or 30 square cm. If made smaller, the radiation is too weak, and larger ones are difficult to fix and manipulate.

Concave apparatus.—This form is particularly useful for application to the eyelids, cheek-bones, etc. It will sometimes be advisable to give the so-called flat applicators a very slight concavity instead of a perfectly plane surface. Indeed, there is always rather better contact at the centre than at the circumference. A very slight depression of the metallic surface would remedy this inequality.

Convex apparatus.—For the naso-malar and naso-palpebral regions the convex form will be found very useful.

Form of apparatus for introduction into cavities, passages, fistulas, and folds.—Here again the shapes vary very much. As a general rule, cylindrical or spherical surfaces should be substituted

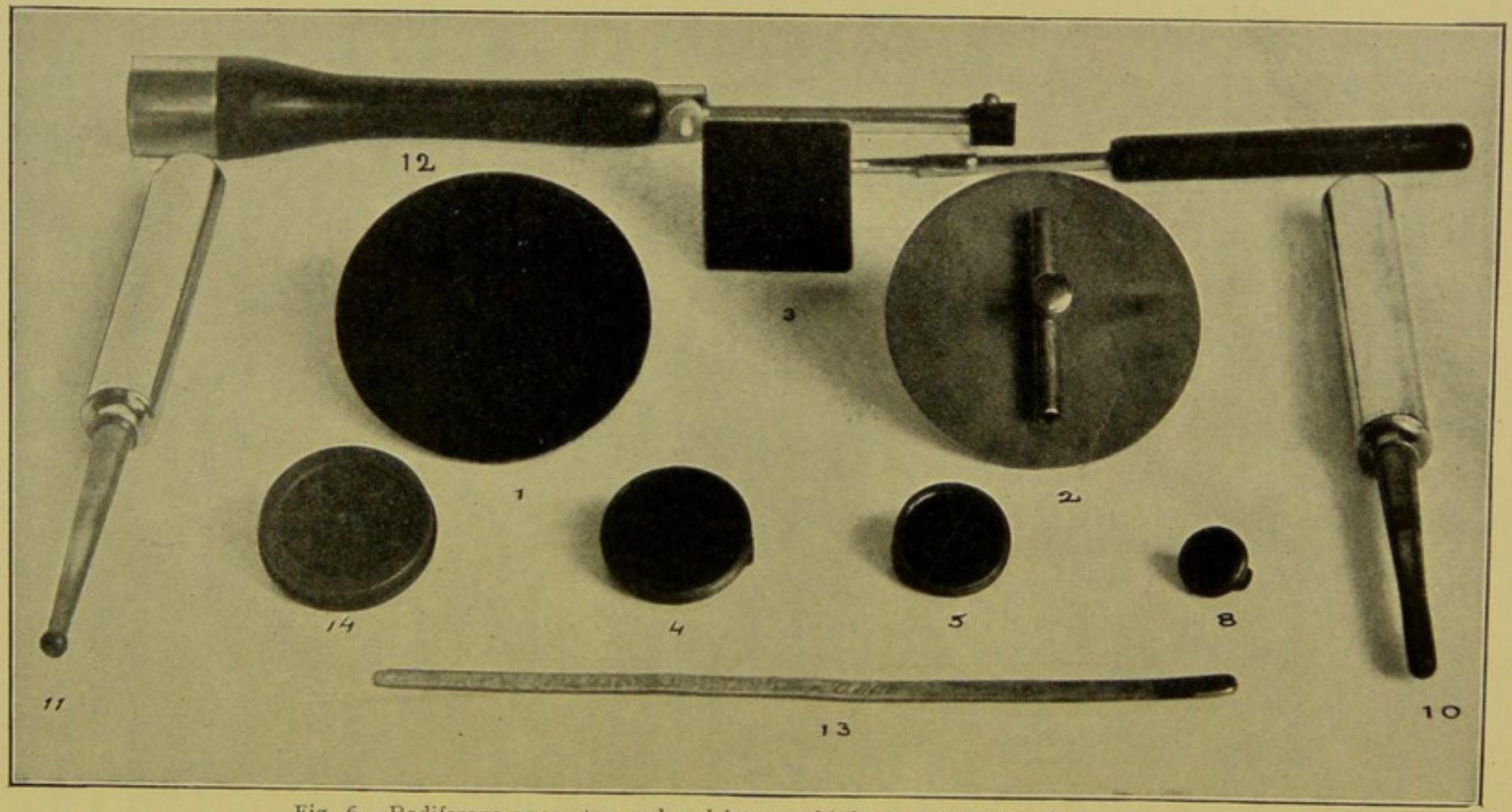


Fig. 6.—Radiferous apparatus, reduced by one-third (*see* description on pp. 41, 43).

The numbers of the apparatus correspond to those of column (1) of the analytical table on pp. 46-47. Except No. 14, these instruments are all covered with fixing varnish.

No. 14, "toile" apparatus. The radiferous "toile" is inside. Its surface is separated from the exterior by an aluminium screen, against which it is laid, and which may vary in thickness. The radiferous "toile" may be removed from the apparatus at will, and used separately. The square plates Nos. 3 and 12 can take any inclination required, and may be unscrewed from the handle. The hollow tube, No. 2, at the back, serves for the insertion of a fixing band. It can be unscrewed, in order to make the apparatus less bulky, when enveloped in a screen.

These instruments may be covered with a series of lead or aluminium screens. *See* radio-uterine applicator and examples of screens in chapter on Gynæcology. Other "toile" and varnish applicators, of different shapes and sizes, possess various advantages. We find the rectangular instruments extremely useful, owing to the possibility of placing them in juxtaposition

for flat ones. Applications to the interior of the mouth, the vaginal canal, etc., should also be made with apparatus belonging to the first category.

Cylindrical apparatus (Fig. 6, No. 10).—The length and thickness of these will vary according to whether the auricular canal, urethra, anus, or uterus is being treated. This is also a convenient shape for introduction into tumours.

Spherical apparatus.—This variety is used to convey the rays into fissures, cysts, blind passages, etc.

Laminated apparatus.—This is a metallic plate, quite flat, and specially intended for treatment of the internal surface of the eyelids, either when they can be everted, or when the apparatus must be inserted between the eyeball and the mucous membrane of the lid.

Holders.—All these applicators can be provided with a holder—long or short, as the case may be—which allows of applying them at a distance. Sometimes, by an arrangement of screws, such as that shown in Fig. 6, No. 12, it is possible to vary the inclination of the instrument on its holder. The round and square shapes also have a hollow tube at the back, by means of which a handle or fastening for fixing the applicator can be introduced. When a minimum of thickness is required the tube can be unscrewed.

We do not intend to describe here all the different forms of instruments. We have only mentioned those which best conform to the requirements of an armamentarium that must be small, although it has to be adapted to many different purposes. It now remains to describe an apparatus combining a flat metallic base with a cylindrical metallic mount, which by the method of its construction can be used for many purposes.

Radio-uterine applicator.—This instrument was devised by Dr. Wickham. It is in the form of a mushroom, or large-headed nail, and consists of three parts screwed together, two of which form the cylinder or stem, and the third the head or disc.* Used as a whole, its stem penetrates the uterine canal, and the head covers the cervix, so that it is well adapted for the treatment of metritis of the body of the uterus, with ectropion of the cervix. When equal action on all parts of the uterus is not required, a whole series of apparatus, with interchangeable parts of different radioactive value, may be arranged in various combinations, or act as a support, without the radium. By removing the distal portion alone, it is possible to operate in the cervix and on its surface; or with the disc by itself, when the stem is

* Wickham, "Présentation d'un appareil dit 'radio-utérin.'" (Geneva Congress, September 4th, 1908.) *See* diagram in chapter on Gynæcology.

removed, on the external surface of the cervix, or even with the cylindrical portion alone, in the uterine canal. As these parts differ in size, and are covered with screens of varying thickness, the manifold uses to which such an apparatus can be put may be easily imagined. It is chiefly intended for the uterus, but may also be employed, either as a whole or in its constituent parts, for application in various regions, such as the anus, entrance of the vagina, ear, etc., and for introduction into tumours. The slightly concave discoid portion may be used alone, for ordinary external applications.

(2) RADIUM VARNISH

The fixing substance with which our apparatus is covered is a special varnish possessing those properties of permeability, solidity, and resistance which we have shown to be so important. When this substance is raised to a high temperature, it becomes sufficiently soft to be poured on to a metal plate or cloth. The required quantity of radium salt is mixed,* and spread in such a way as to obtain as thin a layer as possible of the mass on the plate, and as even a distribution of the salt. The usual proportion is 1 cg. of the salt to 1 square cm. of surface. The varnish is then dried and resined. On cooling, it regains its original solidity, which is very great. Once poured on and hardened, it presents an absolutely smooth, slightly shiny surface of brownish colour. Owing to its transparency the radium grains are visible. When the varnish has just been spread on, the grains are yellowish, but in proportion to their age—for freshly prepared radium salt has a life of its own, and does not reach maturity for some months—they become darker, and change by degrees to dark brown or black. The radioactive value of the varnish naturally depends on the quantity, quality, and proportion to the surface, of the contained radium.

2. "TOILE" APPLICATORS

"Toile" applicators also consist of two parts; the cloth itself and the radium varnish which covers it. These have many advantages. They allow a considerable quantity of α rays and powerful radiations to pass, owing to their construction, which differs from that of the metallic apparatus by the amount and distribution of the varnish. In this "toile" apparatus, the grains are only covered with a thin layer of varnish, especially on the surface opposite to that where they rest on the "toile." The rays, having less thickness to traverse, collectively form radiations of great intensity. The cloths, being very fragile, must

* It is known that the properties of radium are not affected by temperature, however high.

be handled with great care; save in exceptional cases, they could hardly be used without protecting screens, and owing to this circumstance they lose part of their strong radioactivity. Their flexibility is a great advantage. But in this respect, we must distinguish between two kinds of "toile": (1) those of small size, containing radium of very great activity, which have only a limited amount of flexibility; (2) those of large size, but weak in radioactivity, which are extremely flexible, so that applications can be made with them to large surfaces, *e.g.* the arm of a child. The "toile," whether small or large, has, moreover, the advantage of being thin. By enclosing small and very active pieces of it between two sheets of lead united at their circumference, we get a flat apparatus, suitable for regions where an instrument of great thickness could not be used, such as the mouth, vagina, or cervix uteri. Moreover, the degree of flexibility possessed by these applicators, even small ones, is sufficient to permit of producing, when required, slight concavity or convexity on the whole surface of the apparatus and screen, and on the other hand, by reason of their thinness, they can be superimposed, which is often a great advantage. Those of large size and little activity being very pliable, we have frequently been able to utilise them, by folding them in two, or in four, and this use of several layers increases the radiation to a considerable extent. Lastly, the radioactivity is exercised almost equally on either side of the "toile," front or back, thus allowing the instruments to act on different points at the same time, and to radiate almost uniformly over all the parts to be treated, in regions where—as in the vagina—the lesions affect the periphery of the canal. Most of the general considerations which we have mentioned with regard to apparatus with metallic mounting apply also to "toile" apparatus. This rapid sketch will show the numerous advantages attaching to the use of these "toiles."

Numbers (*see* Nos. Fig. 6, p. 42).	Variety and Shape of Apparatus.	Dimensions.	Surface Applied (in sq. cm.).	Activity of contained Barium-Radium Salt (activity of uranium taken as the unit).
(1)	(2)	(3)	(4)	(5)
1	Varnish apparatus, flat, round..	6 cm. in diam.	28·2	$\frac{1}{4}$ pure salt
2	Ditto	6 cm. ,,	28·2	,,
3	Varnish apparatus, flat, square, with rounded angles ..	3 cm. across	9	,,
4	Varnish apparatus, flat, round..	2·5 cm. in diam.	4.9	,,
5	Ditto	2 cm. ,,	3·1	,,
6	Ditto	2 cm. ,,	3·1	,,
7	Ditto	2 cm. ,,	3·1	,,
8	Ditto	1·5 cm. ,,	0·95	,,
9	Ditto	1·5 cm. ,,	0·95	,,
10	Varnish apparatus, cylindrical..	0·5 cm. ,, 1·5 cm. in length	—	,,
11	Varnish apparatus, spherical ..	Diam. of the sphere 1·5 cm.	1·4	pure
12	Varnish apparatus, flat, square	1 cm. across	1	,,
13	Varnish apparatus, laminated ..	square of 0·5 cm.	0·25	,,
14	Varnish "toile" apparatus, flat, round	2·5 cm. in diam.	4	$\frac{1}{4}$ pure salt
15	Ditto	3 cm. ,,	7	,,
16	Varnish apparatus, flat, round	5 cm. ,,	20·5	$\frac{1}{20}$ pure salt
17	Ditto	6 cm. ,,	28·2	,,

NOTE.—(*a*) The figures in column (4) represent the exact surface covered by the "toile" apparatus, an approximate estimate is given of the surface covered by

(*b*) Apparatus which emit α rays also emit soft β rays. The percentage of the

(*c*) The figures of column (11) are given by way of guidance. They are, however, distribution of barium-radium sulphate is homogeneous.

* *See also*, with regard to this apparatus, the curves shown on pp. 72, 73. The with the method which we should now advocate.

† Apparatus No. 3 is one of recent manufacture, and is therefore still in considering the weight of salt incorporated, should be 500,000. Complete maturity of an

‡ and ‖ Applicators 10 and 11 are very difficult to measure, on account of their the case of No. 10, it was thought unnecessary to give the measurement in square

The numbers in column (1) correspond to those of Fig. 6, p. 42.

We make use of many other instruments—"toile," tube, and rectangular. One 1,000,000. The combination of its action in "cross-fire" with that of a "toile"

Weight of contained Barium-Radium Salt (in grammes).	Total available Radiations (activity of uranium taken as the unit).	Proportion of Rays.			Total available Radiations (in sq. cm.). In round numbers.
		α Rays.	β Rays.	γ Rays.	
(6)	(7)	(8) Per cent.	(9) Per cent.	(10) Per cent.	(11)
0·20	580,000*	10	87	3	20,500
0·10	480,000	10	87·5	2·5	17,000
0·09	110,000†	20	71	9	12,000
0·04	34,000	0	90	10	6,900
0·04	55,000	0	90	10	17,700
0·04	50,000	0	90	10	16,100
0·025	50,000	0	90	10	16,100
0·01	25,000	0	90	10	26,300
0·01	13,000	5	85	10	13,600
0·02	150,000‡	50	48	2	—
0·005	180,000‖	50	48	1·5 to 2	128,000
0·007	30,000	10	86·5	3·5	30,000
0·006	19,000	10	86	4	76,000
0·04	450,000	70 to 80	19 to 29	1	112,500
0·06	400,000	70 to 80	18·5 to 28·5	1·5	57,100
0·10	22,000	10	86·5	3·5	1,000
0·20	70,000	15	82·5	2·5	2,400

varnish, which may differ slightly from the surface of the apparatus itself. For the barium-radium salt.

latter is included in the total percentage of β rays.

only useful for comparison (1) when the proportion of rays is identical; (2) when the

proportions given in this table corresponding to it were not formulated in accordance

process of maturation. This explains the quality and quantity of its radiation, which, apparatus is only obtained spontaneously two to three months after it has been made.

shape. The figures relating to them must therefore be considered approximate. In centimetres. (Notes by M. Beaudoin.)

of the latter is 3 cm. by 4 cm., and contains 12 cg. of salt, with an activity of apparatus of the same shape and power gives excellent results.

CHAPTER III

RADIATION (Continued)

II. TECHNIQUE AND METHODS OF OPERATION

I. TECHNIQUE PROPER

When once the general arrangement of the apparatus is understood, there are many ways of utilising and varying the energy it sets in motion, and modifying its application to medical purposes. The questions of technique governing these variations are exceedingly complex and delicate, and do not lend themselves to very systematic division. We may, however, consider that the object of the different methods in use is the modification of energy, as regards both quantity and quality, by weakening and diminishing it on the one hand, or increasing it on the other. They specially aim at influencing either the radiation as a whole, by diminution or increase of the total amount of energy; or the composition of the radiation, in such a way as to change its quality, that is to say, the respective proportions of α, β, and γ rays. But it must always be borne in mind that there is no means of altering the total amount of a radiation without at the same time altering the proportion of the rays. The apparatus may be applied to the tissues direct, or after some substance has been interposed to form a screen. In reality there is always some kind of intervening substance, since even the varnish of the apparatus acts to some extent as a screen. On the other hand, the instruments can seldom be applied unscreened, with the varnish in contact with the skin, owing to the necessity for preserving them. We nearly always envelop them in a very fine sheet of rubber, or fine muslin. These coverings form an additional protection. Their density and thickness can be increased with the object of diminishing the total intensity of the radiation, or of altering the proportion of the α, β, and γ rays composing it. Screens are therefore almost always required, and may be unlimited in number. In the chapter on measurements we shall see what are the doses, what kind of energy is placed at our disposal, and how it varies according to the thickness and density of the intervening substances. Here we shall only deal with the length of application and the different kinds of screens.

1. LENGTH OF APPLICATIONS

The short preceding sketch has already shown us that by means of various screens we can vary the radiation given out by an apparatus to any extent. But there is one consideration which must always influence treatment, especially in the matter of dosage, and that is the time during which the apparatus is left in contact with the tissues, and the method adopted for repeating the applications. The importance of this is shown by the possibility of irritating the surface, whatever be the technique adopted. Whether an instrument of very great total activity be used uncovered, or encased in a lead sheet 2 mm. thick, which only allows of the filtration of radiation having very weak quantitative value, the length of application will, in either case, determine the subsequent production of reaction, whether accompanied or not by inflammation of the surface. This first proposition, which applies to all the methods employed, deserves careful consideration. It might be thought that, by the use of total radiations of intense activity, that is to say, with a preponderating action of β rays, excessive inflammation would always be produced.

One of two methods might therefore be employed—destructive action by the use of total radiations chiefly composed of β rays, or action without destruction, by the use of γ rays alone, and very thick screens. This, however, would not be an accurate way of computing the comparative value of the different processes adopted. In fact, the amount of reaction produced depends on the total effective dosage, which, in its turn, results from the length of application. When we consider the various means of applying the apparatus, with or without screens, we find at the two extremities of the chain: (1) methods which only give very weak quantitative radiations exclusively composed of γ and hard β rays; (2) those which give total radiations of enormous intensity. Now, in the first case, applications of great length result in the accumulation of large doses, and produce intense reaction and irritation. In the second case, very short applications will act without causing the slightest surface irritation. If, therefore, the above-mentioned distinction only referred to the production or prevention of surface inflammation, it would be too arbitrary; but from various other points of view its application, and the reasons for it, are, as we shall show, very significant. Since this question of duration is one of the first importance, we shall discuss it before speaking of screens, selecting various types, from amongst which a whole intermediate series may be devised.

Long applications.—In order to increase the energy of a radiation,

or, in more accurate language, to obtain more intense effects, it is sufficient to prolong the time of contact of the applicators. Being very easily worked, and causing little inconvenience, they can be allowed to remain on for a very long period, even in the case of infants. Given a certain amount of radioactivity, it will suffice to calculate the length of time necessary to convey to the tissues the total amount of energy required. In order to decrease the energy of a radiation, or rather to obtain less intense effects, recourse may be had to fractional doses, shorter applications, and longer intervals between them.

Very short applications.—These are especially useful when treating inflamed and very sensitive surface lesions, such as eczemas on the face, in infants. They should only last one minute, or even half that time. Very powerful instruments with a large surface, used without screening, are employed in this case. These short, but sufficiently strong applications will permit of covering large surfaces, such as the lower limbs or the whole of the head, in a short time, thus refuting the assertion that radiumtherapy is of no practical use except for surfaces of limited extent. For instance, it might be thought that a single application of No. 1* apparatus, having an activity of 580,000 (*see* p. 46), would be destructive, but if the length of application is regulated and reduced, the most sensitive tissues may be treated without resulting irritation.

Fractional doses.—The action of the rays on diseased tissues also depends on the manner in which the application of a given dose of energy is made. Such action varies according to whether the treatment in the first instance is massive, or is divided into fractional doses. In the second case the tissues will bear a total dose of greater energy. If a known total radiation is made to act during a given period, a certain amount of energy will be applied, and a certain effect obtained. But if this period is split up into several portions, the tissues affected will have time, in the intervals, to accustom themselves to the radioactive effect, or to lose part of it, so much so that the fractions of energy will not produce the same effect as the total. The division will ensure a larger total of energy, which will act differently. We have had proof of this in many of our experiments, in which we have seen inflammatory reaction make its appearance after an exposure of a given length, but fail to do so when the same period was subdivided.

Intervals between applications.—By carefully spacing the exposures, the effects produced may be diminished, or, to speak more accurately, different effects may be obtained. If a first application

* The apparatus will be indicated by numbers corresponding to those in the table on pp. 46 and 47, and in Fig. 6, on p. 42.

is calculated to reach the limit of what can be borne by the tissues, and a similar dose is added to it without allowing a sufficient interval of time to elapse, a given amount of reaction will be produced. But if the division and spacing of the doses be properly arranged, this reaction will not occur, or will appear under another form, so that the process will tend to the weakening of the total energy. It is therefore clear that by varying the length of exposure very different effects may be obtained. These result from the total dosage employed, and the way in which it has been distributed and conveyed to the tissues. This is why we can get reaction without superadded inflammation, even with powerful doses, such as those administered with uncovered apparatus. The length of exposure and the spacing are naturally very variable, and will depend on the results desired by the operator, and on the presence or absence of screens. In the course of our discussion of clinical therapeutics we shall indicate the various plans we have adopted as to length of application in the treatment of certain diseases.

"Cross-fire."—There is one process—that known as "cross-fire"—on which we must lay stress. It is adapted to various conditions, and lends itself to that alteration in length of time of which we have just spoken; being equally suitable whether the apparatus be used uncovered, or with the whole series of screens. It possesses so many advantages that it will be found extremely useful in practice. The term "cross-fire" explains itself. This process is a bombardment of the tissues by rays emitted from different points at the same time, and therefore crossing each other, the radiations being chiefly composed of projectiles travelling at immense speed. It originated in a plan adopted by Dr. Wickham, in 1905, for the treatment of deep-seated sciatic pains. Desiring to act at a depth with intense radioactivity, without disturbing the surface, and reckoning on the diffusion of rays emitted outside the apparatus, he covered the part to be treated with several instruments at once, changing their position before the exposure had been sufficiently long to produce erythema at any one point. By this means the action at a depth was made more powerful by the diffusion and crossing of the rays, in proportion to the number of instruments and applications, without the slightest injury to the surface. Starting from this principle, we devised and applied the process of "cross-fire" for the first time to an interesting case, the treatment of an erectile angioma on a baby's forehead. This was the first projecting erectile tumour to be cured by radium. The best way of explaining the reasons for this process will be to mention the circumstances which led us to devise it.

In March, 1907, Drs. Gastou and Artin brought us an infant a few months old, who presented a reddish-violet erectile tumour, cylindrical in shape, projecting 2 cm., and measuring 2 cm. in diameter at the base. It was impossible to ascertain whether the bone of the frontal region was sound, and this uncertainty prevented the application of an apparatus to the upper part of the growth. The tumour was soft, and full of blood; at the least cry it became turgid, and we feared to excite inflammation of the surface, which might have produced serious hæmorrhage. Since it was impossible to fix the appliances, they had to be held in the hand, and the child was restless. The problem to be solved was therefore very complicated. It was necessary to find some method which, in spite of very short applications, would act strongly at a depth, lightly on the surface, and in a parallel direction on the forehead. The "cross-fire" plan fulfils all these conditions. Two instruments, Nos. 8 and 9, were applied uncovered to the lateral surface of the tumour, opposite each other, and kept in place for ten minutes. Their position was afterwards changed twice, but they were always placed in opposite directions, and left *in situ* for the same length of time. This made a total of thirty minutes at a time for each apparatus, divided into periods of ten minutes for each of three places. The applications were renewed every day, in the same manner. By this means they were sufficiently short, and the rays were directed laterally. Moreover, we knew that ten minutes was a period insufficient to interfere with the integrity of the surface, and yet long enough to affect to some extent the superficial tissues. Doses of this length repeated six times gave a total exposure, at a depth, of sixty minutes. The energy of the very penetrating rays, small in quantity, and filtered through the superficial tissues, was multiplied, and even rendered more intense, by convergence at a depth.

The results exactly answered our expectations. The tumour subsided, and became decolorised, without any appearance of surface inflammation. We frequently employed this process afterwards, using either uncovered instruments, or those with the whole series of screens, the latter method being generally employed. It is therefore sufficient, when adopting the same *modus faciendi*, to interpose screens and increase the length of the application accordingly. The crossing of the fires can itself be intensified, when the tumour permits of four applications at once, opposite each other, or when a tube can be introduced into a tumour, the surface being covered with the apparatus. The object of this proceeding is to render the action of the "surpénétrant" rays more intense by their combined effect for a short time, and also making use of the superficial action of the less penetrating rays.

Both the quantitative and qualitative value of the radiation is thus increased. And if this method is employed with apparatus of great intensity, uncovered, or, better still, with screens, very remarkable results may be obtained in the treatment of tumours, and regions suitable for such applications.

2. INTERPOSED SUBSTANCES. SCREENS. FILTRATION

The interposition of screens, of which there is an endless variety, plays a considerable part in radiumtherapy, since they allow the strength of a radiation to be modified to any extent with the same apparatus, giving it a very varied output, and enabling it to be adapted to many uses. With regard to the following descriptions, it must not be forgotten that this chapter only treats of the instruments and the *modus faciendi*. Their therapeutic value will be dealt with in the clinical section. Interposition may be of any kind or quality (solid, liquid, or gaseous). Solid screens are generally used at the present time.

Interposition of air. Applications at a distance.—Before commencing a description of solid screens, we should mention the possibility of using a column of air for this purpose by means of applications at a distance. This method has a special purpose, and is likely to do good service. It was the subject of some experiments by M. Bongiovanni, and has been very ingeniously applied by M. Bayet. We have ourselves also been able to appreciate its effect. The process consists in placing the apparatus at a distance, varying, let us say, from 1 to 5 cm. We generally choose the latter. The support holding the instrument at a distance is a conical shaft of rubber-covered lead (Bayet). The applicator is fixed at the smaller end, the larger end being applied to the tissue in such a way that its outline corresponds to the shape of the lesion to be treated. If the support is of lead, it will be sufficiently malleable to make this adaptation possible. It is kept in place by strips of diachylon, which pass over the large *inverted* end of the cone. By this means the energy of the radiation is greatly lessened. Its diminution will, of course, be in inverse proportion to the square of the distance, and can be easily compensated by a longer exposure. We cannot here take into account the many considerations arising from this interposition of air, with regard to alteration of the radiation in quantity and quality. A description of these belongs properly to physics.

This method allows of—

1. The use of any kind of radiating source; apparatus with salts in varnish, or glass tubes or bulbs containing radium.

2. Alteration of the distance at will; thus making it easy to increase or diminish the energy.

3. The possibility, with a focus of small size, of acting on a much larger surface, by reason of the lateral diffusion of the rays.

Solid screens.—Screens have the double object of lessening the total amount of the radiation, and at the same time modifying its quality by filtration.

These two conditions cannot exist apart. It is, in fact, impossible to diminish the total amount of a radiation without altering its composition. Diminution of the whole radiation is easily understood; the thicker or denser the screen, the weaker will be the quantity. With regard to alteration in quality, the matter is more complicated, and requires some explanation. We have considered (p. 24) the physical theory of filtration. Since the rays possess varying degrees of penetration, some of them are intercepted by certain substances, and the rest, which are more penetrating, can be filtered and utilised. It will be evident from the foregoing remarks how important the use of these screens becomes in practice, since it allows the owner of a single instrument to obtain many different results from it. As we have already seen, the apparatus will not only have various effects when placed directly on the skin, according to the length and method of application, but great variety of action, both as to quantity and quality of energy, will result from the interposition of screens or filters. Filtering has always been used, though involuntarily in the case of the first workers in radium. It is an absolute necessity in radiumtherapy; in the treatment of cutaneous surfaces, indeed, the tissues themselves act in some sort as filters. Since the radium must be contained in a substance of some kind, and since the first layers of tissue absorb some of the rays, and form an obstacle to their passage, it is certain that the energy which succeeds in passing through the enveloping substance and the first cellular layers has really been filtered.

But this is not what is known as filtration in therapeutics. The word there implies voluntary interposition, for healing purposes, of some substance forming a movable and changeable screen between the apparatus and the tissues to be treated. In this sense filtration does not seem to have been used before M. Wickham tried it, in March, 1905. We shall not repeat here what has been said in the Introduction on this subject, or on that of the formulæ of systematic doses as applied to dermatological radiumtherapy. Later on we learned the value of direct applications (with unscreened apparatus), when properly managed, and the importance in many cases of using the largest possible sum of rays, and since the opening of the Laboratoire

Biologique du Radium in 1906, we have studied various modes of direct application, without, however, losing sight of the employment of screens. Our thoughts were chiefly directed to the value which might accrue from the action of extremely penetrating rays. (*See* p. 51, "Cross-fire.") After trying screens of cotton-wool and aluminium, and studying the difference of action arising from the interposition, under the same apparatus, of graduated cotton-wool pads increasing in thickness from a few millimetres to 1·5 cm., we at length treated a patient suffering from ocular trouble (*see* "Various Diseases, Glaucoma") with rays of great penetration. This was in January, 1907. The filtering was effected by sheets of rubber-covered lead, of the kind which act as protectors in X-ray therapeutics.

On the other hand, about April, 1907, M. Beaudoin commenced the investigation of the subject at our laboratory from the standpoint of physics, so as to ascertain the value of radiations filtered through a whole series of lead and aluminium screens of varying thickness. Dr. Dominici then successfully established the systematic use of pure γ rays, isolated and filtered through screens of great density.* We also studied medium filtering, which allows the passage of a certain number of β rays, which can be used at the same time as the γ rays. In certain cases, it was important to avoid the surface irritation often produced by β rays, when carelessly employed; but we had learned from long practice that there are means of overcoming this difficulty, and it seemed a pity, by suppressing all the β rays, to lessen so much of the chief quantitative value of the activity emitted by radium apparatus. It was for this reason that, after comparing different methods, we became convinced of the practical importance of allowing a certain amount of these rays to be present, and to act in the radiation. We then asked the opinion of Sir William Ramsay and M. Debierne as to the power of penetration of β rays. M. Beaudoin had been studying the question in the meantime, and arrived at the same conclusion, namely, that β rays accompany the γ in numbers sufficient for use, even through 1 to 2 mm. of lead (*see* pp. 23 and 73). It now appeared that the use of isolated γ rays, although very useful in individual cases, should generally be replaced by that of radiations composed of more or less hard β rays mixed with γ rays, radiations to which we have given the name of "surpénétrant," † and that in the present state of our knowledge of physics the dosage, at any rate as regards thick filtering, should be regulated by analysis of the quantity of rays rather

* Dr. Dominici gave the name of "ultra-pénétrant" to these pure γ ray radiations in November, 1908, but afterwards recognised that a large number of β rays also escaped filtration.

† Fifteenth French Congress, held at Geneva, September, 1908.

than that of the composition of the rays forming a radiation. We shall return to this subject of filtration considered with reference to reaction, in order to show the *new* qualities possessed by the "surpénétrant" rays. These historical details are interesting, and show the progress which has been made by the Laboratoire Biologique du Radium.

Description of screens.—There are many substances which will serve as screens; silver, gold, copper, tin, mica, etc.; the two best, however, would seem to be aluminium and lead. They differ greatly in character; aluminium being easily penetrated, whilst lead, on the contrary, possesses considerable powers of absorption.

Aluminium screens.—Aluminium possesses many advantages; it can be rolled out in thin sheets (down to the hundredth part of a millimetre), so that the scale of thickness for these screens is very extensive. We generally use the following: $\frac{1}{100}$ mm., $\frac{4}{100}$, $\frac{8}{100}$, often putting several sheets together in order to increase the thickness to $\frac{16}{100}$ or $\frac{32}{100}$. When thicker than this they are extremely hard. Their lightness, however, compensates for this disadvantage, and some useful experiments might possibly be made by means of screens 1 cm. thick.

Lead screens.—Lead can also be rolled out very fine, the thinnest sheets being $\frac{1}{10}$ mm., their scale of progression rising by tenths up to $\frac{5}{10}$, and then by half millimetres and millimetres. The pliability of lead is a great advantage, allowing, as it does, of adaptation to all shapes. Unfortunately, its weight and the necessity of long applications are drawbacks to its use in the treatment of certain regions; *e.g.* the buccal cavity. Silver screens are cleaner, but harder.

We have now explained the object of the screens which we use, and shall specify, in the chapter on measurements, what rays they allow to pass through them. It only remains here to describe how they are employed.

II. OPERATIVE METHODS

Having described our appliances and the means of varying the energy of which they are the source, we will show how they may be used in practice. Applications can be made—

a. Externally, on the surface of the skin.

b. Internally, in tumours, passages, cavities, and sinuses.

A. EXTERNAL APPLICATIONS

We have already seen that the instruments can be applied in three different ways:

1. In direct contact with the part treated.

2. By the interposition of screens between the apparatus and the tissues.

3. At a distance. We will not repeat here what was said on p. 53, about this third mode of application.

1. **Application by contact.**—This will include three processes:

(1) Preparation of apparatus.

(2) Preparation of surface to be treated.

(3) Position and fixing of instrument.

(1) **Preparation of apparatus.**—In the treatment of certain dry lesions, the apparatus can be applied direct and uncovered, without any preparation. It will be sufficient to wipe it, or to leave it for a few minutes beforehand in formaline vapour. But in a clinic where there are many patients to be treated, this repeated cleansing ends in injury to the varnish. We therefore usually wrap the applicator in a very fine sheet of rubber. The reason for this is that cleaning may be avoided, and the varnish preserved from direct contact with warm or damp tissues. Fine muslin can also be used for this purpose.

(2) **Preparation of surface to be treated.**—When the size of an instrument corresponds exactly to that of the lesion, nothing can be simpler; it is easily put in position on the affected part. But it is necessary first to wipe and cleanse the parts very carefully, and remove all traces of moisture and dressings. Crusts must usually be removed, as their presence would intercept some of the rays, and deprive us of part of their action. The cure would also take longer, as the correct dosage could not be exactly ascertained. If, however, the crusts are left they should be considered as screens.

Protection of normal tissues.—But the apparatus sometimes has a surface of action larger than the lesion to be treated. In this case, the tissues which do not require treatment must be protected from the radioactive energy, which would produce useless, or even harmful irritation. With this object, we place under the radium apparatus, whether for long or short exposures (applicators with or without a screen), rubber-covered sheets of lead. We then make a window in these sheets corresponding to the exact shape of the lesion. In order to obtain this, the limits of the region on which the radioactive energy is to be brought to bear are marked on the skin with a dermographic pencil. Laying some tracing-paper on these marks, we get the outline, and apply it to the rubber-covered lead by means of a sharp etching needle. It is then sufficient to follow the traced lines with a penknife, so as to obtain an opening corresponding exactly to the surface on which the radiation is to act. In X-ray treatment, one sheet of this covered lead would be quite sufficient to protect the tissues. This is not the case with radium

rays, which indicates one of the differences between these two methods of therapeutics. We have often proved that when radium rays are emitted from a powerful source, they traverse the protected lead, and, if applied for a long period, act on the other side. It is therefore sometimes well to double the rubber sheets. But there is another aspect of the case to be considered. M. Sagnac has shown that every ray which passes through a metallic substance produces secondary rays. These are easily absorbed, but may cause on the surface of the skin a slight irritation, sometimes followed by pigmentation. It is important to stop these secondary Sagnac rays, and in order to do this, the rubber-covered lead must be protected by another substance which will absorb them, and which is not itself liable to produce other secondary rays. With this object, at the beginning of our experiments, we used to cover our protective lead with a thin aluminium sheet. This, however, was a mistake. The aluminium, it is true, stopped the secondary rays already produced, by absorbing them, but itself in turn produced a certain number. The substances employed are those containing a minimum of metallic elements. M. Sagnac considers black paper the most suitable. Two or three sheets are sufficient; they are sewn on to the rubber which covers the lead, after an opening has also been made in them. We have given the name of "cache" to this little protective apparatus. The same considerations led us to wrap the lead and aluminium screens in sheets of paper and rubber. We also sometimes use very thin mica sheets. These have the great advantage of being transparent and of allowing easy application of the "cache." By placing them entire and without any opening under the latter, they serve to absorb the secondary rays, and also act as a screen to the apparatus.

(3) **Placing and fixing of the apparatus.**—The various preparations having been made, the protective "cache" should be applied, and fixed with strips of adhesive plaster, and then the apparatus can also be put in position and secured. For this purpose we sometimes use bands which pass over the apparatus, sometimes strips of adhesive plaster. For short applications, when the instrument is uncovered, or has a light screen, the arrangement is quite simple; an attendant, or even the patient himself, holding it by a handle. When a baby is being treated, and the region is easily accessible, the mother can do this quite well. The child is sent to sleep, and the application is then made. For the outer surface of the eyelids, the apparatus is first placed flat, and then inverted, drawing up the eyelid in such a way that the rays are not directed on to the eyeball. For the palpebral conjunctiva, the back of the instrument is covered with a sheet of aluminium and

paper, and the whole enveloped in a thin layer of rubber, when, by lightly drawing back the eyelid, the flat apparatus may be introduced on the region requiring treatment. Whatever be the means employed, it is well to distribute the pressure evenly, and not to make it stronger at one point than another, as otherwise there would be a risk of producing more marked action at that point. It is important in the case of tissues, inflamed as in eczema, or full of blood as in some flat angiomata, to use gentle pressure, so as slightly to empty them. The general observations which have just been made apply equally to both kinds of treatment, whether with uncovered instruments or with lead or aluminium screens.*

2. **Application of instruments with screens.**—A screen is cut out, of a thickness suitable to the particular case, and rather larger than the applicator, and turned up at the edges. The applicator is placed on the screen, directly when the latter is of aluminium, or wrapped in a light sheet of rubber when it is of lead; then, in order to stop the secondary rays, a certain number of leaves of black paper are placed on the outer surface of the screen, one sheet being sufficient for short applications with an aluminium screen. Five to twenty, according to the intensity of the source of emission, will be required for lead screens. The whole will then be wrapped in another sheet of rubber, to keep it in place. Applicators covered with aluminium are easy to apply. Those with lead screens, being intended for long applications, should form, with their layers of paper, a well-fixed and uniform whole. This can be ensured by wrapping them firmly in the rubber, which should be turned over the edges, and securely tied at the back. The "cache" is first fixed by small bands of adhesive plaster, and then the instrument is put in position, and kept there by other bands. The strips should be fastened, if possible, from below upwards, so as to avoid displacement owing to a slanting position or its own weight. A Velpeau bandage passing over the whole may sometimes be necessary. When the application lasts long, say for a whole night, and the screens are heavy, it is often convenient to use a special bandage with straps, made by a surgical-instrument maker, particularly for the head, lower jaw, etc.†

* The instruments may be used in many different ways. Two of rectangular shape, for instance, can be placed in juxtaposition according to their length, or width, or in different directions. They may be superimposed, or used for "cross-fire."

† *Note by Dr. Wickham.*—When the back of the apparatus comes in contact with the tissues, or must itself be used—when, for instance, it has to be placed under the arm, or in the mouth or the vagina—a thick screen (which is only protective, unless action is necessary on the side opposite the varnish) must be used. If it be desired to act on the side opposite to the varnish, account must be taken even of the metallic base of the apparatus, which to some extent forms a filter.

B. INTERNAL APPLICATION

1. To cavities.
2. To tumours.

1. **To cavities.**—Stems covered with radium can be introduced into the interior of the nasal fossæ, the auricular canal, etc., either simply wrapped in rubber or protected by lead or aluminium screens; they should be held with care, and the application, which can seldom last long, must be attentively watched, on account of the ease with which they are displaced. For the mouth, the small instruments which we have described permit a handle to be attached, which will facilitate application to the tongue, cheek, gums, or soft palate. For the tonsils, the skin must first be painted with cocaine. Heavy screens, owing to the length of time required, can only be used for the anterior surfaces. These applications are fatiguing, and it is important to lessen the thickness of the screens to some extent, so as to shorten the exposure and make the treatment practicable. In many cases (nævi, leucoplakia, and vegetating epitheliomata of the tongue), we have not hesitated to make use of powerful radiations with short applications and light filtering, and have found them very satisfactory. The practical difficulty as to long applications can be overcome by repeating them frequently. On the lower lip, a heavy instrument applied to the convexity will be kept in place by its own weight. For the vagina and uterus, as for the skin, the applications may be short with light filtering, or very long with thick filtering. There is no difficulty here about long exposures. But, as moisture penetrates the slightest breach of surface, for these regions, the same as for the lips and the tip and edges of the tongue, the screens must completely cover the apparatus, and form a box hermetically closed by soldering. By this means the healthy mucous membrane touching the back of the apparatus will not be irritated. The flatter and thinner the instruments and screens, the easier they will be to use. Radium "toiles," encased in lead sheets, fulfil these conditions admirably, on account of their thinness. In the vagina, according to whether the walls or the culs-de-sac are affected, recourse may be had to cylindrical stems or to flat apparatus, which, entirely covered by sealed lead screens, can be left in place as long as required. In the uterus, the radio-uterine instrument described on p. 43 will be found easy of application, and will allow of action at various depths in the cavity. When exposures of long duration with thick screens are made, it will be sufficient to use a fixing plug of moistened cotton-wool.

2. **To tumours.**—In this case, with the help of cocaine, we must have recourse to a small surgical operation, which consists in making in

the tumour a cavity for the radium tube. The tube should be wrapped in some sterilised substance which will not oxidise, or cause irritation. We might have a combination of encasing tubes, varying in shape and thickness according to the filtration, the effect desired, and the possible length of application.

[*Note by Dr. Wickham.*—It is obvious that the filters which we have mentioned can be adapted to all kinds of apparatus—flat instruments with varnish and radium "toiles," or tubes. In the latter case, a whole series of lead or silver filter-tubes may be used, into which glass tubes are introduced. They may be $\frac{1}{10}$ to $\frac{5}{10}$ mm., 1 mm., 2 mm., etc., in thickness. As we shall see in the chapter on cancer, they can be introduced into flexible catheters, and by this means conveyed to the tumour. For instance, a hollow catheter introduced into the urethra, artificial anus, rectum, œsophagus, etc., will bring the glass tube, which is supplied with the necessary filter-tube, into contact with the lesions to be treated. In such cases neither paper nor rubber is used, the catheter being sufficient to intercept the secondary rays.]

CHAPTER IV

RADIATION (Concluded)

III. MEASUREMENTS AND DOSAGE

We have considered the instruments at present used in radiumtherapy, and their method of application, and also how the energy emitted by an apparatus can be varied. The present chapter will set forth the different hypotheses as to measurements and dosage. We insisted at the very beginning of our researches on the necessity of studying radiumtherapy, which was then in its infancy, more systematically. Ever since we possessed radium apparatus, it has been our constant care to indicate useful measurements, and to determine scientific doses and quantities. Before this period, the only things considered were the amount of the salt contained in the apparatus, and the degree of radioactivity which it possessed. For instance, it was said of one applicator that it contained 0·05 of the salt, with an activity of 100,000; of another that it contained 0·20 of the salt, with an activity of 500,000. One worker in radium stated—and this loose use of terms, against which we have always protested, is still only too common—that he had healed a certain epithelioma by using an apparatus containing 0·03 of pure radium. Such language is inexact, and falls short of scientific requirements. It is certainly useful to have some notion of the original strength of the radium, but from a therapeutic point of view—and this cannot be too often repeated—it is important to estimate carefully, not so much what is in the apparatus as what comes out of it, and can be utilised by the operator. The epithelioma in question was not healed by the radiation of 0·03 of pure radium, but by a radioactivity diminished to some extent by the passage of the rays through the walls of the apparatus; and as these walls vary in thickness, in the study of an experiment which ought to give accurate results one meets with uncertainty about the very quantity on which the value of the experiment depends. Indeed, an experiment is useless unless it can be verified by other observers, and the statement about 0·03 of pure radium does not indicate clearly the means of arriving at a corresponding therapeutic result, since we are not told how much radioactivity was emitted by the apparatus. We will now set forth to the best of our power the different data required for really practical scientific measurements and doses.

Maturation of apparatus.—It should first be mentioned that the instruments have a life of their own, and improve spontaneously for some months, until they reach a state of maturity. When newly prepared, the radioactivity which they supply is comparatively weak. The radium particles seen through the transparent varnish are yellow. During the following weeks their strength increases rapidly, reaching, about the third month, a certain degree of development which constitutes the maturation of the apparatus. The grains are now dark brown, and the output has acquired sufficient stability. Later on, some increase of activity may be observed; but this subsequent growth only takes place very slowly, and depends, to a great extent, on alterations and deterioration which take place in course of time in the fixing varnish. This phenomenon of maturation is due to the presence of the emanation in an active state. Although this gas, in the case of varnish apparatus, cannot be employed directly, on account of its slight power of diffusion, it plays a considerable part indirectly. Inserted in the varnish, it behaves in the same way as in a closed vessel, and in a ratio corresponding to the loss resulting from the radiation restores the radioactivity. It is produced at first in considerable quantities. A radioactive equilibrium is subsequently established between the production and loss of the emanation. An applicator should be measured at the end of the third month; after that, every six months. So long as the varnish remains intact, little change will be noticed.

Analysis of radiation.—The radiation emitted by apparatus which is used either uncovered, or with screens, must be analysed from the double point of view, first of its total intensity, and then of its composition. This is what we call quantitative and qualitative analysis.

Quantitative analysis.—This relates to the radioactivity possessed by the total radiation considered as a whole, the value of which is expressed by numbers, 100,000, 500,000, etc. We have seen (p. 18) that, in the manufacture of radium, the fractionisation was carried to its highest degree, in order to obtain a radium salt as nearly pure as possible. Its purity is verified by the spectroscope and Curie electrometer. It has been proved that this salt has an activity of 2,000,000 *per surface unit*, that is to say, it ionises the air 2,000,000 more than the same quantity of uranium would do, this metal being taken as the unit of measurement.*

* It sometimes happens that an apparatus containing a salt with an activity of, say, 500,000, will have, if a large amount of the salt be present, a greater external radiation, *e.g.* 580,000. This is not an anomaly, for the radiation from a radium salt is not only the result of its activity, but also that of the way in which it is distributed over the surface. To say that the relative activity of a salt of radium is 500,000 is to say that, per surface unit, this salt will ionise the air 500,000 times more than uranium. If there is enough to cover a large surface, it is obvious that its intensity will be increased according to the extent of surface over which it is spread.

Pure radium bromide obtained at the end of fractionisation serves for the production of any degree of radioactivity which may be needed. Thus, to prepare a semi-pure salt, a certain quantity of pure radium bromide is weighed, and an equal amount of pure barium bromide added to it. The two products are dissolved, and the solution stirred, so as to mix them thoroughly, the mixture being then concentrated. The product with an activity of 500,000 has one-fourth part of pure salt. The product 100,000 contains one-twentieth of pure salt. To obtain a weight P from a salt with an activity A, the corresponding quantity of pure radium bromide p is taken, by reference to the following table, and the quantity $(P-p)$ of pure inactive radium bromide added to it.

Percentage of Pure Radium Salt.						Amount of Corresponding Activity.
0·5	per cent.	of	pure	radium	gives an activity of	10,000
1	,,	,,	,,	,,	,,	20,000
2·5	,,	,,	,,	,,	,,	50,000
5	,,	,,	,,	,,	,,	100,000
25	,,	,,	,,	,,	,,	500,000
50	,,	,,	,,	,,	,,	1,000,000

Therefore, when we say that the salt of an apparatus has an activity of 100,000, we mean that, to a given quantity of pure radium, twenty times that amount of pure barium bromide has been added. By this means any given activity may be ascertained. As to the figures showing the radioactivity emitted outside the apparatus, when it is said, for instance, that a certain apparatus emits an activity of 45,000 or 64,000, these figures signify that, analysed by the electroscope or Curie electrometer, the radiation from such apparatus has a radioactive power of 45,000 or 64,000 times greater than that of an equal quantity of pure uranium under similar conditions.

Kilo-uranium or kilurane.—But the mind can only grasp such vast numbers with difficulty. In X-ray treatment, for the sake of convenience, a similar measurement has been adopted, and the terms 10 H, 15 H, etc., are used. In the ordinary measures of length, weight, etc., multiples and sub-multiples are in use, such as kilometre, kilogramme, etc. It would seem to be important, especially from a clinical point of view, to create similar multiples for the measurement of the activity of radium. M. Beaudoin, to whom we owe this idea, suggests the term "kilo-uranium" or "kilurane." To state it more simply, 1,000 uranium units might be designated by one letter, U, for instance; so that, instead of saying "activity of 500,000, 1,000,000,

etc.," we should say, "500 U, 1,000 U." This would simplify the nomenclature, but we do not think that such a multiple would correspond to a definite and fairly constant clinical activity, since the results would be very different, according to whether the radiation were composed of very penetrating or slightly penetrating rays. For instance, 4 U, or 4 kilo-uranium, expressing an activity of 4,000, would be quite as well adapted to a "surpénétrant" radiation composed of rays acting at a depth after they had passed through thick screens, and producing a special clinical action, as to the total radiation of an apparatus with a very small original radioactive percentage, intended for action on the surface.

Qualitative analysis.—This relates to the composition of the radiation as regards α, β, and γ rays. We have already ascertained the proportion of these rays when emitted by radium in the free state, but it is very different in radiations emitted outside the varnish of our applicators. Figs. 2 and 3 (p. 25) show the comparative amount of α, β, and γ rays entering into the composition of the radiation emitted by radium in the free state, or by varnish apparatus, after filtration through the varnish. In the first case, the α rays have an immense preponderance, viz. 90 per cent.; the β only amounting to 9 per cent., and the γ to 1 per cent. But after filtration, the proportions are altered, and these are of special interest to practitioners, since they must be known for therapeutic purposes. There is then only a trifling proportion of α rays, and few γ are present, the β having a percentage of 90. These diagrams show the great importance of β rays in the radiation from the varnish apparatus. They also show the deviation of the rays produced by a magnetic field. The β rays are deflected to the greatest extent; the γ are not affected in any way. It should be noticed that the α and β rays which remain, and filter through the varnish, are those least capable of deviation. In proportion as thicker and denser screens are interposed, the percentage is again altered; there are no more α rays, the β diminish in number, and are less and less deflected, whilst the quantity of γ is very little changed. This is the quantitative and qualitative analysis to which we have already referred.

Uniformity of radioactivity. Possibility of fixed measurements.—In the first place, it is of some importance to observe that the radiation from radium can be measured, and that the measurements obtained remain constant for a considerable time. In this respect it has an advantage not possessed by other radioactive bodies. A Crookes tube, for instance, varies even during the exposure, and needs constant attention in order to obtain sufficient uniformity of action. Radium instruments, on the contrary, when in a state of radioactive equilibrium, possess the great advantage over the vacuum tube of emitting a radiation which is practically constant over a considerable period. We, therefore, only

need a single preliminary measurement, and it will be sufficient to repeat it about once in six months, unless the varnish of the apparatus should have lost its integrity. If this is impaired by wear and tear, cracks, or the action of corrosive chemical agents, the proportions of the radiation will vary very much, when the varnish scales off. Some of the particles being uncovered, the total activity increases in intensity, the α rays becoming relatively more numerous, so that the measurement must be calculated again. It is, therefore, necessary to preserve the varnish, as far as possible, from the slightest contact, and as we have already recommended, to avoid cleaning and washing, by using the apparatus—with some few exceptions—only when enveloped in a protective sheet of muslin or fine rubber. The measurement of apparatus is certainly not absolute, for we cannot pretend to strict mathematical accuracy in so delicate a matter as radioactivity, but still it allows of more exactness and a better method of analysis than would appear to be the case with that employed for the X-rays, at any rate from the standpoint of physics.

Methods of measurement. Electrical method.—There are several ways of analysing radiations: colorimetrical reaction; impression on a photographic plate; effect on phosphorescent materials; and lastly, electrical action. The three first present some advantages, and may perhaps some day be in common use, but that of electrical action, for many reasons, seems very much better, at any rate for such final analysis as shall be capable of verification and useful to all experimenters. We will now show how it may be carried out, and what advantage is to be gained from it. We owe all these data about measurement to M. Beaudoin, whose kind collaboration we have much pleasure in acknowledging here.

Ionisation.—Let us take a metallic rod which has been carefully insulated from surrounding bodies, and convey to it a certain amount of electricity. If the air be dry, we shall find that no loss worth mentioning takes place, and the rod will remain charged for several hours. If we now bring near it a radioactive body, we shall see that the loss becomes considerable, so that the discharge is complete in a few minutes, or even in a few seconds. This phenomenon is explained by saying that the air is *ionised*, or made a conductor of electricity, by the rays from the radioactive body. The more radioactive the body, the more strongly will the air be rendered a conductor, and the more rapidly will the discharge be effected. The velocity of discharge of the electrified body will therefore be proportional to the activity of the material. Let us then attach a thin leaf of gold to our metallic rod, and charge it again. As the rod and the gold-leaf receive electricity of the same sign (whether

positive or negative does not matter), it follows that they are mutually repelled, and since the rod is fixed, the gold-leaf will be deflected. If we now bring near to it, as before, our radioactive material, the system loses its electricity, and in proportion as this loss occurs, the repelling force between the rod and the leaf is diminished, so that the latter falls back by degrees, until it recovers its first position against the rod. It will therefore be sufficient to measure the velocity of fall of the gold-leaf, first for a material having a known activity equal to the unit, and afterwards for the substance to be studied, in order to obtain a ratio which will give the activity of the latter in numbers.

Electrical instruments of measurement.—In order to calculate the velocity of fall of the gold-leaf, it will be necessary to measure by

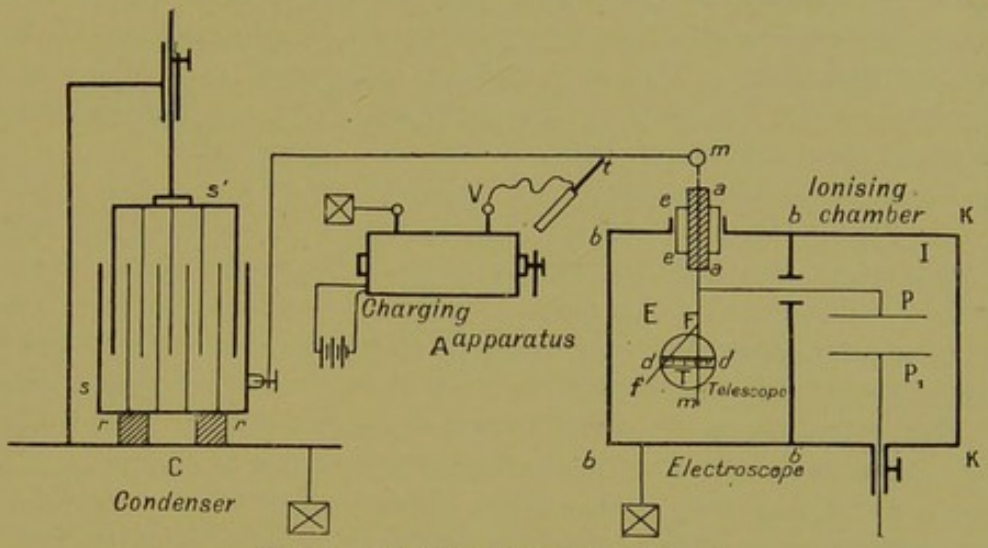


Fig. 7.—Apparatus for measurement.

chronometer the time during which it has been lowered to a given extent, but it is obvious that if the material is very active, the fall will be too rapid to be estimated chronometrically with precision. This drawback may be remedied by adding to the rod and gold-leaf system, which forms an electroscope, appliances called condensers, the object of which is to hold considerable quantities of electricity. The relative loss due to ionisation will afterwards remain small enough to be susceptible of measurement.

We will now give a short description of a set of apparatus for the measurement of radiumtherapeutic instruments (Fig. 7). Its principal parts are:

Telescope, T.
Ionising chamber, I.
Condenser, C.
Charging apparatus, A.

"1. *Electroscope.*—The electroscope E is composed of a metallic rod *mm*, furnished with a flat plate at the lower part, and fitted into an amber plug at the upper part, being itself protected by an ebonite plug *ee*. On the flat plate a thin gold-leaf F*f* is stuck, which can be moved round the point F; the latter acting as a pivot. The metallic case *bbbb* is earthed.

"2. *Telescope.*—The telescope shown in projection by the circle T serves for estimation of the velocity of fall of the gold-leaf. For this purpose it has a micrometer on the glass *dd*, and, for taking measurements, it is sufficient to calculate by chronometer the passage of the gold-leaf between two divisions of the micrometer.

"3. *Ionising chamber.*—The chamber for ionisation I is essentially formed by the two plates P P. The upper one is in connection with the stem of the electroscope. The lower one, on which is placed the apparatus to be measured, is attached to the metallic case *b*KK*b*, and in this way is connected to earth; it can also be moved vertically, and thus permits of alteration in the distance between the two plates. This is a useful arrangement, as it allows of study of the variation in intensity of the radiation from the radiumtherapeutic apparatus in the ratio of its distance from the upper plate.

"4. *Condenser.*—The condenser C consists of two systems of metallic sheets *s s'*, fitting into each other. The system *s* is insulated by means of amber wedges *r r*, and attached to the stem of the electroscope; the system *s'*, movable vertically so as to allow of varying the capacity, is earthed.

"5. *Charging apparatus.*—An ordinary electroscope is charged by means of a simple amber rod, because the capacity of such an instrument is generally weak. But when, as in the present case, it reaches a very high value, it is necessary to have recourse to more efficacious systems of charging. A small Ruhmkorff's coil may then be used, the primary of which is supplied by one or more batteries, one of the terminals of the secondary being earthed. The other end of the secondary V carries a flexible wire terminating in a metallic rod fitted into an ebonite shaft. It is this metallic rod *t* which charges the electroscope."

This is the improved electroscope with which M. Beaudoin analysed the radiation emitted by our apparatus; but for very weak radioactivity we must avail ourselves of the Curie "piezo-electric quartz." The electroscope described not only gives the measurements of the total radiation, but also permits of the specification, up to a certain point, of the percentage of α, β, and γ rays composing it. These measurements include two quite distinct methods:

1. The analysis of uncovered apparatus, in a state of maturity, and with perfectly preserved varnish.

2. The analysis of apparatus with screens whose thickness and density become gradually greater.

The table given on pp. 46, 47 represents the analyses of the first category of some of our appliances. The analyses of the second

category, that of apparatus covered by a whole series of screens, relate both to the total collective radiation and to its quality, that is to say, to the percentage in α, β, and γ rays. The following is the method of absorption adopted by M. Beaudoin to satisfy the requirements of the complex and delicate matter of measurement through a series of screens. We give *in extenso* the notes he sent us.

Method of absorption.*—"When an apparatus is screened in a particular way, with a view to clinical application, the operator has to decide the two following questions: (1) the intensity of radiation emitted by the instrument; (2) the composition of such radiation.

"Let us first take two straight lines O X and O Y, the latter perpendicular to the former (Fig. 8). On the straight line O X, taking O as the starting-point, and in the direction O X, let us draw any number of arbitrary, but equal lines, O $a = a\,b = b\,c\,\ldots = i$J, and let it be agreed that each of such lines represents $\frac{1}{100}$ mm. of aluminium; we shall then be able to number them 1, 2, 3, etc. We thus form a scale in one-hundredths of a millimetre of aluminium, and the length OJ represents $\frac{10}{100}$ or $\frac{1}{10}$ mm. Let us then, from the point J, continue the length JK, KL, etc., equal to OJ. We thus form a scale in $\frac{1}{10}$ mm. of aluminium, till we reach $\frac{10}{10}$ or 1 mm., continuing in this way as far as desired.

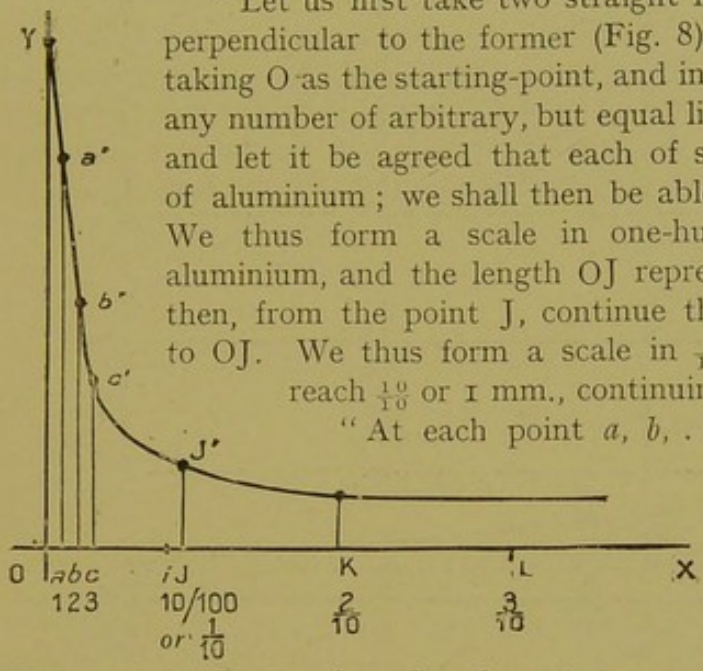


Fig. 8.—Curve showing absorption of rays in proportion to increasing thicknesses of aluminium.

"At each point a, b, ... J, K, L, of the straight line O X, let us draw lines perpendicularly to it, and upon them carry on the lengths aa', bb', JJ', etc., representing the intensities of radiation from the radium apparatus after $\frac{1}{100}$, $\frac{2}{100}$, $\frac{1}{10}$ mm. of aluminium. Lastly, let us join the points obtained, a', b', ... J', by means of a curve. This curve will represent the absorption of the rays, in proportion to the regularly increasing thicknesses of aluminium.

"From the moment when the rays become unequally absorbed, according to their degrees of penetration, the curve ought to show a bend every time that one group of rays becomes totally absorbed. This is, in fact, what actually happens, as we shall proceed to show by a few examples."

Interpretation of results.—"Let us suppose that, operating in the way just indicated, we have established for a radiumtherapeutic apparatus the curve shown in Fig. 9; it will then be easy to learn the total external radiation of the apparatus after passing through an aluminium screen of given thickness. For this purpose, it will be sufficient to turn back to the figure on the line of

* There is another method based on electrical measurement; that of deflection by means of magnets. It possesses some advantages, and may perhaps be employed at some future time.

thicknesses indicating the one required, and after following the vertical line of the number until it reaches the curve, to trace, from right to left, the horizontal line from the point of intersection. The meeting point of this horizontal line with the axis of the activities gives the particular activity required. By way of explanation, we have drawn the lines of construction necessary to find the external radiation of the apparatus through 0·12 mm. of aluminium (line DEF, dotted, and indicated by arrows).

"It now remains to establish an approximate value for the percentage. We shall show what must be done in order to give at each division of the

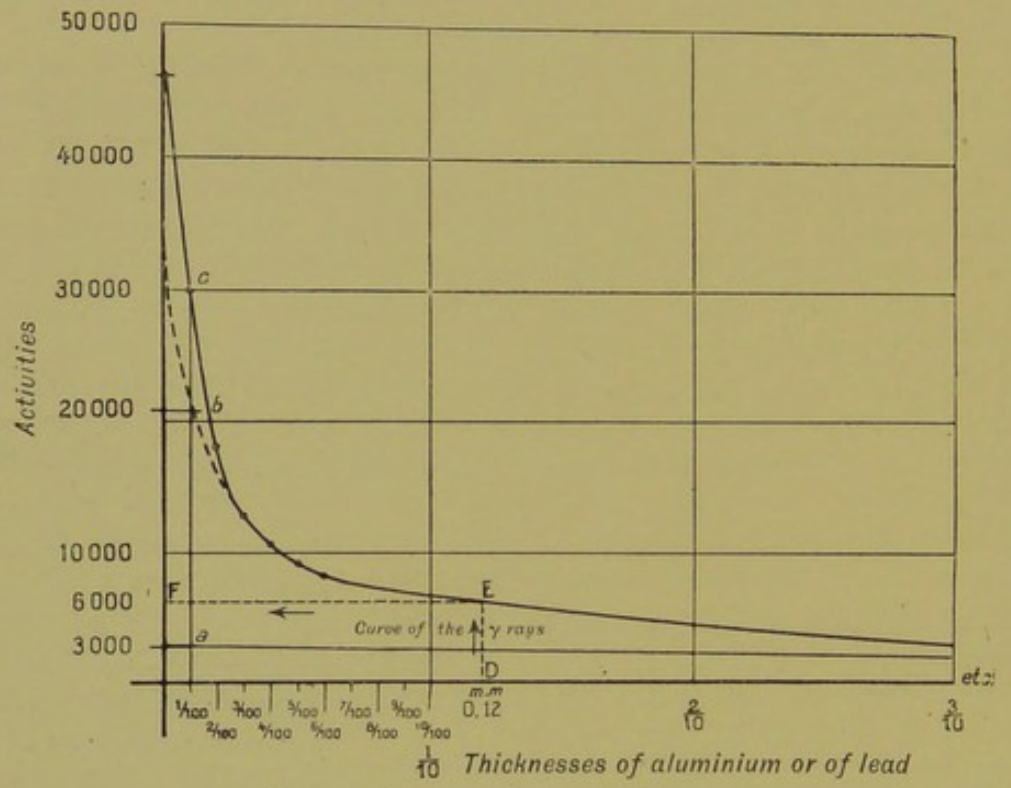


Fig. 9.—Diagram of absorption curve.

1. The curve E, *b*, *c*, etc., is the curve of absorption of α and β rays. 2. The curve ascending from E and terminating in a dotted line is the continuation of curve of absorption of β rays. 3. The horizontal line corresponding to the number 3,000 is the continuation of curve of absorption of γ rays. 4. The junction of curves 1 and 2 must be carried down lower, on to the vertical line corresponding to 3/100.

curve—that is to say, for all the thicknesses of aluminium employed—the percentage of α, β, and γ rays. The same procedure will apply to the division of the β rays themselves into soft, hard, and medium β. When a varnish apparatus gives out α rays, they proceed from α particles situated at different heights in the mass of varnish, so that when they emerge they have not all undergone the same amount of absorption. It is, however, unusual for the absorption to be completely negligible, and we may consider without much risk of error that only a small quantity of α rays will pass through a screen of $\frac{3}{100}$ to $\frac{5}{100}$ mm. of aluminium placed on the apparatus. The points of the curve obtained for $\frac{5}{100}$, $\frac{6}{100}$ mm., etc., of aluminium, therefore correspond to the absorption of a total of β and γ, in addition to the α rays, and as the interception of γ rays is small compared to that of β, the portion of the curve

in question may be taken as representing the suppression of β rays, and especially of soft β. It is therefore reasonable to suppose that the law governing the absorption of β rays on the other side of $\frac{5}{100}$ or $\frac{6}{100}$ mm. of aluminium also governs it on this side, and that the unknown part of the curve may be compared to the prolongation (or extrapolation, as it is called in physics) of the part already known. If this curve coincides with the real curve, there are no α rays; their number will increase in proportion to the distance to which the former is withdrawn. By thus continuing the curves of absorption of the β and γ rays, we possess all the data necessary for determining the percentage.

"In order to make this clear, let us suppose that we wish to determine the proportion of α, β, and γ rays, passing through a screen of $\frac{1}{100}$ mm. of aluminium, which covers the radium apparatus. Let us take the perpendicular line corresponding to the number $\frac{1}{100}$; this straight line meets the curve of the γ rays produced to point a, the curve of the β rays produced to point b, and the original curve to point c. If corresponding horizontal lines are drawn through points a, b, c, we get the following activities:

For a	. . . . .	about 3,000
,, b	. . . . .	,, 21,000
,, c	. . . . .	,, 30,000

"Activity α will therefore represent

$$\frac{30,000 - 21,000}{30,000} \times 100 = 30 \text{ per cent.}$$

"Activity γ will represent

$$\frac{3,000}{30,000} \times 100 = 10 \text{ per cent.}$$

"Lastly, activity β will represent remaining percentage, that is, 60 per cent.

"This would be the case with any other aluminium screen. It will be seen that the percentage of α rays will be *nil* after about $\frac{3}{100}$ mm., and only β and γ rays will be left. All that has just been said applies equally to the curves of absorption obtained with lead screens; these curves, moreover, will resemble each other more than those of aluminium, because they apply to harder rays, over which the varnish has less influence."

These are the descriptions given by M. Beaudoin. Amongst the curves which he has made relating to our apparatus, we will choose two (Figs. 10 and 11), by way of example, referring to apparatus No. 1 of the table on pp. 46, 47 (one curve for aluminium screens, and one for those of lead).

The activity of this apparatus, as stated in the table on pp. 46, 47, differs from that shown at the commencement of the following curves. The reason is that the two analyses were made at an interval of two years, and the apparatus having been much used during this time, the

varnish corroded, and became thinner, allowing a more considerable α ray radiation to pass. This instance shows that it is always better to preserve the varnish by some kind of covering.

Figs. 10 and 11 show how much the radiation is diminished for a given thickness of screen. They also show what screens must be used to obtain different kinds of rays.

Suppose, for instance, that we desire in practice to suppress the α and soft β rays, it will be sufficient, according to the curve in Fig. 10

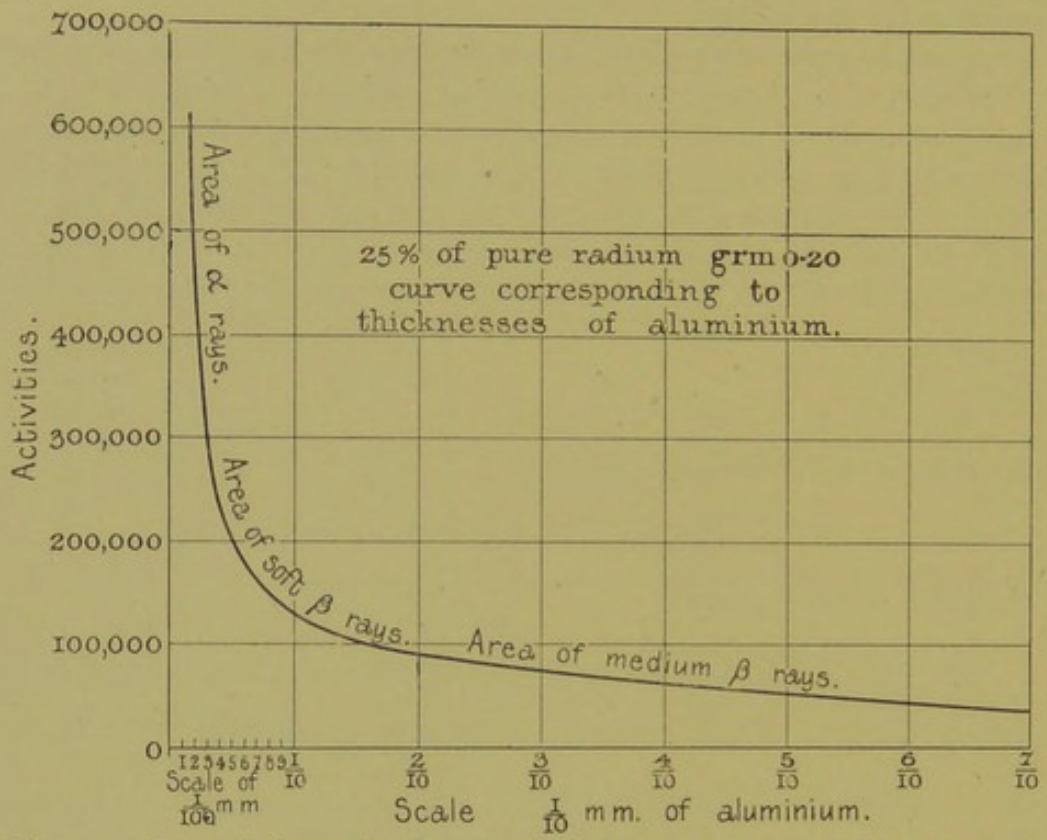


Fig. 10.—Curve of absorption, by means of aluminium screens, of rays emitted by apparatus No. 1 (pp. 46, 47).

to choose a screen of $\frac{1}{10}$ to $\frac{7}{10}$ of aluminium, in order to produce a radiation of about 100 U. Our apparatus will still be very powerful, and on the other hand, it will include the majority of medium and hard β rays, and γ rays. Fig. 11 shows the curve relating to radiation from the same apparatus used with a series of lead screens. This is a most interesting curve. It shows that after $\frac{7}{10}$ mm. of lead, when only γ and hard β rays can pass, the absorption between one millimetre and the next is almost *nil*. This will be easily understood when it is remembered that nearly 10 cm. of lead is necessary to intercept the radiations entirely. The dotted line X Y being considered as the line of γ rays, and the curve of these rays being negligible, we see that hard β are added to γ rays to form the "surpénétrant" radiation after passing through several

millimetres of lead. Up to 1 mm. the proportion of these β rays is considerable. By turning back to the calculations previously worked out, we shall be able to estimate, for the apparatus in question, the proportion reached by β and γ rays in the radiation, through a thickness of 1 mm., and then of 2 mm. of lead.

For a thickness of 1 mm., let us consider lines A B and B C. According to the calculations made, we shall get the following proportions:—

$$\frac{6{,}700 - 4{,}580}{6{,}700} \times 100 = 31{\cdot}6 \text{ per cent.}$$

After 1 mm. of lead, there will be a radiation of 6,700 units, still containing about 30 per cent. of β rays.

For a thickness of 2 mm., let us consider lines D E and E F; we shall then get—

$$\frac{6{,}250 - 4{,}580}{6{,}250} \times 100 = 10{\cdot}72 \text{ per cent.}$$

After 2 mm. of lead, there will be a radiation of 6,250 units, which still contain about 10 per cent. of β rays.

It follows that if we possess curves of analysis relating to all the instruments, we can calculate roughly from the standpoint of physics the value of the different methods employed.

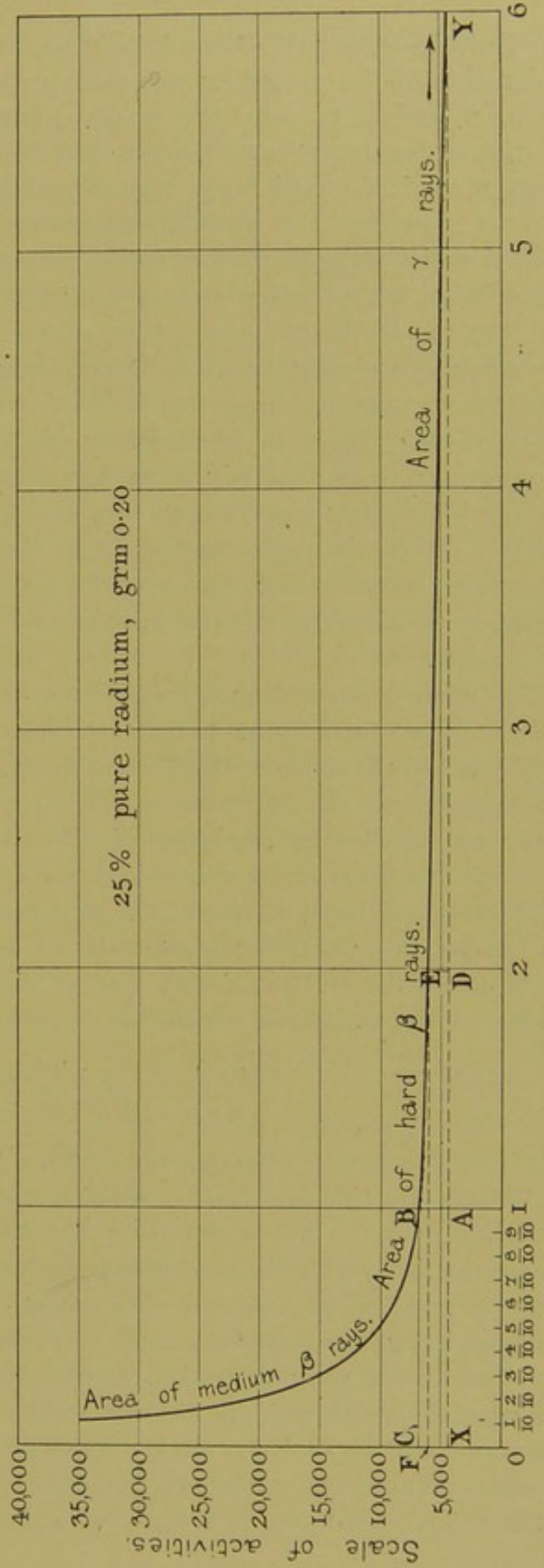


Fig. 11.—Scale in millimetres of lead (apparatus No. 1, pp. 46, 47).

But, to quote M. Beaudoin, "we must not deduce from a consideration of the preceding curves any physical law as to the absorption of α, β, and γ rays by the material; the establishment of such laws demands far more care than would be possible in radiumtherapeutic dosage, and it would be premature to push the analysis of a radiation too far at present. It would first be necessary to study and fix the relation which exists between the physical measurement and the clinical action on a large scale, before approaching specific examples, and it seems to us that the method of absorption, as we have stated it, might well serve for such an investigation. It is certainly better to try to get as much benefit as possible from this method without expecting more from it than it can give. It is evidently inaccurate in some cases, and has no pretence to be anything more than a useful, though imperfect, system."

The foregoing remarks are very important, and we entirely concur in them. It is nevertheless true that these measurements, in the form in which they are now presented to us, form an essentially scientific basis upon which to lay the foundations of a radiumtherapeutic system of dosage.

It is obvious that such measurements, by themselves, do not supply all the data necessary for practice. Although they are specially concerned with the whole surface of an instrument, it is possible, by a calculation of proportions (p. 47, column II), to ascertain approximately the radiations emitted by one portion of its surface; and this idea deserves careful consideration, since, in practice, it is precisely one such particular part which is most frequently used alone. But, in the numerous cases in which this portion corresponds to an irregular or distorted surface, it is more difficult to determine, in a sufficiently definite manner, the value of the radiation which has been used.

SUMMARY OF DATA REQUIRED FOR CALCULATION OF THERAPEUTIC RESULTS

The value of a therapeutic result can only be estimated by taking into account the principal conditions governing and varying the radioactivity. These fall under two headings; the first being concerned with the lesion itself, its nature, its more or less accessible position, its size, etc.; the second depending on the operator, that is, the person using the apparatus and selecting the doses.

The first conditions relate to clinical practice, and will be the subject of special consideration. In this section, we shall only group together those of which we have already spoken, and which concern the instruments themselves. The energy represented by each apparatus, constructed as we have just shown, varies according to—

1. The original activity of the barium salt of radium incorporated in the apparatus.

2. The weight of this salt.

3. The size and surface of the apparatus.

4. The distribution of the salt.

5. The quality of the fixative substance.

6. The intensity of the total available radiation, according to whether the entire surface of an apparatus or only a part of such surface is considered.

7. The qualitative value of this radiation, *i.e.* the proportion of α, β, and γ rays.

The first five of these data can be learned from the construction of the instrument, and have been definitely fixed.

The two others can only be ascertained after the apparatus has been constructed, and even then it is necessary to wait for a certain time, the radiation, which is weak at first, only reaching its maximum value in several months, according to the period necessary for maturation of the radium. This value is subject to variation with time, and must be verified about once in six months. It usually improves; that is to say, the instruments give a better output in course of time.

1 and 2. **Original activity and weight of salt contained in apparatus.**—The importance of this variation in energy will be easily understood. It is evident that a large amount of very active salt will provide a more powerful instrument than a small amount of weak salt, and we shall find the greatest differences in energy according to the different values of the incorporated salt. Its activity can pass through all the intermediate stages, from the state of pure radium salt, *i.e.* 2,000,000, down to 1,000, according to the amount of barium sulphate added to the pure radium salt, in the form of an inert, diluting substance. It should, however, be noted that a small quantity of very active salt will give a less powerful result than a large amount of much weaker salt, and the rules about surface and distribution, upon which we cannot too strongly insist, are based on this truth.

3. **Size and surface of apparatus.**—As early as 1906 we had shown how important it was to consider this subject of surface, in order to estimate the total energy of an apparatus, as well as the therapeutic reaction it is capable of producing. The condition of the surface may modify and disturb the proportion of values in a given original radioactivity of great strength.

Take, for instance, a flat, disc-shaped apparatus with a diameter of 0·002, containing in its varnish 0·002 of pure radium. If it is applied to

a lesion of the same size, we should expect to get, by reason of the intensity of the pure substance, a strong and rapid reaction, in any case much quicker than that given by an apparatus 2 cm. in diameter, containing 0·02 of radium, with an activity of 500,000. Quite the contrary, however, is the case. Our small apparatus would have to be applied much longer in order to have as marked an action as that produced by an instrument of weaker radioactivity, but larger size. The problem concerns the extent of surface, a point which is too often overlooked. The comparison between two instruments should, and indeed can be made only for the same surface. If, in the second apparatus mentioned, only a portion of 0·002 is used, this part of the apparatus will then be weaker than the first. A most important deduction follows from this, namely, that, in any calculation intended to be absolutely correct, it is necessary to indicate carefully what extent of surface of the apparatus has been used. It also follows that in the method selected for treatment of a particular lesion, account must be taken of the portion of the apparatus to be employed, and as it seldom happens that the entire surface can be utilised, the importance of these considerations will be obvious. Moreover, they are in harmony with what has been shown by the measurements for external radiation. Our applicator No. 1 (*see* table on pp. 46, 47) has an external radioactivity of 580,000 ; but if we use only 1 square cm. of its surface, the radioactivity of this portion will be only 20,500. It follows from this that the small instruments should generally be supplied with pure radium. On the other hand, large ones may do good service, even though the activity of the radium be weak.

4. **Distribution of salt.**—The foregoing remarks only refer, of course, to unequal distribution. For if a large quantity of salt be accumulated on a given surface, the value of the radiation will be increased. Most of our instruments are constructed in such a way that the best output is obtained by 1 cg. of salt to 1 square cm. of surface. On the other hand, the distribution will yield a different total, according to whether the salt be spread over a flat surface, or over one which is either cylindrical or spherical. All the rays combine their action more or less on the former, and it therefore accumulates ; whilst it is easy to understand that, on a cylindrical surface, rays proceeding from particles in directly opposite positions can scarcely increase each other's power.

5. **Quality of fixing substance.**—We have already spoken at length about the part played by the fixing substance.

6. **Total available radiation.**—We have already emphasised this essential point, and mentioned the means of obtaining the measure-

ment of apparatus, whether uncovered or with screens. This is a most important scientific guide in practice. It is therefore worth while to find out whether there is any way of analysing a radiation on the spot, immediately before it is applied. The combination of screens is so varied that it would be impossible to analyse all the instruments in accordance with it. Can we then calculate roughly the radioactive output when a screened apparatus is ready for application? There is no absolutely exact system, but with a certain amount of practice, more particularly in the case of lead screens, we may take advantage of the phosphorescent reaction of a "toile" in barium platino-cyanide, and of the discharge of a simple, non-graduated electroscope. These methods are only approximate, and subject to different interpretations by each operator. As regards the luminosity of platino-cyanide, it may perhaps some day be possible to get a scale of colours corresponding to the known degrees of energy. When we notice a scarcely visible luminosity, and a very slow discharge from the electroscope, produced by radiation emitted from an apparatus covered with a lead screen, we know that with such a screen the apparatus can be left in position for several nights without disadvantage. The discharge of a simple electroscope is obviously a very rough way of measuring the energy. As this instrument is discharged, the gold-leaf will fall more or less quickly, according to the intensity of the energy supplied by an apparatus. From the rate of this fall the amount of radiation can be approximately calculated at a glance, but only if the fall is sufficiently slow, which never occurs except with weak radiations. This method, however, primitive as it is, may sometimes be of service. Here also it might be possible to make the condenser electroscope a sufficiently accurate means of temporary measurement. A graduated scale, in front of which the gold-leaf will be displaced during the time necessary for it to pass from one point to the other, and the calculation of distance of the apparatus from the fixed rod to the small external knob, will enable us, with the help of a table, to estimate the energy. These measurements can be made by keeping the window of the "cache" against the radium apparatus. The radiation emitted through the opening, which radiation proceeds from the only portion of the surface utilised, can thus be estimated.

7. **Qualitative value of radiation.**—This point is generally as important as the preceding one, since we know that the rays, whether slightly penetrating, of medium penetration, "surpénétrant," or "ultra-pénétrant," produce different reactions. The two former act on the surface. They usually occur only in intense total radiations of great quantitative value, and are used for short applications.

The latter, on the contrary, act at a depth, occur in an isolated state only when weak in quantitative value, and require long applications. It is therefore necessary to take into careful consideration the proportion of α, β, and γ rays in the radiation.

It will be seen from the foregoing remarks that the therapeutic dosage relating to the instruments enables us to arrive at a great many data, amongst which the qualitative and quantitative value of the radiation, and the amount of the surface of the apparatus utilised, are of paramount importance.

Having ascertained these, it remains to determine the position and duration of applications, their spacing, and the arrangement of the series of exposures necessary to obtain certain results. We have already explained the means of regulating these, and shall next proceed to consider them from a clinical point of view.

The conclusions which we have so far reached are the extreme convenience and adaptability of the instruments; the number of different applications which can be made with a single applicator; the many combinations possible in practice; and lastly, the variety of the radioactive energy placed at our disposal. This energy is quite peculiar to radiumtherapy, and clearly marks it off from other physiotherapeutic agents. Its originality and specificity are due both to the activity of the α and β rays, and to the great power of penetration possessed by the radiations.*

* We have seen in the physics section that α, β and γ rays, although similar in their nature to anode, cathode and X-rays, differ from them in their greater power of penetration. A very interesting difference of action between X-ray treatment and radiumtherapy results from this in practice, since the anode and cathode rays are not available, and the X-rays are stopped by about 1 mm. of lead.

PART III

CLINICAL THERAPEUTICS

CHAPTER I

GENERAL CONSIDERATIONS ON REACTION

In the first Part of this work we explained the nature of radium and radioactive energy.

In the second Part we showed how such energy might be varied, measured, and applied.

It now remains to describe the results given by these methods in the treatment of diseased tissues, and how the tissues behave under the influence of the rays ; in short, how reaction takes place.

The study of this reaction is connected with that of the pathological groups subjected to radium. It will be considered from a special point of view in the course of the chapters on therapeutics, but since it admits of certain generalisations, it will be more convenient to give a summary of them first in a special chapter, in order to make the subject clear.

HOW REACTION IS TO BE EXPLAINED

When the cellular elements of morbid tissues are subjected to radium rays, a special effect is produced on them, and they react in a way peculiar to radium treatment.

Reaction is therefore the response of the tissues to the disturbance resulting from their penetration by radioactive energy. It includes all the alterations produced in them by the influence of radium, whether visible or clinically invisible. It may sometimes be very intense, without causing the slightest trace of inflammation, or, on the contrary, it may be accompanied by a certain degree of inflammation which may increase until it produces necrosis of the tissues.

The term " reaction " does not *necessarily* imply a harmful effect, since no curative action can take place without it. But although reaction certainly leads to healing, it is necessary not only to distinguish between its various degrees, but also to recognise, in addition to useful,

therapeutic and curative reaction—whether visible or invisible, inflammatory or otherwise—that which, from a therapeutic standpoint, is useless. (*See* table on p. 93.)

These different degrees are determined both by the nature of the tissues and by the quantity and quality of the energy introduced.

I. REACTION DEPENDING ON NATURE OF TISSUES AND QUANTITY OF ENERGY EMPLOYED

The principle may be laid down that no tissue which has been penetrated by a sufficient quantity of the rays, can escape a certain degree of reaction.

According to the rays used, the dosage administered, and the nature of the tissues, this will be produced at different depths, beyond the limits of the points of application, and with varying intensity.

Some tissues can be influenced very easily; they are susceptible, and easily acted on by the rays. Others are more refractory, but the resistance they offer is never quite complete. Indeed, we may affirm that no tissue escapes reaction, since, even in cases of resistance or inertia after the employment of comparatively strong doses, an effective result may be obtained by increasing the doses. A time always comes when the cell, whatever its resistance, undergoes a certain degree of degeneration. It is injured in some way, and, being no longer able to react, is destroyed. In these individual cases, either an ulcer or a crust is formed.

Such destructive action is very valuable in the treatment of certain lesions. It is commonly but inaccurately described as a "burn." As it was by this excessive reaction that the effect of radium was revealed when it first began to be used (the "burns" of Becquerel and Curie), it is natural that it should have made a great impression on the public. Even now, the word radium is for most people only another name for "burn." This impression is still so strong that many physicians—without, however, denying what we have frequently demonstrated,* namely, that tissue degeneration may be followed by good and useful repair—can see in radium nothing but a destructive agent. Even authorities on the subject have sometimes been unable to free themselves entirely from this idea, and confuse reaction with degeneration or destruction. We have shown, however, from the commencement of our work, that effective reaction is of two kinds, inflammatory and non-inflammatory, whereas they recognise only the former. We consider that the greatest value of radium resides in its selective action, which may be called

* Wickham and Degrais, French Medical Congress, Paris, October, 1907: "Valeur des tissus de réparation."

"specific," and is independent of all visible superadded inflammation. We will now describe in what this action consists.

Selective action of radium.—Certain pathological tissues react to radium in such a way that the expressions "specificity," "special selectivity," are perfectly appropriate to the action produced. The tissues undergo retrogressive changes, and are modified without the production of a visible inflammatory stage.

This retrogression may be obtained either by comparatively weak doses or by strong doses, and with rays of strong or weak penetration. Even in selective tissues, it is easy to recognise very marked differences of resistance. The doses necessary for the cure of certain lesions by selective action are much larger than those which could be borne by others.

We shall often have occasion to return to this subject. It is the total dosage in the course of a whole treatment which determines reaction, and this must be constantly varied, according to the nature of the tissues and the results desired.

We presented a communication on the specific action of radium at the Tenth French Medical Congress, held at Geneva, September 5th, 1908, and as this point deserves special elucidation, we reproduce here the principal passages of this paper.

"At the Ninth French Medical Congress, held in Paris, we read a paper on the repair of tissues following the ulcerative reaction produced by radium. This caused an erroneous belief amongst many of the members that our methods only brought about the results stated after a *necessary* stage of severe reaction and ulceration.

"It is true that in the treatment of some affections (pigmentary nævus, tuberculosis, fibro-sclerotic cicatricial bands, etc.) it seems necessary, in most cases, to have recourse to the destructive power of radium, and the remarkable manner in which spontaneous repair usually takes place justifies the frequent use of this method. But to limit the action of radium to its destructive effect would be a strange misunderstanding of its true value, and a failure to appreciate the biological interest attaching to its study.

"Radium is, in many cases, an agent of special selection which acts as a specific agent and fully deserves this epithet; that is to say, that without superadded intense reaction, without destruction, without radium dermatitis—in a word, by the 'dry method' (Danlos) tumours may be resolved, and diseased tissues altered and deviated from their pathological course, giving place to healthy ones. This specific action is particularly clear in some forms of carcinomatous neoplasm, both large and small. Our later investigations have confirmed these earlier experiments, and by extending them to other pathological tissues we have been able to establish

and formulate the systematic use of various processes by which the specific action of radium rays has been manifested.

"It is, in fact, entirely a question of dosage. Our object was to ascertain what doses (as regards both quantity and quality) were necessary in order to obtain the specific action of radium.

"We have studied carcinomata of the breast, uterus, etc., and are now in a position to state that, in several inoperable cases, a decided effect has been obtained on the tumours. Their development has been temporarily arrested by the treatment, and in some cases they have been reduced, with decrease in the accompanying pain, and without added inflammation.

"Another action of radium which should be noticed is that which extremely penetrating rays may have, without causing surface irritation, on glandular masses infiltrated by an invading new growth. In a case of carcinoma of the breast, which was inoperable on account of the presence of glandular masses developed in the axilla, and above and below the clavicle, with symptoms of pressure on the trachea, we have obtained very considerable diminution of these symptoms. In another instance an œdema of the arm was clearly reduced in consequence of applications made in the axillary region; all these results being obtained without surface reaction.

"Do not these facts afford sufficient proof of what has been stated? Is anything more needed to show the truly selective and specific properties of radium with regard to carcinomatous neoplasms?

. . . . . .

"In the course of our investigations with regard to the cure of angiomata by radium, we have been led to conclusions of the same kind. Large angiomatous areas (prominent, erectile, and pulsating), angiomatous tumours, actual cavities containing blood, and port-wine marks could not be subjected to severe and destructive inflammation without risk of hæmorrhage. It was necessary to avoid any solution of continuity of the surface, and we succeeded in reducing some of them without added inflammation.

. . . . . .

"But the specific action of radium is not confined to carcinomatous and angiomatous tumours; cheloidal tumours are also benefited by it. Enormous cheloids can be reduced without visible inflammatory reaction, and the turgid appearance of some cheloidal cicatrices disappears, to be replaced by a flat cicatrised surface, which is more easily concealed. The specific action of radium has also relieved the accompanying pain, often very severe.

. . . . . .

"There is another class of diseases, of quite a different order, in which radium may act in the same way as a specific agent. Secondary inflammation can, and indeed must, be avoided in the treatment of certain pruriginous dermatoses. By means of very short applications—one to three minutes on each occasion—and the use of large and powerful apparatus, we have been able to cure, without inflammation, chronic eczema, lichenification, neurodermatitis, local pruritus, and superficial neuralgia, especially that following zoster.

"Can it then be said that the best methods are always those which avoid inflammatory reaction? Certainly not, and from a practical and therapeutical point of view, combined methods are often very useful. The object of this paper, however, is not to discuss the best means of employing radiumtherapy. We only wish to establish the principle of the specificity of radium, as shown by our first researches, on a wider basis, and we think that we have succeeded in doing so by means of our recent experiments."

Value of inflammatory reaction alone or combined with specific action.—From a theoretical point of view, it was of the utmost importance to lay stress on the specific rôle of radium, and to show the weight we have always attached to it. The subject, moreover, is one which possesses great scientific interest. From the practical point of view it must never be lost sight of, so that it may be employed as frequently as possible, above all when æsthetic results are desired.

But to have recourse to selective action alone would be to fall into the opposite error or exaggeration. This would greatly lessen the value of radium, and render only a portion of its advantages available. There are lesions which are not amenable to specific action, but which benefit by destructive action. With the practical object of saving time, even in diseases in which specific action alone would be sufficient for a cure, but only after a long period, it is sometimes well to proceed partly by destruction, and thus to combine the two methods.

Inflammatory reaction from a clinical point of view.—The disorganisation produced by radium has an absolutely unique interest, because it does not in any way resemble that produced by caustics or other destructive means. Its clinical evolution with respect to non-inflamed tissues, such as vascular and pigmentary nævi, is as follows:

When radium has been applied in a dose sufficiently strong to produce inflammation, a period elapses, varying from one to three weeks, during which the tissues preserve a normal appearance. The surface then reddens, itches slightly, is tender to the touch, swells a little, and becomes gradually covered with a crust. Sometimes a bulla, followed by serous exudation, precedes the formation of crusts. Some days later, according to the degree of reaction, this crust will rest on a base which may be comparatively dry, or, on the other hand, markedly ulcerated and purulent. It has a peculiar appearance and colour, usually suggesting the crust of impetigo. It lasts from a week to a month, during which period it frequently falls off, and is formed again, being less thick each time. There is no fixed rule for the date of the appearance of the crust, the length of the inflammatory period, or the repair of the tissue; they are in direct relation to the dosage employed and the nature of the tissues.

With respect to inflamed and ulcerated tissues, such as epitheliomata and ulcerated lupus, if the rays have been used for a destructive dose, the inflammatory reaction will extend beyond the diseased tissues, and will produce a fresh ulcer, covered by a crust, which must be distinguished from the crusts produced by the neoplasm. By degrees the ulcerated base will dry up, and the crust will fall off of itself, leaving a smooth and uniform surface, with a healthy appearance.

When healthy tissues are strongly affected by the rays, their reaction is similar to that which we have just described for inflamed tissues.

Reaction from the histological point of view.—In dealing with the histological aspect of the question, we cannot do better than quote *in extenso* the interesting paper on this subject published by Messrs. Dominici and Barcat, in 1908, in the *Archives des maladies du cœur, des vaisseaux et du sang.*

Action of radium on vascular connective tissue.—"In the present state of our knowledge of pathological anatomy, it would seem that the disappearance of inflammatory conditions and tumours on which radium exercises a curative action must essentially depend upon two phenomena, which are as follows :

"1. The destruction by Becquerel rays of the anatomical elements modified by inflammation and by the progress of the tumour.

"2. The absorption of degenerated tissue by the phagocytes and its replacement by sclerotic tissue.

"We admit that some affections treated by radium—lymphoid tumours amongst others—are cured in accordance with the histological process in question. On the other hand, we cannot consider this process to be the only result of employing radiumtherapeutics in the healing of diseased tissues. This opinion is justified by a study of the effects of radium applications on inflammatory conditions, and on tumours of the connective tissue, as well as on epithelial tumours. Instead of hastening the degeneration of connective-tissue cells injured by inflammation, or by the progress of the tumour, the radium rays, in many cases, revive the vitality of these elements, and subject them to an evolution differing from that which the pathogenic influences were producing. The special action of the Becquerel rays is then substituted for that of these pathogenic influences. Their effects are manifested either by the arrest of the inflammatory process or by the resolution of the tumour, and by a change of structure in the connective tissue. This change consists (*a*) in metamorphosis of the vascular connective stroma into angiomatous embryonic tissue ; (*b*) in transformation of this embryonic tissue into connective fibrous tissue of regular texture. In such a case, the healing of inflammatory conditions or of tumours is the function of a special cellular evolution produced by Becquerel rays. The healthy connective tissue itself undergoes this evolution. The study of the

changes in normal connective tissue under the influence of radium rays must naturally precede that of the alterations in pathological connective tissue.

"**Modification of normal connective tissue.**—If we expose the skin of an adult guinea-pig, in a normal state of health, to a series of radium applications of a therapeutic nature, according to the technique indicated below, and if the animal be examined a month after the application, we shall see that those portions of the integument which have been irradiated appear as small hairless zones, smooth, colourless, and supple. At this stage the structure of the skin is entirely changed; the hair bulbs, sebaceous glands, and sweat glands are atrophied, whilst the vascular connective tissue of the corium is transformed into embryonic tissue. In this article the modifications of the corium will be specially considered. We shall describe and follow these changes, after briefly recalling the normal structure of the cutaneous connective tissue of the adult guinea-pig.

"The papillary and sub-papillary layers and the derma are formed of connective-tissue bundles and a network of abundant elastic fibres, crossing each other, in varying degrees of obliquity, in a loose system of meshes on the surface of the derma. The interstices of the connective-tissue bundles are occupied by fixed cells, scanty, atrophied, and isolated. Here and there bunches of smooth muscle fibres cross the connective-tissue field, which is intersected by lymphatic capillaries, and traversed by small blood-vessels. Under the influence of radium this texture is completely changed. The connective-tissue bundles and elastic fibres have almost disappeared, and are replaced by innumerable connective-tissue cells, ramified and spindle-shaped, approaching each other and anastomosing in a network of narrow oblong meshes. The elements of this network are no other than the fixed cells of the connective tissue which have been multiplied, after undergoing a kind of embryonic degeneration. The cellular network lines the walls of numerous cavities filled with red corpuscles and leucocytes, amongst which ordinary polynuclears predominate. These cavities are those of the small blood-vessels, which have dilated and become transformed into embryonic capillaries (transformation of the true cells of the vessel walls into embryonic cells of the cellular network, plasma-cell formation of the endothelium). These embryonic capillaries are, moreover, extended by budding of their terminal points. Finally, the vascular connective tissue acquires a structure at once embryonic and angiomatous. The new formation is pure, for it is free from any inflammatory character. Here and there some red corpuscles and lymphatic cells exude into the meshes of the cellular network, but the lymphatic cells in question are of the embryonic type. There is no sign of deposition of fibrin in the meshes of the cellular network, of diapedesis of the polynuclears, of phagocytosis, or of transformation of lymphatic cells into plasma cells. On the other hand, as regards the vessels, there is no thrombosis, swelling, proliferation of the endothelium in the vascular cavities, nor thickening of the coats of these vessels, for they undergo embryonic retrogression, and become blended with the myxomatous tissue which forms the network of connective-tissue cells.

Myxomatous tissue prevails over angiomatous tissue, and this predominance of cellular proliferation over the development of vessels becomes marked in proportion to the evolution of the histological process. Indeed, in the second stage, the size of the blood cavities diminishes, and the capillaries shrink to such an extent that their lumen becomes practically non-existent. Some of them are even transformed, in consequence of the adhesion of their walls, into complete spindle-shaped cells, placed end to end, and apparently incorporated in the connective-tissue network (two or three months after the last application). During this time the anastomosing connective-tissue cells throw out fibrils. The myxomatous tissue is then transformed into a sort of flat, fibrous tissue, the fixed cells of which preserve in many particulars a conformation similar to that of myxomatous tissue. Thus the final cicatrix is gradually produced, a cicatrix having neither the structure of the corium of normal skin, nor that of post-inflammatory sclerotic tissue. Its texture differs from that of the corium of normal skin, the newly formed connective-tissue bundles and the cells which separate them being regularly superimposed, and forming lines parallel to the surface of the body. This arrangement differs from that of the adult corium of the regular type, which is a collection of thick connective-tissue bundles, crossing one another in every direction, and forming a boundary to fissures in which are placed sparse fixed cells, having an uncertain direction. The structure of the cicatrix differs from that of the sclerotic post-inflammatory tissue by its regularity, its uniformity, the absence of fibroid perivascular rings and of vascular obliteration. It is composed of connective-tissue bundles, separated by elongated fibroblasts. The fibroblasts and connective-tissue bundles are parallel both to each other and to the surface of the skin. This texture is comparable to that of a fibroma, and even suggests that of a young fibroma, considering the quantity, conformation, and relations of the connective-tissue cells which contribute to the formation of the cicatrix. The fibroblasts are numerous, and at certain points their mass exceeds that of the connective-tissue bundles, their substance being formed of a more or less thick chromoplasm, containing a still bulky nucleus. Their anastomoses continue to be visible in many places. But we hasten to add that this is only a matter of analogy. The new formation differs from the fibrous tumour in two ways: (1) the tissue of which it is formed does not exceed, either in surface or depth, the limits of normal connective tissue; (2) it is transformed by degrees into connective fibrous tissue, rich in elastin. The fixed cells become rarefied six or seven months after the beginning of the experiment; their substance and nucleus grow smooth, whilst their chromoplasm disappears, becoming changed into hyaloplasm; the anastomoses which unite them cease to be visible, and the connective-tissue bundles separating the layers of fibroblasts thicken, while the elastic fibres reappear in increasing proportions, those portions of the derma which have been subjected to the influence of radium being differentiated from those not affected by it by the alternation and regular direction of the connective-tissue bundles and fibroblasts. Their texture is analogous to

that of a flat fibroma with connective-tissue bundles and stratified cells arranged in a regular manner.*

"The three following figures (Figs. 12 to 14) refer to the normal skin from the biopsy of a guinea-pig, fixed and stained thirty days after the completion of a series of radium applications.

Commencement of applications	April 11th
Completion	May 11th
Number of applications	10
Duration of each application	5 minutes
Entire duration in one month	50 minutes

"Round varnish apparatus, 2 cm. in diameter, containing 0·025 of radium sulphate, with an activity of 500,000.

Activity: total radiation	62,000
α	2
β	84
γ	14

"*Results.*—On May 8th a small crust appeared on the surface at the point of application, followed by a slight ulceration. On May 14th the crust fell off, leaving white skin, without hair or pigment.

Fig. 12.—Portion of skin of guinea-pig which has not been submitted to the action of radium, but is situated close to the irradiated region (Dominici and Barcat).

1, Lower portion of epidermis, situated under horny layer, and above derma. D, derma showing connective-tissue bundles, fixed cells, smooth muscular fibres and blood capillaries; the connective-tissue bundles appear like undulating filaments crossing one another in every direction; the connective-tissue cells show only their more or less opaque nuclei, their substance being almost invisible under normal conditions; under the same conditions, these cells are widely spaced in the derma. C, connective-tissue bundles. 2, nuclei of fixed cells. 3, bundles of smooth muscular fibres. 4, lateral part of a hair bulb. 5, blood capillary, on the right of which is a second capillary.

"Action of radium on the histological processes of inflammation and of connective-tissue and epithelial tumours.—Radium rays are capable of modifying diseased as well as healthy skin. It is for this reason that experimental cutaneous tuberculosis of the guinea-pig, certain atypical sarcomata of the human skin, and also epitheliomata, can be healed by means of complete transformation of sarcomatous tissue into tissue of a fibrous nature.

* Two points must be noted with regard to the structure of this new formation: (1) the tissue of which it is composed does not superficially exceed the limits of normal connective tissue; (2) elastic fibres are formed in considerable proportions, and at the same time as the collagen of the connective-tissue bundles. These two points explain the regularity and suppleness of the cicatrix after the application.

"*Experimental cutaneous tuberculosis.*—The action of radium on cutaneous tuberculosis is characterised by three phenomena, viz.:

"1. Diminution of the simple inflammatory perituberculous reaction (disappearance of the accumulation of polynuclears of macrophagocytosis, transformation of lymphatic cells into plasma cells, and development of nodules possessing a lymphoid structure).

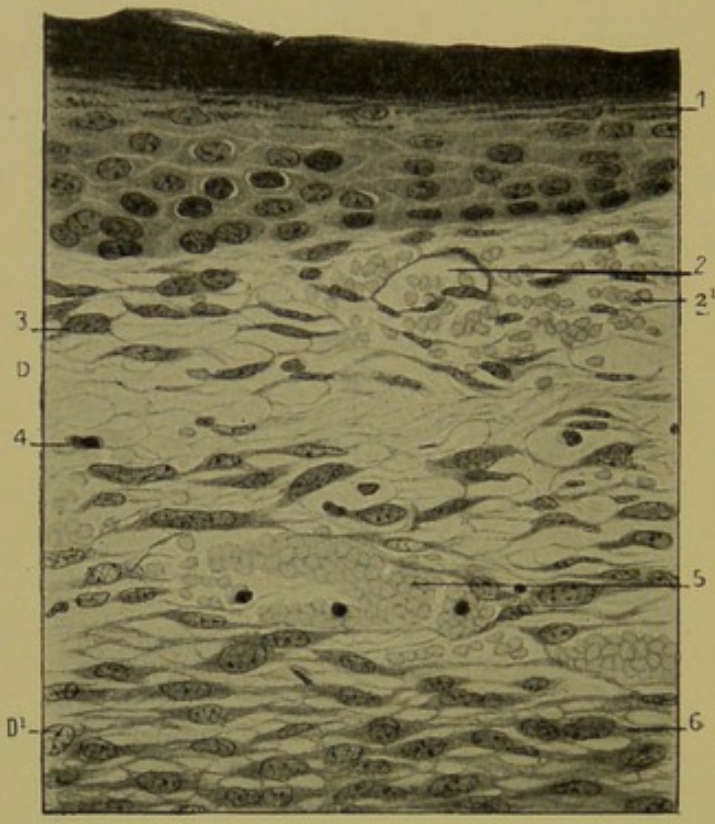


Fig. 13.—Portion of skin of guinea-pig, subjected to radiation, and removed from the periphery of the zone of application of the radium (Dominici and Barcat).

1, Thickened epidermis. D, subepidermic portion of derma. D', derma proper; in these two lesions vascular connective-tissue reactions may be seen, viz. (a) multiplication and hypertrophy of fixed cells, and their grouping in a network; (b) dilatation of blood capillaries and extravasation of red corpuscles, the reaction being more marked in the deep portion of the derma D' than in its superficial portion. 2, dilated blood capillary. 2', red corpuscles extravasating into the interstices of connective tissue. 3, hypertrophied fixed cells. 4, lymphatic cells or migration into connective tissue. 5, capillary much distended by congestion of blood. 6, network formed by anastomosis of connective-tissue cells of derma.

"2. Organisation of the vascular connective-tissue stroma, which was the seat of this simple inflammatory process, following the type of the angiomyxoma described above.

"3. Extension of this process to the tuberculous follicles themselves, the epithelioid cells of which lose their globular conformation, elongating and anastomosing in a network of fixed cells of embryonic type.

"As a result of this the epithelioid tissue of the tubercles is changed—at least, in part—into embryonic myxomatous tissue.* The cure is completed by the transformation of myxomatous into sclerotic tissue having a texture identical with that of a pure fibroma.†

"*Sarcomata.*—The retrogression of atypical sarcomata takes place—at least, in some instances—according to the law which we have just formulated. The size of the body and of the nucleus of its enormous cells gradually decreases. As they shrink the neoplastic elements elongate, the contours of their nuclei become regular, and they finally assume the

* We say that this transformation only takes place in part, for it is quite evident that elements which have undergone the commencement of caseation are incapable of taking part in a histoblastic process. Such elements will be destroyed and absorbed.

† It will be obvious that we are only considering here cases in which radium rays, employed in the manner we have indicated, influence an early tuberculosis, where the sclerotic effects peculiar to that disease have not yet been produced. In more advanced cases we should find ordinary sclerosis in the irregularly arranged fibrous bundles, perivascular sclerosis, endovascularity, etc.

form of large embryonic connective-tissue cells, anastomosing in a cell mass similar to that of the myxomata. The resemblance is the more striking as they are surrounded by myxoid tissue, in which connective-tissue fibrils are gradually developed. The tissue of the sarcoma is thus transformed into myxomatous tissue, which ultimately changes into tissue resembling that of a fibroma.

"*Epitheliomata.*—Under the influence of the radium rays, the cells of cancroids of the skin or of the muco-cutaneous regions (the lips) gradually diminish in size. This atrophy corresponds—not to the metamorphosis of these definitely formed elements, but to their destruction. The epitheliomatous cells disappear, either by means of a progressive absorption of their protoplasm and nuclei, or by a sort of granular dissociation of the two parts forming the cell. During this time the inflammatory processes which accompany the development of every epithelial tumour are arrested, whilst the vascular connective tissue is organised according to the method which has just been described.

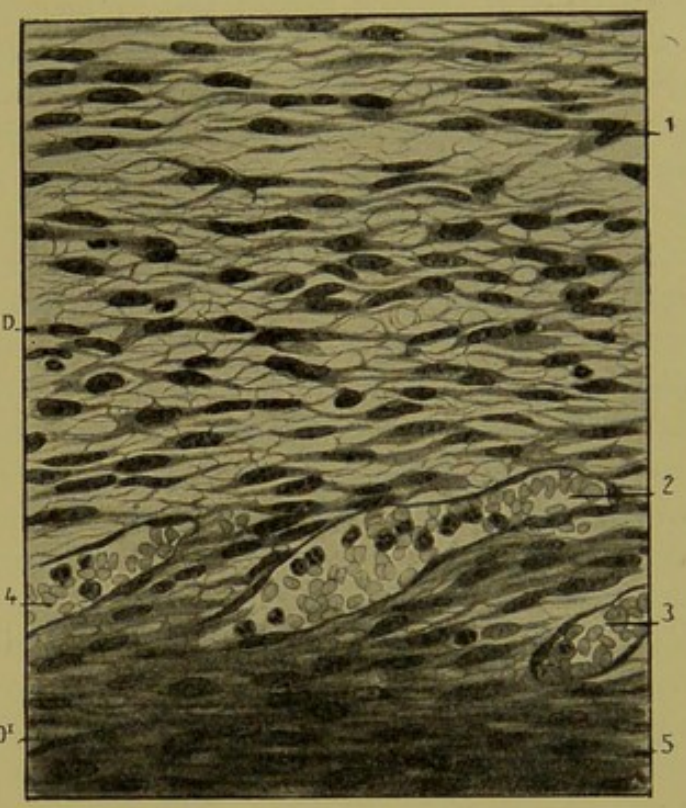


Fig. 14.—Central part of irradiated zone of skin of guinea-pig (Dominici and Barcat).

D, Upper portion of derma. D', lower portion of derma. The reaction of the connective-tissue cells is less marked in the upper than in the lower part of the derma. 1, network formed by anastomosis of fixed cells of upper part of derma. 2, 3, 4, blood capillaries with extremely dilated embryonic walls, containing both red corpuscles and a larger quantity of polynuclears than normal. 5, network formed by multiplication and anastomosis of fixed cells in deep portion of derma.

. . .

"In fact, the action of radium on the integument (at least in therapeutic applications) can be shown to produce the same effects, whether the condition of the skin be normal or diseased. The elements of the epidermis, physiological (hairs, sebaceous and sweat glands), or pathological (epitheliomatous cells), are absorbed by degrees and disappear, whilst the overlying Malpighian epithelium persists. The cells of the vascular connective tissue, whether normal, or modified by inflammation or by a sarcomatous process, have an alternating evolution. In the first stage, they return to the state of embryonic connective-tissue cells; in the second, they again arrive at maturity, under the form of elongated fibroblasts, which are superimposed, and follow the regular lines of stratification, again forming connective-tissue bundles and elastic fibres."

These researches of Messrs. Dominici and Barcat explain what our clinical practice had already shown us. We have, indeed, more than once insisted * on the value of the clinical repair which follows inflammatory reaction, and which sometimes allows us to give the new tissues the name of "tissus de reconstitution." It is precisely this special tendency communicated by radium to the elements of repair which justifies a preference for its use in place of caustics and other means of destruction. The restored surfaces are usually supple, smooth, and uniform, neither raised nor depressed, and lighter in colour than the normal skin. All degrees of restoration may be observed, according to the amount of reaction, from almost a normal aspect of the tissues down to the appearance of actual scars.

Complications detrimental to æsthetic appearance of repaired tissues.—There are, however, three complications which sometimes spoil the picture, viz. depressed scars, telangiectases, and pigmentation. They do not occur when the selective action of radium is alone employed. On the other hand, they are not of much importance in the treatment of tumours of a grave character, or lesions which cause disfigurement, such as large and deeply coloured prominent vascular tumours. It is, however, otherwise when the lesions treated are not very marked and easily concealed, and when radium treatment has an æsthetic object, as, for instance, the reduction of prominent cicatricial bands, or decolorisation of pigmentary or vascular nævi which are flat, superficial, and very pale. It is especially with regard to such lesions that depressed scars, telangiectases and pigmentation must be taken into serious consideration. This subject will be treated of more particularly in the chapter on angiomata, but it is now necessary to show what are the indications for their treatment by radium, how they can best be avoided, and what ultimately becomes of them.

Depressed scars.—Depression of cicatrices is very rare. It must not be confused with reduction of pathological tissues, which were somewhat raised before treatment, to the level of normal tissues. When true contraction occurs, it is the result of too large doses and excessive inflammation.

But there is another cause of atrophy and contraction which seems to us sufficiently obvious, and easily avoided; it is quite as frequently due to too much care as to the want of it. Too much attention—such as removal of the crust every day, cleansing of the ulcerated surface with strong antiseptics, too frequent dressings; in short, the care usually advised for ordinary wounds—does not seem suitable for the inflammatory

* Wickham and Degrais, French Medical Congress, Paris, October, 1907: "Valeur des tissus de reconstitution."

reaction peculiar to radium. The repair must be allowed to take place *spontaneously*. The crust following the inflammation will be the best protective dressing. It should be allowed to remain, only the periphery being cleansed. The cure will be more rapid, and the result better.* When there is want of care, *e.g.* neglect of cleanliness, secondary infection, hairs caught in the crust, scratching with the fingers, tearing off of the crust, it is evident that every complication which accompanies infected and neglected ulcers may be expected.

Telangiectases.—The possessor of radium seldom fails to apply his apparatus first to his own skin, and in most cases he sees the scars resulting from strong reaction covered, after a certain time, by small telangiectases. This fact made us very cautious at the beginning of our experiments, and, indeed, it must always be a cause of anxiety to the radiumtherapeutist. We ascertained by degrees that these telangiectases, though frequent on healthy skin, occurred less often on pathological tissue. Many of our cicatrices date back several years, and show no trace of them. We have, however, observed the appearance, from the third to the eighth month, of numerous and closely grouped telangiectases on the areas exposed. Now this complication is almost always produced by too large doses and neglect of inflammation. In the majority of cases it could, no doubt, be avoided. Indeed, what we have just said about the cause of depressed scars applies equally to the production of telangiectases. When once produced, they may be treated by thick filtering; we have obtained their removal, in several cases, by the isolated action of very penetrating rays and long applications. They can also be treated by the galvano-cautery.

Pigmentation.—Pigmentation is sometimes produced, either at the periphery of the surfaces treated, or in small points disseminated in the centre of these surfaces. We have not exactly ascertained its cause. It seems to appear more readily on skins which are seborrhœic and abound in pigment, and we believe that it also results from a want of homogeneity of action. The perfect distribution of the grains of radium salt on the surface of the apparatus will be found a good preventive. The secondary rays of Sagnac, which should be intercepted, may play some part in its production. The method of application at a distance, which enables the tissues to be permeated in a more uniform manner, would seem to be one way of avoiding it. When it has been produced, there is no occasion, except in some few cases, to attach much importance to it, for it becomes almost obliterated in course of time.

* An exception must be made if, the proper doses having been exceeded, a crusted ulcer is formed which is slow in healing. It will be then necessary to remove the crust once or twice, to cleanse with diluted Alibour water, and to allow it to form again, until repair takes place by itself.

So far, we may consider these sequelæ, taken as a whole, very rare, and for the most part preventable. Sometimes they are of secondary importance; sometimes, on the contrary, they require such attention as we have recommended for flat, superficial, and slightly coloured nævi. Certain idiosyncrasies which may produce the preceding complications, in spite of carefully regulated dosage, must also be taken into account. It should be repeated here that the correct and effective application of radium requires very long and thorough experience.

We are now in a position to formulate the following conclusions from the general indications given above:

1. Reaction does not necessarily imply a destructive effect; there may be strong reaction without inflammation or destruction.
2. Destructive inflammatory reaction is sometimes useful, and even necessary; it should not be rejected at first sight.
3. Specific, non-inflammatory reaction must not be overlooked.
4. All reaction, of whatever kind, is determined as much by the dosage adopted as by the nature of the tissues.

In order to make these statements clearer, we have put together in the table on page 93, which must only be considered from a clinical and schematic point of view, the general conditions of reaction. Some of the divisions are incomplete, but it will help to make plain the various meanings of the word "reaction."

II. REACTION ACCORDING TO QUALITY OF RAYS. RESPECTIVE VALUE OF α, β, AND γ RAYS

ISOLATED "SURPÉNÉTRANT" RADIATIONS. RADIATIONS CONSIDERED AS A WHOLE

We have hitherto studied the nature of reaction, the changes which constitute it, and the proper interpretation of the term. In order to determine the respective values of α, β, and γ rays it is important to ascertain whether it is possible to attribute a special kind of reaction to each group of rays, considered individually, and also whether this varies according to the rays by which it is called into action. In the chapters on physics and mensuration, we have considered the characters which distinguish the rays from each other, and we must again lay stress on those which it is most important to remember in order to form a correct estimate of reaction, viz.:

1. Power of penetration, a knowledge of which will show theoretically the depth at which the rays produce reaction.
2. Quantitative intensity (chiefly determined by the number

TABLE OF REACTIONS

- **A. Therapeutic Reaction** (correctly proportioned doses).
  - On pathological tissues extending more or less deeply and affecting the cutaneous or mucous layers.
    - *a.* Without any added ulcerative stage, or surface irritation.
      - This form of reaction exists only in diseases which yield to the specific and selective action of radium. — *e.g.* cheloids, carcinomata, eczemas, angiomata, etc.
    - *b.* With a destructive stage, ulcerative or necrotic, affecting the surface of the tissues.
      - *a.* For diseases of the first group in which this reaction is not *necessary*, it is sometimes *useful*, in order to gain time.
        - In this case the specific and destructive actions are combined in various degrees. There is destructive action on the surface, and specific action in the deeper tissues.
      - *b.* This form of reaction is necessary in diseases which do not appear to be influenced by the selective action of radium. In other words, to cure these lesions we must have recourse to the destructive power of radium, and rely upon the reparative power of the tissues. — *e.g.* pigmentary nævi, cicatricial fibro-sclerotic bands, tuberculosis, etc.
  - On pathological tissues extending more or less deeply, but not affecting the cutaneous or mucous layers.
    - *a.* Without clinically visible inflammatory stage.
      - *a.* When the disease yields to specific action. — *e.g.* carcinomata, vascular tumours.
    - *b.* With clinically visible inflammatory stage.
      - *b.* When the disease does not respond to specific action. In this case it is necessary to modify the overlying tissues in order to proceed to the destruction of the subjacent pathological tissues.

- **B. Non-Therapeutic Reaction** (errors of dosage, or individual susceptibility and idiosyncrasy).
  - When the reaction has been—
    - (1) Insufficient or excessive.
    - (2) Accidental and unforeseen.
    - (3) Useless or injurious.
  - Such reaction produces either—
    - (1) Radiumdermatitis (burn).
    - (2) Unfavourable stimulation, which may excite morbid evolution.
    - (3) Complications caused by depressed scars, telangiectases, pigmentation, and deep crust formation, which are slow of repair.

of rays emitted by the apparatus) with which the rays influence the tissues.

3. Their proportion in certain radiations.

An adequate appreciation of the respective therapeutic value of the rays can only be formed from a knowledge of these data.

1. α **Rays.**—These rays being easily absorbed, it is probable that the reaction which they produce is exercised only upon the most superficial layers of the tissue. Is this a reason for considering that their action is negligible? Far from it. In the radiation from varnish apparatus their proportion is very trifling, but in that from radiferous "toile" it is most important, 50 to 80 per cent. These rays, if skilfully directed, may be used with great advantage in the treatment of chronic, superficial inflammatory diseases.

Radium "toiles" containing a salt of weak activity (10,000 to 20,000) may be large without being too heavy, and, owing to their flexibility, an arm, for instance, can be enveloped in them, and local effects thus obtained on the surface.

A screen of $\frac{4}{100}$ to $\frac{5}{100}$ mm. of aluminium is sufficient to intercept the α rays of the radiation. But it is difficult to specify in the series of screens the exact moment at which they are entirely absorbed. Moreover, their action does not appear to be very different from that of soft β rays, which, in the curves of penetration, follow almost imperceptibly on α rays.

In reaction which results from the use of collective radiations having an intense quantitative value, the exact share taken by α and β rays can scarcely be determined, since there is no means of isolating them.* We may suppose, however, when the exposures with unscreened apparatus are extremely short, and result in modification of the surface, with or without reaction, that the effect is produced by some α rays and very numerous soft β, medium β playing an inferior part. As to γ and hard β rays, it does not seem that they could have time to act, if we consider the extreme length of application which is known to be necessary, when they are isolated, to enable them to influence the tissues. However this may be, the difficulty of practically isolating these rays with absolute certainty, which we shall meet with again when studying the rôle of the other rays, has hitherto prevented any entirely conclusive statement as to their respective value.

2. β **Rays.**—In physics, the β particle, or electron, has a considerable share, for, as we have seen, no less a rôle is assigned to it than that

* Quite recently M. Marckwald has succeeded in isolating polonium, in the state of a chemically pure salt. Up to that time this radioactive substance had been known only as a deposit on various metals. These experiments make it possible to study the clinical action of α rays, the only ones emitted by polonium.

of the primordial atom of electricity, which is the basis upon which all the theories of modern physics rest. In radiumtherapy, we hold β rays, all things considered, to be of equal importance. They are present, in large numbers, in the most effective and most frequently used radiations, being found as primary, and again as secondary rays. The primary rays predominate largely. Analysis of uncovered apparatus, when the varnish is not injured, almost always gives them a proportion of 80 to 90 per cent., as against 1 to 10 per cent. of γ rays. We may therefore consider that in a total radiation, emitted by a varnish instrument without a screen, they exceed the γ rays in number. For instance, if we take apparatus No. 1 of our table (pp. 46, 47) we see that, for a total radiation of 580,000, there are respectively:

Of α rays	. . . . .	10 per cent.	= 58,000 units
Of β rays	. . . . .	87 ,, ,,	= 504,600 ,,
Of γ rays	. . . . .	3 ,, ,,	= 17,400 ,,

β rays have therefore the advantage of numbers.

They have also the advantage of being heterogeneous, that is to say, of possessing amongst themselves different qualities of penetration. It follows from this that they can permeate the whole thickness of the tissues at various stages. By passing from soft to very hard β rays through medium and all intermediate β, a whole scale is placed at our disposal, which allows of the production of reaction in cutaneous lesions at various depths.

It has been inferred from the constant presence of γ rays in all the radiations—for β cannot be employed without also using γ—that γ rays play the truly curative part in the results obtained, the β only producing an irritation which often proves injurious. This conclusion, however, is not correct. The following considerations show in some degree the biological and curative action of β rays, independently of that of γ rays.

When almost isolated γ rays can be obtained, by means of sufficiently thick lead screens of 5 mm., very long exposures are required in order to produce a reaction. It is therefore improbable that they can act in ten to fifteen minutes. Now, certain chronic eczemas are modified and cured without intense reaction, by applications with uncovered varnish apparatus of high power, lasting from one to three minutes, the application being repeated three or four times. We are therefore justified in saying that γ rays are overpowered, and remain to some extent unused in these short applications without a screen, which, on the other hand, make great use of the action of soft and medium β rays. Nor can it be the α rays which have predominated in the action, for, even

in cases in which we have used screens of $\frac{3}{100}$ to $\frac{5}{100}$ mm. of aluminium, which intercept them, similar results have been produced.

It is therefore evident that β rays have a real action which may be as truly selective without inflammation of the tissues as, in other cases, it is destructive, and this is very fortunate, for since their quantitative value is extremely powerful, their suppression, or the demonstration of their uselessness, would have deprived radium of much of its claim to originality, and greatly reduced the therapeutic usefulness of this precious metal.

It is difficult to ascertain exactly where the penetration of hard β rays ceases, for they accompany γ rays through screens of a thickness beyond which operation would be scarcely practicable. Moreover, we shall see that a part of their effect is blended with that of γ rays, and the reaction which they produce is therefore more profound than was supposed.

3. γ **Rays.**—We know that the proportion of γ rays is comparatively very low in the radiation from unscreened apparatus. They scarcely amount to 1 to 10 per cent., and this leads us to suppose that their share in massive and intense total radiations, without a screen, is very inconsiderable, and need scarcely be taken into account, since such an application only lasts for a few minutes. But, after filtering, the study of γ rays leads to very interesting considerations, for although we could not hope to isolate α and β rays, the case is quite different—at any rate in theory—with γ rays.

The idea of obtaining γ rays and causing them to act alone arose from a consideration of the mechanism of filtering, of which the following is a summary :

γ rays pass through all substances. The other rays, on the contrary, are absorbed according to a scale proceeding from α through soft and medium β to hard β rays. If, therefore, an apparatus is covered with an entire series of screens of increasing thickness, the external radiation will be modified, both as to quantity and quality.

The quantitative value of the total radioactivity will become weaker and weaker, descending, for instance, from 600,000 to 5,000, and from 3,000 to 1,000, when the lead screen is 3, 4, or 5 mm. thick.

The qualitative value, that is to say, the proportion of α, β, and γ rays, will be altered ; that of the γ rays being changed to a very slight extent only, whilst the loss will take place in the others ; first in α and soft β rays, then in medium and hard β. The β will resist to some extent, and will be found again with the γ rays, after tolerably thick screening.

Various questions are therefore suggested :

1. What thickness of screens is required before γ rays can be considered isolated? When isolated, are they of practical use?

2. If they are accompanied by hard β rays, after having passed through thick screens, are these rays to be taken into account?

3. Lastly, how should the action of γ rays be interpreted?

1. In theory, we may certainly succeed in isolating γ rays; but what interests us, as physicians, is to know whether in ordinary practice such rays can be utilised alone. Beyond 2 and 3 mm. of lead, the weight of the apparatus and extreme length of exposure required, owing to the quantitative weakness of the radiation, give rise, as a rule, to conditions usually incompatible with clinical practice. Now Sir W. Ramsay calculates that there may still be some hard β rays left after using a screen of 5 mm. of lead. M. Beaudoin's curve (*see* p. 73) gives to 2 mm. a proportion of 10 per cent, and to 1 mm. a proportion of 30 per cent. of hard β rays.

According to M. Debierne, between thicknesses of 5 mm. and 1 cm., the exact moment at which β rays cease to pass through the screens is not known. It therefore would seem very difficult to determine, with absolute certainty, the individual biological rôle of β and γ rays. Moreover, the most eminent physicists are not yet agreed as to the respective powers of penetration of the various rays.

2. It follows, then, that hard β rays almost always accompany γ rays. Are these hard β rays negligible, since they are only present in very small quantities when thick screens have been used? We do not think so.

If the resolution of epitheliomatous vegetations, for instance, by means of thick screens (2 and 3 mm. of lead), which allow few β rays to pass, took place in a few hours, we might justly consider the presence of this small number as negligible, and deny them any useful action. But it is only on condition of making the exposure last from 40 to 100 hours that such resolution is obtained. Now this interval is quite long enough to permit β rays to accumulate in sufficient doses, especially when, as in the above-mentioned analyses, with 2 mm. of lead there are still about 10 per cent. of hard β rays.

3. The action of γ rays now remains to be explained. Some physicists appear to be surprised when surface reaction obtained by isolated γ rays is mentioned. It is true that these rays are extraordinarily penetrating; they traverse the human body, lighting up uniformly a radioscopic screen placed on the other side of it. Moreover, when thick filters are used, the rays which pass through represent a selection from those which are most penetrating. How, then, can we explain the fact that such rays are capable of modifying the most

superficial cells of the tissues? There is an anomaly here to be accounted for.

The following is the explanation which we suggest, and which tends to extend still further the share of the β elements.

γ rays act not directly, but by the production of secondary β rays. We have seen that over their whole course, in proportion as they come in contact with the material penetrated and its various layers, they give birth to secondary rays chiefly composed of β electrons. These electrons, it is true, are very easily absorbed, and would only have a limited sphere of action. But each cell attacked would be acted on by such secondary rays; and in this way, even in the action of γ rays, the β elements, of secondary formation, would play a great part indirectly. It is thus that the action exercised by γ rays on the most superficial layers of the tissues should be regarded.

It is easy to see how important a part might be assigned to β rays taken collectively, if the action of secondary β could be added to that of primary β. We are careful, however, to avoid definite assertions and conclusions. Considering the extreme reserve with which physicists speak of the separation of the rays, the limits of their penetration, and various other characteristics, physicians should guard against a tendency to formulate too definitely therapeutic methods based on the value of certain rays.

It will be well to consider the action of two kinds of grouping: the hard β rays and the γ rays which, isolated or combined, form the "surpénétrant" radiation, and the bundles formed by the *ensemble* of all the rays.

1. **"Surpénétrant" radiation.**—Radiations composed exclusively of hard β rays and γ rays, in varying proportions, have a special clinical significance. Since the curves of absorption bend very slightly from the moment when these radiations, after filtration, are freed from the other rays, they form a definite therapeutic entity, and deserve the special designation which has been given them.

With regard to collective radiations in which weak and medium rays are concerned, their use and the proportion of the elements of which they are formed are too variable to receive any special name; the term "rays of weak and medium penetration" will be sufficient to indicate the α rays, and the soft or medium β which they include.

Regarded in this way, "surpénétrant" rays, when made use of in certain ways, produce special reactions of great importance, and point to certain general conclusions, the principal of which are as follows:

i. "Surpénétrant" rays are obtained by the interposition of lead screens of from $\frac{1}{10}$ mm. to 2 or 3 mm.

ii. They form radiations of weak quantitative value. Fortunately this weakness can be compensated by the total length of the applications, either by continuing them for some hours in succession, and even for whole nights, or by making them shorter, but frequently repeated. The object is to accumulate, by a weak but very protracted radiation, a dosage having a sufficiently large total. For many parts of the body, the ease with which applications can be made admits of this method of treatment. Strips of diachylon fix the apparatus on the skin during the night, and it does not disturb sleep. In the vagina and uterus long applications are also easy. Unfortunately, this is not the case with buccal mucous membranes, where it is necessary to give shorter applications, frequently repeated.

iii. Preference should be given to high-power apparatus when it is only desired to produce reaction with "surpénétrant" rays; for, on the whole, in applications weak in quantitative value, the duration of the exposures, however long, does not entirely replace or equal in value radioactive intensity. With a very intense source, "surpénétrant" rays will be fairly numerous. The total radiation which they represent when used alone should have an activity of not less than 3,000 to 4,000; and the greater this activity, the stronger will be the reaction. This explains the excellence of the "cross-fire" process, when used for such radiations, since this method increases the intensity of the rays, and does so in a proportionally shorter time.

iv. "Surpénétrant" rays act on tissues at a depth, with very little irritation of the surface. Their feeble emission, the doses being of necessity comparatively weak, is valuable when one wishes to work at a great depth, gently and on a small scale, avoiding inflammation and respecting the surface. Of course excessive duration, or doses which would accumulate too large a number of rays, might cause surface irritation; but on the one hand, this would only occur as a result of a serious error in dosage, or such a disproportion in time as could only be due to great inexperience; and on the other hand, such severe reaction or radium-dermatitis seems to heal fairly quickly, when it is not very marked.

The "surpénétrant" rays being few in number, and the others, on the contrary, being present in considerable quantities, the latter will require greater delicacy of treatment. An error of some hours in the technique of "surpénétrant" rays will be of comparatively little importance. If, however, a mistake of a few minutes in excess be made with regard to the use of slightly penetrating rays, a very different reaction will be produced. The manipulation of the latter therefore requires greater care.

It will be seen that reaction with superadded inflammation (radium-

dermatitis) is not connected with the operative process, which may or may not intercept rays of weak penetration, but simply depends upon the dosage ; and this was to be expected.*

2. **Total or collective radiation.**—Rays of weak penetration from unscreened apparatus and those with light filters have been considered with reference to α and soft and medium β rays, and we have seen that they form radiations possessing great total activity. They therefore offer the advantage of short applications in the course of which all the rays act at varying depths. By the use of different methods we may succeed in modifying the surface reaction and acting at a depth. To do this is, in many cases, to obtain the greatest possible advantage from a radium applicator. We should then, as a principle, try to employ collective radiations as often as possible, and intercept α and soft and medium β rays only when it is quite certain that their presence will be harmful, or produce a less valuable result. This amounts to saying that, if equal results can be obtained, preference should be given to the more practical method of short applications.

When the employment of the whole of the rays produces inferior results, it is necessary to have recourse to other methods of procedure ; but before making use of very dense screens, and consequently only "surpénétrant" rays, it is well to consider the possibility of using the whole series of medium screens, aluminium and lead. By the employment of such medium filters we have obtained very valuable reactions. They share the advantages of the extreme methods.

The technique of "cross-fire" should here be recalled. Since this method allows of the accumulation and increase in intensity of action of "surpénétrant" rays, at the same time making use of those of weak or medium penetration, it is as well adapted for uncovered apparatus as for applications with screens. If, then, the use of dense screens of medium thickness is combined with the benefits offered by this "cross-fire" method, sufficiently deep reaction will be obtained in many cases, without the necessity of very protracted exposures.

In ordinary practice these different values may be combined with great advantage. The object of all our therapeutics is to select, from the aggregation of different forces, those which, by their union, will give the largest output. By the various methods of application

[* *Note by Dr. Wickham.*—It must be understood that these remarks only refer to quantities of 5 to 10 cg. of pure radium. When we are able to deal with it on a larger scale, say in *grammes*, these statements will, no doubt, have to be modified.]

without screens, by that of "cross-fire," and by the alternation of suitable screens, the combination of radium rays can be indefinitely modified, both in quality and quantity, and a great variety of reactions of a therapeutic nature may be consequently obtained.

Note by Dr. Wickham.—We have seen from the Beaudoin curves that the power of very penetrating rays, selected by filtration, is proportionate to the thickness of the filters. In theory, therefore, it is quite certain that intense radiations can penetrate the tissues very deeply. It does not, however, follow that they can act therapeutically at great distances from the surface, for the fact of penetration to a certain depth does not necessarily imply therapeutic action. To be effective the radiation must possess a sufficient quantitative value. It is, in fact, the *number* of the rays that have penetrated which determines their healing influence, and a very intense radioactive source must be used, in order to obtain a sufficiently large number, after heavy filtering. Deep therapeutic action, with a screen of given thickness, will therefore be in direct proportion to the intensity of the source.

For instance, if 1 mg. of pure radium is placed behind a lead filter 3 mm. thick, the rays which pass through it, although very penetrating, will be unable to produce any therapeutic effect, in spite of applications of indefinite length, on account of their small number.

If, however, instead of 1 mg. of pure radium, 10 cg., or even, as may soon be possible, 1 grm. be used, there will be enough rays to produce deep action.

It must be remembered that the thickness of the tissues traversed itself acts as a filter. If very deep action is required, it will be necessary to use a source capable, in spite of the thickness of the metal or tissue filters, of accumulating at the required point, during a limited period, sufficient rays to permit of therapeutic action.

The foregoing remarks may be summed up in the following formulæ:—

1. Therapeutic action is only produced at a given depth without surface inflammation when a sufficient number of rays can be accumulated in a space of time too short to produce such inflammation.

2. To obtain such a result it is necessary to co-ordinate, regulate, and combine in the proper proportions, the intensity of the radioactive source, the thickness of the metallic filter, and the total length of the applications, and also to take into account filtering by the tissues themselves.

3. The deeper the action desired, the more necessary will it be to increase at the same time, and in suitable proportions, the intensity of the source, the thickness of the metal filter, and the total length of the exposures. The method of placing the instruments opposite each other (cross-fire) allows very deep action from intense sources to be obtained, without using excessively thick metal filters—in these cases the tissues act as special screens—and without necessitating too long applications.

It will be seen that the question of the depth at which radium can act

is very complex, and cannot be easily decided. Some workers in radium,* relying on histological experiments, have recently stated that it cannot act beyond a depth of 2 to 2½ cm. I have, however, succeeded in modifying a tumour of the mediastinum to such an extent that the patient, who was choking and coughing incessantly, was completely freed from his trouble in a month. Similar results of X-ray treatment have been reported. Why, then, should not radium rays, the greater penetration of which has been practically demonstrated, act at a still greater depth ? The only difficulty is to ascertain under what conditions such action can be obtained, and this is the point which I have endeavoured to elucidate.

It is well known that many combinations are possible when several factors can be combined at will. In radiumtherapy, four entirely distinct primary factors can be united, each combination producing different therapeutic effects. They are as follows :—

1. Radioactive source, variable in quantity, quality, form, etc.
2. Filters.
3. Length of exposures.
4. Nature of tissues treated, their position, resistance, and individual reaction

Each of these factors can be varied *ad infinitum*.

* See a statement of the interesting experiments made by MM. Delbet and Herrenschmidt on the normal gastric mucous membrane of the dog. Société pour l'Étude du Cancer, April, 1909.

CHAPTER II

THERAPEUTIC RESULTS

We now proceed to consider reaction in detail with reference to certain groups of diseases, and to give particulars of the therapeutic results which we have obtained.

This subject will comprise eight divisions :

1. Carcinomata and other malignant growths.
2. Cheloids and disfiguring scars.
3. Angiomata.
4. Pigmentary nævi.
5. Muco-cutaneous tuberculosis.
6. Analgesic action of radium, in pruritus, neuralgias, and chronic inflammatory dermatoses.
7. Various diseases.
8. Gynæcological radiumtherapy.

In this study we have invariably given the first place to clinical facts. We can best indicate the possibilities of radiumtherapy by a description of these, together with the methods and dosage indicated. The conclusions given are deduced from these cases.

I. CARCINOMATA AND OTHER MALIGNANT GROWTHS

We begin this part of our work with the group of carcinomatous diseases because we studied them first, and they are those in which radium seems to us calculated to render the greatest and most opportune service ; also, because the various modes of radiumtherapeutic action are here most manifest, and finally, because the progress in apparatus and technique made during the last few years can be dealt with in this chapter.

When, in March, 1905, Dr. Wickham commenced the study of radiumtherapy, his attention was naturally directed to cutaneous superficial epitheliomata. At this period, indeed, experiments had been chiefly made on these lesions, and many successful results had already been recorded.

M. Danlos must be mentioned first, for his work dates from 1900. After the study of a large number of small and superficial cases, spread over a period of three years, he arrived at the conclusion that radium had a curative action on the majority of benign epitheliomata, both by the

wet and dry methods. M. Robert Abbé, who acquired radium shortly after the discovery of M. and Mme. Curie, had also announced favourable results. Then there appeared in succession the works of Béclère, A. Darier, Sichel, Williams, Krylov, Lassar, Follard, Repmann, Myrou Matzenstaum, Branstein, Mackenzie Davidson, and many other of the earlier pioneers. These authors were able to report very few successes, except in the case of benign lesions, and the conclusion drawn from their work was that, although radium had a very beneficial action, it could not lay claim to the treatment of anything beyond small and innocent superficial lesions, which responded quite as readily to other therapeutic methods. This is why the radiumtherapy of carcinomata remained so long in the background. To-day, on the contrary, the use of radium for carcinomata extends to huge ulcers, enormous tumours, lesions situated on the mucous membranes, and subcutaneous growths, and frequently also to cancers which no other method has been able even to alleviate. It therefore follows that, in the course of the last few years, extensive modifications have taken place in the methods of its employment. Such changes have been directed

(1) To development of the instruments, which has put us in possession of apparatus of considerable radioactivity with large surfaces;

(2) To improvement in technique (various methods of direct application, filtering, "cross-fire," introduction into tumours), which has made such apparatus available at a depth, as well as on the surface. These have been described in the preceding chapters.

Our cases at present amount to about six hundred, but we can only give statistics for certain forms of mucous and cutaneous epitheliomata which have been treated in sufficient numbers, and during a fairly long period. Indeed, in the matter of cancer, where relapse must always be taken into account, statistics are only valuable when confirmed by time and numbers. This is a rule which cannot be too strongly insisted upon. The results obtained will form the subject of a first chapter.

Other forms of carcinoma have been successfully treated, although in smaller number. These results need confirmation, but, at any rate, they open out a wider horizon to radiumtherapy. They will be grouped in the next chapter.

I. EPITHELIOMATA OF MEDIUM GRAVITY

Our first group will include benign lesions, or those of medium gravity:

1. Vegetating cutaneous epitheliomata.
2. Superficial epitheliomata, ulcerated (ulcus rodens) or otherwise.
3. Epitheliomata in special sites.

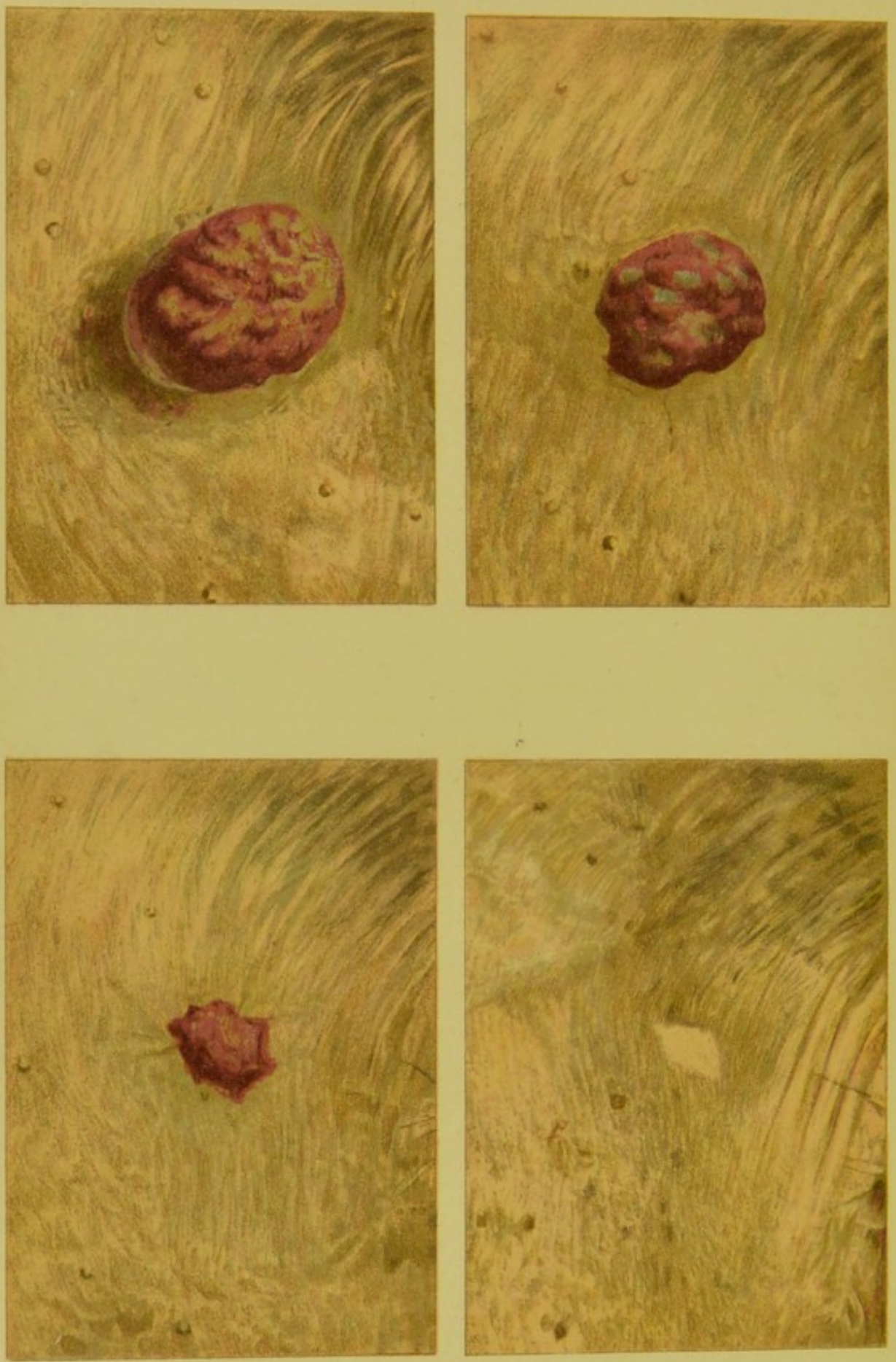


PLATE I.—FUNGATING EPITHELIOMA OF TEMPORAL REGION

PLATE I

FUNGATING EPITHELIOMA OF TEMPORAL REGION (p. 105)

Before treatment, a thick crust covered the growth. It was removed for the first application, and did not form again.

FIG. 1.—State of growth on second day; the surface is already much drier.

FIG. 2.—Thirteenth day of treatment.

FIG 3.—Thirtieth day. On the thirty-fifth day, the cicatrix was formed.

FIG. 4.—Cicatrix photographed a year after completion of treatment. Its surface is perceptibly reduced in size.

1. FUNGATING CUTANEOUS EPITHELIOMATA

Epitheliomatous vegetation is a growth particularly suitable for the action of radium, and there are numerous techniques adapted to it. Direct application of the apparatus and methods of filtering, either with thin, or with thick and dense screens, can show a sufficient number of cures to testify to their respective value. Any of these methods may be employed, according to the requirements of the clinic, the convenience of the patient, and the apparatus at disposal. We usually prefer direct applications.

Direct applications.*—By this method of applying apparatus without a screen, curative reaction is produced very quickly, sometimes even resulting from the first application. If, for instance, after removing the crust covering a large vegetation, a collective radiation having an external total activity of 50,000 (apparatus No. 4), composed of 90 per cent. of β rays and 10 per cent. of γ rays, is applied for an hour, the next day the surface appears less moist, and there is less oozing and tendency to crust formation. After the second application, the modifications are more clearly marked. The tumour has decreased in size, and on the following days the gradual removal of the growth by absorption takes place very rapidly, in proportion to its impregnation by the rays. If the total dosage adopted has exactly reached the required amount, without exceeding it, reaction occurs exclusively in the superfluous tissue, the resistance of which becomes weakened. A complete cure is obtained without subjecting the tissues forming the base of the growth to a stage of ulcerative reaction. In this case the cicatrix which follows is much improved. The surface is usually smooth, uniform, supple, and whitish in colour, of excellent appearance, and seldom depressed. In some few cases, it is impossible even to distinguish it; it blends so well with the surrounding tissues that after some months its limits cannot be exactly traced.

(1) **Fungating epithelioma of temple** (Plate I).—This is a very remarkable case, the more interesting as the growth, instead of showing the usual indolent character, was, on the contrary, undergoing a marked and acute malignant evolution. The cure, however, was very rapid.

In July, 1906, an old man had on the back of the hands two small ulcerated epitheliomata, which we subjected to radium. Besides these two lesions, which disappeared entirely without leaving any scar, towards the end of July we noticed a small tumour on the temple, resembling a comedo, or sebaceous cyst. The skin in that part was only slightly stretched, and the small swelling was rather hard. Indeed, we had

* The apparatus is, however, always wrapped in a fine protective rubber tissue.

scarcely noticed the little cyst during the time that we were occupied with the hands, and Dr. Coyon, who sent the patient to us, had not mentioned this trifling lesion. On September 6th, thirty-six days afterwards, it had grown, mushroom-fashion, in such a way that it formed a fleshy mass, 2½ to 3 cm. in height and 3 cm. in width. It was now a prominent epithelioma of seborrhœic origin, the tumour being soft, red, spongy, moist, and crusted. Apparently the lymphatic glands were not affected. We immediately commenced treatment by radium. After removal of the crust, the tumour was treated by thirteen applications (the first being made on September 7th, and the last on September 29th), each one lasting an hour, with No. 4 apparatus. The surface was cleansed before each operation. As shown by the figures in Plate I, on the thirteenth day the tumour had greatly diminished, and on the thirtieth day, October 8th, it had completely resolved, leaving only a small surface in process of cicatrisation. Considering the conditions of acute evolution in which this epithelioma was found at the beginning of treatment, the rapidity of its resolution is very remarkable. The operation was exceedingly simple, the patient himself holding the apparatus, and feeling not the slightest unpleasant sensation. At the present time, three years and a quarter after the disappearance of the epithelioma, the scar is perfect in stability and appearance. The fourth figure of Plate I is a photograph taken a year after treatment. Since then, the mark of the scar has become still further effaced; it is scarcely visible, and shows no sign of depression or telangiectasis.

But, better still, there are some instances in which no sign whatever of a scar remains. The patient whom we are about to mention was shown to our friend Dr. Oudin nearly a year after treatment. Having been told that the epithelioma was situated on the ear, he was unable even to find the place where it had been. Cases of such complete obliteration are rare; we have only about ten examples.

(2) **Fungating epithelioma of ear** (Plate II, Figs. 3 and 4).—A fungating epithelioma, about the size of a one-franc piece, was situated in the upper half of the interior of the auricle. The patient was entrusted to us by M. Dominici in 1907. The limits of the lesion formed a regular circumference, and were stopped by the thick border of the external ear. It was painful, and covered with a soft crust of brownish green colour, from which exuded a sanguinolent liquid. The removal of the crust disclosed a vegetating tissue extending over the whole surface. The growth projected about 3 to 4 mm., and its base seemed very shallow. (This latter fact would lead us now, as a result of further experience, to use moderate doses.) No. 7 apparatus exactly covered the epithelioma; it was adopted and applied without any screen. There

EXCAVATING CANCROID OF NOSE

FUNGATING EPITHELIOMA OF EAR

PLATE II

PLATE II

EXCAVATING CANCROID OF NOSE (p. 119)

FIG. 1.—The excavating ulcer with punched-out edges had resisted various forms of treatment.

FIG. 2.—The cicatrix is still very satisfactory, two years and a half after treatment.

FUNGATING EPITHELIOMA OF EAR (p. 106)

FIG. 3.—The photograph was taken two days after the first exposure. The crust did not form again. Cure by thirty-fifth day.

FIG. 4.—The new tissues present the appearance of normal skin. There is no sign of any scar.

were six applications, of one hour each, on six consecutive days. The growth disappeared with extraordinary rapidity, and, from the fourth day, showed hardly any prominence. There was no longer any need to renew the applications, and our persistence occasioned too strong a reaction ; the ear swelled and an erysipelatous condition was produced. We feared that this excessive dose might result in an ulcerating radium-dermatitis, but nothing of the kind occurred. The swelling soon subsided, and, strange to say, on the thirty-fourth day of treatment, the cure seemed complete, in spite of the transitory inflammation. A year later there was no sign by which the repaired tissues could be distinguished from those surrounding them. About fifteen months after treatment, a small, suspicious-looking point made its appearance on the edge. Fearing a relapse, we applied No. 8 apparatus for an hour, and the tissues resumed their normal condition.*

This case gives rise to various interesting considerations. Amongst other things it proves that the dosage was too large, and should have been moderated, on account of the delicacy of the auricle and the absence of induration of the base. We should now, in a similar case, limit the length of the exposures to three or four hours at most, with the same apparatus, in fractional doses of twenty minutes each. The curative action of rays of medium penetration is very clearly shown in this example. The radioactivity emitted outside the apparatus was 5,000 for γ rays, and 45,000 for β rays. Now, owing to the use of thick lead screens, it has been possible to study radiations with an activity of 5,000 units, composed entirely of γ rays, and experience has shown that their action is slow, and that an exposure of not less than twenty hours is required to obtain a sufficient effect in such cases. It seems most unlikely that so strong a reaction and so rapid a resolution of the vegetation can be attributed to the γ rays, considering the small number and short length of the applications. The only logical conclusion is therefore that β rays, with their activity of 45,000 units, had the principal share in this reaction.

Filtering.—But there is a very different method of procedure, requiring different dosage ; viz. the use of thick screens from the beginning. Vegetations can be removed quite as well with this technique by making use of " surpénétrant " rays alone ; but only after long exposures, which is a disadvantage. This process must, therefore, save in exceptional cases, give way to the more rapid one of direct application. When it is desired to have recourse to screens, it will generally be best to use thin ones, which allow a fair proportion of medium β rays to filter through.

* *Note by Dr. Wickham.*—Another suspicious point appeared six months afterwards which also disappeared after an application of No. 8 apparatus for one hour.

By this method, which steers a middle course between applications with uncovered apparatus and the use of " surpénétrant " radiations, we may obtain a more prolonged action on the deep-seated tissues, and it will be at the same time sufficiently massive. We now give two examples of treatment with the interposition of screens ; one with a thin screen, being the first experiment made in therapeutic filtering ; the second with a screen of 2 mm. of lead.

(1) **Vegetating epithelioma of pubic region.**—Dr. Wickham's first case.—" In March, 1905, M. Armet de Lisle had just entrusted to me a set of radium apparatus when, by the advice of Dr. Montgomery, of Chicago, an American lady, who was suffering from three fungating epitheliomatous tumours in the left pubic region, came to consult me. Relapse had repeatedly followed the use of X-rays. The largest of the growths had an extent of about 3 cm. and a height of 1 cm. ; it was covered with a thick crust, and the epitheliomatous surface was oozing, sanious, and painful. The second was half the size, dry, and indolent. The third was the size of a large pea. These three lesions represented the recurrence of an enormous epithelioma. They were situated at the extremities of the cicatrised surface resulting from the previous action of the X-rays, and formed three distinct carcinomatous foci.

" The apparatus which I possessed was the kind with radium in varnish (p. 7) now in general use. But I had then no data or means of comparison, M. Danlos' results having been obtained with different instruments. This applicator seemed to be extremely powerful. An exposure of five minutes on the skin of my forearm left a very marked erythema, and on the shaved skin of a guinea-pig the reaction denoted considerable activity. The instrument possessed an external activity of about 60,000 to 80,000. I therefore resolved to proceed with caution. Knowing that the radiation from radium was composed of elements endowed with very unequal powers of penetration, and that, in spite of its walls, positive therapeutic effects could be obtained from the old-fashioned apparatus, and knowing also from the practice of X-ray therapeutics that slightly penetrating rays caused irritation, and that, in order to avoid too rapid superficial action, the tube must be made hard, the idea occurred to me of interposing a screen between the apparatus and the epithelioma. This experiment convinced me that I should be able in any case to diminish superadded inflammation if it should be produced, and to vary the thickness of the screens as required. *This was my first use of filtering in therapeutics.* It was not a question of the filtering which is indispensable in all radium-therapeutic operations, seeing that the rays are compelled to pass through

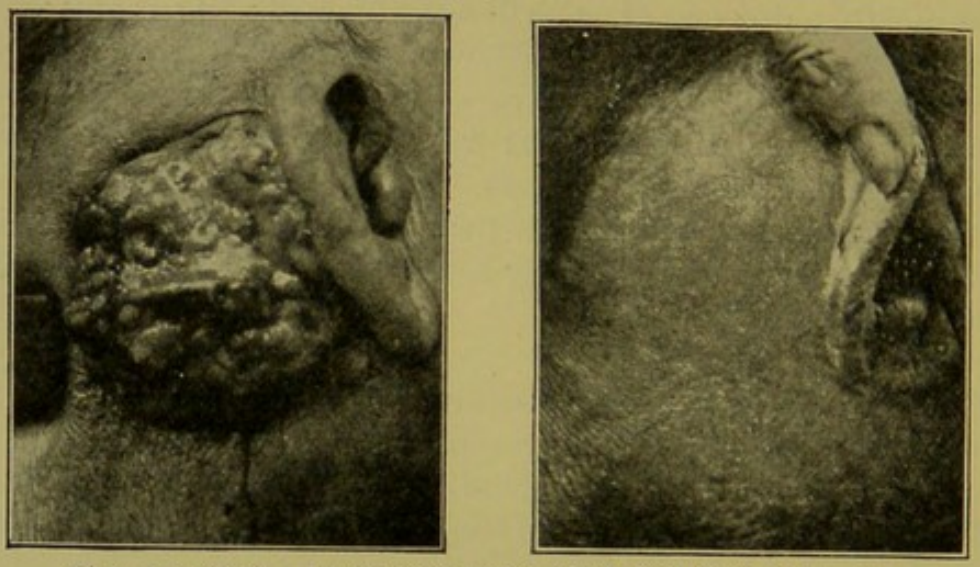
the fixing substance which holds the radium salt, and forms part of the apparatus. What was needed was a supplementary filtering, capable of being applied and altered at will. It must have a special purpose, and consist in the interposition of an additional and specially devised apparatus. I took some absorbent cotton-wool and compressed it, so as to make a hard pad, which was then wrapped in two leaves of Hamilton's gold-beater's skin, such as that found in Langlebert's ouataplasm.

"The first application was for thirty minutes (apparatus No. 2, p. 7); each of the three epitheliomata being treated separately. I resumed treatment two days later, and repeated these applications of thirty minutes, at intervals of two days, several times. At the end of the first month, a decrease of one-half was obtained without any apparent inflammatory reaction. The tumours simply shrivelled up and became much reduced in size. In the course of the following month I lessened the thickness of the pad by about half, but continued applications of the same length at the same intervals. At the end of the second month, scarcely anything remained, and in the course of the third the cicatrisation was complete. I have recently heard from this lady that the cancer has not reappeared."

The gravity of the following case places it outside the limits to which it was intended to confine this group. We record it here, because it will serve to show both the progress made in the technique, and the almost equal value of different methods in the treatment of epitheliomata of the same kind. Having described the method of procedure with uncovered apparatus, and also of that with screens of cotton-wool, we now give an illustration of the use of lead screens.

(2) **Fungating epithelioma of lymphatic origin** (Figs. 15 and 16). —A patient in the clinic of M. de Beurmann, aged 72, had a large crusted ulcerating epithelioma occupying the whole region of the right temple. Glands were present behind the ear and at the angle of the inferior maxilla, but were not specially marked. Severe pain, however, was felt in the whole retro-auricular, parotid, and superior cervical regions. Only the temporal ulceration was treated at first. Apparatus No. 1, enveloped in a fine protective sheet of rubber, was applied to the temporal lesion for six hours in succession. Improvement took place with such rapidity that the cure was accomplished in three weeks, without superadded inflammatory reaction. This is an excellent example of the power with which β rays can act, when used in massive doses and short exposures. During this time, however, the retro-auricular lesions which existed at the time of the patient's arrival had developed,

and produced an enormous vegetating mass, 6 cm. in diameter and 4 cm. in height, which soon became the site of frequent hæmorrhage (Fig. 15). Every dressing was accompanied by profuse bleeding, and it was often necessary to change the bandage during the night, as it became soaked through. The patient was in a bad state generally, and very weak from this constant loss of blood. A diffuse lymphatic swelling was situated in the retromaxillary angle. The pain continued to increase. We then applied, day and night for fifteen days, that is to say during a period of three hundred and sixty hours, No. 15 apparatus, with a covering of 2 mm. of lead, only allowing a very weak "surpénétrant" radiation to pass through, and thus obtained gradual resolution of the



Figs. 15 and 16.—Large epithelioma which healed in eight weeks.

lesion (Fig. 16). The region might be considered healed, but of course it was necessary to watch for any appearance of relapse. The very severe pain felt by the patient disappeared at the same time as the epithelioma.

This example shows that radium can be applied, not only to small cancroids, but also to epitheliomata of grave character and large size. The following chapter will be devoted to a description of such cases. The case illustrates, too, the reduction of congested lymphatic glands, for, as we have said, there were hard masses at the retromaxillary angle, covered with normal skin, and these were reduced by degrees. In order to hasten this evolution, we treated them with "surpénétrant" radiations for seventy hours, in the same way as the large tumour, and the retrogressive action continued until they entirely disappeared. And lastly, this example shows very clearly the hæmostatic action of radium. The frequency and abundance of the hæmorrhage de-

creased rapidly from the time of the first applications, and at length ceased altogether.

From a consideration of these facts, regarded as a whole, we have been enabled to formulate the following conclusions:

(i) Epitheliomatous vegetations, even when of large size, may subside and disappear without undergoing superadded inflammation, and may leave a cicatrised surface which is often quite firm and solid, and scarcely visible.

(ii) The methods producing such a result are very various, radiations comprising a majority of γ rays being quite as effectual as those comprising a majority of β rays.

The latter are often preferable, on account of the brief length of the applications, which makes the treatment convenient in practice. We will, however, add two different methods. On the one hand, if the base of the vegetating surface is indurated and deep-seated, two methods of application will be desirable. The object of the first will be to reduce the superficial portion by means of exposures of great intensity (unscreened apparatus), whilst the second is intended to act at a greater depth with "surpénétrant" rays alone. If, on the other hand, as in the case of our first example, the growth should be sufficiently prominent to be covered by two simultaneous lateral applications, we may take advantage of this circumstance to act by means of "cross-fire," applying the apparatus without a screen, and in opposite directions. Since the rays are almost parallel to the base, there will be no risk of irritating it, and the apparatus may be left in place for a considerable time. In this way the growth is quickly destroyed; and the base is afterwards treated in the manner already indicated.

The following is an instance in which "cross-fire" proved very effective. A man, aged 45, had an enormous fungating epithelioma in the middle of the left cheek. Its situation allowed of the employment of "cross-fire." We applied apparatus No. 3, enclosed in 1 mm. of lead, to the mucous membrane, for an hour at a time, ten days in succession. Externally, apparatus No. 1, with similar filtration, was employed for the same time. The rapidity of the result was astonishing. A month after treatment the surface of the cheek was normal, and the tissues were supple.

(iii) The time required for cure varies greatly, depending, as it does, on many conditions. The size and extent of the vegetation, the depth of infiltration, and the operative method and dosage adopted, are all factors which modify the duration of the healing process. Taking a

growth the size of a nut as an average, three to six weeks must be allowed.

On the whole, radium has a powerful effect on fungating epitheliomata, and failure seems to be very rare. The technique is varied and many-sided ; the method to be used in any particular case should be determined by the exigencies of practice and the needs of the patient. It is obvious that the cicatrisation must be carefully watched, and any subsequent developments at the edges of the scars should be specially noted. The effect of radium continues long after an apparent cure ; the patient often feels, two or three months afterwards, a sensation which he compares to the crawling of a minute insect, and from time to time slight scaling may be observed, which plainly indicates that the cicatrised tissues are still undergoing modification. During the two or three months following a cure, there is no occasion to be uneasy about the appearance of small growths, visible under a magnifying glass. It is sufficient to keep them under observation, as they will usually disappear spontaneously. If they persist, or if a small swelling appears after three or four months, there should be no hesitation about repeating the application for two hours, with apparatus No. 8, for instance. Relapse will then most probably be averted. It is therefore indispensable to warn the patient of the necessity of being examined, from time to time, by his doctor, in order that the slightest tendency to relapse may be detected and combated at once ; though such cases are very rare. When, for any reason, a patient cannot remain under our observation, we prefer at all costs to increase the dosage, and produce a more intense reaction on the base. By this means relapse has hitherto been avoided in every case.

2. SUPERFICIAL EPITHELIOMATA, ULCERATED OR OTHERWISE (" ULCUS RODENS," EPITHELIOMATOUS NODULES AND RIDGES)

In contrast to fungating epitheliomata, we group here more or less superficial growths, ulcerating and covered with a crust, or with a dry surface. They may be considered under four different headings :

(1) Small ulcerative sluggish cancroids with superficial base.

(2) Cancroids with dry surface.

(3) Ulcers with thick, indurated base, presenting certain malignant characters.

(4) Superficial ulcers of large size.

These forms of cancer of the skin react admirably in the direction of cure under the influence of radium. They are all capable of healing by simple modification, without any ulcerative, crusted, or severe

stage of reaction, whether the various methods of direct application be used, or those with the interposition of screens. The establishment of these facts is extremely interesting from a theoretical point of view, particularly as in these cancerous forms the special selective action, that specific action to which we shall often have occasion to return, is nowhere more definite or more manifest; and in some cases, as we shall see, very small doses are sufficient for a cure. Considered from a practical point of view, in most instances, with the exception of forms having a deeply indurated base, the use of the specific, to the exclusion of the inflammatory action of radium, is inconvenient for the patient, and causes loss of time, neglect of valuable apparatus, and a more complicated method of operation. It is therefore generally better to act energetically, and to use destructive doses at first, followed by selective doses.

(1) Small Ulcerative Sluggish Cancroids, with Superficial Base

This group and the following one are by far the most important, owing to their number. They generally include seborrhœic lesions of the skin, which, having undergone an epithelial transformation, have already reached a stage at which a bleeding ulcer or obstinate epitheliomatous nodules indicate the rebellious and malignant nature of the disease. Sometimes a crust covers the lesions, which bleed slightly when it is removed. The margin of the ulcer is bounded by a hard, typical edge, which is diagnostic of the condition. But at this stage the lesion is seldom deep, and if there is a tendency to extension, it is usually on the surface. Speaking generally, when cancroids are superficial, do not exceed 2 to 3 mm. in depth, and show no sign of malignancy, and when no obstinate or refractory character has been revealed by the failure of other therapeutic means which should normally have brought about a cure, we may be contented with a small total of doses, which is often successful. For instance, for an ulcerating cancroid 2 cm. in diameter, with a superficial base, the application for an hour of apparatus No. 5, unscreened, after the removal of the crusts, may be speedily followed by favourable modifications. The crust will not form again, and the ulcerative base changes in colour and aspect, and becomes covered from the tenth to the twentieth day. We have met, though very rarely, with cases in which a single weak application of this kind for an hour or an hour and a half produced the final cicatrix, of which the following is an instance in point.

i. **Epithelioma of slow evolution originating in senile warts.**—A patient, aged 60, had had for four or five years two

epitheliomata of slow evolution and senile verrucous origin on the right cheek, one of them being the size of a 50-centime piece, ulcerated and covered with a crust. When the crust was removed, the ulceration appeared in the shape of a cup, the edges being cleanly cut, but not prominent. The whole surface was even and deep red, bleeding slightly. There was no swelling or hard projection on the cutaneous portion of the edge. The diameter was about 1 cm., the bottom of the cup being 3 to 4 mm. The base was not indurated. No. 7 apparatus was applied direct, for half an hour. The raw surface was very soon modified, and the cavity filled in, two more applications being made in the course of a week. We then considered it unnecessary to continue the treatment. Ten days afterwards the lesion was completely healed. Granulation tissue had been formed without any intervening inflammatory stage. At the present time, after the lapse of a year and a half, no trace of the epithelioma remains.

It would, however, be imprudent to rest content with doses so weak, which might involve relapse. A second and a third hour of application, with an interval of a day or two, would be desirable, when dealing with these superficial cancers. A slight brownish crust, produced by inflammatory reaction, and usually dry, will be formed towards the tenth or twelfth day, and will fall off about the twenty-fifth to the thirtieth day, disclosing tissues well on the way to repair.

ii. **Small ulcerating and crust-forming epithelioma.**—A patient, aged 58, came to consult us on August 28th, 1906, who had on the right side of the nose an ulcerating and crusted epithelioma, the size of a 50-centime piece. It was a cancroid, or "ulcus rodens," commonly met with on the face. It was extremely sluggish, and slightly concave, and bled a little. The edges were hard and pearly, but not ulcerated. At its first appearance, and for several years afterwards, there was only a small crusted wart; the epithelioma having developed later. The patient would not have troubled about it if it had not caused latterly a very disagreeable pruritus. We decided to use apparatus No. 2 (p. 7). As this exceeded the limits of the ulcer, we protected the neighbouring healthy tissue in the following manner: A hole adapted to the size of the ulcer was made in a rubber-covered lead sheet about 2 mm. thick. The apparatus could then be applied to the ulcer direct, on the surface left exposed by the hole. The treatment was begun on August 28th, and continued on September 1st, 7th, 10th, and 14th; each exposure lasted forty-five minutes, making a total application of three hours and three-quarters. On September 8th the wound already looked healthier, and the bleeding had ceased. The base became filled in, and the epitheliomatous crust did not form again. There was no longer any itching. Some days

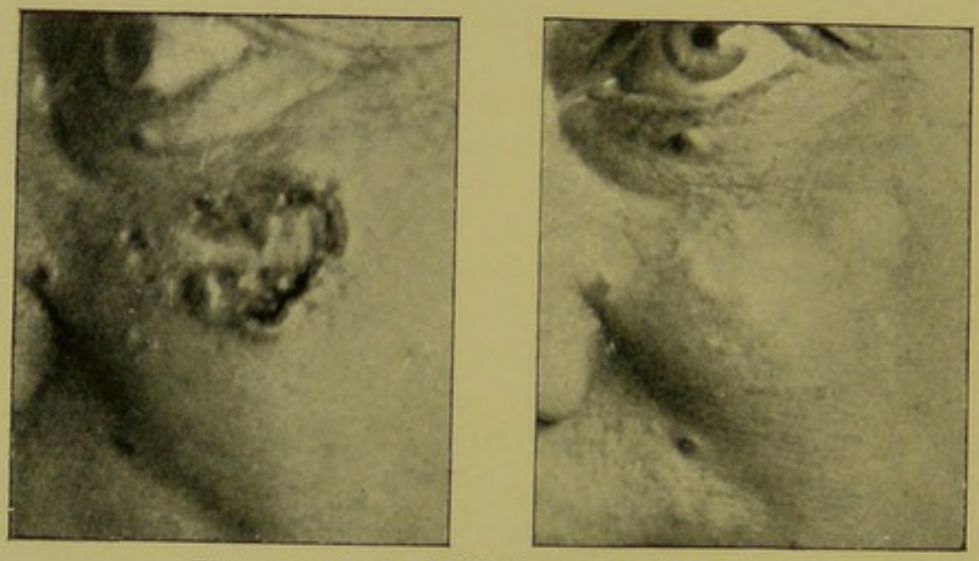
after the completion of the treatment reaction set in, though not very severely. This time, however, a new, slightly impetiginous healing crust was formed. This is what we call the *radium crust*, and it must be distinguished from the dark crust, mingled with blood, of crusted epithelioma. On October 23rd the patient came to see us, much distressed, because, as she said, the crust was there the same as before. But it was now dry and only slightly adherent; a touch with the spatula removed it, and the underlying tissues were in admirable condition. The cicatrix afterwards improved; it has continued quite solid, is perfectly smooth and healthy, and almost invisible, and now—three years after operation—shows no trace of telangiectasis.

Epitheliomata of this kind are evidently curable by various other therapeutic agents, as well as by radium. It sometimes happens, however, that elderly patients will not hear of an operation, such as cauterisation or curetting, and the ease with which radium is applied suits them very well. The cure is accomplished quite simply, by means of short and painless applications, and without any need of coercion, so that radium would seem to be the most practical and effective treatment for such persons. We have also used it for infirm patients who could not have left their homes to undergo X-ray treatment. And lastly, we know an instance of a distinguished personage who was unwilling to submit to any treatment likely to hinder him in his affairs. The apparatus was arranged for a period of two hours. It had only to be brought to him, applied and removed, and the cure was accomplished.

As we have already said, healing can be brought about quite as well by apparatus with screens, of which the following case is an example.

iii. **Epitheliomatous ulcer on right side of nose.**—An epitheliomatous ulcer was situated on the right side of the nose, in the form of a band extending horizontally from the lobe almost to the commencement of the cheek. It was 3 cm. long, and not more than ½ cm. wide. Very superficial in the middle, and at its two extremities, especially at the back, it was excavated, and had the appearance of perforating. This lesion had already been treated several times. The patient had been subjected to X-rays, cauterisation, and even radium, by other operators. None of these methods had produced a permanent result; scar formation had taken place to some extent, but there was very rapid relapse. Consequently, the patient came to us in January, 1906, in a very sceptical frame of mind, being quite convinced of the futility of our endeavours. After seven applications of an hour each, spread over a fortnight, with apparatus Nos. 5 and 8 (p. 7), in the course of the following month we saw the ulcer dry up by degrees, and then become filled in and cicatrised, without

the least sign of superadded inflammatory reaction. We operated by means of filtration, this being our usual custom for the first year. The apparatus was enveloped in an aluminium sheet, $\frac{1}{100}$ mm., and separated from the tissues by a screen of cotton-wool about 1 cm. in thickness. The objects of this proceeding were diminution of the total intensity of the radiation, avoidance of massive doses and too violent reaction, and the use of more penetrating rays. This example, therefore, is an instance of an ulcer which, when treated by filtering, healed very quickly, without any visible change beyond the regression and absorption of the neoplastic tissues. The condition of the patient, whom we saw again recently, is still perfectly satisfactory. A faint cicatricial



Figs. 17 and 18.—Epithelioma of malar region.

streak can only just be distinguished. Unless previously told of it, one would never notice it.

We may sum up by saying that radium has so far given very favourable results in many cases of this form of epithelioma. We consider it an ideal treatment.

(2) Sluggish Epitheliomata with Dry Surface, Surrounded by Nodules

The observations made in the preceding paragraph apply in all respects to epitheliomata with a dry surface. These lesions only differ from those just mentioned by the absence of ulceration. The prominent epitheliomatous nodules, smooth, stretched, and pearly, which surround the ulcers of the former group are found again here, but the centre of the surface is smooth and even, without break of continuity. These growths are usually very superficial and sluggish, and in some cases cover large

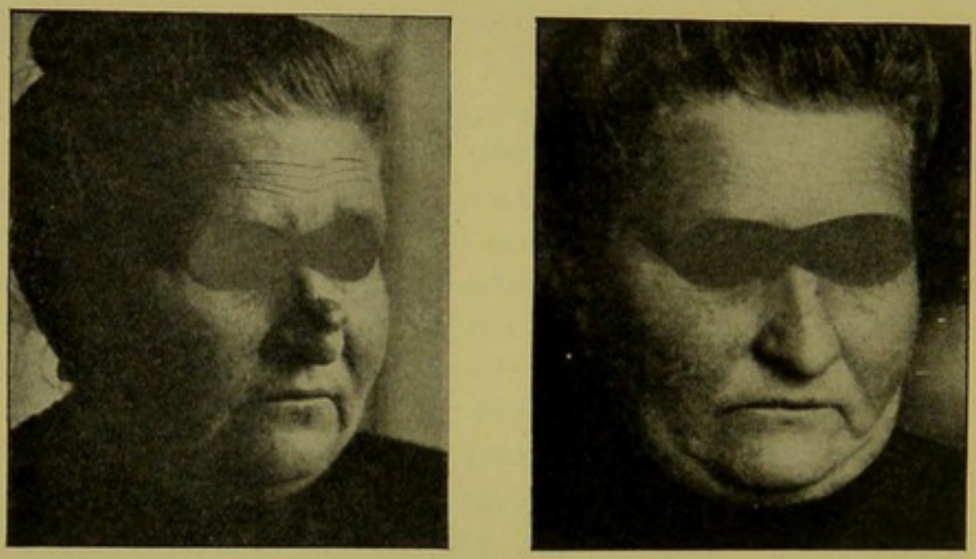
areas. But on the other hand they may consist of a single epitheliomatous nodule, either on the first appearance of the growth, or in the event of a relapse. The lesions heal very easily, with or without superadded ulceration. The following example shows the effect which may be obtained by direct application of the apparatus.

i. **Epithelioma of malar region** (Figs. 17 and 18).—A patient, aged 43, presented an epithelioma of the left malar region. The lesion measured about 9 cm. square on the surface. It was characterised by a collarette of large epitheliomatous nodules surrounding a depressed centre, which was cicatrised but not ulcerated. This growth had first appeared thirteen years previously, after the patient had attempted to remove a comedo with a pin picked up in a circus. The only methods previously tried were galvano-cautery, scraping, and hot-water applications, and they were all unsuccessful. The lesions had begun to spread three or four months before the patient came to us. We applied apparatus No. 1 for half an hour on August 7th, 1907, and for one hour on August 8th, 9th, and 10th. In order to form an estimate of the total dosage, it should be noticed that the lesion being smaller than the surface of the apparatus, the radiation available was proportionately less than the amount indicated in the table. On the 19th an erythema made its appearance, followed by a scanty flow of serous fluid. A crust was formed which dried quickly, and adhered firmly at its base. A month afterwards the crust fell off, disclosing the newly formed surface, which was smooth, even, of satisfactory appearance, and showed no trace of nodules. A year later the cicatrix was still in admirable condition, and relapse appeared most improbable.

The slow methods of thick filtering also lead, as we shall see, to the healing of epitheliomatous nodules, but for these forms we prefer rapid methods with great radioactive intensity, merely suppressing the α and some of the soft β rays by the interposition of $\frac{4}{100}$ to $\frac{8}{100}$ mm. of aluminium. The two following cases were treated by filtering.

ii. **Epithelioma of the right cheek.**—An epithelioma of the right cheek occupied the whole region situated between the lower eyelid, the lateral surface of the right side of the nose, and a line joining the external angle of the eye to the right ala nasi. It presented many different aspects. Near the nose was a scarred and erythematous surface, which threatened a relapse. Below the eye and under the skin were aggregations of non-ulcerative nodules, almost amounting to a small tumour. Below this, and in the nasal groove, slight ulceration existed. For the dry lesion situated below the eye, which was the principal growth threatening to ulcerate, and which denoted the

spreading of the epithelioma and its extension towards the eye, it was necessary to act at some depth. We therefore applied to this place for nine consecutive nights, from 9 o'clock in the evening to 8 in the morning, apparatus No. 5,* enclosed in 1 mm. of lead. The erythematous lesion was treated for five days, two hours daily, with apparatus No. 5, covered by $\frac{1}{10}$ mm. of lead. We treated the slight ulceration with the same apparatus, and $\frac{8}{100}$ mm. of aluminium, for two hours daily, during a period of four days. The results were exceedingly good. Every part responded to treatment exactly as one could have wished; and five weeks afterwards smooth, even, and supple cicatrised surfaces, of excellent appearance, had replaced the affected parts.



Figs. 19 and 20.—Epitheliomatous tumour of bridge of nose treated by penetrating rays.

iii. **Epitheliomatous tumour, treated by "surpénétrant" rays** (Figs. 19 and 20).—A patient, aged 53, in July, 1907, presented, on the bridge of the nose, an epitheliomatous tumour, slightly transparent. This lesion had made its appearance twelve years before, as the result of a blow, but had only increased in size during the previous six months. The skin was not ulcerated, but it adhered to the underlying neoplasm. The treatment of this tumour consisted of three series of applications of twelve hours each, spread at almost equal intervals over five or six days; the first, from July 8th to 11th; the second, from August 12th to 19th; the third, from September 16th to 20th. On July 29th the neoplasm was already considerably reduced, and on September 16th it was level with the surface, no inflammation having been produced during the process of resolution. At the present time the surface presents an almost normal appearance; it is smooth and even, and

* *See* column 1 of p. 46 for analytical table of apparatus.

shows no tendency to relapse. Apparatus No. 14 was used for the first and second series, enclosed in a lead sheet of $\frac{3}{10}$ mm.; and for the third series a sheet of 1 mm.*

(3) Ulcerative Cutaneous Cancroids showing Malignant Characters by their Tendency to Deep Extension

In contrast to the preceding epitheliomatous forms, for which doses administered on a large scale and in a small number of applications are to be preferred (uncovered apparatus or light screens), we give here, in a single group, those examples of cutaneous carcinomatous growths which seemed to us to respond best to doses that were large as regards their total, but were administered in applications with a very small number of rays (medium screens).

Some epitheliomata, on account of the depth of their infiltration, and their malignant and perforating characters, must be considered as *noli-me-tangere*. It therefore seems more reasonable to treat the different stages of these growths alike. A large dose administered in the first instance, which would have too strong an effect, particularly on the superficial layers, might perhaps incur a risk of irritating, and to some extent stimulating, the deep layers. This does not, however, imply that such massive doses introduced at the beginning must of necessity prove injurious. We have ourselves frequently obtained very good results with them, even in difficult cases. The following example is a proof of this.

i. **Excavating cancroid** (Plate II, Figs. 1 and 2).—A patient presented, on December 6th, 1906, on the right ala nasi, a crusted ulcer 2 cm. long by 1 cm. broad. This lesion had been unsuccessfully treated by X-rays and cauterisation. Some improvement took place, but it was never satisfactory or permanent, having always been followed by relapse. When the crust was removed, an ulcerated cavity was disclosed about 6 or 7 mm. deep; the lower edge being punched out. The bottom of the wound was yellowish, and of alarming appearance. On account of the failure of previous attempts, and the signs of malignancy, we adopted at first the following doses: On December 6th, one hour of apparatus No. 7, applied without a screen, and twenty-five minutes of apparatus No. 12, on a part not covered by the first apparatus; the same applications being repeated on the 7th and 10th. The yellowish base already showed signs of improvement, and some tendency to become filled in. The crust, which formed again from the 7th to the

* It should be understood, once for all, that, in order to simplify description, we do not mention each time the wrapping of the metallic screens in sheets of paper and rubber tissue.

10th, was easily removed without making it bleed. Ten applications of apparatus No. 7 were afterwards made, each time for an hour. On January 10th the reaction was at its height. A yellowish crust, honey-like, and impetiginous, covered the whole surface treated. On pressure, a drop of sero-purulent fluid oozed out. The tissues undergoing reaction then dried up quickly, and on January 25th the crust fell off of itself, disclosing a healthy-looking surface in course of repair. On February 12th the cure appeared to be complete. There was no subsequent relapse, and in November, 1908, the region examined was remarkably supple. The tissues were smooth and even, showing neither depression nor telangiectases. We think that the dosage was too

Figs. 21 and 22.—Epithelioma on pigmentary nævus.

large in this case; six or seven hours, as in the next example, would have been sufficient.

ii. **Epithelioma on pigmentary nævus** (Figs. 21 and 22).—On the lower third part of the cheek of a woman of 51 there was a pigmentary nævus of the variety known as "beauty-spots." Seven years ago this nævus underwent an epitheliomatous transformation. An ulcer formed by degrees, which, when we saw it, was the size of a one-franc piece, the edges being punched out. A month previously an ulcer of the same kind, but of very rapid growth, had developed near the external angle of the eye. The symptoms were grave, and demanded prompt and energetic intervention, the more so as it was necessary to prevent invasion of the eyelid. We applied apparatus No. 6, without a screen, for six hours in succession, to each ulcer; and a fortnight afterwards inflammatory reaction of average intensity, with ulceration and crust-formation, was produced on the surface of

each growth. The crusts came away about the sixth week, and showed a smooth and even surface, of healthy appearance. The cicatrices have remained quite firm for eight months, and show no tendency to relapse.

Our reasons for resorting to filtration in the treatment of these lesions are mainly theoretical. The aim is to impregnate the whole thickness of the carcinomatous tissue, slowly and gradually. Filters of medium thickness are usually the most suitable for these lesions; they consist of aluminium or lead sheets, $\frac{1}{10}$ mm. thick. The methods are very numerous; the choice of screens, length and division of applications, varying according to the time at the disposal of the patient, the nature of the lesion, and the apparatus which can be obtained. We will confine ourselves to a few examples. The knowledge and experience of the operator must determine the choice of these methods. For cases similar to No. 1 (p. 119) we should occupy, with apparatus No. 5, for instance, a total period of ten to twelve hours, spread over ten or twelve days, with a screen of about $\frac{8}{10}$ of aluminium. With $\frac{1}{10}$ of lead, fifteen to twenty hours would be necessary, divided into four or five applications in the course of twelve days. Epitheliomata which are complicated by erythema and lymphangitic inflammation are also amenable to these doses. Such inflammatory growths, when they do not yield to ordinary mild applications, give rise to much anxiety; they are often particularly sensitive, and have a tendency to extend deeply. They are *noli-me-tangere* in the highest degree, and it is therefore better to use for them "surpénétrant" rays filtered through lead sheets, say $\frac{5}{10}$ to 1 mm. thick, or sometimes even 2·5 mm., as in the following case.

iii. **Infiltrating epithelioma.**—An ulcero-crustaceous epithelioma of the pre-auricular region with peripheral inflammation presented a punched-out perforating ulcer when the lesion was freed from its crust. Careful examination revealed a detached border of 1 to 2 mm. over the whole circumference of the ulcer, and on the upper part this border reached a size of 1 cm. Pressure on this spot was extremely painful, and produced a little drop of purulent fluid. The extent of the epithelioma being much greater than appeared at first sight, the treatment had to be directed, on the one hand, to the ulcer, and on the other to the regions covered with skin, which, though apparently healthy, was detached. The case was a serious one, and had resisted the X-ray treatment. We therefore decided to resort to the action of "surpénétrant" rays alone, and to push the treatment to the stage of ulcerative reaction. We used the No. 3 square apparatus enveloped

in 2·5 mm. of lead, and it remained in place from 9 o'clock in the evening till 8 in the morning, every night from August 26th to 31st. We afterwards increased the thickness of the lead to 3 mm., and the apparatus was left on for the same length of time from September 2nd to 8th. On September 14th the part was red, oozing with blood, and much inflamed, the detached portions being exposed. On the 21st a crust formed which covered the whole lesion, and below it there was an abundant serous discharge. The upper part, which had been to a large extent detached, and painful to the touch before treatment, was no longer sensitive. Little by little the secretion diminished, and the edges of the crust, having become quite dry, were loosened. On October 5th the whole crust came off and disclosed a very healthy-looking restored surface. This condition was maintained for five months.

This instance proves that inflammatory reaction can be obtained, even by the employment of "surpénétrant" radiations containing but few β rays. The object of this reaction, which has an almost uniform effect on the diseased tissues, is to destroy the neoplasm at any stage of its development, without producing injurious results. In this way we have arrived at excellent results by very different methods, with and without a screen. In fact, radium furnishes us with many very useful methods of treating these serious and troublesome forms of cancroid. It is extremely valuable as a therapeutic agent, and has given, so far as we can judge, permanent results.

(4) Superficial Ulcerative Epitheliomata with Large Surface

When radium was first used for medical purposes it was believed that radiumtherapy would be limited to the treatment of small benign cancroids. In the preceding paragraphs, we have already been concerned with epitheliomata which presented some characters of malignancy, and we shall now see ulcers of large extent reduced and healed. Even in August, 1907, at the Congress of Rheims, we were able to assert that, by the use of powerful instruments, it was possible to reduce such epitheliomata. The following observations refer to neoplasms exceeding in virulence those hitherto described. We have already seen such an example on page 110 (Fig. 15). These growths have been usually treated with massive doses, and the results prove that this method which, by reason of the intensity of the reaction produced, has caused an unreasonable fear of excessive inflammation, is often an excellent plan for bringing about the cure of epitheliomata of large extent, even when the neoplasm happens to be situated in regions where

a bad cicatrix would occasion great injury from an æsthetic point of view. This method has given us particularly satisfactory tissues of repair.

i. **Ulceration of nose.**—An ulcer covered the whole left ala nasi, three-quarters of the lobe, and the whole middle of the base, both to right and left. The total area of the ulcerated surface was about 32 cm. square. This extension took place a year ago, following erysipelas, but the ulcer itself dates back seven years. The following method was adopted: Twelve hours, spread over a period of ten days, of direct application of apparatus No. 1, its position being changed at each exposure so as to affect the whole surface. This was an intensive dose.

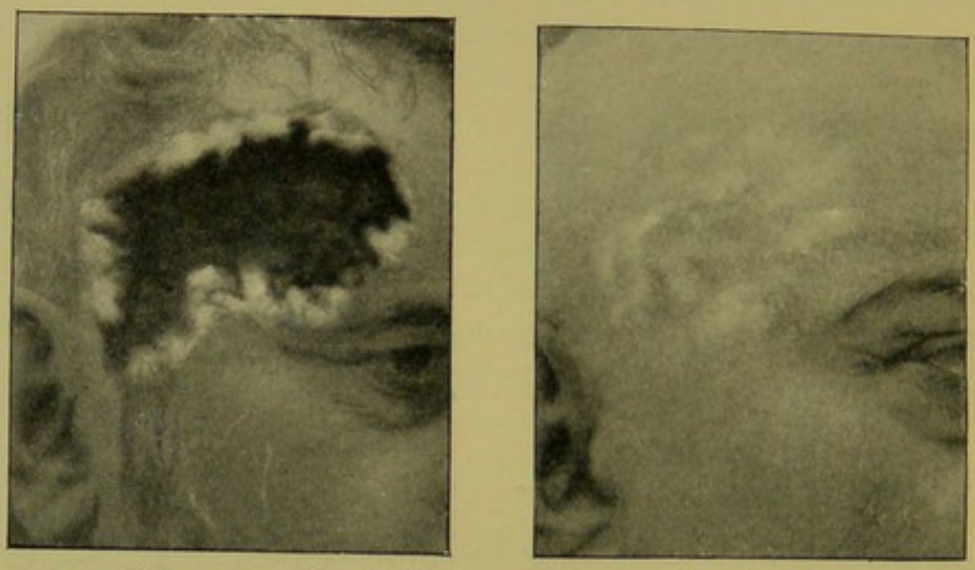
Figs. 23 and 24.—Ulcerated and crusted epithelioma of forehead.

After exceedingly strong reaction, the treatment, begun on January 14th, 1907, terminated with a healthy scar. The case, when presented on November 6th, 1908, to the Société Médicale des Hôpitaux, attracted notice by the excellence and stability of the scar tissues.

ii. **Ulcero-crustaceous epithelioma of forehead** (Figs. 23 and 24).—The patient, aged 45, who was brought to us by Dr. Favre of Poitiers, at the advice of Professor Raymond and Dr. Brocq, presented an epithelioma of the median portion of the forehead, measuring 6 cm. by 5. From the middle of the lower edge, which extended from one eyebrow to the other, there was an extension towards the root of the nose, and another which, passing beyond the left superciliary arch, threatened to reach the upper eyelid. The edges showed epithelial nodules. The ulcerative and vegetating centre was the site of constant serous exudation, which became solidified, and formed a crust of great thickness. The epithelioma appeared fifteen years ago, and since then has

never ceased growing; many methods of treatment had been tried, but none of them had succeeded in arresting its extension.

We applied every day for an hour, for six consecutive days, apparatus No. 1, enveloped in fine rubber. In consequence of this treatment a very marked crusted reaction was produced about the fifteenth day. The thick crust only fell off towards the twenty-fifth day, and gave place to a new one, not so thick, and reduced in size; a fortnight afterwards this in its turn dried up. Cicatrisation then proceeded very actively, and was complete two months later.*



Figs. 25 and 26.—Epithelioma of temporo-frontal region.

The following is an instance of a still larger ulcer, which, however, healed quite easily.

iii. **Epithelioma of temple** (Figs. 25 and 26).—One of Dr. de Beurmann's patients presented an enormous epithelioma, occupying the right half of the forehead and right temporal region, as far as the zygomatic apophysis. This lesion measured 15 cm. long by 8 cm. wide. It was bordered by large epithelial nodules the size of a pea, the ulcer being covered with granulations, which bled at the slightest touch. The treatment consisted in the application of two instruments, Nos. 1 and 3, each simply wrapped in rubber, and left on for six consecutive hours. They were placed in juxtaposition on the different points of the epithelioma.

Improvement took place slowly. Fresh applications of a similar

* *Note by Dr. Wickham.*—Six months after cicatrisation a small crusted ulcer was produced in the centre of the scar. It was not a relapse, but a radiumdermatitis of late development. We have often noticed a similar occurrence when the destructive method has been used to excess. It is well to be on the watch for it, for harm may be done if it is mistaken for an epitheliomatous relapse, and again treated with radium. The inflammation should be allowed to die away of itself, or be treated with emollients.

kind were made two months afterwards, and repeated at the end of a second period of fifty days. By the seventh month there was no longer any tendency to relapse.

3. EPITHELIOMATA OF SKIN AND MUCOUS MEMBRANE IN SPECIAL SITES

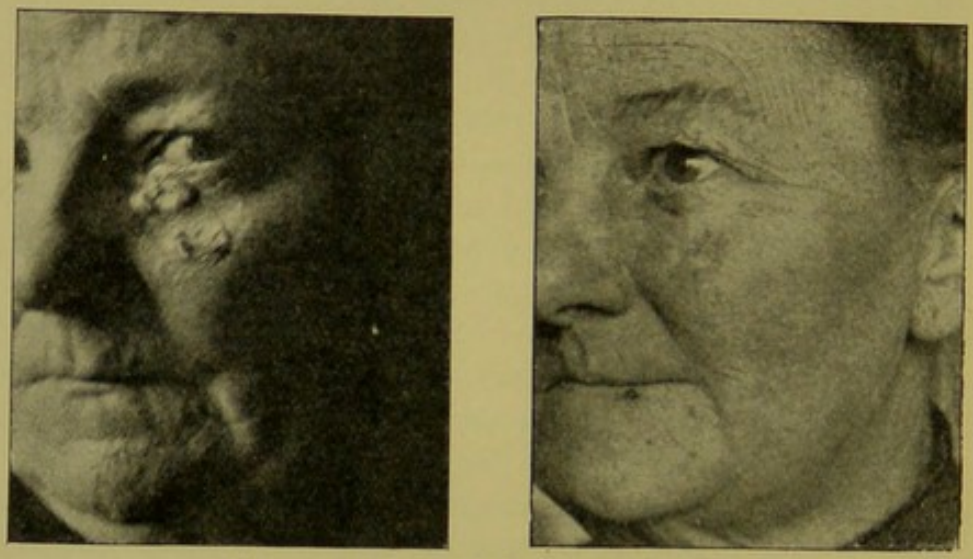
We have already shown that the adaptability of radium instruments permits of the treatment of regions which can scarcely be reached by other therapeutic agents. In this section we have collected cases showing still more clearly this advantage, which is most marked in the treatment of epitheliomata of the conjunctiva and the eyelids.

(1) **Epitheliomata of conjunctiva.**—i. An epithelioma affecting the whole region of the left lacrymal caruncle, and the inner third of the conjunctiva. The patient, who was sent to us by Dr. Hallopeau, had suffered from this growth for six years. The cutaneous lesions in the neighbourhood of the conjunctiva were treated with apparatus Nos. 8 and 9, applied for three hours, without a screen. They yielded to treatment in the ordinary way, and were not specially refractory. The conjunctiva itself required more delicate treatment, but owing to the flatness of its surface, it was possible to slip apparatus No. 13, enveloped in rubber, on to the caruncle and conjunctiva. Twelve exposures of ten minutes each, making a total of two hours, and spread over ten days, were prescribed for the first series. Two similar courses were employed at intervals of a month. The epithelioma of the mucous membrane diminished by degrees, without inflammation, and, a month after the completion of the third course, appeared to be healed. However, eight months afterwards a slight relapse occurred near the caruncle, which was treated by an hour's application of No. 11. There has been no recurrence for the last sixteen months.

ii. In a case of an epithelioma situated at the bottom of the outer conjunctival cul-de-sac of the left eye, the conjunctiva formed a swelling on the eyeball. The epithelioma itself projected as far as the level of the skin; epitheliomatous vegetations filling the whole region. The spherical apparatus No. 11, and the flat apparatus, No. 13, were applied daily, the former in the bottom of the cul-de-sac, and the latter on the flat surfaces, both wrapped in aluminium $\frac{2}{100}$ mm. in thickness and in rubber. One instrument was used one day, and the other the next, in short exposures of fifteen minutes, in such a way that every part was almost equally affected. It would have been difficult to operate for longer periods without irritating the mucous membrane. The congestion of the conjunctiva diminished by degrees, the vegetations being reduced; and after several series of applications, the region had

lost its induration and thickening. Dr. Abadie thought that the cure was complete, since the cul-de-sac was in good condition, but ocular troubles made their appearance and slowly grew worse, necessitating, after a delay of two months, the enucleation of the eye. M. Abadie then discovered that the epithelioma had penetrated to the wall of the orbital cavity. Curetting was employed for the latter lesions, and since then no relapse has occurred.*

(2) **Epitheliomata of eyelids** (Figs. 27 and 28).—i. A patient showed, in the substance of the lower eyelid, an aggregation of epithelial nodules. It was necessary to avoid any treatment which might produce inflammation of the eye, and with this object we adopted apparatus



Figs. 27 and 28.—Epithelioma of eyelids.

No. 7, with a screen of $\frac{1}{10}$ mm. of lead, and inverted it, so as to direct the rays downwards. The length of application was for one hour, six days in succession. After three similar courses at intervals of six weeks healing was obtained without any irritation of the eye.

ii. An ulcero-crustaceous epithelioma of the upper eyelid, developed from a seborrhœic wart, was specially difficult of treatment, on account of the proximity of the eye, for it reached the ciliary margin. The square apparatus No. 3, enveloped in $\frac{6}{10}$ mm. of lead, was applied for eighteen hours, one or two hours at a time, from May 1st to 13th. These applications were followed by a crust of medium thickness, which fell off in less than a month, leaving a smooth and supple surface. This did not cause the least injury to the eye, disfigurement of the palpebral fissure, or mutilation of the eyelid.

* *Note by Dr. Wickham.*—Since this was written, a relapse took place, and the patient died. No radium had been tried on the deep cancer, as the patient lived some distance from Paris.

iii. A patient, aged 47, was sent to us by M. Balzer in October, 1907, for an enormous epithelioma of the lower eyelid, the ciliary margin of which was entirely destroyed. This growth had appeared sixteen years before, in the internal angle of the eye, in the form of a small nodule, which was operated on, and did not recur for five or six years. Ten years ago, on the site of the cicatrix, a vegetation appeared, and continued to increase. A year ago its growth was so rapid that the whole ciliary margin of the lower eyelid and the lacrymal caruncle were both destroyed. Some adhesions were formed between the free margin of the lid and the ocular conjunctiva, and limited the movements of the eye to some extent. On the skin itself, and all along the ciliary margin, from the external to the internal angle, on the latter of which there was a large pearly nodule with hard edge, a series of small crusts and ulcers was seen. Photophobia and abundant epiphora were also present. Apparatus No. 13, wrapped in rubber tissue, was applied to six places, for two hours; a quarter of an hour on each place. A second series of applications, made a month afterwards, produced serous oozing; the epiphora was less abundant, and the photophobia had disappeared. The edge of the eyelid has been cicatrised for ten months, and no relapse has occurred.

These few examples show the use that can be made of applicators with flat and spherical surfaces; they also prove that the conjunctiva is not easily irritated by radium. On the other hand, epitheliomata of which it is the site respond more quickly to doses which would be insufficient for cutaneous growths of this nature. Radium is, therefore, a very suitable means of treatment for epitheliomata of the ocular mucous membrane, both on account of the adaptability of the instruments and the value of the therapeutic action itself. It might seem that on account of the proximity of the eye and the risk of causing retractile cicatrices, any process liable to produce inflammatory reaction must be carefully avoided. This, however, is not in the least the case, and it is one of the advantages of radium to allow of the re-formation of perfectly supple tissue after such reaction. In spite of this, we usually employ non-irritative doses for these regions.*

(3) **Epithelioma of auricular canal.**—M. ——, aged 70, presented an ulcero-crustaceous epithelioma of the auricular canal. The lesion extended to a depth of about 1·5 cm., and had spread externally to the cavity of the concha. After having ascertained the exact limits of the growth, we used apparatus No. 10, in $\frac{1}{100}$ mm. of aluminium,

* *Note by Dr. Wickham.*—The beneficial effect of radium treatment on the eyelids has long been known, and recorded by many observers, especially A. Darier, in France, and Mackenzie Davidson in England.

in applications of twenty minutes each, for fifteen hours, spread over a month, and obtained complete resolution. The external part was treated with No. 8, applied for three hours.

It is difficult, when dealing with epitheliomata of the auricular canal, to keep the cylindrical apparatus for long in a good position, and exactly at the level of the ulcerated parts. It is therefore well to make use of very high radioactivity, so as to operate by means of short exposures, frequently repeated.

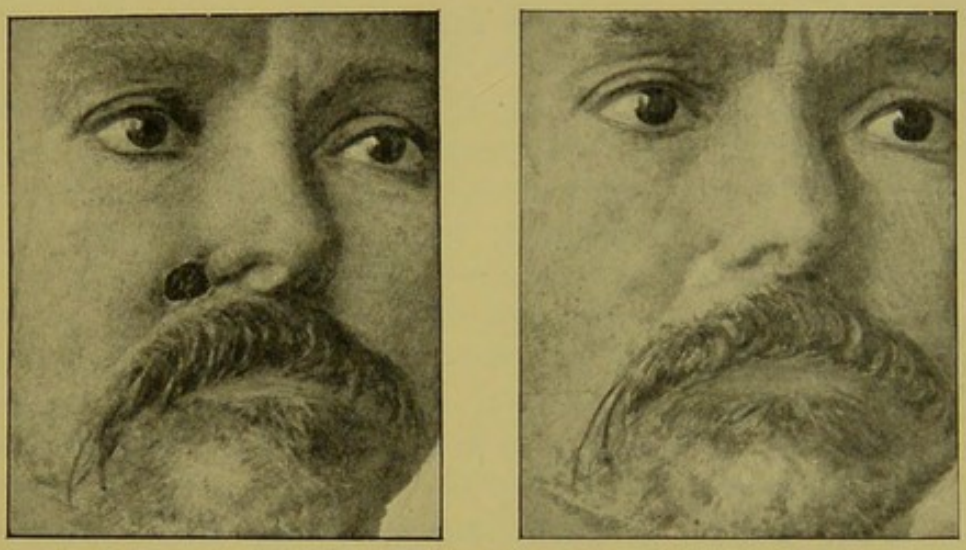
(4) **Epitheliomata of nasal mucous membrane.**—i. An epithelioma of the nasal groove and the corresponding nasal mucous membrane began twenty years ago with a small nodule; by degrees the skin became ulcerated and covered with a crust. On moving the tip of the nose, a fissure was seen under the crust, showing the beginning of detachment of the left nostril, and pressure on this spot produced a little drop of purulent fluid, which appeared to come from the interior of the nose. There was also difficulty in breathing. Dr. Caboche, the rhinologist who kindly examined the state of the mucous membrane, reported as follows:—

"The patient presents an ulcerative intranasal lesion, of the same character as the ulceration of the sulcus. It occupies the front part, the floor and the outer wall of the vestibule as far as the head of the inferior turbinated bone, which is not affected. There is internally a fissure which threatens to detach the ala nasi, but I have been unable to discover any communication between the intra- and extranasal ulcers."

It was important to ascertain whether, by acting only on the cutaneous surface of the nose, and by using rays of great penetration, the intranasal lesions might also be improved at the same time. With this object, apparatus No. 3, in 1 mm. of lead, was applied as a bridge, from the nose to the cheek, the air between the centre of the instrument and the lesion acting as a screen. An application of two hours was repeated for twenty consecutive days. The first phenomena to be observed were the cessation of the discharge, and the drying up of the crust. Towards the fifth week, the crust fell off, disclosing a clean, smooth surface, with a healthy-looking scar. The difficulty of breathing through the right nostril had disappeared, and the epithelioma of the mucous membrane, when again examined by Dr. Caboche, showed evident signs of diminution. The ulceration was considerably modified; it was much less marked, and only persisted in the upper part of the vestibule. The cylindrical applicator, No. 10, was then applied for two hours in the nostril to the remains of the growth. The intra- and extranasal lesions may now be considered healed. The action of the rays on the epithelioma

of the nasal mucous membrane through the whole thickness of the nostril was very remarkable.

ii. A patient (Figs. 29 and 30) had for some months seen the development in the nasal groove of an ulcer which became more and more depressed, and developed very rapidly. The nose was perforated, as far as the mucous membrane. The edges were punched out; the ulcerated periphery was red and bleeding, the base being lined with a yellowish scab of unhealthy appearance and offensive odour. All these symptoms taken together gave the growth a specially malignant character. We employed apparatus No. 8, in $\frac{4}{100}$ of aluminium. In the course of eleven days, the instrument was applied for a total period of eighteen



Figs. 29 and 30.—Epithelioma of nasal mucous membrane.

hours, in exposures of two hours each. A month later, after a crusted reaction which did not last long, the ulcer became finally cicatrised. The scar, when it was seen two years later, had remained in excellent condition.

These examples show not only the efficiency of radium, but also the convenience and adaptability of instruments which lend themselves to the treatment of such widely different regions.

PRECANCEROUS AFFECTIONS

Papillomata and senile warts.—These lesions are often the starting-point of epitheliomata. It would be unnecessary to mention the action of radium on affections so trifling, and so easily curable by many other modes of treatment, if it were not specially effective. One or two hours' application of apparatus No. 7, for instance, will easily cure an aggregation of two or three small papillomata of the

scalp, or seborrhœic and senile warts. It is merely from the fear of their being precancerous that it is necessary to mention such lesions in this chapter.

GENERAL CONSIDERATIONS

From the analysis of this first group of facts, a certain number of conclusions stand out clearly, the principal of which are as follows :—

1. Radium is applicable not only to small, sluggish, and benign epitheliomata, which are easily curable, as was known before we began our work, but also to forms of epithelial cancer which, refractory to other treatments, have relapsed into a bad condition, forms which show a malignant character (rapid evolution, perforation, punched-out edges, inflamed periphery and base, and large surface); and yet all these unfavourable cases have scarcely altered our statistics for the worse.

2. Our statistics include, among the epithelial cancers of this first group, only those the treatment of which was completed before January 1st, 1908. The most recent cases are more than a year old, the older ones dating back nearly four years; the element of time—an indispensable condition for the value of records of this sort—will therefore be sufficiently allowed for. Out of 59 cases, we have noted 3 which were unsuccessful. These figures, compared with those obtained from other therapeutic measures, seem relatively favourable. The failures were due to relapse which occurred when the patients were out of reach of our supervision. When symptoms of relapse show themselves—which, however, seldom happens—they are usually relieved without difficulty. We have had other failures, but these were in carcinomata of special gravity, and are quite outside the scope of our first group.*

3. The æsthetic value of the scars is an interesting point for consideration. Absence of retraction, depression, and prominent bands is the rule, and this is a great advantage in the treatment of ulcers in the neighbourhood of orifices, especially those situated on the eyelids. The scars are usually smooth, even, supple, and can often be distinguished from the neighbouring healthy tissue only by their lighter colour. They are seldom the site of subsequent pigmentation or telangiectases. In several cases they are completely effaced; the epithelioma of the ear in Plate II being a good example.

4. Convenience of application, absence of all constraint, and freedom from pain are all great advantages in the treatment of these epitheliomata, which so often attack old people. The patient can

* *Note by Dr. Wickham.*—At the present time, after an experience of five years, I am able to record similar results.

himself hold the apparatus when once it is put in position. It is better to have the instrument fixed by a band; it can then be allowed to remain for a long time without causing fatigue. There is nothing striking or noisy about the apparatus, a fact which is calculated to encourage timid persons. Moreover, there is so little appearance of "treatment" or of having anything remarkable done, that during the ten or twelve days following the application, in the course of which nothing appears to have resulted from it, the patients are sometimes sceptical, and it becomes necessary to reassure them.

5. The possibility of adapting the shape of the apparatus to the regions to be treated, and of conveying the radioactivity into depressions, cavities, and passages, is an advantage which has been recognised from the commencement of radiumtherapy; but we must recall the fact that in the case of hidden and hardly accessible regions having a small surface, this advantage only obtains when radium salts of very great intensity are used, for the small applicators required for these lesions emit an inferior radioactivity on account of their limited surface.

6. The selective action of the radiation on certain carcinomatous cells is evident. We consider that this consideration predominates in importance over all the rest, for by means of this selective action epitheliomata can be cured without ulcerative reaction, doses and methods can be regulated, and the most serious cases of carcinoma can be treated. Moreover, histology has shown that the regression of epitheliomatous neoplasms has quite special characters.

7. Only scientific dosage can ensure the progress of radiumtherapy, and we have therefore always been anxious, from the very beginning of our work, to act with precision. Dosage may be regarded from two very different points of view, that of physics and that of therapeutics. Physical dosage may be fairly exact. We have seen, indeed, that by means of electrometrical analysis the available radioactivity emitted outside the instruments can be estimated, whether they are used uncovered or with screens. Therapeutic dosage, that is to say, a knowledge of the quantity and quality of radioactivity suitable for particular cases, cannot be indicated with the same certainty. It does not depend entirely on experience gained in the use of the technique; it also proceeds from a knowledge of the clinical characters of the epitheliomata and of individual susceptibility. Now such characters being particularly variable, it would seem very difficult to establish any general rule for all the cases treated. By reference to our experiments, the plan which we have adopted in each particular case may be ascertained. We may, however, recognise, from a therapeutic point of view, two principal groups, corresponding to two different methods.

In the first we put cutaneous epitheliomata, which may be ulcerated or non-ulcerated, sluggish, large or small, superficial, and not exceeding 3 or 4 mm. in depth ; also fungating epitheliomata of all sizes.

In the second group we place epithelial carcinomata accompanied by inflammation, perforating in character, and with deeper infiltration, and epitheliomata of the ocular and nasal mucous membrane.

In the first group massive doses (radiations applied collectively) are the most suitable. The apparatus should be used without screening, or with very light screens, $\frac{1}{100}$ to $\frac{4}{100}$ mm. of aluminium, so as to furnish the largest possible amount of activity. The duration of the applications is therefore short, an average of three to six hours, distributed if possible over several days, or concentrated into a single exposure. For instance, for a superficial epithelioma, with 4 square cm. of surface, applicator No. 4, emitting a total radiation with an activity of 50,000, should be left in contact for five or six hours. If it acts over the whole of its surface, apparatus No. 1 will furnish a sufficient dose in four hours. For a small applicator such as No. 8, eight hours will be necessary. These are average doses.

In the second case, where it is important to avoid hastening cellular modification, and to act uniformly and simultaneously upon the entire thickness of the neoplasm, the energy must be dealt out more slowly, in small doses, whether we employ all the groups with unscreened apparatus, or only " surpénétrant " or intermediate rays. The first condition is realised by means of frequently repeated exposures of very short duration, as in Case 2 (p. 126). The second requires the method of long exposures, as in Case 3 (p. 121). In either case it will be possible to calculate the doses of radiation by reference to our tables and scheme of dosage.

The method of long duration (with screens of 1 to 2 mm. of lead), using " surpénétrant " radiations in which γ rays occur in large numbers, is the best for perforating growths and deep infiltration. Between the principal groups which we have indicated there exists a whole series of intermediate cases, for which intermediate techniques will be suitable (screens from $\frac{1}{10}$ to $\frac{3}{10}$ mm. of lead). These are the cases most frequently met with, and they require very careful discrimination. But there is no absolute rule. We have always refrained from asserting that only one particular dosage or method is suitable for certain cases, knowing from experience that this would bring down on us well-merited criticism. Quite different methods may achieve similar results. A growth may be healed just as well by the action in 100 or 120 hours of a " surpénétrant " radiation, with an activity of 4,000, as by the action in six hours of the total radiation from the same apparatus used without

a screen. Moreover, in the selection of a technique, great stress must be laid on the requirements of the patient and other practical considerations. Facts, experience and common sense are not of less importance in radiumtherapy than in other healing agencies.

From these considerations regarded as a whole we learn, amongst other things, that the dose of radioactive energy can easily be varied in such a way as to permeate deep epitheliomatous tissue, on which it exercises a special selective curative influence. They show the possibility of extending radium treatment to carcinomata with deep infiltration, and to those which are mucous and subcutaneous; in fact, to growths of a very serious character. Some of the following examples will show that this is not a matter of hope or conjecture, but of accomplished facts. Recent improvements in the instruments have enabled us to obtain far more important results than those previously mentioned. When, in the large instruments, which are from 10 to 30 cm. square, radium salt in the proportion of one-fourth can be replaced by pure radium; when we know how to combine the simultaneous action of several of these instruments; when we can at the same time introduce tubes, injecting into neoplasms radiferous solutions of great activity—then we are convinced that the limits of the healing effect of radiumtherapy will be gradually extended. Its future depends upon the amount of energy available. We now have at our disposal extremely great radioactive intensity, by means of the "cross-fire" method, whenever it is possible to apply it, and means have been found of increasing the intensity in other ways. The clinical examples with which the following chapter opens will serve to confirm what has just been stated.

CHAPTER III

THERAPEUTIC RESULTS (Continued)

I. CARCINOMATA AND OTHER MALIGNANT GROWTHS (Concluded)

II. MALIGNANT NEOPLASMS

We shall now treat of neoplasms which are of a grave character on account of their position, nature, extent, or size. They will be divided into four groups, according as they are situated—

1. In the skin and subcutaneous tissue.
2. In the lymphatic glands.
3. In the breast.
4. In the buccal mucous membrane.

The application of radium to carcinomata of the uterus will be considered in the chapter reserved for gynæcology.

In each of these groups we have observed various degrees of improvement under radium treatment; the selective action of radium has nowhere been more evident or more valuable. Although the examples are not as yet very numerous, we may be able to draw some general conclusions from the cases analysed in this chapter.

1. CUTANEOUS AND SUBCUTANEOUS CARCINOMATA

Amongst the cases grouped under this head we choose the six following, because, when we undertook them, they did not seem more amenable to any other therapeutic measures, and, in some cases, had resisted other forms of treatment.

(1) **Epithelioma with perforation, affecting half the face.**—A patient, aged 64, appeared with her head, including the eyes, entirely wrapped in bandages and linen, soaked in pus and blood. The removal of the wrappings caused pain, and disclosed the most horrible lesion imaginable. It was a fungating epithelioma of enormous size, forming a large and prominent tumour, which affected three-quarters of the left cheek. On the upper lip there was an immense vegetating mass, spreading below the labial commissure and covering the lower lip. The left side of the nose had disappeared under a fungating growth,

having a projection of 1·5 cm., which, having covered the whole bridge of the nose, was spreading to its right lateral surface, and was itself the site of an erythematous infiltration. The eye was hidden under epitheliomatous masses. This tumour, the aspect of which produced a most painful impression, had a fetid and repulsive odour; a blood-stained purulent liquid was flowing from it, which entered the eye, nose, and mouth. From the centre of this mass it was possible to penetrate into the left nasal fossa, and the attachment of the upper lip, destroyed at one point, allowed of the passage of a probe, which came out again at the mouth. The patient wore a bib, on which saliva, blood, and pus had accumulated. The poor creature was in a very bad state of general health, for she was badly nourished, and the carcinoma was the source of frequent and abundant hæmorrhage, which exhausted her.

This neoplasm had begun only six months previously, with a small seborrhœic wart on the cheek; its development had therefore been very rapid, although it had not been neglected. Dr. Vigoureux had tried X-ray treatment for several months. At length, seeing that the progress of the tumour was not arrested, our distinguished colleague used some exposures of high frequency, but with no better results, and he then thought of radium. Dr. de Beurmann kindly received the unfortunate woman at his clinic, where the treatment was undertaken. A month afterwards, radical improvement had been effected, both in the general state of health and the local condition. On the occasion of the two first applications of the remedy, such severe hæmorrhage took place that it was feared the patient would not survive it. But this quickly diminished, and eventually ceased entirely. By February 1st one portion of the tumour was completely reduced; the eye and upper lip were set free; the offensive odour existed no longer, and the part took on the reddish colour characteristic of tissue which is well on the way to repair.

The following dosage and technique were employed. We applied "toile" apparatus No. 15, in 2 mm. of lead, over the whole circumference of the tumour. The pliancy of the "toile" permitted the fashioning of a concave apparatus adapted to the enormous peripheral edge. Left in the same place for twenty-four hours, the apparatus was fixed each time next to the region where it had been on the previous day; in a fortnight, it had been used in each place for a total of fifty-two hours. In the centre, for three consecutive days, that is, seventy-two hours, we applied an apparatus containing 12 cg. of sulphate of radium, with an activity of 1,000,000, in 2 mm. of lead.

A new series of applications was made from February 1st to 15th. At the present time (March 1st, 1909), the improvement is very marked,

cicatrisation having taken place over the whole periphery. There is no longer hæmorrhage, and what remains of the growth resembles curetted tissue, only needing repair. The patient has now recovered her normal health ; she has a good appetite, and is growing stouter.

It is interesting, moreover, to note that six years ago this same patient had, on the right temporal region, a small epithelioma for which M. Balzer had scraping performed by a surgeon. Then, relapse having taken place, an excision was made. The lesion having again relapsed, M. Balzer sent her to M. Danlos, to be treated by radium.

In spite of this improvement, as the reduction of the vegetating masses has permitted of more exact knowledge of the extent of the deep lesions, particularly the invasion of the floor of the nasal fossæ, this case must not be considered as permanently successful. Very energetic treatment should be again resorted to, in the hope of affecting the base of the neoplasm.*

In the following case the carcinoma had destroyed the tissue over an extensive surface, and had reached the underlying osseous regions which had a blackish, necrosed appearance.

(2) **Ulcer covering left half of forehead, and temporal region, and affecting osseous wall.**—(A patient of Dr. Jeanselme's, treated at Dr. de Beurmann's clinic).—The ulcer measured, 12 cm. by 8 ; it occupied the left half of the forehead, and the entire temporal region. Its upper edge was 2 cm. from the roots of the hair ; below, it encroached upon the necrosed superciliary arch. Indeed, this huge ulcer was so deep that the external frontal table was necrosed over an extent of 3 cm. by 6, and from its dark appearance formed a contrast to the rest of the ulcer. The superciliary arch was destroyed, the upper eyelid had been invaded and detached, and was the site of a groove, which was spreading to the upper conjunctival cul-de-sac. On the exterior of the ulcer there was a huge vegetating mass, the edges of which were punched out. Everywhere else the growth was surrounded by a large ridge, and its surface was intersected by vascular dilations. The internal edge, especially above the base of the nose, presented a thickening of about 1 cm., the pain being very severe in this region. The left eye was attacked by exophthalmos and chemosis. This neoplasm had commenced eighteen months previously, and made rapid progress.

The treatment consisted in applying every day, on the edges of the lesion, apparatus No. 15, covered with 2 cm. of lead, in such a way that each part should be treated for sixty-two hours. After the first applications the fungating portion improved, as well as the large peripheral rim,

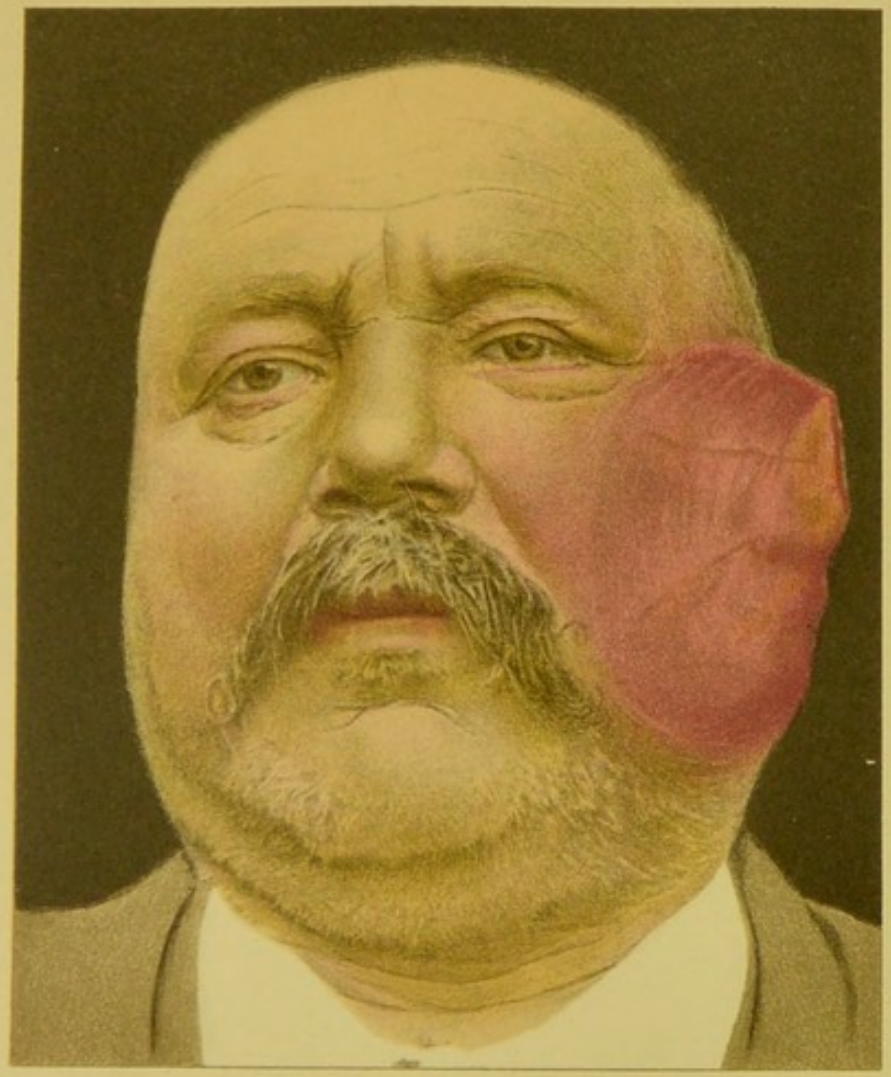
* *Note by Dr. Wickham.*—The patient has since died of meningitis, the growth having developed high up inside the nose, on the upper part of the bone.

PLATE III

EPITHELIOMA OF PAROTID REGION (p. 137)

FIG. 1.—The epitheliomatous tumour was not quite so red as shown in the plate. The overlying skin, raised by the neoplasm, was smooth, adherent, stretched, and inflamed, but showed no ulceration at the periphery of the tumour. Only one part was ulcerated. It was about the size of a two-franc piece, and situated at the upper part of the growth.

FIG. 2.—A full-face photograph was taken, so as to allow a comparison to be made between the patient's physiognomy before and after treatment. But the part is not quite normal. It is the site of two small, hard, movable projections, which appear to be fibro-sclerotic remains, produced in course of transformation of the epithelioma.



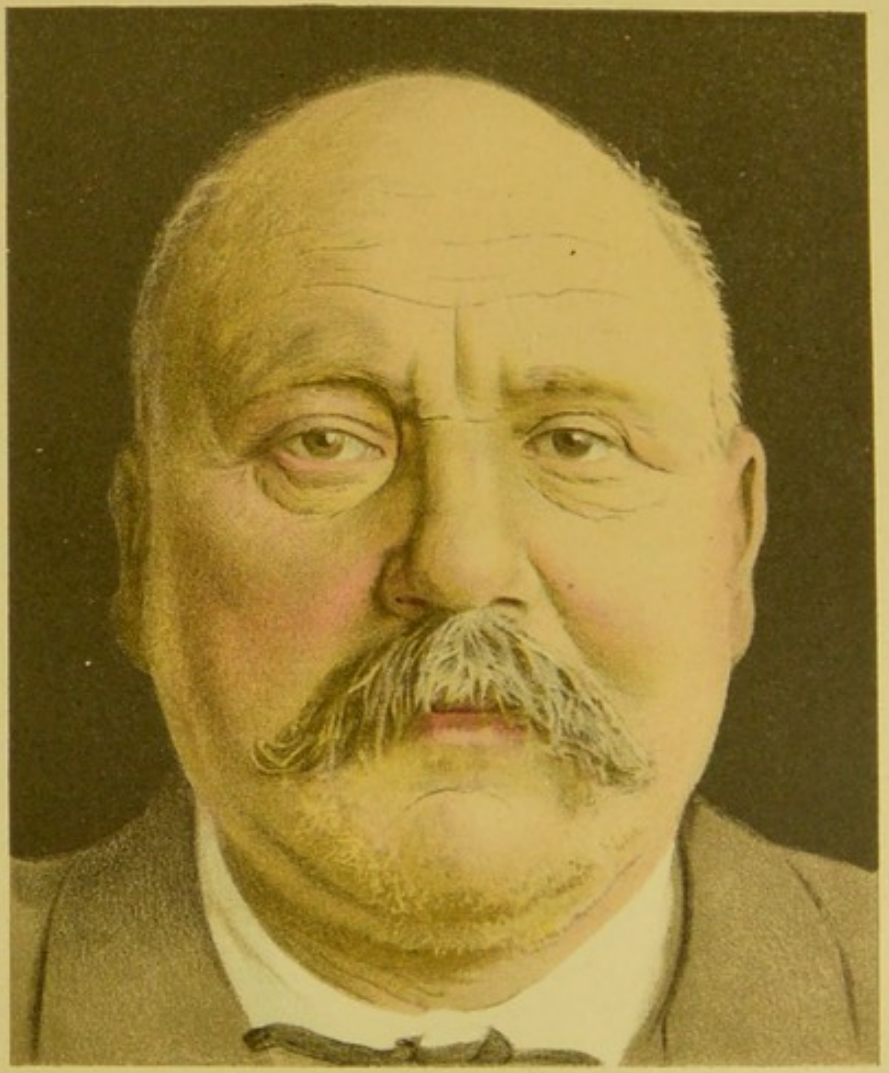


PLATE III.—EPITHELIOMA OF PAROTID REGION

which had been the starting-point of the cicatrisation. The pain entirely disappeared. The necrosed osseous portion was partly exfoliated. Improvement and cicatrisation took place rapidly.

The next case dates farther back; it was shown, in course of treatment, to various learned societies, and is a most remarkable instance of the results to be obtained from radium.

(3) **Tumour of parotid region** (Plate III, Figs. 1 and 2).—A patient, aged 55, presented on the left cheek an enormous projecting tumour. It was solidly rooted in the deep tissue, and could not be moved without also moving the head, with which it was united. It was as hard as plaster, and extended transversely over an area of 9 cm., from the external ear to the inner fourth of the cheek, and vertically over 12 cm., from the temple to the vicinity of the edge of the lower maxilla. Its most prominent part was nearly 5 cm. high. The skin covering it was everywhere red and inflamed, smooth, stretched, and traversed by large veins; it was impossible to fold it, but it was intact over the greater part of the growth, only showing solution of continuity at the top, where there was a sero-purulent bleeding ulcer, the size of a two-franc piece. The surface was uneven, as if several tumours were united in one. A slight glandular swelling was present in the submaxillary region. The patient did not complain of pain. Dr. Duprey, of Château-Chinon, who had known him for a long time, wrote to us that a swelling of benign aspect had existed in the preauricular parotid region for ten to fifteen years. It was not at first progressive, but in May, 1908, rapid development had taken place. The histology of the case, described by Dr. Dominici after a fortnight's treatment, when the tumour was already considerably reduced, showed the following changes:

"Lobulated epithelioma having cells with budding nuclei, numerous ordinary multipolar karyokinetic figures, and slight horny growth."

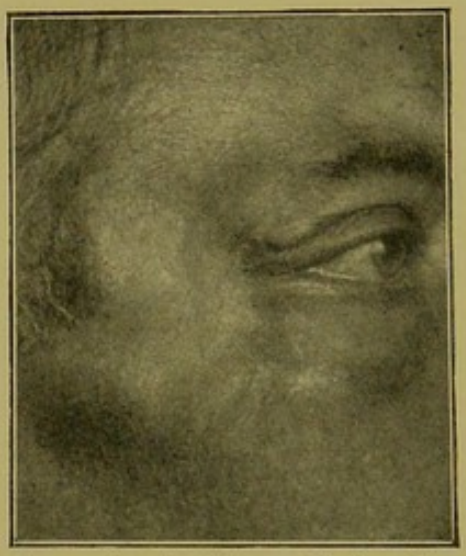
On November 6th, 1908, eleven weeks after the commencement of treatment, the tumour, when shown to the Société Médicale des Hôpitaux, projected above the surface only 1·5 cm. It was entirely detached at the base, and the neoplasm was easily moved. By February 28th it was nearly healed. The skin had almost recovered its normal colour, and the ulcer had become cicatrised. In the course of these regressive changes the submaxillary induration diminished to such an extent that no complication seemed threatened from this quarter; but a lymphatic gland and a hard nodule of fibrous consistency remained in the lower part.

We must lay stress on the therapeutic treatment pursued, for it was a combination of several different methods. It was desired to concentrate

the largest possible total of radioactivity in the depth of the epitheliomatous mass, without injuring the surface. But it was necessary to act promptly, on account of the progress of the malignant growth; and we were therefore obliged to work on all points at once. These various requirements were satisfied by the method of "cross-fire." We have already explained that a given intensity of radiation acts much more energetically when concentrated into a short space of time. By means of "cross-fire" the effective power of the radiations is multiplied by the number of rays crossing each other and striking simultaneously on the same place. If, therefore, four instruments placed opposite each other are employed for an hour, two and two, at the four cardinal points of a tumour, an intensity not only quadrupled, but of special quality, is concentrated into that period; and it was in this way that we worked. Applicators Nos. 2, 3, 4, and 7 were covered with lead screens 1 or 2 mm. thick, in such a way that only "surpénétrant" hard β rays and γ rays were employed. These instruments were left on all night, and at each fresh application they were moved so that the same portion of the skin was not affected two nights in succession. By acting in this way we avoided too great irritation of the skin, and on the other hand considerable radioactive power was brought to bear on the interior of the tumour.

But the accumulation of rays introduced into the tumour was even greater than has been indicated. Apparatus No. 1 was placed directly on the ulcerated surface, simply covered with protective rubber. Moreover, during four periods of twenty-four hours, a tube giving "surpénétrant" rays with a radioactivity of about 2,000 was introduced, and kept in place in the centre of the tumour. The rays emitted by this tube crossed those coming from the surface. In this way the "cross-fire" system, filtering by means of thick screens, the application of uncovered apparatus, and the introduction of tubes, were all utilised. The energy available was very great, all the instruments being of high power. Applicators with screens were applied every night for a fortnight in the first series, and for a fortnight two months afterwards; each instrument yielding a "surpénétrant" radiation of 2,000 to 6,000. Apparatus No. 1 was used unscreened on the ulcer, for three hours in each course. The process of reduction was marked by strong reaction in the interior of the tumour. Fragments of a slough were extruded by the ulcerated part. By pressure on the lateral portions of the tumour a peculiar whitish milky fluid oozed out in rather large amounts. About the fifteenth day a decrease in the hardness of the tissues was produced very rapidly, particularly in a lower protuberance, where it seemed that a collection of fluid had formed. As this had no outlet, it was easy to put it in communication with the central

ulcer, and after incision, a considerable quantity of the same whitish milky liquid, which was very thin, came out. The skin remained uninjured, except in several places where ulceration had been produced, especially at the periphery of the central ulcer, on the spot where the unscreened apparatus had been applied. The patient felt slight feverishness and discomfort for a week when the reaction was at its height; after which everything became normal. Resolution of the growth is at present almost complete, except in two places, where the nodules mentioned still persist. We would specially call attention to the detachment of this tumour at its base, since it was so firmly rooted before treatment. This is a favourable symptom which we shall meet with



Figs. 31 and 32.—Cancer of temporo-malar region involving orbital wall.

again in the section on carcinoma of the breast; it shows the action of the rays at a depth.

(4) **Carcinoma of temporo-malar region, affecting orbital wall** (Figs. 31 and 32).—This was a case of a neoplasm small in size, but serious on account of its position and its fistulous course. It was situated in the neighbourhood of the eye, which slightly protruded, and it affected the osseous wall. The patient, aged 57, was sent to us in November, 1908, by Dr. Galand. The growth had commenced fifteen years before as a wart; for four years previously, in spite of various treatments (electricity, cauterisation, etc.), it had extended deeply, invading the subcutaneous tissue and the osseous wall. At the above-mentioned date, at the level of the external angle of the eye, and even affecting it, an ulcer covered with a greenish grey crust was present. It was thick and very adherent, extending over a surface 3 cm. in diameter. The growth surrounded the lower part of the

orbit, and at this point there was a deep sinus. The entire peripheral region was bulging out, hard and painful to the touch; exophthalmos, together with some weakness of sight on the side and lancinating pain, made us fear pressure on the orbital wall, and encroachment on the orbit itself. The tissues in this region also adhered strongly to the subjacent bony plate. The aim of the treatment was to act at a great depth as far as the orbit, and we calculated on the selective power of radium on epitheliomatous cells to influence the neoplasm, without injuring the eyeball. It was always possible to cover the protruding part of the eye with a protective "cache."

Apparatus No. 3, covered with 1 mm. of lead, was applied three times for twenty-two hours in succession, once a week, on November 15th, 22nd, and 29th, 1908; that is, for sixty-six hours in all. On February 1st the patient appeared to be cured. The whole region in the neighbourhood of the external angle of the eye was scarred over without any retraction of the eyelids. In the lower part, at the opening of the sinus, where this joined the orbital wall, one small point was slow in becoming cicatrised, as often happens in regions where cellular subcutaneous tissue is wanting. The exophthalmos decreased, and the sight returned. This result was specially interesting, for an operation would have been accompanied by considerable injury to the tissues, and probably followed by retraction of the eyelids; neither fulguration nor X-rays could have acted easily at a depth, and integrity of the surface could scarcely have been maintained.*

(5) **Epithelioma invading almost the whole nose and destroying half its left wall.**—When epitheliomata are situated on osseous or cartilaginous tissue, in regions where the skin has no bed of cellular tissue (bone and cartilage of the nose, orbit, and frontal region), it will be necessary, both for applications with uncovered apparatus and for those with screens, to employ doses with a weaker total than when operating on the cheeks, for instance. Inflammatory reaction is produced more easily, and is much longer in disappearing. Weak divided doses are therefore generally to be preferred.

A patient came to us with an ulcer which had destroyed almost the whole surface of the nose, except the extremity of the lobe. The cartilage and part of the bones were denuded, and half the left wall was perforated. The lesion dated back four years and a half, but the ulcer had only assumed this character of acute

* *Note by Dr. Wickham.*—About the month of September the local condition, which had been excellent, and showed an apparent cure, began to relapse, but no persuasion from us could induce the patient, who lives in Central France, to return for treatment. Fortunately, the relapse does not seem to be making rapid progress.

malignancy some months previously. It had spread very rapidly. In the neighbourhood of the inner angle of the left eye the peripheral induration of the edge, which bounded the growth in every direction, was particularly marked and threatening. The treatment had to be vigorous over the whole circumference, and much more gentle on the denuded osseous and cartilaginous portions. There was, therefore, much difficulty in knowing what technique to adopt. Many courses of application were made during a period of five months, the plan generally pursued being as follows :

i. On the peripheral edge, an application with apparatus Nos. 5, 6, 7, 8 and 9, uncovered, or with only a light screen ($\frac{8}{10}$ mm. of aluminium), for three to five hours, half an hour at a time, during about ten days.

ii. On the parts laid bare, apparatus No. 3, with 2 mm. of lead, for forty hours, in divisions of three or four consecutive hours, spread over about three weeks. There were three series in all, with a month's interval between them, on both sides of the nose. By the fifth month, although the perforation was not filled in, its edges were well on the way to cicatrisation ; the epitheliomatous rim had disappeared ; the appearance of the tissues was good, and the danger of extension towards the lacrymal caruncle seemed to have been averted.

(6) **Subcutaneous relapse, with rapid extension of epitheliomatous tumour of cheek, extirpated by surgical operation. Severe inflammatory reaction on surface and at a depth obtained by the use of "surpénétrant" radiation.**—A recurrent tumour, the size of a small nut, was situated in the malar region. Indurated and prominent ridges extended from this growth towards the eye and middle of the cheek. The whole formed a hard mass about 20 cm. square, the surface being intersected by bands of scar tissue, the remains of a previous operation. The skin was stretched, but not ulcerated, and could only be folded with difficulty. The relapse had taken place in the connective tissue.

In the treatment of this lesion we resorted to "surpénétrant" radiation. Application was made of apparatus No. 1, from nine o'clock in the evening to eight in the morning. The first night, 2 mm. of lead ; the second, 2·5 mm. ; for eight nights in succession, 3 mm. From this time a diminution in the height of the growth was observed. For two nights more, 3·5 mm. ; and 4 mm. for the four last nights. In all, about 165 hours, in divisions of eleven consecutive hours, for fifteen days in succession, with a "surpénétrant" radiation of 2,000 to 4,000. Fifteen days after the completion of treatment the tumour was obliterated and the swelling had disappeared, but the skin was very red, showing the probability of strong and deep reaction. Indeed, a fortnight after

the patient had returned to his home in Provence he wrote to tell us that the whole region treated was painful and inflamed. At various points fissures occurred, through which a whitish milky liquid flowed abundantly. (We have often met with this liquid in the treatment of epitheliomata when there was severe and deep reaction.) We thought the dosage must have been too strong, but this excess was really necessary; the patient being unable to return, we were obliged to aim at a definite result.

This case proved to us that no method can entirely avoid surface irritation. Even when using only "surpénétrant" radiations, too large a total of doses accumulated in the course of the applications ends by producing both superficial and deep inflammatory reaction. We may, therefore, again assert that whether or not inflammation supervenes is determined by the dosage rather than by the methods. (*See* Reaction, p. 79 *et seq.*) On the other hand, this case also shows that inflammation produced by excessive doses of "surpénétrant" radiations is generally quickly healed. Indeed, after several weeks of such reaction, the tissues dried up, everything resumed its normal condition, the hard masses disappeared, and now (four months afterwards) nothing remains of the relapse, at least in appearance. The skin is supple and movable, although crawling and itching sensations continue.*

2. IMPLICATION OF GLANDS

Relapses affecting the glands respond to some extent to radium treatment, as we have often seen, on account of the possibility of acting at a depth without ulcerating the surface, and for this reason they may be classed with subcutaneous carcinomata covered with skin, which require careful treatment. The three following examples deserve mention.

(1) A very old lady had a retroauricular glandular growth resulting from an ulcerated epithelioma of the auricular canal. The tumour, covered with thin and stretched normal skin, had formed in the retroauricular fold, and developed rapidly. It was doughy, and about the size of a pigeon's egg. No surgical operation was possible. The tumour was strongly adherent at its base, uniting with the subjacent bony tissues of the ear. The injury done by an operation would have been very great, and the patient would have been unable to bear it, on account of her advanced age. It would have been difficult to preserve the skin intact with X-ray treatment, and this was not practicable, since the patient was unable to leave home.

* *Note by Dr. Wickham.*—In the last two cases healing has been permanent, but I have heard nothing for a long time of the two former ones.

"Surpénétrant" radiations were adopted in weak doses (1,000 to 2,000 units). The applications were made in series of five or six consecutive nights, each course being separated from the previous one by two to four weeks' rest. By degrees a reduction of the tumour became evident. According to Dr. Paillotte, who was attending the patient, it diminished slowly, acquiring a harder consistency, of sclerotic nature. After several months the neoplasm was reduced to a fourth of its original size. The skin was never the site of any irritation. These results were obtained quite simply, the process causing very little fatigue or discomfort. This is a decisive proof of the specific action of radium and the ease with which it can be employed.

(2) In the next case the dosage was excessive, and produced a surface inflammation which was long in healing, but strong measures were absolutely necessary.

It may be asked whether in urgent cases, it is not better to incur a superficial radiumdermatitis, lasting five or six weeks (a period during which, after a course of treatment, the patient is in any case obliged to rest), rather than deprive him of this vigorous treatment, which alone has any chance of arresting an acute growth.

The patient in this case, as the result of a somewhat indolent epithelioma at the back of the throat and tonsils, rapidly developed an enormous hard prominent mass throughout the whole left cervical region. There were symptoms of pressure and discomfort, and the head was immovable. The skin was fine, smooth, and stretched, being simply raised by the tumour. It was difficult to fold it.

Every other night, from November 25th to December 11th, eight times in all, application was made of apparatus Nos. 5, 6, and 3. No. 3 was reinforced by the addition of two "toiles" containing 4 cg. of radium salt, having an activity of 500,000. These instruments were covered with 2 mm. of lead. On the intervening days, application of apparatus Nos. 3, 5, and 7 covered with 2 mm. of lead. The tumour was therefore treated for sixteen days in succession. The apparatus was used in such a way as to oppose the rays to each other, and to spread them over the enormous growth. In spite of the use of screens, radiumdermatitis was produced; but at the present time, two months after treatment, the tumour, which had been growing rapidly in a most alarming manner, has considerably diminished in size, and the whole of it has become softer. The patient is able to bend his head to the left, and the intolerable pain experienced in the left half of the head has disappeared.*

* *Note by Dr. Wickham.*—The patient has since died from the extension of the throat cancer, which was inoperable, and had not been treated by radium. The glandular mass, however, had entirely disappeared.

(3) Another case, similar in all respects to the last, and even more advanced, the origin of which was probably a carcinoma of the larynx, necessitating tracheotomy, has recently undergone vigorous treatment by "cross-fire," with "surpénétrant" radiations, as in the preceding case. Softening, slight decrease in size, and very marked diminution of the violent pain in the head soon took place, this time without superficial inflammation.

(4) One of Dr. Cazin's patients presented considerable glandular infiltration, resulting from carcinoma of the breast, tumours existing in the pectoral, axillary, and cervical regions. There were signs of pressure (pain, difficulty of breathing, and œdema of the arm). In such a case treatment could aim at nothing further than the relief of the patient. This was obtained to some extent; for two or three months there was certainly relief of pain and difficulty of breathing, and even reduction of part of the growths treated. It was vacation-time, and the patient would not consent to remain in Paris in order to continue the treatment. We heard of her death two months afterwards.

This collection of cases shows how important the use of radium has become.

3. NEOPLASMS OF BREAST

The breast is a region particularly suitable for radiumtherapeutic processes, especially the "cross-fire" method, combined with the use of screens. The four principal conditions to be fulfilled by the technique are as follows:

i. Penetration of the lung by the rays should be avoided, as far as possible. Indeed, in carcinoma of the breast, when the lungs are often sensitive and irritable, it is sometimes well to diminish the total amount of rays reaching them; this may be effected by the "cross-fire" plan, which allows of the greater number of the rays being directed laterally.

ii. Even in superficial carcinoma of the breast, as in Paget's disease,* it is necessary to act at a depth, and to reach the entire thickness of the mammary tissues considerably beyond the nodosity and infiltration which reveal the neoplasm to the touch. We have to search in the dark for the smallest corner to which the growth could have spread. Now, theoretically, the power of extreme penetration possessed by "surpénétrant" radiations, which, as already mentioned, can pass through lead several millimetres thick, ensures the influence of radioactivity over all parts of the mammary region, whatever their depth.

* Wickham, "Maladie du mamelon dite de Paget." Contribution à l'étude de la pathogénie du cancer. Thèse de Paris, 1890.

iii. The radioactivity must be very strong. In addition to choosing an apparatus with a large surface, containing an exceedingly active radium salt, some of those operative combinations which aim at the increase of intensity must be adopted. These are—superposition of the applicators ; introduction of radiferous tubes into the interior of the carcinomatous tissue, a very useful plan when the skin is already ulcerated ; multiplication of the apparatus and points of application. A breast may be covered by four instruments, acting opposite each other, and crossing their fires. In this connection we would repeat that the simultaneous action of two radiations directed towards each other yields better therapeutic results than the action of the same two instruments placed one above the other. The breast, as we have said, is admirably adapted for this " cross-fire " method. In some cases these three ways of operating may be combined, and from this we see the possibility of permeating the whole mammary region with radiations which are at once numerous, penetrating, and very intense.

iv. The skin must be safeguarded. While introducing considerable radioactive energy into the growth, we should seek to avoid surface inflammation. Now, even when the epidermis is already affected, red, and resembling the skin of an orange, or that of an abscess which is on the point of bursting, improvement can be obtained without bringing about ulcerative reaction. Putting other considerations aside, filtration will produce this result if the screen is sufficiently thick (2 to 3 mm. of lead) and the exposure sufficiently long.

The " cross-fire " system, in which the position of the points of application is changed, allows of the use of thinner screens, and consequently of more rays, fulfilling the four conditions we have laid down, and rendering the treatment more rapid, practical, and effective. The breast is therefore a region particularly suitable for demonstrating one of the chief properties of radiumtherapy, as well as the progress made by the filtering methods of the Laboratoire Biologique du Radium. Convenience of application, which can easily continue for entire days and nights, without any alteration in the habits of patients, who are usually aged, and without causing them any discomfort ; flexibility of the instruments, which allows of many operative combinations ; and the possibility of covering exactly the whole of the mammary region in the direction required with numerous, intense, and extremely penetrating rays, without superficial inflammation of the skin,—these are advantages which, taken together, belong to radium, but not to any other therapeutic agency. X-rays, in particular, can make no claim to them.

In considering the various measures adopted for carcinoma of the breast, it should be observed that, whatever the means employed to

obtain neoplastic destruction (various kinds of cauterisation and fulguration), and whatever the extent of the operation, there is always a further region where the germs of disease may remain out of reach. If, therefore, radium can succeed in reducing a neoplasm of the breast, its method of action must be superior, both in theory and practice, since the rays must have reached the neoplastic elements at all parts of the mammary region, even beyond the zones usually accessible. It is certain that the detachment of the neoplasm at its base, and the mobility thus given to tumours in course of treatment, even before the growth itself is reduced—which we have noticed not only in carcinomata of the breast, but also in case No. 3 (p. 137), in carcinomata of the uterus, and in other tumours which were originally fixed and adherent—clearly prove that the curative influence is exercised at a depth. On the other hand, the absence of any superadded process of inflammation, and the quiet and painless reaction that takes place, are conditions which favour healing, and form a contrast to the danger of stimulation, subsequent glandular invasion, and general absorption which sometimes accompany ordinary surgical procedures.

These considerations, to say nothing of the complete absence of mutilation, are real advantages, to which must be added the possibility of treating, under the same conditions, not only glands where infiltration is known to exist, but also (as a prophylactic measure) those of the axillary and pectoral lymphatic regions, which have apparently not been involved. If, in addition to the various qualities mentioned in the chapter on Reaction, we consider the special value of radium with respect to epitheliomata, radium-therapy for malignant neoplasms of the breast will certainly be seen to possess peculiar practical importance, as the following instances will show.

(1) **Carcinoma of breast treated through rubber-covered lead of the kind used for protection from X-rays.**—A patient, aged 72, was sent to us by Dr. Triboulet, on November 6th, 1907. She presented on the left breast a tumour the size of a small tangerine orange, which was fixed on the costal plane, and had spread over the whole surface of the skin, to which it was united. The nipple was retracted, and an ulcer about the size of a one-franc piece existed just outside it. The rest of the surface resembled the skin of an orange, red and apparently about to ulcerate. There was a lymphatic gland in the left axilla. Very severe radiating pains were present in the whole left side of the thorax. This tumour had made its appearance a year previously; it was evidently a carcinoma of the breast. Dr. Triboulet, for many reasons, more particularly on account of the great age of the patient, was afraid of an operation, especially with chloroform, and applied to us, hoping that radium might arrest the growth of the carcinoma.

The presence of the ulcer might have induced us to employ unscreened apparatus in order to act with intense total activity; but by this time our experiments as to filtration through screens of cotton-wool, aluminium, and rubber-covered lead had shown us how to act at a depth. As such deep action was of the utmost importance for our patient, and it was particularly necessary to use very penetrating rays, we operated from the first in the way previously tried, as in the case of an inoperable glaucoma, treated on January 23rd, 1907. (*See* Glaucoma, p. 277.) We interposed, between the growth and apparatus No. 1, a sheet of rubber-covered lead; one of those, 1·27 mm. thick, which are specially constructed as a protection from X-rays. Through this layer, apparatus No. 1 discharged the electroscope, and lighted up a barium platino-cyanide screen. The filtering only allowed very small quantities of the most penetrating rays to pass. The results answered our expectations, although the doses were much smaller than those which we should now employ.* We were surprised, on looking back, to think that with doses so weak, results could have been obtained which, though very slow, were nevertheless effective. Apparatus No. 1 was applied for an hour and a half, eleven times, from November 6th to 18th. On December 11th there was very marked decrease of pain. The tumour was reduced in a transverse direction from 4·5 cm. to 3·8 cm. The part nearest the sternum appeared to be softening. (We have since noticed, in several other cases, this softening process, but without consecutive ulceration.) Further treatment of the same kind, but for an hour only on each occasion, ten times, from December 11th to 23rd. On February 3rd the ulcer was almost healed; the tumour was more easily moved, and the redness and orange-skin appearance had diminished. From February 3rd to 12th, ten applications of one hour each were made, after which the healing became quite evident; there was no longer reason to fear that the growth would spread. So great a change had taken place in the consistency, size

* *Note by Dr. Wickham.*—It should be clearly understood that I am not recommending radium as the ordinary treatment for cancer of the breast. I only desired to show from my own cases (which now number about 30) how useful it may sometimes be.

In practice, I always advise that patients be sent to a surgeon, and that radium be used only in the following cases:

1. When the patient firmly refuses an operation.
2. When the surgeon considers the case inoperable.
3. *After* complete surgical removal, if there are enough very powerful radium instruments to cover a large extent of the surface. Otherwise X-ray treatment would be more suitable.

Radium is therefore useful as a help to surgery, and in those slightly advanced cases in which, a young patient refusing mutilation by the loss of a breast, the surgeon may be called on to remove the whole subpectoral and subaxillary lymphatic chain, radium treatment being used for the breast itself.

and mobility of the tumour, that the fingers could be inserted between its posterior surface and the costal wall. The ulcer was completely cicatrised, the skin being no longer red. The axillary lymphatic gland was reduced, and there was no more pain. A surgeon who had feared to operate before treatment was again consulted, and now thought that the operation might be easily performed by simply using cocaine as an anæsthetic. Being satisfied with the results obtained, the patient preferred to continue the radium applications. Every two months a fresh course of exposures was made, with the same *modus operandi*. In September, 1908, apparatus No. 1 was used for ten hours, with a simple lead screen of 0·5 mm., not covered with rubber. At present the lesions are so much reduced that only a fibrous nodule, about the size of a nut, remains round the nipple. The nodule can be easily moved on the costal wall; and the skin is in excellent condition, never, indeed, having been injured. This result is remarkable, since the tumour, which, left to itself, would certainly have continued to extend, seems to show no danger of this at present (eighteen months after commencement of treatment), and has been very successfully modified. The diminution of the lymphatic gland, without direct exposure to radium, should be noted.

(2) **Cancer "en cuirasse."**—On December 11th, 1908, a patient, aged 78, was sent to us by Dr. Moutard-Martin, with a carcinoma of the left breast for which operation seemed impracticable, for many reasons. The neoplasm had appeared about two years before. It occupied the external portion of the gland, which was much atrophied. Its base was firmly adherent, and characteristic induration was present. In its right half, however, there was a softer, almost fluctuating, portion; the skin at this level being red, like that of an orange. The whole of this part of the tumour resembled an abscess ready to burst; everywhere else skin of normal colour adhered to the neoplasm, and formed part of it. A lymphatic gland, as large as a nut, and slightly movable, was present in the axillary region. The pain was lancinating, and sometimes caused insomnia.

The plan adopted was that of "cross-fire," combined with filtration by 2 mm. of plain lead. The instruments used were No. 1 for the lower part, and No. 3 opposite, on the upper part. The applications were repeated fifteen times in the course of a month, each exposure being followed by an interval of one day. The applicators were fixed about nine o'clock in the evening, and removed about eight in the morning, a total of 160 to 180 hours. No. 1 was always put in the same place; No. 3, which is smaller, being slightly moved from time to time. This dosage seemed to us suitable; and an interval of one day was found to be beneficial. During a period of forty-eight hours the treatment

lasted eleven in all, and the tissues were allowed to rest for thirty-six. We think that this plan of uniting the method of fractional doses to that of "cross-fire," applied with a small number of very penetrating rays, offers great advantages, and avoids the risk of too hasty action. Resolution took place in quite an ordinary and regular way. During the following two months we observed an improvement in the various symptoms we have indicated. The inflammation was lessened, the skin had recovered a certain amount of flexibility, the nipple was less retracted, and, a specially important symptom, the base was detached. There remained, on February 1st, on the site of the tumour, a hard, elongated cord, movable and indolent in character. Fresh applications of a similar kind were afterwards made; ten exposures of twelve hours each, with an interval of one day. At the end of March there remained only an induration, which appeared to be nothing more than tissue in process of cicatrisation. The pain was no longer felt. The lymphatic gland was treated by six applications (six nights), with one night's interval, of apparatus No. 7, covered with 1 mm. of lead. All these results were obtained without causing ulceration of the surface, and there was only slight reaction, which ceased in a fortnight.

The case is, of course, too recent to permit of any final conclusion, but it is interesting to have obtained to such an extent, and with so much ease, the reduction of a neoplasm the malignant evolution of which was becoming rapidly accentuated.*

(3) **Carcinoma of breast of large size.**—A patient, aged 47, presented on the left breast a typical carcinoma, with retraction of the nipple, adhesion of the skin over a small area, where it cannot be folded, and adhesion of the base to the thoracic wall. The tumour was very large, and seemed to occupy the whole gland, which was normally much developed. The axillary and subclavicular glands were enlarged. The pain was very severe; it radiated especially from a point in the back, and complicated the general state of health, which was bad. The patient was highly neurasthenic. She had painful gastric crises, and sometimes showed symptoms of spasm of the larynx. She was badly nourished and emaciated. Surgical intervention was out of the question.

The treatment was similar to that of the preceding case, except that the applications were repeated four or five times a week, instead of three, and the screens were 1 mm. of lead for the first five applications, and afterwards 2 mm. On account of the large extent of the surface, it was possible at every exposure to choose places opposite each other,

* *Note by Dr. Wickham.*—At the present time (December, 1909) the first patient is still quite well. The second patient is fairly well, but if radium treatment is stopped for long the cancer begins to grow again.

different from those of the day before. There were fifteen applications. Two months after the commencement of treatment it was obvious that the tumour was rapidly diminishing in size. It had become detached from its base, and of softer consistency. The portion adhering to the skin was more supple. The pain in the back had ceased, and the patient herself acknowledged a great change. Her nervous condition was improved. A second course was commenced, and the improvement became more marked. The nipple was freed, and the mobility of the gland perfectly restored. Resolution was proceeding quite satisfactorily, when the patient caught a cold, which turned to serious broncho-pneumonia, to which she succumbed.

(4) **Peri- and intracanalicular adeno-fibroma.**—A patient, aged 33, was sent to us by Dr. Robinson with a tumour the size of an orange, situated in the left breast. The growth, movable in the substance of the breast, disturbed the patient, owing to the radiating pains from which she suffered in the left side and arm. But there was another circumstance which, not unnaturally, made her uneasy. She had had a similar tumour in the right breast two years before, the removal of which had been performed by Professor Berger. The histological examination of the tumour gave the following particulars :—

"The matrix, according to the regions examined, is dense and of coarse fibre, fine and of light texture, or œdematous and myxoid. The glandular elements extending into this stroma are in the form of groups of dilated acini, irregularly enlarged and stretched, and taking strange shapes. They form small cysts with gelatinous and transparent liquid contents. A single layer of cubical or cylindrical cells covers their internal surface. In their mutual relations the matrix and glandular tissue behave inversely. Where the connective tissue has become dense and scirrhous, the glandular formations are only slightly developed. On the other hand, where the connective tissue is lax, the adeno-cystic growths are well developed. Finally, in some places where the stroma is very fine and rich in cells, cellular masses push into the adenomatous cavities, which, pressed on unequally from different sides, take star-like forms, impossible to describe. Two small axillary lymphatic glands, when examined, were free from metastases. A certain amount of irritation was evidenced by hypertrophy of the lymphatic endothelium. Diagnosis : peri- and intracanalicular adeno-fibroma."

On account of the firm refusal of the patient to submit to removal of the other breast, we attacked this tumour by the "cross-fire" method with two applicators, one 12 cm. square, containing 12 cg. of radium sulphate, with an activity of 1,000,000, the other 16 cm. square, containing 16 cg. of radium sulphate, with an activity of 500,000. Each of these was covered by 3 mm. of lead. Placed, one above and the other below, and then, on the third day, one on the right and the other

on the left, the instruments were thus transposed at each application. During one month we made fifteen applications of twelve hours. After the first, the painful symptoms were greatly relieved, and the size of the tumour gradually diminished. The growth, which before treatment was the size of an orange, was now only that of a large nut. There was no longer any question of an operation, although the surgeons previously consulted had declared it imperative.

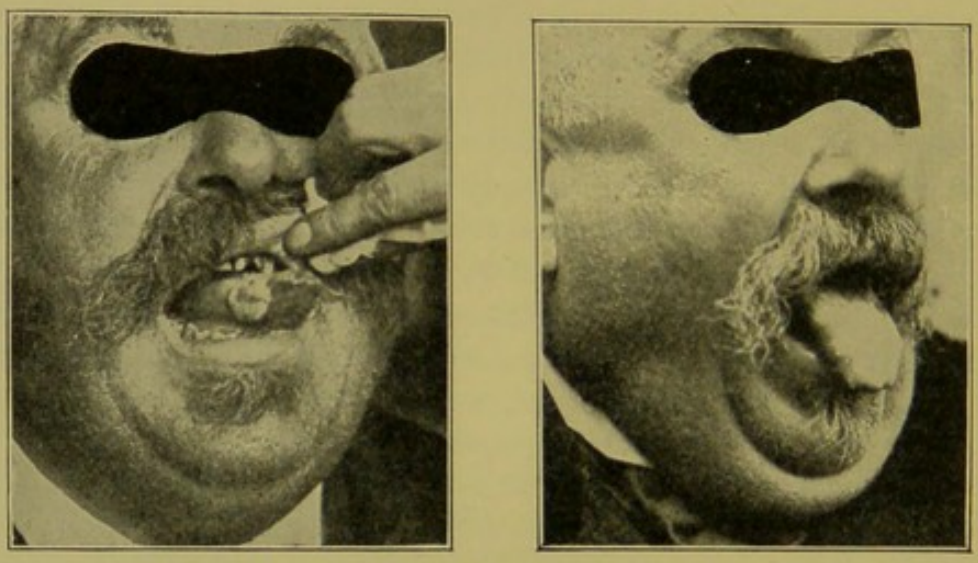
These clinical examples, selected from many others, resemble each other in more than one point, at any rate as to the regularity of the reduction; in our opinion they show the effects produced by radium, and the advantages which it offers. In cases of relapsing nodules in an operation scar we have obtained successful resolution. In several cases where the lesions had reached such proportions that there was no longer any question of interference, except with the humanitarian object of affording relief, not only were the pain and discharge diminished, which was what we expected, but there was even some passing improvement in the general state of health, an improvement corresponding to partial decrease of the tumours, and very probably prolongation of life under less painful conditions. These results, however, need not cause surprise; the specificity of radium had been clearly demonstrated by our experiments, which showed curative action at a depth without surface destruction, and exercised in many parts. These properties of radium, moreover, may be put to good use after surgical removal of a growth. Even in the dressing which follows the operation, during the period of cicatrisation, apparatus covered with lead screens may be introduced into the cotton-wool, and allowed to remain for the necessary time, in a different place each day. This will be the best method of searching at a depth for foci of disease which have been left, and of avoiding relapse. In short, the practical conclusions which we have drawn from these cases seem to us very favourable to the claims of radium.

4. CARCINOMA OF BUCCAL MUCOUS MEMBRANE

Carcinoma of the mucous membrane, except as regards the conjunctiva, has only recently become the object of systematic and regular study. Two cases of cure have been quoted in papers on the subject, one of sarcoma of the lower gum, the other of cancer of the tongue, both obtained by Dr. Abbé. Dr. Etner, in 1905, announced the resolution of an inoperable cancer of the buccal mucous membrane, without relapse during a period of two years. Dr. Danlos had met with success in several cases of leucoplakia. We have mentioned in the previous chapter a whole series of epitheliomata of the conjunctiva which were reduced and healed

by the action of radium; in these cases the facts were numerous enough and of sufficiently long standing to warrant statistics, and, moreover, they corroborated the results previously obtained by Dr. A. Darier. In two cases of cancer of the nasal mucous membrane we gained positive results. The present section will be devoted to buccal mucous membranes. Amongst other cases of the tongue we must specially note the two following.

(1) **Carcinoma of tongue** (Figs. 33 and 34).—M. G.——, aged 50, formerly suffering from syphilis, had a leucoplakia of the tongue. On the right edge an induration had appeared six months previously, which began to proliferate rapidly. The lesion was the size of a one-franc piece.



Figs. 33 and 34.—Fungating epithelioma of tongue.

The histology of the case showed that it was an epithelioma; this examination was indispensable, for the patient presented palmar syphilides. On account of the proliferation we used at first collective radiations. Apparatus No. 4 was employed for eight hours, an hour at a time, on successive days, simply wrapped in rubber. The growth subsided in the course of the following month, and by the second month it was entirely level with the surface. The deep hard portion, forming the pedicle of the large vegetation, was much diminished. This in its turn was treated by filtration. The patient is still undergoing treatment.

The history of this case is of some importance, seeing that we had recourse to total radiation. It is generally desirable, according to Professor Gaucher, to avoid all irritation in the treatment of carcinomata of the buccal mucous membrane, and total radiations, if carelessly used, run a risk of producing it. In this instance there was never any superadded inflammation. The lesion melted away without any complaint

of discomfort from the patient. We are convinced of the importance of filtration in the treatment of mucous membranes (*see* Carcinoma of Lips, below), but a distinction will certainly have to be made in future between forms amenable to collective radiations and those for which weaker radiation is more suitable.

Another case of cancer of the tongue was treated on December 15th, 1908. The patient attacked by it, who was syphilitic and a great smoker, observed a small fissure forming by degrees on the right edge of the tongue, which grew larger and deeper, and of which the objective characters were alarming. On being touched it appeared to be not only the anterior surface which was attacked, but the whole thickness. A tumour the size of a hazel-nut was enclosed between the two surfaces of the tongue. The patient complained of rather sharp pain when speaking and eating. The position of this lesion was suitable for the employment of "cross-fire." For this purpose we used an angular apparatus forming two valves, joined together on one side, and open on the other, allowing of the introduction between them of the edge of the tongue; each valve contained a "toile" covered with 0·04 grm. of radium sulphate, covered with 1 mm. of lead. This apparatus was applied for fifty hours, in divisions of two hours each. The first result was a change in the fissure, its yellowish-grey aspect disappearing and giving place to a reddish colour. The consistency of the tumour altered; it then gradually diminished in thickness, and this regressive movement continued.

(2) **Carcinoma of lips.**—The radiumtherapy of these growths has been very thoroughly investigated by Gaucher and Dominici. The following are some of our own cases.

Upper lip.—A patient came to us with an epitheliomatous ulcer on the right side of the upper lip, in December, 1907. It was a post-operative relapse, encroaching on the mucous membrane. The operation had produced great loss of substance of the mucous membrane and the surrounding tissue. Apparatus No. 6 was applied for four hours, and resulted in a reaction which took some time in disappearing, as occasionally happens on tissue which has been modified by previous cicatrices. Cicatrisation was effected by degrees, the irreparable loss of substance causing a deformity of the lip. The case is a year old, and no relapse has since occurred.

Lower lip.—i. A patient came to us on May 10th, 1907, presenting a leucoplakia of half the lip, in the middle of which was a fungating epithelioma, with indurated base. We operated with light screens and weak doses, knowing how sensitive the mucous membrane is. An aluminium sheet of $\frac{1}{100}$ mm. was interposed. Apparatus No. 7 was applied for half an hour each day; twenty times in all. Six weeks afterwards

the cure appeared to be complete, in spite of slight reaction. This is the case which we mentioned at the Congress of Rheims, on September 7th, 1907. The result did not fulfil our expectations, for three months after the end of treatment acute relapse occurred, necessitating an operation, which resulted, at the hands of Dr. Ombrédanne, in an admirable repair of the lip. Unfortunately, a relapse took place shortly afterwards from sublingual glandular invasion, followed by ulceration and vegetation; and this required a second operation. A year later a fresh recurrence appeared in the same region. An abscess formed in one of the glands, which became the site of a huge inoperable mass, implicating the floor of the mouth. After having had the abscess opened, we treated this region by radium. Apparatus No. 2, covered with 2 mm. of lead, was applied for a month, every two days, for a period of twelve hours each night. From the time of the first applications, as usually happens in such cases, the suppuration dried up, the odour diminished, and the lips of the wound formed by the incision made to drain the suppurating gland assumed a satisfactory appearance. After treatment the size and hardness of the tumour diminished by degrees. The discomfort was considerably less, the movement of the head, which had previously been hindered, regaining greater freedom.

ii. (Plate IV, Figs. 1 and 2.) An epithelioma was situated in the median part of the lip, not encroaching on the skin, but on the buccal surface, in such a way that to see the whole of it one had to evert the lip. A serous or sanguinolent fluid came from the lesion, which was fungating. There was very hard infiltration through the whole thickness of the lip. On the right was a submaxillary lymphatic gland, which, though not large, was plainly visible. The first course of treatment, from August 7th to 9th, 1908, consisted in daily applications, for two hours, of an apparatus composed of two "toiles" placed in juxtaposition, with an activity of 500,000, and alternately covered with 2 mm. of lead one day and $\frac{4}{10}$ mm. the next. The object was to act very strongly on the superficial fungating portion, and with weaker action on the deep layers. After this treatment the whole vegetating part subsided. From September 4th to 16th, and October 10th to 15th, second and third courses identical with the first. In November, for eighteen hours, spread over ten days, we treated the tumour between two fires, placing one apparatus in front on the skin, and another in the gingivo-labial groove, covering each of these instruments with 2 mm. of lead. As the result of this treatment we obtained cicatrisation of the surface, and gradual reduction of the deep infiltration.

iii. (Figs. 35 and 36.) A patient, aged 22, presented, at the muco-cutaneous edge of the lower lip, a deeply ulcerated epitheliomatous

EPITHELIOMA OF LIP

CHELOID OF NECK

PLATE IV

PLATE IV

EPITHELIOMA OF LIP (p. 154)

FIG. 1.—The growth is vegetating, and infiltrates the upper portion of the lip.

FIG. 2.—The ulceration is cicatrised, but a slight induration may still be felt on palpation.

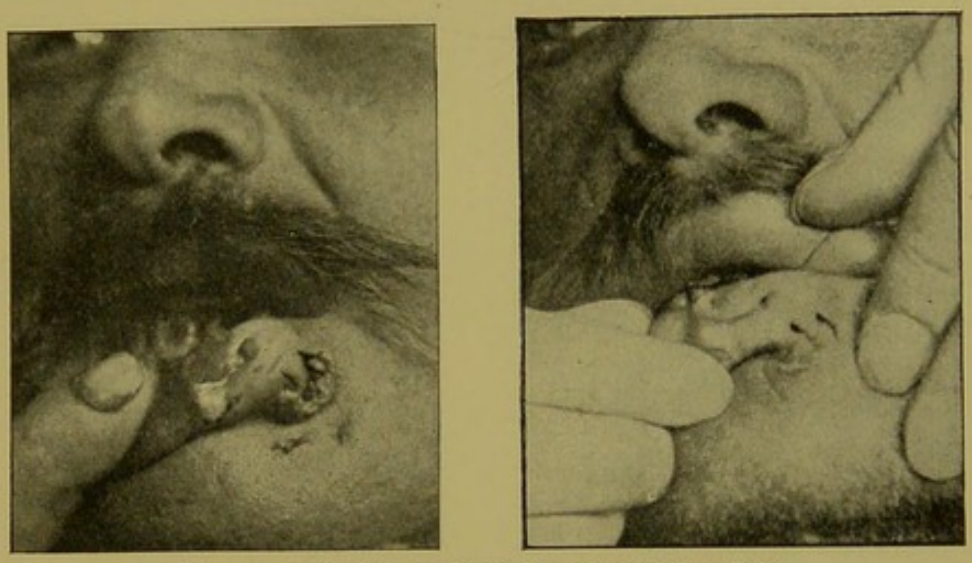
CHELOID OF NECK (p. 167)

FIG. 3.—The cheloid is hard and distinctly prominent; it has a fairly deep-seated base.

FIG. 4.—The cheloid is reduced to a flat surface; there is no longer any deep induration, and the skin has recovered its normal consistency.

tumour; on palpation it gave the sensation of a deep cartilaginous infiltration. Indurated lymphatic glands were present under the chin and on the sterno-cleido-mastoids, at the level of the angle of the maxilla. This lesion was painful. From May 14th to 27th we applied, for twelve hours, in divisions of three hours in succession, on the skin and muco-cutaneous region, a "toile," with an activity of 500,000, containing 0·04 grm. of radium sulphate, in $\frac{6}{10}$ mm. of lead. The first results obtained were diminution of the ulceration and suppression of the pain.

By July 6th the region had become dry and supple, but as slight induration remained, a new series of applications similar to the last was made. At the present time, six months after treatment, the lip is



Figs. 35 and 36.—Ulcerating epithelioma of lip.

in excellent condition. The depressions of the healed surface shown in the photograph are due to loss of substance, but the tissues are perfectly pliant and have cicatrised.

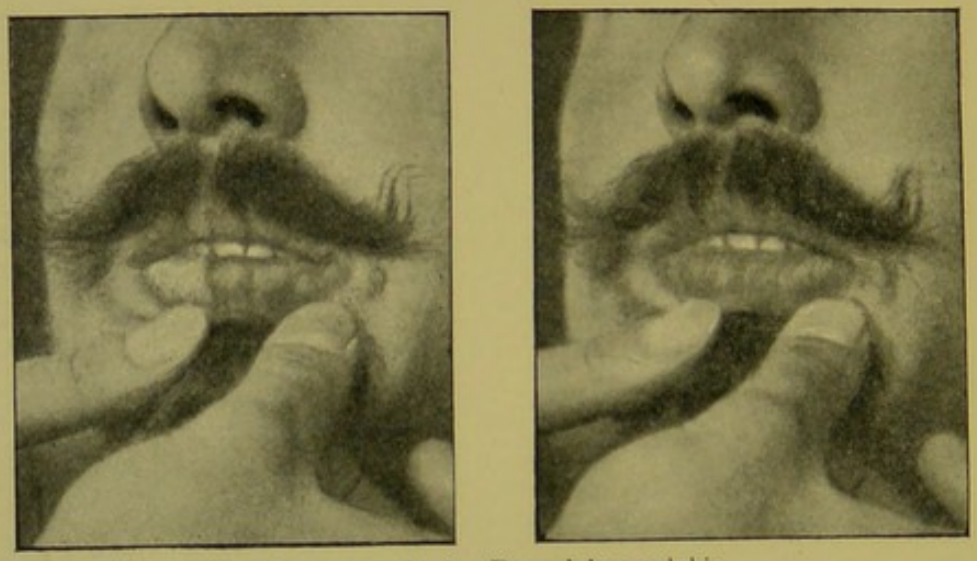
(3) **Leucoplakia.**—On account of its frequent epitheliomatous transformation, leucoplakia requires mention in this chapter. We have treated several cases, some successfully, others with less appreciable results.

i. In case No. 1 (p. 153) the leucoplakia of the lip was entirely removed.

ii. In the case of leucoplakia accompanying cancer of the tongue, mentioned on page 152, we obtained very marked modification. It was thick and mammillated, with irregular surface; after treatment, which consisted in the application of apparatus No. 4 for two hours —an hour on two consecutive days—the parts treated became smoother and more even, but remained of a greyish colour.

iii. The most interesting case that we have had is that illustrated in Plate V. After applications of apparatus No. 4, enclosed in an aluminium sheet 0·04 mm. thick, for six hours, spread over eight days, there was surface inflammation, followed by very evident reduction. Fig. 2, Plate V, shows the state of the tongue when the patient left us, two months after the commencement of treatment. The mucous membrane afterwards assumed a greyish tint, as in the preceding case, but the irregularity and fissures in the skin, and the pain which had previously been felt, entirely disappeared. The surface is smooth and supple, and no deep-seated induration can be made out.

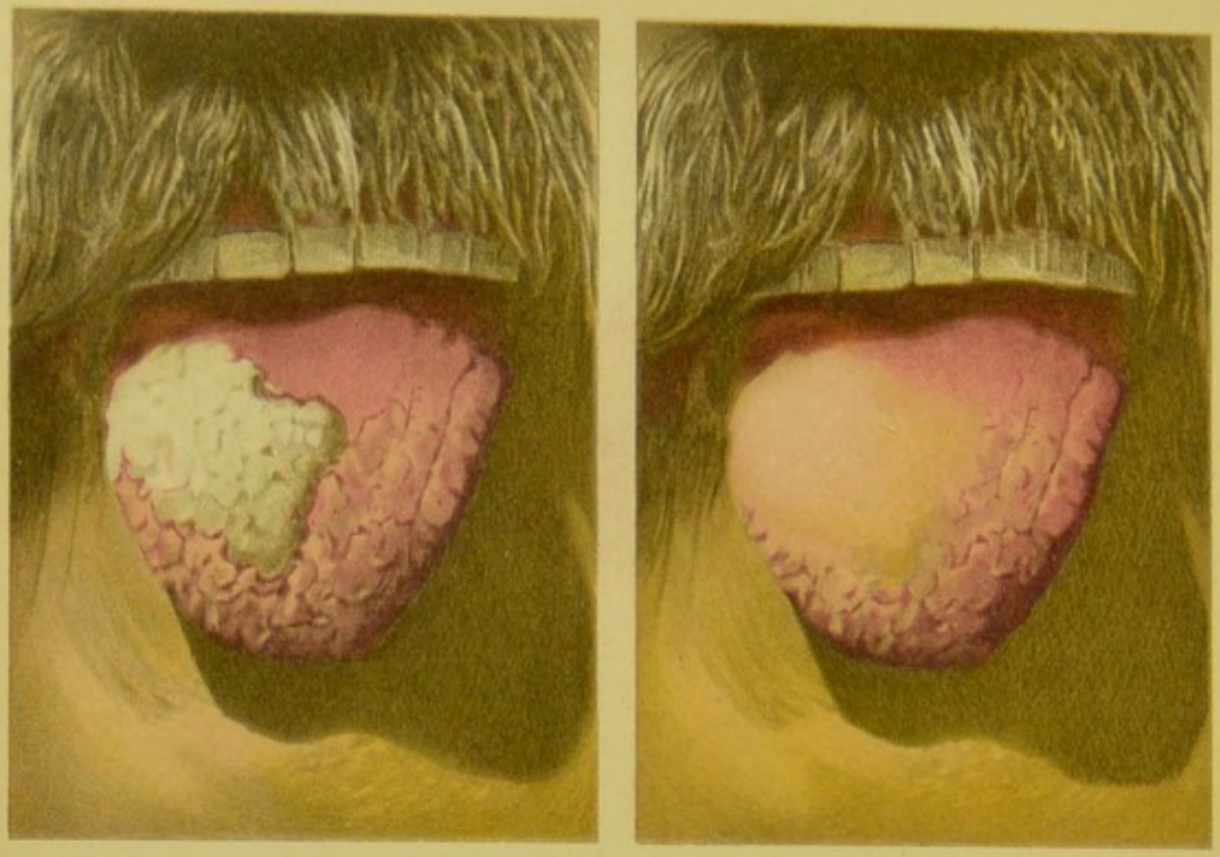
iv. (Figs. 37 and 38.) A patient, aged 45, formerly syphilitic,



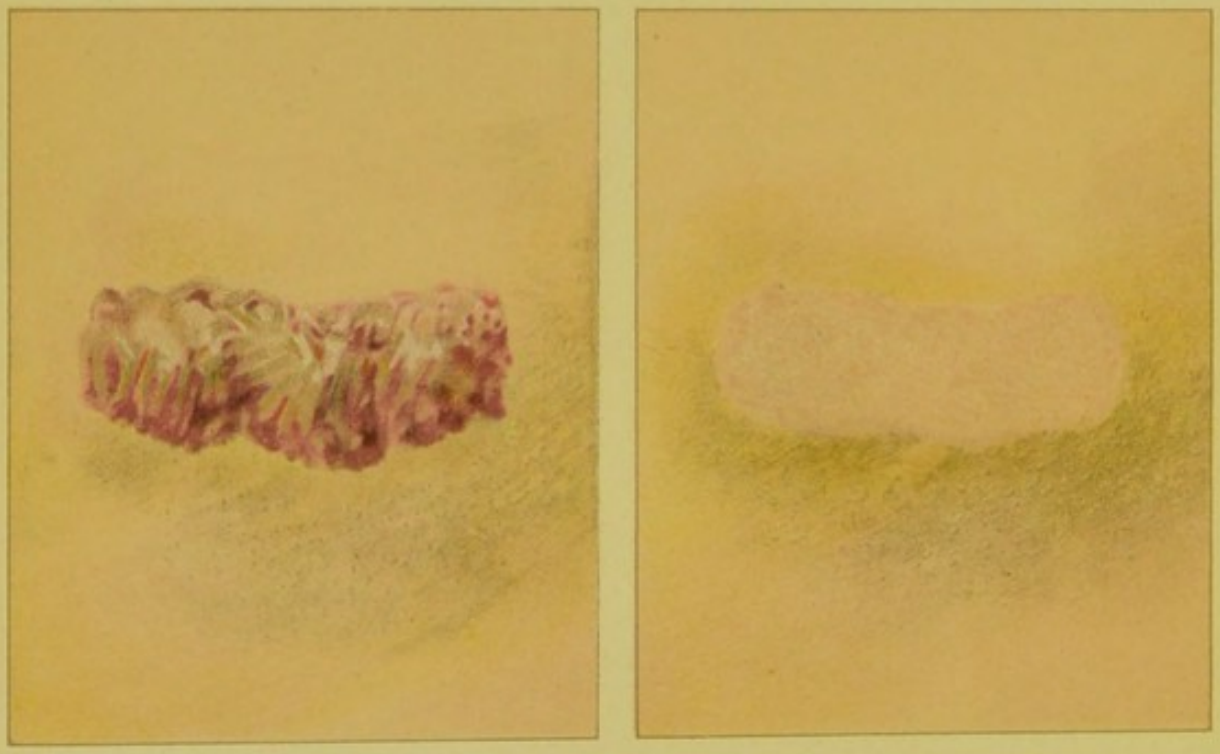
Figs. 37 and 38.—Buccal leucoplakia.

presented a nacreous leucoplakia on the lower lip, near the commissure. Eleven applications, of one hour each, were made every day with apparatus No. 9, enclosed for the first three in 1 mm. of lead, and then in $\frac{6}{10}$, $\frac{4}{10}$, and $\frac{3}{10}$ mm. in succession, for the remainder. The last exposure was made without a screen. After slight reaction the tissues recovered their normal appearance.

Experiments with regard to the buccal mucous membrane are few in number, and too recent to permit of a final estimate. But, from the standpoint of comparison with other therapeutic methods, they justify us in considering radium valuable in the treatment of cancers in this situation. We have several cases under treatment at the present time, which it would be premature to narrate, although satisfactory retrogression has so far been obtained. Quite lately an epithelioma of the buccal mucous membrane, affecting the entire thickness of the cheek, which



LEUCOPLAKIA



PRESTERNAL CHELOID

PLATE V

PLATE V

LEUCOPLAKIA (p. 156)

FIG. 1.—The patch is thick, rounded, and much raised, resembling porcelain.

FIG. 2.—Since this figure was drawn, a slightly greyish tint with a few white streaks has recurred, but the mother-of-pearl patch has disappeared. There is now no prominence.

PRESTERNAL CHELOID (p. 165)

FIG. 3.—Presternal cheloid, deeply coloured, and very prominent, with irregular surface.

FIG. 4.—Not the slightest induration remains. The skin is soft and pliable. Improvement took place without any superadded inflammatory reaction.

was considered by the patient's medical advisers beyond the scope of any therapeutic treatment, was reduced to an unexpected extent in one month, by the use, inside and out, of a rectangular instrument containing 12 cg. of salt, with an activity of 1,000,000, applied with screens for 120 hours on the skin, and five hours on the mucous membrane.*

RADIUMTHERAPY OF CANCERS IN GENERAL

In concluding our communication of November 6th, 1908, to the Société Médicale des Hôpitaux, on the treatment of cancer by radium, we called attention to the necessity, on such a subject, of avoiding definite conclusions based on cases which were few in number and had been recently treated. Relapse must always be looked for, and unfortunately no treatment is exempt from the possibility of complications. All we can do is to recognise and endeavour to estimate the qualities and special properties of radium, and the advantages which it may possess over other methods of treatment. In this respect the cases recorded in this and the preceding chapter, which strengthen and confirm each other —and to these must be added the results obtained in carcinoma of the uterus (Chap. X)—have not failed to impress favourably those who observed them, in spite of the reserve inseparable from a scientific attitude of mind. These cases lead to a certain number of general considerations, most of which have already been stated, and need not be repeated here.

The most striking point in our investigations was that the results were not confined to small epitheliomata, and were far better than those obtained by the first observers. In lesions for which there is no hope of cure, it is sometimes possible to prolong the lives of patients, and to relieve their sufferings, even in cases where surgical, electrical, or X-ray treatment can no longer be employed with advantage.

* *Note by Dr. Wickham.*—In spite of many cases of sarcoma which were very successfully modified, and several instances in which cancer of the lower lip and of the palatal arch was *apparently* cured, the researches made by Dr. Degrais and myself from the completion of the French MS. to the present time (December, 1909) have led us to the conclusion that, with the instruments now at our disposal, the use of radium in the treatment of cancer of the buccal mucous membrane gives results greatly inferior to those at first recorded, and to those that we have obtained in other regions. I think that there are several causes for this failure :—

1. The special sensitiveness of the mucous membranes.
2. The rapidity of invasion of the lymphatic vessels.
3. The weight of the thick filters required, which is a source of irritation.
4. The impossibility of leaving such heavy instruments in contact with these cancers for a sufficiently long time.

I believe that when we can employ much more powerful radioactivity, and when other methods—we are now experimenting with some which seem superior to those previously used—have been tried, the results will be better. However that may be, there is no doubt whatever that, in the present state of radiumtherapy, it is necessary, with few exceptions, to resort at once to surgery, using radium afterwards (in strong doses, " surpénétrant " rays, and fairly short exposures) simply to heal the scars.

In ulcerating neoplasms one usually observes, in the first place, arrest of pain, hæmorrhage, and discharge, and the disappearance of offensive odour; analgesia and diminution of congestion afford great relief in subcutaneous neoplasms. These are all valuable services to patients of this class, whose condition is hopeless.

In growths of less serious character the improvement does not stop here, but is accompanied by other symptoms of resolution. Tissues are modified; the tumours become detached from their adherent bases, and diminish in size; vegetations subside and disappear; ulcers become cicatrised and gradually replaced by new tissues of excellent appearance. Subcutaneous neoplasms, in consequence of their fibrous transformation, frequently leave hard, indolent, and movable foci after treatment.

We have obtained no less successful results with other tumours of various kinds (lymphadenoma, sarcoma, lymphosarcoma,* and mycosis fungoides).† We have not specially mentioned malignant neoplasms which are only accessible with difficulty, since the study of these growths is still proceeding, and the examples of them are recent, but some of the results obtained are now sufficiently clear and precise to permit us to assert the value of radium in a larger field than had hitherto been thought possible. This is not a mere idea or opinion based only on conjecture, but a principle founded on the special selective action of radium, and we are able to profit largely by its therapeutic properties, viz. the great power of penetration possessed by the rays, the flexibility of the instruments, their convenience and the ease with which they can be adapted to the regions to be treated, and the improved technique which allows of strong dosage. The value of these properties has been fully demonstrated in the preceding cases. By way of illustration, we may mention some of the regions difficult of access where radium has been able to produce good effects. It will be easy to devise a combination of instruments appropriate to the treatment of any particular carcinoma, according to its position, extent, and gravity.

In cancer of the prostate gland, one can act either on the perineal region or on the gland itself, by the introduction of an apparatus into the rectum, or of a radiferous tube into the growth. In carcinoma of the rectum it is sufficient to locate carefully the site of the tumour,

* H. Dominici and Barcat, "Un cas de lymphosarcoma traité par le radium."—*Presse médicale.*

† *Note by Dr. Wickham.*—In all cases in which local reduction has been obtained, it is necessary to persevere with the treatment. With few exceptions, the patients cannot be considered "cured." It is only a question of prolongation of life, for in these diseases relapse, or invasion of other parts by metastasis, is sure to take place, sooner or later.

and to introduce an instrument at the required distance. For the œsophagus an œsophageal catheter can be used. Abdominal carcinomata may be treated by the application of apparatus to the walls of the intestines by means of an artificial anus, followed by the introduction of a radium catheter. Cancer of the cervix of the bladder may also be treated by means of a catheter.

Lastly, the properties peculiar to radiumtherapy may also be found beneficial after surgical removal, for, in any case where X-rays are considered useful with the object of preventing relapse, radium offers still greater advantages, on account of the greater power of penetration of the rays, and the facility with which apparatus covered with screens can be fixed in the dressings, and left in place for a very long time without inconveniencing the patients, or producing inflammation. In the treatment of these different kinds of very deep-seated neoplasms, recourse should always be had to a high degree of radioactivity; the most intense radiation will also be the most valuable. If the regions only permit of very short applications, the apparatus should be covered with extremely light screens, and the exposures frequently repeated. If, on the contrary, they allow of long-continued action, the instruments should be covered with thick screens.

Finally, we should never forget, whenever such a course seems practicable and beneficial, to combine the injection of virtually non-absorbent substances containing a soluble or insoluble salt with the application of apparatus to the surface of tumours and the introduction of tubes into their interior; a method which is exclusively confined to radium.

[*See* addendum to this chapter by Dr. Wickham on pp. 300-2.]

CHAPTER IV

THERAPEUTIC RESULTS (Continued)

II. CHELOIDS AND DISFIGURING SCARS

At the beginning of our experiments in radiumtherapy we had the opportunity of seeing two cheloids of the presternal region disappear under the influence of the rays; the fibrous cicatricial bands complicating scrofula becoming level with the surface. This was an indication that systematic study of these lesions should be undertaken, a study which, it appears, had not been previously made. Indeed, in the literature of the subject there were only two cases, recorded by Williams, concerning cheloids, and no mention was made of treatment of such cicatricial bands by radium. After having related in various papers the experiments we had made, collected a sufficient number of successful results, and established the main lines of the technique, we laid before the Academy * the following conclusions:—

1. Radiumtherapy can be advantageously employed for the reduction and improvement of certain kinds of disfiguring scars, especially those complicated by cheloids and fibro-sclerotic prominent growths.

2. True cheloids, in most of their forms, are particularly amenable to radium treatment.

Since this communication our cases have been much more numerous, without in any way causing us to qualify our early conclusions; they have, indeed, decidedly confirmed them. On the other hand, our methods themselves have benefited by longer study, so that the following data can be established on a wider basis. In the first place, a distinction must be made between cheloids and fibrous cicatricial bands. The action of radium is so different in these two cases that it would be well to separate the study of them entirely, were it always possible clinically to distinguish one from the other. But, in addition to forms in which the difference of diagnosis is plainly indicated, there is a whole series of prominent disfiguring scars about which it is difficult to ascertain clinically whether the tissues are either cheloidal or sclerotic, or whether,

* "Traitement par le radium de certaines cicatrices vicieuses: chéloïdes, acnés chéloïdiennes, écrouelles, brides fibreuses saillantes." Acad. de Méd., May 26, 1908.

as often happens, there is a combination of the two processes. In the first section we shall speak of tumours which are obviously cheloidal; prominent cicatrised bands form the subject of the second section.

I. CHELOIDS

Marked healing influence of radium on cheloidal tissues.—The various methods hitherto placed at our disposal for the treatment of cheloids are far from satisfactory. Surgery can only hope to obtain good results by free excision, both superficially and at a depth, far beyond the visible limits of the lesion. Even in the case of an ordinary presternal cheloid, as for instance that shown in Plate V (Fig. 3), it tends to produce great loss of substance. Now operations, even on a large scale, do not always prevent relapses from taking place, and these are usually troublesome, their size sometimes being double that of the first lesion. Case No. 8 (p. 171) is an instance of a cheloid operated on three times, which, each time, relapsed to double its original size, ending in an enormous tumour. Scarification and electrolysis, even though recently improved, give uncertain results. The number of operations required for cheloids of considerable size discourages patients, and, in any case, the pain they cause makes them difficult to bear. Good isolated results have been obtained by X-rays, but there have been no systematic investigations which would justify comparison, and to radium workers who have been able to try both treatments, radium seems to possess advantages over the X-rays. Two new methods have been much advocated lately; one, by de Beurmann, consists in first surgically scraping the cheloid, and then subjecting the wound to X-rays; the other, by Gaucher and Louste, follows up the scarification by fulguration.

In radium we possess a therapeutic agent which exercises a very marked healing influence on cheloidal tissue. Our statistics concerning true cheloids relate to about 50 cases, and in none of them have we so far met with absolute resistance or relapse. The results consist, in varying degrees, and after greater or less length of treatment, in levelling of prominences, decolorisation of erythematous cheloids, analgesia of those which caused pain, recovery of elasticity by the deep-seated tissues, and the possibility of folding the epidermis on the surface on which the growth was situated. These results sometimes, especially with recent cheloids of small size, lead to recovery of the normal state. When once obliterated, the growths frequently leave a surface which, although very satisfactory in appearance, is smoother, drier, more even and glazed, than the surrounding skin. It is not covered with down, and its colour is sometimes redder and sometimes whiter than the normal skin.

Technique.—The treatment of cheloids lends itself to various combinations, and the same successful results may be attained by different processes. These lesions, generally so refractory to therapeutic agents, in many cases even responding to their action by redoubled vitality, show themselves, on the contrary, particularly amenable to the action of radium. That is why we advise beginners in radiumtherapy, or possessors of new and untried apparatus, to choose cheloids as the subject of their first experiments. If the doses are insufficient, the cheloidal process will not be made more active; if, on the other hand, the doses are excessive, and produce severe reaction, the tissues will be easily repaired, and will not become the site of a relapse. Nevertheless, it will be well to state the line of procedure which we have hitherto found to give the best practical and æsthetic results. Above all, the principle which governs the technique, and which the operator must never lose sight of, is the necessity for influencing the cheloids to the extreme depth of their base, and acting on their peripheral prolongations, which sometimes extend far beyond their visible limits. The treatment of a cheloid should only be considered complete when the tissues show an almost normal elasticity on palpation, even at a depth. There are two very different methods, one deriving its effects from the specific action of radium, the other from its destructive action.

Specific action of radium.—The amenability of cheloidal tissues to radium is due to the fact that the rays can exercise on them a special action, which causes them to disappear by simple absorption, by gradual regression, without exhibiting the least revulsion, or clinically visible inflammation. In opposition to the destructive inflammatory action, which radium always possesses in certain doses, and which might indeed be utilised in the treatment of cheloids, this special action, which we have called specific, is nowhere more marked than on such tissues. And it is not the least of the advantages of radiumtherapy that it enables us to watch the easy disappearance of tissues which are usually so refractory. In order to produce this selective action it is sufficient to use doses which are not strong enough to produce surface irritation. These are calculated according to the methods which are given in the chapter on Carcinoma, but they may be much stronger for cheloids, since these neoplasms are very much more refractory than others.

It is possible, then, to make use of total radiations of great power, composed largely of β rays, and employ them in frequently repeated exposures of short duration; or of "surpénétrant" radiations of weak quantitative value, allowing them a sufficiently long action; or of the simultaneous application of several instruments acting opposite each

other, by the system of "cross-fire." By these means, which lead to the absorption of the growths, we can utilise the selective power of radium. But they are sometimes slow, and in order to gain time it is often well to act more energetically, undeterred by the fear of producing a certain degree of destructive inflammation. In the application of these different processes, two important data must be borne in mind, viz. (1) the great resistance shown by cheloidal tissue, from which results the possibility of using fairly large doses, without producing any reaction worth mentioning; (2) the futility of aiming at the entire avoidance of superficial inflammation. If the "specific" dose be slightly exceeded, a small dry crust with a dry base is produced which will not in any way hinder the course of treatment. If there is any hesitation as to which of two doses, intended to obtain simple modification without destruction, shall be chosen, there can, therefore, be no objection to deciding on the stronger. Cheloids which respond most readily to the employment of specific doses are those of recent formation in process of evolution, and those of young children. The following are three cases, amongst many others, which show the possibility of reducing these growths without causing inflammation.

1. **Cure of cheloid caused by application of thapsia, dating back nearly four years, with no trace of inflammatory reaction.**—A cheloid was situated at the level of the fourth intercostal space, 6 cm. to the left of the border of the sternum. It was the size of a haricot bean, and rather more than 1 cm. in diameter. The growth did not appear to be deep-seated. It was easy to take hold of it and roll it between the thumb and first finger. Its consistency was very hard, and the surface smooth, even, and redder in colour than that of the neighbouring skin. It had been caused by an application of thapsia. The inflammatory agent had acted rather more strongly at its left inferior extremity, and the growth had developed at this point.

This case gave one of us the opportunity of trying the effect of radium on this variety of neoplasm for the first time, in April, 1905. No. 4 apparatus with a screen (p. 7), by means of which Soupault had discovered the influence of radium on arthritis in 1904, was chosen for the treatment. It covered the surface of the cheloid fairly well, and contained an aluminium sheet $\frac{1}{10}$ mm. in thickness, forming a screen sufficient to intercept some of the rays; its active surface was a disc 1 cm. in diameter. "With this apparatus, we produced no inflammatory reaction on the skin by exposures lasting less than fifteen minutes, and repeated for several days on the same place." * The applicator

* Wickham: "Note sur l'action du radium en thérapeutique." *Annales de Derm.*, October, 1906, p. 3.

was used for fifteen minutes on six different occasions, equally distributed over a fortnight. Fifteen days after the commencement of treatment, the tumour had decreased in size, and seemed less hard. The surface became slightly erythematous, but no desquamation took place. Improvement was more marked during the following weeks, and by the third month there remained absolutely nothing of the cheloid but a darker and slightly pigmented area. The tissues at this level had recovered their original elasticity, and the epidermis could be folded in the ordinary way. Eventually the pigmentation itself disappeared, and the region resumed its normal aspect. This was the first cheloid treated in a systematic fashion with a definitely fixed dosage, and our conviction of the specific action of radium on cheloids dates from this time. The case is an instance of the complete restoration of tissues to their normal appearance, without relapse during a period of four years.

2. **Presternal cheloid following application of sinapism. Cure without relapse for more than three years.**—The treatment just recorded was hardly finished when a second patient, whose case was similar in every respect, was entrusted to our care. Clinical practice has some strange coincidences. It was a growth of the same size, almost in the same place, of the same appearance and of recent development, with a similar slightly infiltrated base, and a similar induration. It originated in a sinapism, instead of thapsia. The Soupault apparatus with a screen was naturally adopted on account of the previous success. The exposures were for thirty minutes instead of fifteen, but only to the number of three, and with an interval of three days between them. A few months later the cheloidal tumour had disappeared. Some time afterwards, and again, still more recently, we were able to examine the patient. The tissues were absolutely supple, and no longer showed a trace of the former lesion.

This case agreed with the first in all respects, particularly as regards dosage and the specific value of radium, of which it afforded weighty and conclusive proof. Moreover, these two examples induced us to undertake the study of the effects of radium on cheloids in a systematic manner. It should be remarked that β rays played the principal part in the technique followed in the treatment of these two cases. Indeed, it would be difficult to underrate their importance, considering, on the one hand, the large proportion of β rays (87 per cent.) contained in the radiation employed, and, on the other hand, the extreme shortness of the applications, which prevents us from attributing a really effective part to the γ rays, in view of their small proportion and the time of application which we know to be necessary for their action.

The following is a third example of the healing of a cheloid, without

superadded inflammation, by specific action, but this time with the use of " surpénétrant " radiations, including a large majority of γ rays.

3. **Presternal cheloid cured without inflammatory reaction** (Plate V, Figs. 3 and 4).—A patient came to consult us about a presternal cheloid, dating from April, 1907. A small swelling appeared on the breast at this period. The patient, wishing to dress for the evening and go out, pricked it with a pin. Such severe inflammation almost immediately ensued that she was obliged to remain at home. An abscess formed, which was incised, and a small cheloid developed in consequence of this operation. This was surgically removed, but relapsed to three times its previous length and thickness, and finally attained the proportions shown in Plate V. This growth, prominent over the whole of its surface, was more so in the centre, where it measured 1 cm., and presented a sort of ridge from which descended the two halves of the cheloid. Patches separated by slight depressions also existed in a transverse direction. The whole of the growth was reddish violet, and studded with numerous telangiectases, being much more deeply coloured than is usual with cheloids. It was 4 to 5 cm. long by 1.5 cm. wide, and very hard to the touch, its base being rather deep-seated. The skin which covered it could not be folded.

Apparatus No. 2, covered with $\frac{6}{10}$ mm. of lead, was applied for eight hours, an hour a day. Fifteen days after the last application, a diminution could be observed in the thickness and redness of the growth. Four weeks later, apparatus No. 2, with $\frac{5}{10}$ mm. of lead, was used for six consecutive hours, in one exposure. There were three more applications, at intervals of five weeks from each other; the first, for twelve hours in succession, with No. 2, covered with $\frac{5}{10}$ mm. of lead; the second for the same time with No. 1 and $\frac{4}{10}$ mm.; the third with the same apparatus and duration, but with a screen of $\frac{3}{10}$ mm. These applications were only followed by very slight desquamation. The tendency to levelling and suppleness became more marked after each treatment. From the time of the last exposure, the skin took on an almost normal appearance, scarcely to be distinguished from the healthy surrounding skin. When pinched between the fingers it showed normal elasticity, and there was no longer any deep induration.

We have several times obtained the regression of cheloids by using thick filtration (2 mm. of lead), and leaving the apparatus in place for several consecutive nights.

These examples not only demonstrate the specific action of radium, but also indicate that the results may be obtained by means of very different techniques and degrees of radioactive intensity.

In the next paragraph we shall show that it is often desirable to act on cheloids in a more energetic manner.

Combination of specific and destructive properties of radium.—We have said that, in practice, it is sometimes well to combine the destructive and specific properties of radium. The possibility of producing rather strong inflammation of cheloids, without the risk of relapse, is due, not only to the special process according to which the repair of diseased tissues takes place, but also to the filtration effected by the first layers of cheloidal tissue. Indeed, whilst the latter receive intense and massive total doses, the deeper layers are only affected by the more penetrating rays, which, having passed through in small numbers, exert a gentler specific action. A double action is therefore simultaneously produced; destructive in the superficial portion of the cheloid, and specific beneath that region. The specific action produced on the cells underlying the inflamed regions explains why these cells do not undergo the harmful influence which it would seem must be produced by the severe inflammation in their neighbourhood. These are the considerations which have frequently induced us to employ methods that utilise and combine this double action of radium, especially for patients in the country, whose stay in Paris is short. In many cases we have avoided much loss of time in this way. These methods may be employed in three different ways:

1. The first consists in acting by two exposures: (a) massive doses of full radiation from unscreened apparatus, intended to destroy the prominent portion of the cheloid (for instance, No. 1, applied for three hours in succession); (b) "surpénétrant" radiations used immediately after the first applications, before inflammatory reaction has set in, in order to act specifically on the deeper parts—*e.g.* No. 1 apparatus covered with 2 mm. of lead, applied for about twenty-four hours.

2. Treatment with "surpénétrant" radiations can also be easily managed, by leaving the instruments in position for a considerable period, until doses are accumulated which produce some degree of superadded inflammation. For instance, No. 1, enveloped in 1 mm. of lead, would be left in place for two or three days.

3. Lastly, medium filtering with $\frac{1}{10}$ to $\frac{6}{10}$ mm. of lead can be used, and we now as a rule have recourse to these. With such filtration, four or five long applications for several nights, with long or short intervals, made with No. 1, for example, yield excellent results. It is evident that the doses and length of exposure must vary according to the thickness and extent of the surface treated. We will select some cases which illustrate these different doses for cheloids differing in origin (cauterisation, burns, traumatism, scrofula, acne, etc.).

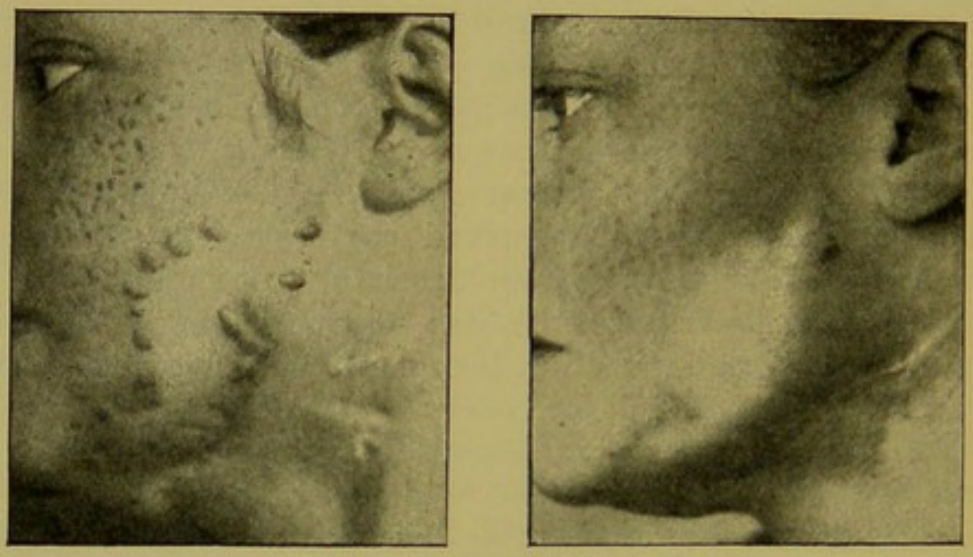
1. **Cheloids of anterior surface of neck following inflammation produced by iodised cotton** (Plate IV, Figs. 3 and 4).—In consequence of the application, in early infancy, of iodised cotton soaked in hot water, a blister was produced on the anterior part of the neck of a girl of 12, followed by the formation of a crust, and then by degrees by a cheloid of large extent. This was thickest at its centre, where it formed a hard mass 6 or 8 mm. above the level of the skin, and was situated in front of the cricoid cartilage, extending above to the thyroid cartilage. From the median portion of the neck there were prolongations or cheloidal processes which extended over a region limited above by a line passing through the upper part of the thyroid cartilage, below by the upper edge of the gladiolus of the sternum, and laterally by the sterno-cleido-mastoid muscles. The whole formed a cheloidal patch of large extent, as will be seen from Plate IV. On palpation the cheloidal induration was found to be rather deep. The skin could not be folded, and was the site of erythema, and somewhat severe pruritus.

The treatment consisted in the application of apparatus No. 3, in $\frac{6}{10}$ mm. of lead, for ten hours, spread over three days (two exposures of three hours, one of four). About the sixth week improvement of the cheloid at its left lower extremity was observed, otherwise there was little change. A second series was then made; in the centre, No. 3 was applied with $\frac{3}{10}$ mm. of lead, for twenty hours, two hours a day; on the sides, No. 4, in $\frac{1}{10}$ mm., was placed for eight hours on the right, and four on the left. A slight crust made its appearance in the centre, fifteen days after the last application, only lasting ten days. Six weeks after the commencement of the second series we employed No. 2, with $\frac{3}{10}$ mm. of lead, for twenty-four hours in three nights, eight hours each night. Two other applications were made successively for twenty-four hours in two nights, with an interval of two months, one with No. 2, covered with $\frac{1}{10}$ mm. of lead, the other with No. 3, covered with $\frac{2}{10}$ mm. After each course the tumour improved, and became more supple. The special object of the two last exposures was to do away with the deep induration, for levelling of the surface had been already obtained. What remained of the growth was scarcely visible, and a little whiter than the normal skin.

The essential point to be noted was the suppleness of the tissues. The skin could be folded without any difficulty, and, when taken between the fingers, the region treated presented no induration.

2. **Numerous cheloids of face, following cauterisation for tuberculous lupus** (Figs. 39 and 40).—A patient attacked by tuberculous lupus of the left cheek had been unsuccessfully treated by actual cautery. Cheloids had been produced on many of the places cauterised. Photo-

therapy had afterwards cured the lupus, but not the cheloids. These formed a series of hard elevations, separated from each other, and placed at the periphery of the cicatrix of the lupus which they encircled. Instruments Nos. 6 and 7 were applied for three hours on each growth. There was slight inflammatory reaction. Three months afterwards the cheloids of the anterior edge of the lupous cicatrix had disappeared, the others being only reduced in size. Treatment was resumed with No. 6, successively applied for two hours on each of the remaining cheloids. From that time the growths entirely disappeared. Nothing remained but a smooth, even, scarcely visible surface. No relapse has occurred during the eighteen months since the date of this cure.

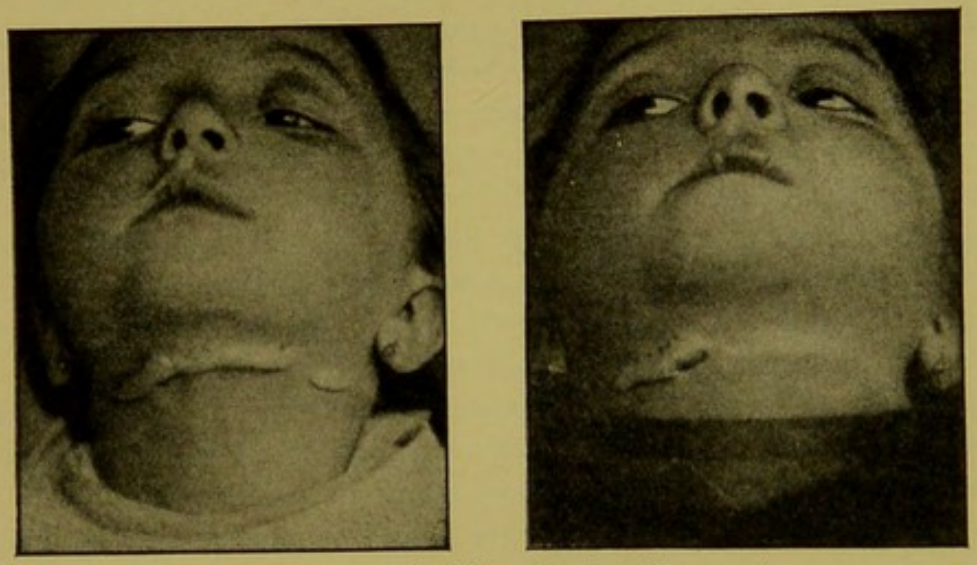


Figs. 39 and 40.—Cheloids of face.

3. **Cheloid of submaxillary region following burn** (Figs. 41 and 42). —A child, aged 5, was burnt, a year ago, by scalding fat. The result was a cheloid 1 cm. wide, with a projection of 8 mm. This large, hard ridge, studded with fine vascular ramifications, began at the left sterno-cleido-mastoid, was absent for a distance of 1 cm., and then reappeared, crossing the submaxillary region and continuing to the sterno-cleido-mastoid of the right side. In the first series, the whole cheloid was treated, place by place, with applications of apparatus No. 4, six hours on each area. The result was a certain degree of levelling of the whole growth. In a second series, the left portion alone was treated by the application of No. 5 for three hours, and complete resolution was afterwards obtained, as may easily be seen from comparison with the right portion, treatment of which was not continued.

4. **Huge cheloidal patch on back of hand, following burn.**—A patient of 34 had been burned on the hands and face eight months

previously in consequence of the explosion of a spirit lamp. The scars were complicated with cheloids. On the back of the hand there was an extensive reddish area of hard cheloidal tissue, deeply coloured, with extension towards the fingers and wrist. It projected as much as 6 mm. in places. The movements of the hand were much impeded, and the fingers could not be bent. A portion of the surface, 28 square cm., exactly in the middle of the cheloidal patch, was treated by two exposures of twelve hours each, with eight days' interval, of apparatus No. 1, with a screen of $\frac{2}{10}$ mm. of lead. Slight, though somewhat painful, inflammatory reaction ensued. No crusts were produced. During the two following months we observed the gradual regression



Figs. 41 and 42.—Cheloids of submaxillary region.

of the lesions. The tissues lost their colour, and became flatter and more supple, so much so that the place treated, which is now level, again clearly showed the red cheloidal tissue surrounding it.

5. **Painful cheloid following cauterisation of pigmentary nævus.** —In the postero-external region of the right arm a patient presented a small pigmentary nævus which had formerly been an ordinary "beauty-spot." Four years before, however, the cautery used for its removal had transformed it into a cheloid, which gradually increased in size. When the patient was sent to us, the growth had a projection of 5 to 7 mm., and occupied a surface of 4 square cm. It was exceedingly painful. Indeed, for two years this growth had been the site of very severe pain, with daily or nightly exacerbations. Pain was also felt in the neighbourhood of the lesion, extending to the shoulder, and descending as far as the elbow. No relief had hitherto been obtained by the patient, whose sleep was constantly disturbed. It was, therefore, removal of the pain,

rather than of the little tumour, which was required. Apparatus No. 7, covered with rubber, was applied for eight hours a day, every two days. After this first treatment partial flattening of the cheloid and diminution of the pain were produced. Two months afterwards a second series of the same applications ended in completely levelling it. But as, six months afterwards, the painful symptoms had not quite disappeared, and a hard portion still remained below the level of the skin, we employed isolated " surpénétrant " rays for a third course. Apparatus No. 6, with 1 mm. of lead, was left in position for thirty-six hours. Complete relief was almost obtained, but very slow reaction set in seventy days after the application, causing some attacks of pain. This, however, is a symptom which now seldom occurs. Four months afterwards we used three applications of No. 7 with 2 mm. of lead, for twelve hours. Since then considerable improvement has taken place in the painful symptoms, which have only returned at long intervals. The treatment is not yet finished, and if the pain reappears we intend to continue the use of " surpénétrant " rays.

6. **Presternal cheloid following burn.** — A child, 3 years of age, was sent to us by Dr. Hontang for a cheloid of the chest. This growth had begun six months previously, following the application of a mustard poultice, which had caused a burn measuring 10 to 12 square cm., slightly to the left of the border of the sternum. The cheloid had only developed in the centre, around which could be seen scar tissue resulting from the burn, but not presenting a cheloidal character. There was a small cheloid on the back, which had originated in the same way. The treatment consisted in the application of apparatus No. 1, covered with $\frac{1}{100}$ mm. of aluminium, and left in position for two hours in all, half an hour every two days. Fifteen days afterwards a crusted reaction appeared, which lasted three weeks to a month. The influence of the radium became evident during the four following months, for the parents observed continual improvement for the whole of this period, during which time, being detained in the country, they were unable to bring their child. Five months after the first course of treatment we noticed a very evident diminution of the cheloid in extent and prominence. The opening made in the protective " cache " was now too large at every part of its outline. A new series of applications was made in the same way, and the skin recovered its suppleness some weeks afterwards, became level, and now has only a slight appearance of scarring.

7. **Cheloid following application of leeches.**—A child, aged 10, presented, as a result of the application of leeches in the right and left lumbar regions, three cheloidal scars on each side. These growths were

the size of a large pea on the right side; on the left they had a starlike appearance, reproducing the shape of the leech-bites. The tumours were the site of very severe itching, which disturbed the child's sleep, and injured its health. We applied instruments Nos. 6, 7, and 8, enveloped in $\frac{4}{10}$ mm. of lead, on the left lumbar region, for twelve consecutive hours. In the right lumbar region, the three cheloids being close to each other, we were able to make openings, of the same size as the lesions, in a single protective "cache," and to apply apparatus No. 1, wrapped in $\frac{4}{10}$ mm. of lead, for twelve hours in succession. These applications reduced the lesions to a level with the surface, and caused the disappearance of the itching. Two points still remained, one on the right side, and the other on the left, where subsidence was only half effected, and where itching still occurred from time to time. No. 8, in $\frac{2}{10}$ mm. of lead, was applied to each of these places for six hours and a half. Complete reduction of the lesion and disappearance of the itching were then obtained.

Cheloids frequently follow scrofula, but they are rarely purely cheloidal, as in the following case, being usually mingled with cicatricial irregularities and fibrous bands, and therefore belonging rather to our second division.

8. **Huge cheloid of neck, following scrofulous cicatrices, relapsed three times after three surgical operations.**—It is well known that the skin of the black races is liable to cheloidal growths. The young negress whose history follows is a remarkable instance of this tendency. In 1893, at the age of 20, a cold abscess appeared on the right side of the neck. It burst, and the resulting scar became the site of a cheloid. This unsightly and troublesome tumour was surgically removed. The first excision was followed by a relapse which produced a cheloid twice the size of the first. This was again operated on, but relapsed once more. Finally a third operation was undertaken, which was also followed by an extremely rapid cheloidal process, that developed upon the cicatrix and at every point of the suture. These successive growths caused the formation of an enormous cheloid, 20 cm. long, extending from the right sterno-cleido-mastoid to the left half of the neck, on which it slightly encroached, after crossing the thyroid cartilage. It measured posteriorly 4 cm. wide, and gradually diminished, being only 1 cm. in width at the anterior extremity. Its thickness was considerable, the projection above the skin, in the widest portion at the back, reaching 2·5 cm., and it decreased in front, being only 0·5 cm. near the median line of the neck. In the middle of this cheloid, above and below, there were three others the size of a haricot bean, formed at the points of suture. The tumour was extremely hard to the touch, and appeared to extend

very deeply into the subcutaneous tissue. It was a growth of enormous size, such as is rarely met with.

Treatment was divided into two parts. The first was intended to reduce the lesion by acting with extremely destructive doses, as we knew from experience that inflammation was not followed by relapse in cases of this kind. In the second, we used chiefly " surpénétrant " rays by " cross-fire," acting on the tissues even when in a state of inflammatory reaction.

First course : Apparatus No. 1, wrapped in rubber, for six hours on each place, an hour at a time, six days in succession. Very severe and painful inflammatory reaction ensued.

Second course : Begun on the ulcerated tissue six weeks after the first. The posterior region of the cheloid, although already much reduced after the first treatment, was still thick enough to enable us to use our " cross-fire " method, placing apparatus No. 7, with $\frac{3}{10}$ mm. of lead, for twenty hours above, and No. 6, with the same screen, below.

After a month's rest a new course was begun. The patient then had to go to America, and we were unable to watch the retrogressive changes which usually take place by degrees during the three months following application, and are still evident many months afterwards. At any rate, when she left us, four months after the beginning of treatment, the lesions had been gradually reduced by more than two-thirds, and in proportion to the decrease of the projection the tissues regained their elasticity, both on the surface and at a depth. We afterwards received a letter from the patient expressing her satisfaction, the cheloids having become still smaller.

The next examples show the efficacy of radium in a specially refractory class of diseases, viz. acne cheloid.

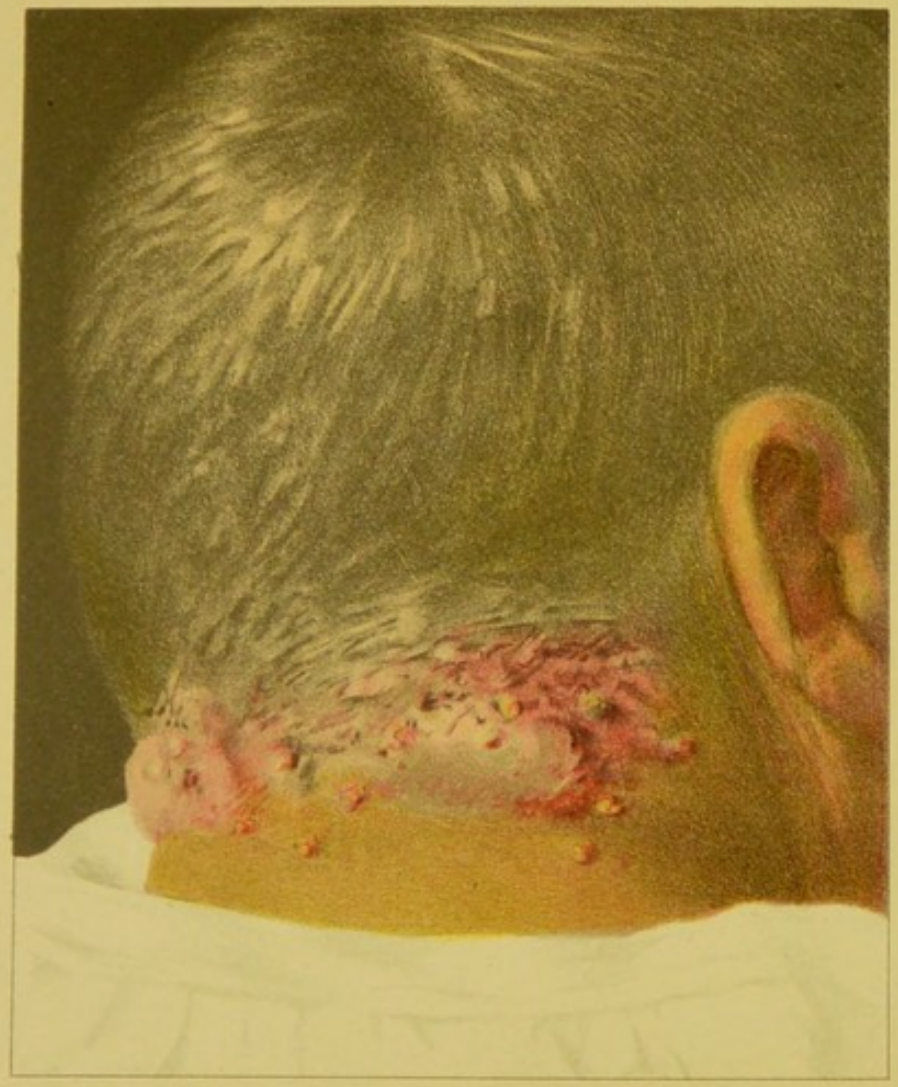
9. **Extensive acne cheloid of nape of neck** (Plate VI).—A workman, aged 43, presented on each side of the nape of the neck a large acne cheloid tumour which had made its appearance three years before. The rubbing of his clothing against the lesions, and the large size of the tumours, inconvenienced him when at work. Many scarifications had been made without lasting improvement. Radium treatment was then proposed. Apparatus No. 14 was applied for four hours on the left side, and No. 2 on the right. A month afterwards the cheloids were reduced to half their size, and had become much less painful and troublesome. Most of the acne elements had disappeared. Treatment was then resumed with the same instruments applied for a total of five hours, distributed over five days. These applications were repeated on two subsequent occasions, with a month's interval. Six weeks after the last course the cheloidal lesions had entirely disappeared. A year after completion

PLATE VI

ACNE CHELOID (p. 172)

FIG. 1.—The tumours were sufficiently large and troublesome to compel the patient, who is an artisan, to give up his work, in order to undergo treatment.

FIG. 2.—The levelling process is complete, and the acne pustules have not appeared again. The deep induration is much less marked.



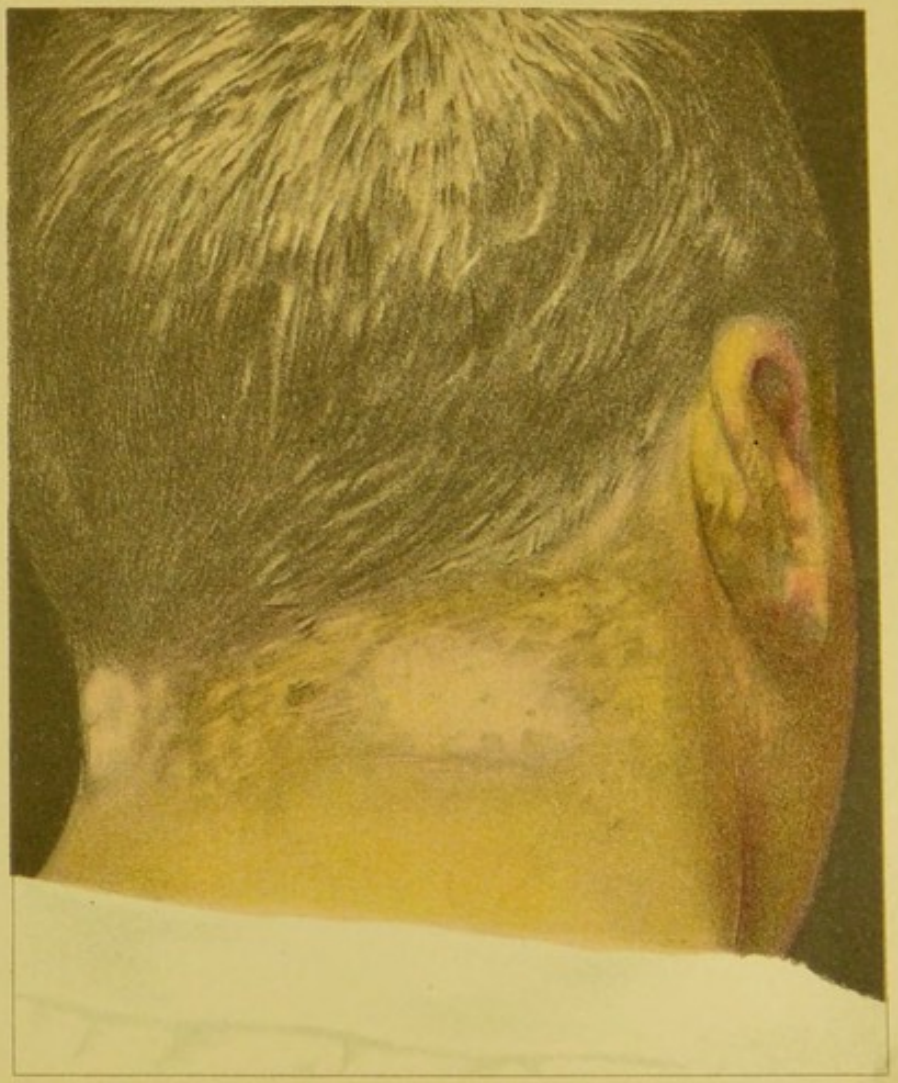
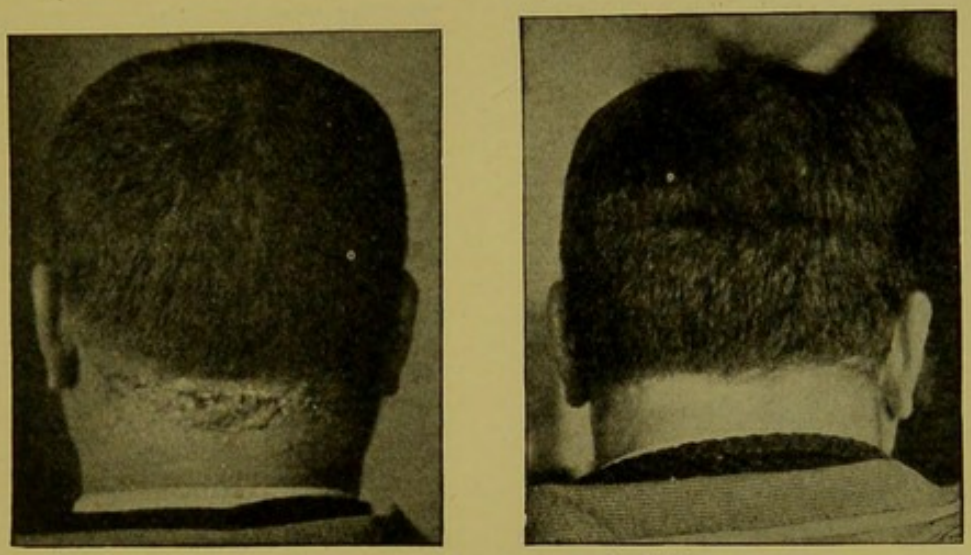


PLATE VI.—ACNE CHELOID.

of treatment the tumours had not recurred. The deep tissues were supple, and the surface treated was lighter in colour, smoother, and more even than the normal skin.

This case is interesting for several reasons. (1) So simple a cure of acne cheloid deserves special attention. One of the reasons for the peculiarly refractory character and relapse of these lesions is the constant recurrence of acne papules, and in this instance they did not reappear. (2) It proves that cheloidal tissue can sometimes bear very intense total doses of radioactivity, without the production of severe inflammation. If, however, this should occur, it is quickly repaired and exercises no exciting action of a nature to produce relapse.



Figs. 43 and 44.—Acne cheloid.

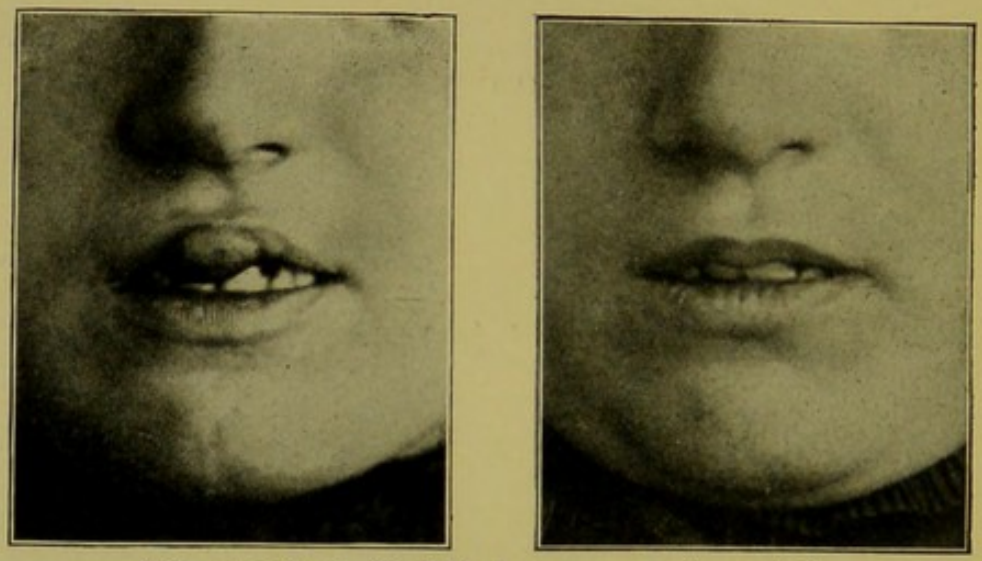
10. **Acne cheloid of nape of neck** (Figs. 43 and 44).—A workman, aged 37, consulted us for acne cheloid of the nape of the neck. There had been first an eruption of folliculitis, which appeared just at the place where there was friction from the collar. By degrees these growths became the site of cheloids, occupying the entire back of the neck. The beginning of the cheloidal development dated back eight years, during which time various forms of treatment had been tried without success. The lesions constantly became the source of fresh eruptions of folliculitis, and there was severe itching.

The treatment consisted in four series of exposures, with apparatus No. 3, left on each place for three hours, at intervals of six weeks. Six months after its completion the appearance of the part was admirable. There was no trace of the cheloid, nor had any signs of acne reappeared. This case confirms the preceding one. We have treated other examples of acne cheloid with similar results, and therefore think

that radiumtherapy is clearly indicated in such cases. But these cases, which illustrate the reduction of follicular and acneiform inflammatory lesions, lead us to hope for new and important developments of the therapeutics of sycosis and acne rosacea.

Before concluding this section on true cheloids, the conclusions from which will be stated at the end of the following section, we will give a case which is unique in our series, and interesting both from its clinical character and from the therapeutic result obtained.

11. **Cheloid of mucous membrane of lip** (Figs. 45 and 46).—Cheloids rarely occur on the mucous membranes. So far as we know, the only two



Figs. 45 and 46.—Cheloid of mucous membrane of lip.

cases published are one by de Beurmann and Gougerot,* and the other by Jourdanet and Barré.†

On February 1st we were consulted about a tumour of the upper lip, which had appeared as the result of a furuncle. This growth was hard and cheloidal, the mucous membrane at the same spot being slightly discoloured. We applied apparatus No. 5 for two hours, and three weeks afterwards the tumour had become reduced to a remarkable extent. It first became softer, and shortly afterwards shrivelled up, until no trace of it remained.

II. FIBRO-SCLEROTIC CICATRICIAL BANDS

We have seen that it is difficult in many cases to distinguish true cheloids from prominent cicatricial fibrous bands. The technique that should be used is, however, different in one respect. Although tissues

* De Beurmann and Gougerot, Société derm., February, 1906.
† Jourdanet and Barré, Polyclinic of Dr. Jacquet at the St. Antoine Hospital.

PLATE VII

REDUCTION OF CICATRICIAL FIBROUS BANDS FOLLOWING SCROFULA (p. 175)

FIG. 1.—The patient suffered from lupus of the face and of the conjunctivæ at the same time. The cicatrix consisted of depressions and prominent bands.

FIG. 2.—Reduction was effected in such a way that the smooth, uniform cicatrix which remains has to a great extent lost the scrofulous appearance which was so distressing to the patient.

PLATE VII.—REDUCTION OF CICATRICIAL FIBROUS BANDS FOLLOWING SCROFULA

obviously cheloidal are adapted to the selective action of radium, this is not the case with fibro-sclerotic bands, which can only be levelled by destruction of the growths. The benefit of the treatment in this case consists only in the convenience with which destruction is obtained, and the usually excellent quality of the tissues of repair. If there is any doubt as to the nature of cicatricial prominences, specific doses could be tried first, and then, in case of failure, recourse might he had to destructive doses. But there is one point which we cannot too strongly emphasise. Our communication to the Academy in 1908 has erroneously caused some of our fellow members to infer that all disfiguring cicatrices can be subjected to radium. Hollowed-out scars, narrow bands which only project slightly, soft bands, swellings and deformities of the normal skin, very extensive scars, etc., cannot be classed among the cicatrices amenable to radium treatment. The only claim of radium is to level, more or less, fibro-sclerotic bands which are hard, prominent, and fairly large, and sometimes to affect the colour and relieve the pain of scars. It is therefore necessary that these bands should present a sufficiently large surface, for we know how much the radioactive value of an apparatus is reduced when only a small portion of it is used.

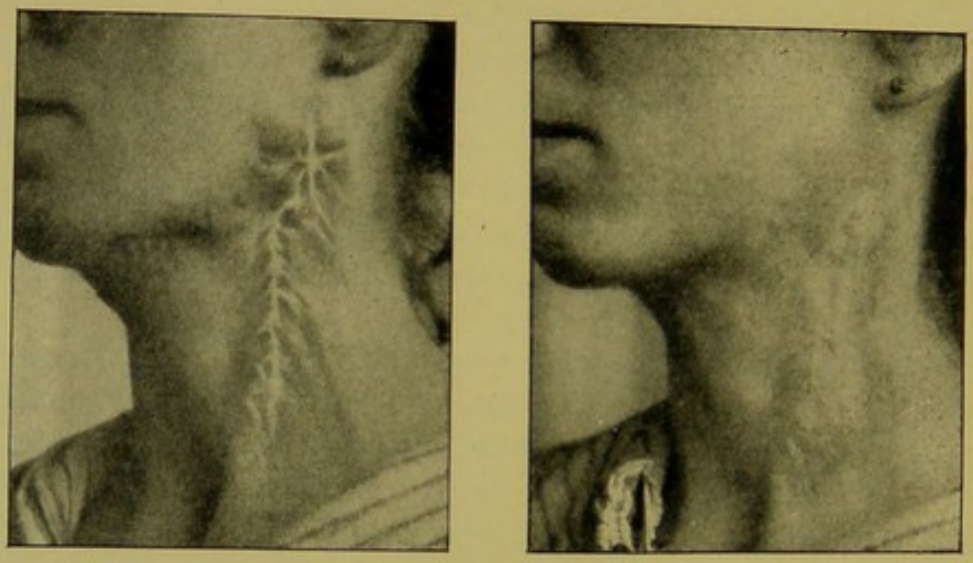
The action of radium on these fibrous bands sometimes renders unlooked-for services. The results obtained with the girl whose history we give on p. 177 are a remarkable instance of this. In some cases not only are the bands levelled, but they become unexpectedly softened to so great an extent that it has been possible to correct a deformity or retraction. In these very successful cases, the cheloidal process probably existed for the most part in the retractile band. It has often happened that, having refused to treat a particular scar, we have yielded to the entreaties of the patient, and obtained, to our surprise, much better results than could have been expected. We therefore advise that a trial be made of radium in cases where unsightly deformities exist, after, of course, warning the patient of the doubtful value of such treatment. In general, although it may be necessary to have recourse to destructive doses, one must be careful not to overdo them, for ulceration produced on fibro-sclerotic bands is long in scarring over, and telangiectasis may occur.

The following are some examples of cases in which radium reduced such bands.

1. **Cicatrices with fibrous bands following scrofula** (Plate VII).—An erythematous lupus of the face, in a woman of 25, was treated by the Finsen method in the clinic of Dr. de Beurmann. She presented, at the same time, on the left side of the neck, a little below the

angle of the inferior maxilla, a disfiguring scar, 4 cm. by 2, following a suppurating adenopathy, which had healed several years before. This puckered surface, which was very conspicuous and unsightly, was covered with rather hard bands, the one in the centre appearing to be cheloidal.

The treatment was very simple, a single application of apparatus No. 14, for two consecutive hours, without a screen, being sufficient to produce the result shown in Fig. 2. Slight inflammatory reaction occurred, lasting about a fortnight; and then we observed that the tissues underwent repair, the bands subsided, and the whole surface was gradually levelled so thoroughly that no other application seemed



Figs. 47 and 48.—Cicatrices with fibrous bands following scrofula.

necessary. The treatment took place more than a year ago, and the region is very much improved. The surface is smooth and even, a little lighter than normal skin, but it no longer has the appearance characteristic of scrofulous scars, and it is not the site of telangiectases.

2. **Cicatrices with fibrous bands following scrofula** (Figs. 47 and 48). —A patient, aged 32, showed numerous disfiguring scars following an adenopathy, which had been suppurating for seven years in the masseteric region, and along the right and left sterno-cleido-mastoids. The lesions on the right side exhibited more particularly a cheloidal character, and consisted of hard whitish enlargements. Along the left sterno-cleido-mastoid there was a long process formed of swollen sclerotic tissue, with depressions and projections of hard thick bands, irregular in surface, and plainly showing the character of the strumous lesions which caused them. Small lupous nodules which had appeared round these scars had been healed by phototherapy. All the lesions to right and left

were treated with apparatus No. 4, wrapped in rubber, and left in position for four hours. The patient returned several months afterwards. The appearance of the part was completely altered, the cheloids having melted away and the fibrous bands disappeared. The lesions no longer had the appearance of scrofulous scars, the tissues being smooth, even, and whiter than the normal skin. Some small points still persisted, and fresh applications were made with No. 4, for two hours. The present state has existed for fourteen months, and continues very satisfactory.

3. **Cicatrix with fibrous bands following syphilitic gumma.**—On the left side of the chest a patient presented an irregular reddish cicatrix, crossed by prominent bands. This was the remains of a syphilitic ulcerating gumma, healed by specific treatment. The scar greatly worried the patient, and he was most anxious to get rid of it. Apparatus No. 1, simply wrapped in rubber tissue, was applied for an hour and twenty minutes, in two sittings, two days in succession. After inflammatory reaction lasting fifteen days, the surface was restored, becoming more and more even, and two months afterwards the tissues had lost their unhealthy colour, and were smooth and much more supple. They are, of course, still scarred, but have a much less disfiguring appearance.

4. **Fibrous bands and cheloids following burn.**—In the case of a young girl of 16, disfiguring and cheloidal cicatrices of the back of the hand were the result of a burn which had occurred fourteen months previously. The surface of the skin was scarred and wrinkled, and showed at certain points prominent bands which, from their reddish colour, were very conspicuous against the paler background. Some of these had a cheloidal consistency. The treatment was tried on a band reaching from the styloid process of the ulna to the third metacarpal. Apparatus No. 1, covered with $\frac{1}{10}$ mm. of lead, was applied for four hours, an hour at a time, every other day. The inflammatory reaction was somewhat painful, and lasted fifteen days. Five weeks afterwards the band became flat. Treatment was resumed, three months later, on another band with No. 1, covered with $\frac{5}{10}$ mm. of lead, and applied for four hours, an hour at a time, on alternate days. In consequence of this treatment the lesion was levelled, and a normal colour of the skin obtained, the tissues recovering much of their elasticity.

5. **Cicatricial bands, resulting from burns, producing deviation and deformity of the commissures of the lips.**—The cheeks and chin of a young girl, who is now 15, were burnt at the age of 3. These regions showed an irregular scarred surface, studded with diffuse red spots and telangiectases. There were also cheloids on the chin. The labial commissures were encircled on each side by two fibro-sclerotic cicatricial bands, which became more marked when the child opened

her mouth, hindering its movements, and strangely disfiguring her face. By way of trial, treatment was at first limited to the commissural band on the left side, and to several patches of telangiectases in the centre of the cicatricial tissue. Apparatus No. 8 was applied for three hours, an hour every day, for three consecutive days, on the different points of the sclerotic band. Two months afterwards softening of the tissues became evident, the telangiectases had disappeared, and the region treated was smooth and of a whitish colour. The period of inflammatory reaction was comparatively short, and not very marked. These results seeming to the father of the child sufficiently encouraging, treatment was undertaken on the right cheek. In this way, pursuing the same mode of operation, the various places were dealt with, and two months afterwards the child's face had a satisfactory appearance. The commissures were less drawn and deformed, and the tissues more supple. Six months after completion of treatment the scars were in an admirable condition. They no longer showed deformities, projections, or redness; the tissues were merely more smooth and glossy than the surrounding skin.

6. **Disfiguring cicatrices resulting from burns.**—A girl, aged 18, was sent to us by Professor Gaucher with disfiguring cicatrices following a burn (from greasy boiling water) dating from the age of 14. The scars were numerous and extensive. Over a large part of the right scapula there were fibrous bands and telangiectases, causing a very unsightly appearance. On the anterior surface of the forearm there was a cicatrised surface of about 3 square cm., with cheloidal growths. The latter place was treated first, together with another selected from the centre of the cicatrised area in the neighbourhood of the scapula, by a six hours' application of apparatus No. 1, with a screen of $\frac{8}{100}$ mm. of aluminium. Eight months afterwards the girl, pleased with the results obtained, came to ask that the other regions should be treated in their turn. The places which have been subjected to the action of radium are, without any comparison, less unsightly than those lying near them. They are flattened, supple, smooth and regular, the telangiectases which crossed them having disappeared. But it should be noted that improvement took place quite differently on the shoulder and arm. Over the scapula the fibrous bands passed through a stage of destruction. The inflammatory reaction was most severe, and cicatrisation very slow in appearing. On the arm, on the contrary, where there were cheloids, the reaction was slight, and the tissues literally melted away. This instance shows both the resistance of cheloids to irritation, and the specific action exercised on them by radium.

7. **Cicatricial bands, resulting from wound caused by motor-car**

accident.—Disfiguring scars (cheloids and bands) developed on the malar, nasal, and temporal regions of a patient of 17, in consequence of a wound caused by a fall from a motor-car. The temporal scar, which was rather large, and the site of cheloids and small bands, formed streaks, and was traversed by numerous telangiectatic vessels which gave it a very turgid erythematous appearance. The nasal cicatrix was situated on the bridge of the nose and extended to its left side, the malar region being likewise crossed by fibrous bands. These scars were treated by the application, for three hours, at three different periods, each with a six weeks' interval, of apparatus No. 1 for the malar and temporal regions, and No. 8 for the bridge of the nose. In estimating the strength of this dosage, it must be remembered that only a portion of apparatus No. 1 was used.

The fact of being able, by means of radium, to soften contracting and deforming fibrous bands is extremely interesting. We know an instance of a girl whose countenance assumed a distorted appearance whenever she wished to speak, and it was impossible for her to laugh. Radium has been successful in modifying the retraction of the commissures so as to make existence less painful for this unfortunate patient. This is not an isolated instance. Professor Gaucher has lately observed, with us, an improvement by radium treatment of a scar of the upper lip, which showed the teeth in a very ugly sneer. This cheloidal deformity followed the cicatrisation of a syphilitic chancre. We applied, on the contracting band, apparatus No. 7, covered with $\frac{2}{10}$ mm. of lead, for six hours, and shortly afterwards the suppleness returned, and the lip partly recovered its normal shape. We have similar cases, particularly that of a baby which had its lower lip drawn and retracted by a cheloidal band. A twelve hours' application with apparatus No. 5, covered with 1 mm. of lead, renewed fifteen days afterwards, softened the tumour, and allowed the lip almost to regain its normal position. As a result of these operations, levelling was obtained.

Conclusions.—Experience enables us to assert that radium has a special selective and specific action on cheloidal growths. It follows that cheloids of every kind, whether they exist alone, or accompanied by fibro-sclerotic tissue, as in the case of prominent fibrous cicatricial bands, can become absorbed and be made to disappear by simple cellular modification, without destructive inflammatory reaction. The cheloid, a growth so refractory to other therapeutic agents, and so baffling on account of its habitual resistance and facility of relapse, disappears and is in some sort melted away by a curative process

which is not shown externally by anything but the disappearance itself. This principle once laid down, it must be acknowledged that, with a practical object, it may very often be advantageous to increase the doses to the point of producing a certain amount of destructive inflammation. We have indicated, in the course of our remarks, the various techniques which are suitable, and shall not, therefore, return to this point.

Whether regression be produced with or without an inflammatory stage, the importance of the result consists not only in the disappearance of the tumour, but in the softening of its base, and also in the possibility of being able, after treatment, to fold the epidermis where the cheloid was situated. This recovery of some degree of normal elasticity is very advantageous in the case of contracting deformities ; and one of the most valuable effects of radium is partly to restore a deformed and retracted lip to its original shape. The disappearance of the congestive symptoms frequently accompanying cheloids, and the cessation of the pain of which they are the source, are very appreciable results.

As to fibro-sclerotic cicatricial bands, destruction is indispensable when the cheloidal element is absent. Here, however, the results are less important and more uncertain. We can succeed, it is true, in levelling such bands, and softening the tissues, but only in part. Besides, as we have shown, it is quite certain that radium can be applied only to special varieties of these bands, and that disfiguring cicatrices do not necessarily respond to the influence of radiumtherapy. The reason, however, why every prominent fibrous band must be subjected—at any rate by way of trial—to radium treatment, is that it is often impossible to be certain that cheloidal tissue is not combined with the sclerotic process. If this is the case, the result is certain to be favourable. As we have already observed, scars treated without much hope of success have frequently been greatly improved. In short, cheloids and a certain number of disfiguring cicatrices with prominent bands can now be very successfully treated by radium, whereas, before its discovery, we were generally baffled by such growths.

CHAPTER V

THERAPEUTIC RESULTS (Continued)

III. ANGIOMATA

(Vascular Nævi—Vascular Tumours)

When we first undertook the systematic study of the treatment of angiomata by radium, only a few isolated articles on the subject were to be found in medical literature, amongst which may be mentioned those of Danlos, Hartigan, Follard, Ekstein, Strasmann, Rehns. These papers only dealt with flat nævi, and in view of the poverty of the apparatus then in use, it did not seem that the application of radium to vascular nævi could be included in ordinary practice. Owing to the improvements made in the apparatus, however, we have been able to treat systematically, and restore to their normal colour, a great many varieties of angioma, by formulating certain rules for the technique. But the cases in which we have found radium of exceptional value were those of prominent growths, and erectile angiomatous tumours, and it does not seem that any experiments of this kind had been made before we demonstrated the specific curative action of radium on such tumours, an action which, judging from the collective results of our work, is one of the culminating points of the present system of radiumtherapeutics. Our attention had been drawn in the first place to certain signs of the relief of congestion by radioactivity which denoted a selective influence on the capillary blood-vessels, and it was this circumstance which induced us, after some successful experiments, to take up the regular study of the therapeutic action of radium on vascular nævi, as soon as our technique allowed of it. Since the date of the paper which we read on this subject at the Académie de Médecine, on October 8th, 1907, our methods have been more systematically recorded, and the number of our cases has amounted to about two hundred, the older ones dating back several years.*

Vascular nævi, considered from the radiumtherapeutic point of view, may be provisionally divided into four groups :

* *Note by Dr. Wickham.*—Up to the present time (December, 1909), we have treated about 500 cases.

1. Flat angiomata, superficial and level with the skin.

2. Flat angiomata, level with the skin, and deeply infiltrating the cutaneous and subcutaneous tissue and mucous membranes.

3. More or less raised angiomata, with smooth or papillated surface.

4. Soft and pulsatile angiomata in fluctuating areas, and erectile angiomatous tumours situated under the skin, or on the mucous membrane.

These divisions are neither exhaustive nor mutually exclusive, for not only are there many intermediate classes between the different groups, but it also frequently happens that quite distinct forms of nævi exist simultaneously in the same patient. Our classification is based on the value of the clinical results obtained, as well as on the technique and dosage suited to each group.

FIRST GROUP: FLAT SUPERFICIAL ANGIOMATA, LEVEL WITH SKIN

In this first group we frequently meet with nævi of a pale colour that are not very apparent, in which case attention should be chiefly devoted to the permanently æsthetic appearance of the newly formed tissue. As such tissue undergoes certain modifications, even after several months of apparently perfect stability, the results obtained can only be estimated after a fairly long period of observation. Side by side with cases in which the colour has not changed, we have sometimes seen pigmentation, telangiectases, and — in some few cases — slight depression of surface, appear after a considerable lapse of time. These objections apply specially to pale nævi, for, when the colouring is strongly marked, and forms an unsightly deformity which it is impossible to hide, even if the result should somewhat deteriorate, treatment would still be a benefit to the patient, since removal of the colour frees him from the deformity from which he previously suffered. He could easily conceal the irregularities produced by means of simple artifices of the toilet. Such was the case of the girl mentioned on p. 188, if we may anticipate the remarks in the next section, to which, however, some of the preceding considerations apply equally well. Since the time when the photograph was taken, she has had eruptions of dermatitis, and telangiectases have appeared, the result therefore not being so favourable as is indicated in Plate X; nevertheless, taking things as they are, it is certain that her appearance is entirely changed for the better. We must not then refuse to apply to these strongly coloured forms a treatment which, in a large proportion of cases, ensures at least very considerable improvement.

As to the technique, it varies according to individual cases; as a rule, we try to avoid inflammatory reaction. From the commencement of our attempts we adopted, with the patient's consent, for pale and easily concealed growths, the plan of treatment now to be described. A single area was first operated on by way of trial, and, after a sufficiently long period had elapsed, the result obtained indicated the subsequent line of treatment. This is a method to which it will often be necessary to resort, and it is dictated by the most elementary common sense. But we have met with individual idiosyncrasies and inequality of resistance. With some patients the results may vary in different places. Doses sufficient for one subject produce scarcely any effect on another. We have learned to recognise some of the reasons which explain this inequality, *e.g.* a dry or greasy skin; a certain doughy softness of the nævi; special colour; the facility with which the normal skin becomes red when rubbed; the degree of decolorisation obtained by pressure with the finger; the fair or dark colour of the skin, and its delicacy. These are all signs to direct us, and nowhere are the experience and judgment of the radium operator more necessary than in the treatment of nævi belonging to our first two groups. Our object must be to avoid inflammatory reaction as far as possible. This result may be attained by different means; we generally use rays of medium penetration, although we have sometimes found very penetrating rays useful. The α rays and some of the soft β should be suppressed, a radiation composed to a great extent of medium β being quite suitable. Moreover, it is important to use sufficiently powerful total radiations; the shortness of the applications will limit the inflammatory reaction, whilst being of great practical advantage. The radiferous "toiles" which we have tried for this purpose during the last year gave the best results; they are flexible, and fairly large, containing radium with an activity of about 50,000. Aluminium sheets of $\frac{1}{100}$ to $\frac{8}{100}$, and even up to $\frac{1}{10}$ mm. in thickness, with the addition of leaves of paper or very fine sheets of mica, are interposed to intercept the α and soft β rays. It will be sufficient to leave these "toiles" in place for less time than would produce irritation, and to renew the applications several times, at more or less widely spaced intervals. The inflammatory reaction can thus be limited to simple desquamation. With varnish apparatus similar results may be attained, and unnecessary irritation avoided, by the same method of procedure.

The foregoing remarks show that we must learn to recognise the flat, superficial nævi which are amenable to treatment, estimate the extent to which they are likely to benefit by it, and choose the operative methods most appropriate to them. When it is thought necessary,

on a place recently treated, to begin a fresh series of applications in order to complete the removal of colour, there is one most important precaution to be taken, on which we cannot too strongly insist. This is —with some few exceptions—never to employ a dosage so intense for these second courses as for the first. In the majority of cases, it will be necessary to use weaker doses. This rule must be carefully observed, especially if the first exposures have only been made three or four weeks previously. Indeed, the rays originally employed continue their action for many months after the last application. Reaction may seem to have been complete for two or three months, and yet the tissues are still undergoing modification. Each new application made shortly after the first therefore produces cumulative action; the tissues being at the time more sensitive and irritable than usual. To neglect this important principle is to run the risk of too severe inflammatory reaction.

With regard to this group and the following one, the site of the lesions largely affects the value of the results. Angiomata of the trunk and limbs sometimes offer much greater resistance to radium treatment than angiomata of the face. When the nævi are situated on the mucous membranes, small and frequently repeated doses easily reduce the colour, but we are seldom specially consulted for flat superficial nævi in this position. The persons attacked trouble very little about them, and it is only occasionally that an opportunity of treating them occurs. The growths are usually somewhat swollen, or they show the deep infiltration of a nævus occupying the whole thickness of a cheek, for instance. We shall therefore turn our attention more particularly to these in the following groups, especially as regards vascular tumours.

So far we have had in view nævi which have not been subjected to any other therapeutic agency. But there are many cases in which electrolysis and cauterisation have been previously tried. The scars often left by these operations are a hindrance to radium treatment, since the surface of the apparatus must necessarily cover the whole of the nævi, the cicatrices as well as the coloured parts. Theoretically we ought only to act on the latter, which is, of course, impossible. The newly formed tissues are less even; but we have often observed, after treatment by radium, a certain levelling and diminution of superficial irregularity, and notable improvement in the scars themselves, due in great measure to its action on the sclerotic tissue. (*See* under Cheloids.)

The following are some satisfactory results which we have obtained, chiefiy during our earlier studies, since it is important to allow for the effect of time.

1. **Flat vascular nævus level with skin, superficial and**

PLATE VIII

VASCULAR NÆVUS WITH FLAT SURFACE (p. 185)

FIG. 1.—This nævus is of the telangiectatic variety. Some portions under the maxilla are raised; elsewhere it is quite flat.

FIG. 2.—The small venules which may be observed under the maxilla are the remains of the nævus, and not subsequent telangiectases. The group of telangiectases situated at the lower part of the neck has not been subjected to radium; the elements are, however, modified, probably by action of the neighbouring parts. Some telangiectases of new formation have since appeared, but only in small numbers.

PLATE VIII.—VASCULAR NÆVUS WITH FLAT SURFACE

of large size, situated on neck of adult (Plate VIII).—A patient presented a flat superficial nævus on the neck, of about 60 square cm. The upper half was very deep purple, and at the angle of the inferior maxilla there were some prominent points, also highly coloured. The colour faded by degrees to reddish mauve in the lower parts. Lower still, fine telangiectases were visible, forming a continuation of the nævus. Moreover, a vascular network could be distinguished below the evenly coloured surface, marked out by a slightly redder colour. This network extended beyond the layer of uniform tint to the clavicle. By the patient's wish the lower telangiectatic part was not touched. Two months after treatment the whole surface of the nævus, which was all of the same tint, lost its colour in a very remarkable way, the affected tissue becoming quite smooth and even, and scarcely lighter than the neighbouring skin. There was almost a return to a normal aspect, without any perceptible reaction. The final treatment dates back for more than a year, and the tissues have continued in good condition.

Apparatus No. 1 was used for one hour, three days running, for the most strongly coloured regions, and only two days for the lighter parts, except for one place where "toile" apparatus No. 14 was used for an hour, on two consecutive days. Only six or seven weeks were required to obtain removal of colour from each of the areas treated. The reaction was slight; it began ten days afterwards in the case of "toile" apparatus No. 14, and fifteen days with No. 1.

2. **Flat superficial vascular nævus situated on cheek.**—A flat superficial vascular nævus, with a surface of about 12 square cm., on the cheek of a girl of 20, presented a very marked colour, much resembling that of port wine. A dull red, produced by small puncta, could be distinguished, standing out against the colour of the background. Apparatus No. 7 was applied without a screen, for one hour only. About the tenth day surface inflammation was produced, which only caused slight itching, followed by a reaction with crust formation, which did not last long. On the thirty-fifth day of treatment no sign of irritation remained, and the unsightly colour had disappeared. The tissues of repair continued to undergo favourable modification during the next three months, after which we observed the peculiar granular appearance of the skin which indicates restoration almost to the normal state. The other portions of the nævus were then treated in the same manner, with similar results. The decolorisation was brought about a year ago, and the tissues on the site of the former nævus have almost the appearance of healthy skin. Unless told beforehand, no one would notice the rather smoother and lighter surface. Results so entirely satisfactory as these are rare.

3. **Apparently superficial nævus of right cheek.**—The following case may be compared with the previous one, on account of the resistance shown by the growth to the action of radium. In the case of a patient of 25, we found below the right malar apophysis a flat nævus the size of our No. 1 apparatus. This was selected for treatment, and on account of the thickness of the skin, the difficulty of reducing the colour by pressure, and the patient's anxiety to leave Paris, we allowed the instrument to remain on without a screen for two consecutive hours, in a single application. It was a case for strong dosage. Five weeks afterwards the patient came to see us again. The normal colour had only been regained over half the growth, and, contrary to our expectation, inflammatory reaction had been very slight. We made a second application with the same apparatus, but only for one hour, in order to avoid too great an accumulation of the rays. At present, eight months after treatment, the restored surface is in excellent condition.

4. **Nævi treated by electrolysis without success.**—In two cases nævi had already been treated by electrolysis without any result except a patch of cicatrices marbling the surface, which was the colour of port wine, with white depressions.

In the first case the rather dark nævus occupied the temporal region and the upper half of the right cheek ; it was covered with small, round, depressed scars, due to electrolysis. A first application of radium was made, by way of trial, on an area situated at the lower part, with apparatus No. 15, left on for an hour, on two consecutive days. Six weeks after rather severe inflammatory reaction had occurred, the surface was smooth, even, and normal in colour, the traces of electrolysis being much less marked. The other places were then treated in the same way, with very similar results.

In the second case, on the cheek, neck, clavicular region, and part of the arm, there was an enormous reddish purple spot, riddled with small, round, depressed scars. The whole cervical region had been formerly treated by electrolysis. In spite of the exhaustion of long and frequent operations, the young girl, who was endowed with uncommon determination, wished the electrolytic treatment to be pursued to the end. Unfortunately, it only succeeded in producing a very unsightly surface by the alternation of white and violet points. When she presented herself for treatment by radium the lesion was not in a promising condition, and yet the result obtained on the cheek and the cervical region, the only parts operated on, was considered successful by Professor Le Dentu and by the patient herself. As in the preceding case, there was partial levelling and effacement of the cicatrices, together with removal of colour from the nævus.

5. **Nævi of large size.**—Lastly, we will record the case of a girl of 21, who presented a huge deeply coloured nævus on the anterior half of the right cheek and the corresponding frontal and temporal regions. On pressure with the finger, decolorisation was easily produced, which appeared to indicate the superficial nature of the angioma. A radiferous "toile," 18 square cm., covered with a salt having an activity of 50,000, and wrapped in an aluminium sheet 0·01 mm. thick, applied in three places, was large enough to cover the whole surface of the nævus. Its flexibility facilitated treatment on the lower eyelid and the malar apophysis. The length of application on each place was ten hours. From the tenth to the fifteenth day slight erythema appeared, followed by branny desquamation. About the fourth week the colour was considerably reduced. Two other applications were made under the same conditions, each at an interval of one month. By the third month this flat angioma had almost disappeared, in spite of its marked colour and large size, without any reaction other than slight erythema after the first application.

SECOND GROUP: FLAT ANGIOMATA LEVEL WITH SKIN, DEEPLY INFILTRATED

Generally speaking, most of the statements made in the preceding section about the value of the results obtained, and the progress made in the technique, apply to our second group of angiomata. We will not repeat our remarks on these points, but as the growths are for the most part very unsightly and deeply coloured, and cannot be concealed, stronger doses and more energetic radioactivity may be fearlessly employed in case of resistance of the tissues. A permanent effect, although on the whole less brilliant than was at first expected, would still be valuable. It is sometimes possible to act on the mucous membrane through the cutaneous and subcutaneous tissues. Thus, in the case of several patients whose angiomatous gums bled easily, the rays, after having penetrated the thickness of the cheek, have freed the mucous membrane from congestion, lessened its colour, and stopped the hæmorrhage. The methods are very varied; we may have recourse either to—

(*a*) Massive total doses like those furnished by two or three hours' application of apparatus No. 1, uncovered, which produce superadded inflammation.

(*b*) The same doses, divided into fractions, and spaced in such a way as to avoid all surface inflammation.

(*c*) Total radiations emitted by radiferous "toiles" containing a radium salt of weak activity, 50,000, for instance, and used so as to produce no surface inflammation.

(*d*) "Surpénétrant" radiations employed for several nights, either in succession or at intervals, by interposing screens 2 to 3 mm. thick between a powerful applicator and the nævus.

We have also obtained improvement and removal of colour, by attacking the tissues from both sides at once, front and back. A lip or cheek allows of the application of instruments placed opposite each other according to our "cross-fire" system. By this means radiations of greater total intensity can be used, and the apparatus allowed to remain in place for a shorter time. This method, by increasing the amount of the radioactivity, renders treatment more rapid and practical. It is the best system when the whole of the lip or cheek is affected, and it can be combined with various filtering. On the mucous membrane surface the exposures must be shorter than those adopted for the skin surface; and medium screens are then to be preferred, *e.g.* aluminium sheets, or lead sheets from $\frac{1}{10}$ to 1 mm. Thicker filters would involve too long application, which would be impossible in the mouth.

We give an example of our procedure. Externally, we applied apparatus No. 1 or No. 2, in lead screens of 1 mm., on the skin surface, for one or two consecutive nights. The apparatus No. 3, enveloped in $\frac{5}{10}$ mm. of lead, was applied simultaneously to the mucous membrane, at the back, for an hour. The following cases show some of the results obtained:—

1. **Flat vascular nævus, strongly coloured, level with skin, infiltrating entire cheek, and covering half of face** (Plates IX and X).—A workgirl came to us from Dr. Brocq, in February, 1907, with a nævus of such size and depth that no permanently successful treatment seemed possible. It covered the left half of the face, was deeply coloured and of enormous size, infiltrating the whole thickness of the cheek, and even colouring the corresponding buccal mucous membrane. The tissues presented a sort of doughy softness to the touch, and all this half of the face seemed slightly swollen or thickened. The nævus also affected the internal half of the upper eyelid and whole lower eyelid, the middle of the forehead, and a small part of the temple. These lesions were of a kind which hitherto had been refused treatment, being clearly beyond the scope of surgery and electrolysis. By the use of radium this growth has now been very much improved. The following method was adopted:—

The surface being very extensive, we decided to treat one part at a time, in successive courses. First of all, a place on the cheek received an application of five hours with apparatus No. 1, an hour at a time, with one day's interval. This exposure afforded an opportunity for an interesting experiment. Continuing our investigation of the effect produced by screens, we made a pad of compressed cotton-wool, enclosed

PLATES IX AND X (p. 188)

FLAT VASCULAR NÆVUS, WITH DEEP INFILTRATION

PLATE IX.—The violet colour shown here is not exaggerated. Owing to the thickening and swelling of the tissues, the nævus produced asymmetry of the face. The infiltration affected the whole thickness of the cheek, and the lining mucous membrane was deeply coloured.

PLATE X.—This coloured photograph was taken a year ago. Since that time a certain number of telangiectases have appeared, which, however, the patient easily succeeds in concealing. A little swelling of the lip remains, and the mucous membrane is decolorised. On the face and at the edge of the nose, the appearance is really better than that shown by the chromo-lithograph. The red and violet parts visible to the right of the nose and lips are an error of reproduction.

PLATE IX.–FLAT VASCULAR NÆVUS, WITH DEEP INFILTRATION

PLATE X.—THE SAME PATIENT AS IN PLATE IX A YEAR AFTER TREATMENT CEASED

in two sheets of rubber tissue, similar to those which one of us had previously used, but, in the present case, of such a kind that the thickness of the screen gradually increased from one end to the other, varying from a few millimetres to 1·5 cm. We were thus able to observe the different reactions produced corresponding to the thickness. Very severe inflammatory reaction at length occurred, lasting several months, and we then feared we had given an excessive dose, but by degrees all came right. The place treated occupied an area of 30 square cm., and was not touched again. The disappearance of the inflammation now dates back twenty months. Plate X shows the present state. After four months of cicatrisation, a kind of spontaneous recurrence of inflammation took place near the centre, which lasted for three weeks. Some small streaks of telangiectases appeared about the seventh and eighth months, producing a marbled appearance, and some inequality in the colour of the part. The other places were successively treated by application for three hours in three days of apparatus No. 1, and each region lost its unsightly colour with perfect regularity. For the upper lip, nose, and frontal and temporal regions the square apparatus No. 3 was used for three hours, No. 7 being applied for a shorter time, but more frequently, on the eyelids. The colour was easily removed from the latter regions, the appearance of which is now satisfactory.* The mucous membrane inside the cheek had also been strongly coloured before treatment, and the applications on the skin brought about its decolorisation, without the least inflammation. This fact has been confirmed by other cases, and clearly shows the selective action of radium. There now remains, in place of the nævus, only a paler surface, still slightly red. This is, of course, not normal in comparison with the skin of the right side, being smoother and lighter in some places, and redder in others, which gives it a somewhat uneven appearance. A few telangiectases also remain. On the forehead, eyelids, nose, and upper lip the edges fade almost imperceptibly into the normal skin; moreover, these regions lost colour, in this particular instance, with extreme facility, in consequence of a moderate amount of reaction. From an æsthetic point of view the results are not complete, but they have given entire satisfaction to the patient. This young workgirl considered herself saved from a frightful and humiliating infirmity, which caused her to be dismissed from workshops, and deprived her of the means of livelihood.†

* An eczematoid eruption has recently occurred on the skin, which is sensitive to cold.

† *Note by Dr. Wickham.*—For two years and a half we have treated these cases, which were formerly incurable, by the use of "toiles radifères," with an activity of 50,000. This method causes the gradual disappearance of the angioma without superficial inflammation. In a case exactly similar to the one illustrated in Plate IX, the removal of colour has been extremely successful. There has been no return of the irregularity of the surface, and no telangiectasis has occurred.

2. **Deep flat nævus.**—A patient, aged 15, presented on the left cheek, left half of upper lip, and left eyebrow a huge infiltrating nævus. All these regions showed the remains of a much more extensive and deeply coloured angioma, which had been treated by electrolysis and the actual cautery. The operations had produced deep scars of the cheek and lip, with retraction of the latter. There was also deformity of the upper eyelid. Apparatus No. 4 was applied for four hours on each place, four days in succession. The action of the rays was doubly interesting in this case, since it effected both the removal of colour from what remained of the wine-coloured mark, and the levelling of scars. The cicatricial bands were softened, so much so that the regions subjected to radium now present an even appearance, more nearly that of their normal condition. The inequality which existed owing to the cicatricial deformities being mingled with the wine-coloured patches was diminished to a great extent. The occurrence of cases of this kind have, amongst other reasons, led us to undertake the systematic treatment of cicatrices complicated by prominent fibrous bands.

3. **Deep-seated nævus affecting two-thirds of face.**—A nævus covered two-thirds of the face of a patient, aged 18. It was dark in colour, and affected the whole cheek, right temporal region, forehead (except the median part), left temporal region, right half of upper lip, and right half of chin. The buccal mucous membrane was also discoloured. Apparatus No. 1 was applied for three consecutive hours on the cheek, temporal region, and forehead. Then the other places were treated in succession with applicators Nos. 3, 5, and 6, left in contact for three hours at a time. The patient was seen again eight months afterwards, when the whole growth was evidently paler. This case was one of those which had hitherto been considered incurable. By the use of radium, removal of colour was effected fairly easily, after moderate inflammatory reaction. There was certainly a want of evenness which detracted from the perfection of the result, but it gave satisfaction to the patient. Telangiectases were produced, but in small numbers, and they have not increased since the termination of the treatment more than a year ago. Lastly, we should mention that the buccal mucous membrane, corresponding to the places treated, was reduced in colour without inflammatory reaction.

4. **Highly coloured, deeply infiltrating angioma, with gingival and nasal hæmorrhage.**—An enormous highly coloured deeply infiltrating angioma was situated on the left half of the face of a patient, aged 30. The tissues were doughy and puffy throughout, especially on the lip. The mucous membrane was highly coloured, and the gums were bleeding, the nasal mucous membrane infiltrated

by the angioma being also the site of hæmorrhage. A place of about 16 square cm. was first treated by the system of thick filters. Apparatus No. 1 was covered by a lead screen of 1·5 mm., and this appliance was left in position for three consecutive nights, about thirty hours in all. In the two following months a certain amount of desquamation was produced, accompanied by slight pruritus. The tissues became less tumid, and more even, and acquired a paler colour. A second series of applications was made with the same apparatus, but for six nights. At the same time the mucous membrane was treated for ten days, an hour at a time, with No. 3, covered with 1 mm. of lead. This time the reaction was more severe, and the pruritus rather marked. There was rather more pronounced desquamation, no inflammation being produced on the side of the mucous membrane. After an interval of three months the region lost its colour over one-half its extent. The mucous membrane of the gums also became paler, and no longer bled. The other places were successively treated with satisfactory results, and without any inflammatory reaction worth mentioning, by means of a "toile," containing a radium salt with an activity of 50,000, left in place for eight hours, with a screen of 0·01 mm. of aluminium. As the result of applications made on the nose, the epistaxis ceased. The treatment is not yet finished, but the whole of the nævus is very much modified.

5. **Large highly coloured nævus.**—In the case of a child, a large strongly coloured nævus occupied a surface 15 cm. by 20 ; pressure with the finger hardly affected the colour. We selected two large "toiles," one having an activity of 5,000, the other of 10,000. Their flexibility allowed of folding them in two, and placing one part on the other. They were enveloped in a sheet of 0·01 of aluminium. The total radioactivity used was about 20,000 units, the length of application being twenty consecutive hours. Slight erythema was produced, which had no result beyond a fine desquamation. Five weeks afterwards some improvement was observed. The same applications were then renewed six times, once a month, on each of the parts of the angioma, and by degrees the loss of colour became very marked, without inflammatory reaction.

6. **Deeply infiltrating nævus of large extent.**—A patient, aged 16, presented a deeply infiltrating nævus, of a purple colour, situated on the left temporal region, and on the whole of the left cheek, which seemed rather larger than the right ; the left half of the gum of the superior maxilla and the mucous membrane of the cheek being also swollen and discoloured. Apparatus No. 1 was applied for three days in succession, an hour a day, on the lower regions of the nævus, all the other places situated above and around the preceding one being treated with No. 3,

left in place for three hours. Three months after commencement of treatment, the result produced, although considerable, was not sufficiently marked, and the patient therefore urged us to repeat the applications, but we preferred to suspend operations, and, owing to various circumstances, did not see her again until a year afterwards. The reduction in colour of the nævus was then very satisfactory, and in course of time became spontaneously more pronounced, so that a second course of treatment was considered quite unnecessary. The mucous membrane also was decolorised.

This instance proves that, in some cases, it is better to wait and be patient before resorting to a new series of applications. Premature intervention might prove useless, and even injurious.

Action of radium on nævi complicated with post-electrolysis scars.—We have already mentioned in our first group the frequent occurrence of disfiguring scars succeeding operations (electrolysis, cauterisation, etc.), and the trouble they cause in radiumtherapy. We have often met with cicatrices of the same order in deeply infiltrating nævi, and these are still more unsightly, the curative effect produced by radium being therefore more obvious. The rays certainly cannot claim to render the tissues perfectly smooth and even, but they succeed in partly levelling the scars, and in suppressing, by reduction in colour of the portions of the growth remaining purple after electrolysis, the marbled appearance resulting from the juxtaposition of the nævi and cicatricial points. We have already quoted one instance (2, p. 190), and some others follow :—

1. A patient, aged 30, presented on the right malar and temporal regions, and upper lip, a large deeply coloured nævus. The purple surface was studded with deep and somewhat discoloured depressions, produced by electrolysis. Apparatus No. 1 was applied on the temporal region for three hours in succession. Two months afterwards, No. 3 was used, for two hours and a half, on the upper lip. Finally, on the occasion of a third journey—the patient, who lived in Brussels, could only spend a day in Paris at long intervals—No. 3 was applied for two hours and a half on the malar region. The places treated were successively levelled and lost their colour ; but some pigmentation and telangiectases appeared during the following months. The scars of electrolysis had to a great extent disappeared.

2. A patient, aged 24, had undergone many operations by electrolysis during three years. An enormous deeply coloured nævus extended over the internal and upper half of her right cheek. The operations, though they had not decolorised it, had covered it with numerous cicatricial

depressions. Apparatus No. 2 was applied for two hours. The scars became modified in such a way that the skin regained a smooth and even appearance.

3. A patient, aged 50, presented in the left cervical region, which was the site of a deep purple nævus, cicatricial bands resulting from the application of nitric acid used therapeutically; no decolorisation, however, had been produced. Apparatus No. 1 was applied for three consecutive hours. The thickness of the prominent cicatrised bands had prevented the application from being equal at all points, so that some places were decolorised, and others still slightly red. As to the cicatricial bands, they diminished in thickness and became softer. This successful action on fibro-sclerotic cicatricial tissues complicating nævi confirms in all respects what has been said in the chapter on cheloids and disfiguring scars.

THIRD GROUP: MODERATELY RAISED ANGIOMATA WITH PLAIN OR PAPILLATED SURFACE

At first sight it would not seem that there is any special reason for the formation of this group, since the cases composing it might be simply considered as the first stage of tuberous erectile angiomata. In radiumtherapy, however, they must be treated neither like flat superficial angiomata nor erectile tumours. These growths, although developed externally, are often hard, and sometimes even sclerotic, seldom showing fluctuating points; therefore the disorganisation of their prominent parts involves no risk, and there need be no fear of hæmorrhage. The lesions are not much raised in the case of children; it is in adults, in whom they very often occur, that they present some of the characters of sclerosis. They cannot be reduced by pressure, and exertion does not increase their size. It is, therefore, not absolutely necessary, as for erectile tumours, to resort to methods acting at a depth without inflaming the surface, and their treatment is thereby facilitated. When such growths are small enough, they can be quite as easily healed by electrolysis. Radium treatment is, however, more suitable when these angiomatous formations occupy a fairly large surface, and, even in the case of small lesions, the painless nature of this treatment will be found of great advantage. One of the reasons which explain the facility of cure in most of the cases coming under this category is that the base is not usually very deeply rooted. The possibility of acting vigorously and leaving the instruments longer in situ gives the "surpénétrant" rays time to influence the base whilst the other rays modify the surface.

No precise limits can be assigned to this third group of angiomata. Between those which are slightly raised, and those in which papilla-

tion is very pronounced, a whole intermediate series exists, forming a transition between our two first groups and the fourth. Some, although raised, have a flat surface, others a surface which is framboesioid and papillated, and these inequalities may vary from the size of a millet seed to that of a pea or a cherry.

The length of application and the dosage must be calculated according to the thickness, hardness, and prominence of the angiomata. As a rule, such lesions respond readily to radium; but in this group, side by side with rapid cures, one meets with others which are refractory and drag on in spite of several courses of applications. The doses are usually stronger than those indicated for the previous group. Apparatus No. 1 can be left in position for four hours, even when acting on the whole of the surface. Nos. 2 and 3 may remain for five hours. For these angiomata —with few exceptions—there is no need of filtering, or of frequently repeated applications; radioactivity with a free, intense action will be best. But we have also observed good results from very penetrating rays used alone. The effects obtained are disappearance of the projections and removal of colour. In slightly raised growths repair very nearly approaches the normal state if the doses have not been too strong. In the very deeply coloured forms with thick, hard, sclerotic papillation, slightly red edges and purple centres sometimes remain after reduction. But the lesions are so unsightly before treatment that these irregularities, when produced, are of less importance than would otherwise be the case.

The study of angiomata of the mucous membrane does not belong to this group. Such growths should in no case be treated by inflammation of the surface; we will therefore postpone the consideration of the therapeutic treatment of these angiomata, when prominent, to the section on erectile tumours.

Each of the four cases about to be narrated has a special interest of its own.

1. **Strongly coloured nævus with flat surface, projecting 3 mm., on a child six months of age.**—This case is the first in which we obtained a prompt and successful result by the use of doses fixed beforehand. The lesion had begun at the child's birth, with a small red spot in the centre of the right cheek, and by degrees this point had spread, and become raised. At the age of six months, the growth was still extending; it was dark purple in colour, and was the size of a 50-centime piece. Its prominent edges were about 3 mm. above the level of the skin; a fine venous network existed at its periphery, and its consistency was rather soft. The child lived in Normandy, and, after seeing it once, we decided to go and treat it. M. Degrais took No. 7 apparatus,

PLATE XI

PROMINENT VASCULAR NÆVUS (p. 195)

FIG. 1.—The two white streaks crossing the nævus are the result of an operation for electrolysis. The patient would not continue this treatment on account of the pain it caused.

FIG. 2.—The reddish surface shown in the chromo-lithograph has considerably diminished in the course of a year. What still remains of it blends with the general tint of the face, which is somewhat deeply coloured.

PLATE XI.—PROMINENT VASCULAR NÆVUS

which we had arranged to apply daily for half an hour, seven days in succession. He himself made the first three applications, and, as these were effected without difficulty, he went away, leaving the care of the four which followed to the mother. A rubber-covered lead sheet, with an opening, exactly covered the nævus. Everything occurred as we had expected. The reaction was slight, and commenced ten to fifteen days after the last application. An inflammatory redness was produced, and then a crust, which fell off about a fortnight later, after which the redness diminished every day. This process, as related by the parents, cannot be considered rigorously exact, and their statements were evidently wanting in accuracy. However that may be, when we saw the child again, a month and a half afterwards, the nævus had disappeared, the surface was level, and even the fine peripheral telangiectases, which had not been directly influenced, were no longer to be seen. The tissues were smooth and even, but rather lighter than the neighbouring skin. A slightly purple point remained in the centre, which disappeared spontaneously in the course of the following month. We exhibited this baby, when cured, to the Société Française de Dermatologie, on December 5th, 1906. This nævus might certainly have been healed by electrolysis, but it was an opportunity for showing the Society that we had succeeded in formulating an almost exact dosage for this kind of growth, and that the action of the rays might be demonstrated on a zone at the periphery of the points of application. Before treatment the child was sent to sleep by putting it to the breast, and the operation was performed during its sleep. The absence of all pain and the simplicity of the procedure should be noted, as these are important points in favour of radium, even in a case like this, which was perfectly amenable to electrolysis. We have just seen the child again. Its condition has continued quite satisfactory, and no subsequent telangiectasis was produced. The place treated is only a little lighter than the surrounding skin.

2. **Flat nævus in adult with projection of 3 to 6 mm. and papillated surface** (Plate XI).—On account of their slow evolution the nævi of adults must be considered more refractory. The following example shows an easily obtained result in the case of a printer, aged 35, who was sent to us by M. Brocq, in February, 1907. The patient had been subjected to electrolysis before M. Brocq had had anything to do with him, and the white cicatricial lines crossing the nævus were the result of the first and only attempt of this kind. The patient, having suffered severely from the operation, had refused to continue the treatment. The framboesioid, papillated nævus was deep purple in colour, and raised from 3 to 6 mm. in parts. Being limited as to time (for the patient, having inherited a hotel in Vichy, was

anxious to leave), we were obliged to use strong doses at the outset, calculated to produce sufficient effect once for all. Apparatus No. 1 was applied four times for half an hour, and three times for an hour (a total of five hours), spread over nineteen days. This dosage was very strong as a whole, but much weakened by being distributed over so long a period. The same amount given in five days would have been much too strong. We took into account the prominence, induration and papillation of the growth, which justified intense action. The reaction was rather severe, but caused little pain, the patient complaining chiefly of itching. An erosion covered by a crust was produced. When he left us, three weeks after the completion of treatment, the crust was dry, and adhered firmly to the underlying tissue. Shortly afterwards he wrote to say that it had fallen off, and that the patch no longer existed, but had been replaced by a normal surface. Dr. Durand-Fardel, of Vichy, was kind enough, at our request, to examine the patient. He informed us that he noticed nothing but an area of erythematous aspect, with a slightly redder point near the eye. The patch was level with the normal skin, and not at all conspicuous. At the present time, two years later, the tissues show no sign of a scar; only a slight reddish tint persists, and this blends to some extent with the general colouring of the face, which is rather strongly marked.

3. **Nævus with scars following electrolysis** (Plate XII).—In the course of our communication to the Académie de Médecine on the treatment of angiomata by radium, we presented this case before treatment as a very favourable type, which might be easily cured. The results only partly justified our anticipations, for there was great and unexpected resistance to treatment. A patient, aged 18, showed on the right half of the upper lip, with extension towards the cheek and naso-labial groove, a raised nævus with very irregular surface. The outlines on the side of the cheek were deeply punched out, and very difficult to limit exactly. The colour was dark red, like port wine, and the projection varied from 4 to 6 mm. The inequality of the surface was accentuated by hard, yellowish striæ, slightly prominent, like fibro-sclerotic bands, and towards the edge of the cheek by white depressed scars. These bands and scars were the remains of electrolysis. The operations, from which good results might have been expected, had been quite unsuccessful, and after several trials it became necessary to abandon this mode of treatment, which had been very painful, and of which the patient had an unpleasant remembrance.

We were not then (October, 1907) aware of the inconvenience and hindrance to radiumtherapy caused by sclerosis following electrolytic operations. Having now had greater experience, we should use

PLATE XII

NÆVUS WITH CICATRICES FOLLOWING ELECTROLYSIS (p. 196)

FIG. 1.—The depressions and yellowish projections to be distinguished on the violet background of the nævus were produced by unsuccessful operations for electrolysis.

FIG. 2.—The satisfactory results have been well maintained, no appreciable change having taken place in the course of fifteen months.

PLATE XII.—NÆVUS WITH CICATRICES FOLLOWING ELECTROLYSIS

intense radioactivity at first. At that time we calculated on an easy improvement, and commenced treatment with comparatively weak doses. Applicators Nos. 4 and 7 were used for an hour, three hours in five days, distributed over the different points of the nævus. Contrary to our expectations, this first treatment had little effect. A second course of applications was then decided on, with No. 2, applied for four hours in four days. After very severe reaction and considerable improvement, the repair still left coloured tissues. It was necessary to begin again, for the third time. Apparatus No. 1 was applied for three hours in three days, and from that time forward, after inflammatory reaction lasting for a month, the desired results were obtained. The nævus has now been healed for fifteen months, and the surface of repair is one of the most satisfactory we have had. It is smooth and even, and no telangiectasis followed the operations. The electrolytic scars, which are much reduced but still visible, somewhat spoil the appearance of the healed surface.

4. **Framboesioid vascular nævus.**—A child, aged 12, was sent to us by Professor Gaucher with a vascular framboesioid nævus of the anterior wall of the axilla. This tumour, deep purple in colour, was in marked process of development; for some months it had been the site, from time to time, of congestive eruptions, becoming slightly larger on each occasion. The friction of the dress at the arm-hole had caused this inflammation. In other instances we have had occasion to notice the influence of repeated traumatisms on the development of angiomata, particularly in a case of flat angioma of the cheek, which was much increased by shaving. Apparatus No. 6 was used six times for a quarter of an hour, with an interval of one day, the same applications being repeated on three different occasions, each at a week's interval. After slight reaction, the tumour became gradually obliterated.

FOURTH GROUP: SOFT ANGIOMATA WITH FLUCTUATING AREAS; AND ANGIOMATOUS ERECTILE TUMOURS

It is in this group that radium renders by far the greatest service. The cases composing it are met with most frequently in infants and young children, but are not uncommon amongst adults. A great number of intermediate forms exist between the two extremes which we have mentioned. We recognise—

1. Fluctuating erectile areas, which are pulsatile, but do not constitute true prominent tumours.
2. Prominent tumours.
3. Tumours specially important on account of their position, chiefly those in the neighbourhood of the eye.

4. Angiomata of the mucous membranes.
5. Deformities, in which most of the preceding forms are found combined.*

These different kinds of angioma have one link common to them all, which explains their being grouped in a single section—the necessity of avoiding too marked an ulceration of their surface, which would entail a risk of hæmorrhage. This contingency, however, is less likely to arise on account of the hæmostatic action of radium. As the skin covering these tumours is usually affected, and deeply coloured, it is well, whilst acting specially at a depth, to use for one part the rays of medium penetration acting more particularly on the surface, and to combine the different methods best suited to influence the entire thickness of the tissues with appropriate doses, strong at a depth, but superficially weak. In other cases there may be subcutaneous tumours, the skin which covers them being usually normal, or partially coloured. It is therefore necessary, whilst acting deeply, to respect the surface, or only to act on its coloured portions.

Various plans can be used and often combined to satisfy these different requirements:—

(*a*) Applications of apparatus without a screen, either frequently repeated, or sufficiently spaced.
(*b*) Methods of filtering.
(*c*) Use of "cross-fire."

"Cross-fire" finds its most accurate and most useful employment in the treatment of these angiomata. By combining it with weak or medium filtering it considerably increases the intensity of the "surpénétrant" rays, whilst allowing some action to those of medium penetration. Thus an erectile tumour is very rapidly impregnated in all its stages with doses of radioactivity sufficient for levelling and decolorisation.

1. ERECTILE FLUCTUATING AREAS

We will give two typical examples of this form of angiomatous tumour, one situated on the face, the other on the arm.

(1) **Subauricular angioma, affecting lobule of ear, highly coloured, swollen in centre, of soft consistency, fluctuating and pulsating, in an infant six months of age** (Plate XIII).—This case is one of the first which we undertook to treat, and we cannot therefore state the dosage quite accurately. We were then at the commence-

* *Note by Dr. Wickham.*—There is also a sixth group, that of subcutaneous and submucous vascular tumours, in which radium has produced good results without superficial inflammatory reaction.

PLATE XIII

FLUCTUATING VASCULAR TUMOUR (p. 198)

FIG. 1.—When the child cried or struggled, the angioma became inflated and throbbed so violently that the pulsation was visible at some distance. The lobule of the ear was twice the normal size. The tumour could be partly reduced by pressure.

FIG. 2.—There is now complete absence of throbbing; the lobule has recovered its normal aspect, and the healed tissues have maintained their admirable appearance for more than two years.

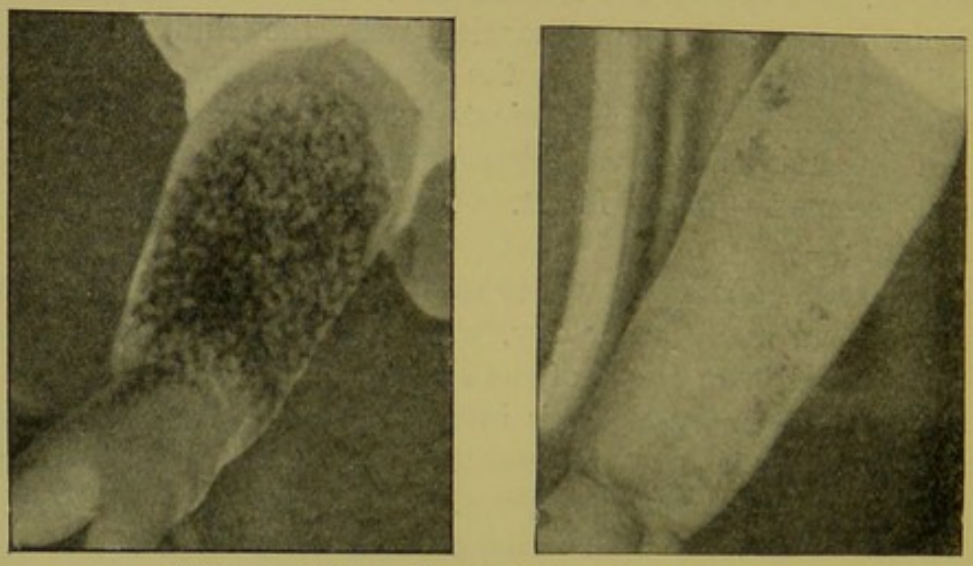
PLATE XIII.—FLUCTUATING VASCULAR TUMOUR

ment of our studies, and obliged to feel our way. We have tried, however, from beginning to end, to keep to the principle of not using doses that might produce too severe reaction. Our present experience would have led us to treat this case with still weaker doses. It was that of a baby, six months old, sent to us by Dr. Boulay. When the child was quiet, the angioma was extremely soft. It had the sensation, when touched, of a fluctuating area; but on movement or the slightest effort, the tumour became hard and swollen, and filled with a greater quantity of blood; it then pulsated so strongly that the throbbing was visible even at a distance. The colour varied from reddish to deep purple, and the lobule of the ear, invaded by the angioma, was pendulous; it was also swollen, and double the normal size. The edges of this tumour formed an imperceptible continuation with the skin, but the mass increased from the periphery to the centre, reaching, under the lobe of the ear, a swelling which projected 1 cm. from the surface. The aspect of the nævus was very distressing, and none of the ordinary treatments seemed suitable for it. The following method was therefore adopted :—

We operated in series of seven to twelve applications of three-quarters of an hour each, every other day, with apparatus Nos. 4, 7, 8, and 9, applied at the different points of the angioma. They were wrapped in a thick layer of cotton-wool. This interval of a day between every two exposures allowed the rays to penetrate in larger quantities, without any risk of too severe action on the epidermic tissue. The infant was allowed to rest for about two months after each set of applications. When we saw it again, two months after the first course, the areas already treated had partly lost their colour, and the swelling of the lobule of the ear and the throbbing were reduced by one half. The treatment was pursued with results which were always clearly visible one to two months after each course; there were three in all. At present, the lobule of the ear is almost normal in shape and colour, the skin being somewhat wrinkled, but not scarred. The pulsation in the neck has entirely disappeared, and the surface of the nævus is level, no longer swelling when the child cries. It is white, smooth, and even, and can scarcely be said to possess a cicatricial character. Only a few points of pigmentation are now visible on the newly formed tissue, especially at the periphery, besides some telangiectatic striæ. This rapid improvement surpassed all our expectations, and has given us great hopes for cases hitherto considered practically incurable. The treatment dates back nearly three years, and the admirable appearance of the surface has been maintained. Eight months ago it was the site of a transient inflammatory attack which is worthy of note. At the beginning of October, 1908,

when the cold weather began, the whole lesion became red, pruriginous and inflamed. Its appearance was that of an eczematoid dermatitis. After the application, first of Langlebert's ouataplasms for three days, then of zinc ointment, and lastly of inert powders, it became normal again in about a fortnight.

(2) **Swollen angiomatous area** (Figs. 49 and 50).—A vascular nævus occupied the lower half of the forearm of an infant five months old, forming a swollen area which affected two-thirds of its circumference, and ended at the wrist in a thick edge, a number of small red spots standing out against a dark port-wine coloured background. The consistency was soft, and rather doughy. By taking the two wrists in the hand,



Figs. 49 and 50.—Turgescent angiomatous area.

it was easy to calculate the increase in size caused by the angioma, which produced the sensation of a fluctuating area. When the child moved and cried, the mass became hard and increased in size, and was then pulsatile. The need of treatment was urgent, for the tumour was in full process of development, and this made the mother uneasy, and induced her to consult Dr. Cottu, who referred the patient to us. As the surface of the lesion was circular and very extensive, the use of our large radiferous "toiles" was indicated, and their flexibility allowed the nævus to be covered. Two "toiles" were placed one above the other, one with a total activity of 20,000, the other of 10,000, the length of application being eleven hours, almost equally spread over five days. An aluminium sheet of 0·01 mm. was interposed. A month afterwards we observed that the tumour had ceased to spread. It had become smaller, and its surface was decolorised. A second course of the same kind was undertaken, which was also followed by very marked improvement.

PLATE XIV

ERECTILE VASCULAR TUMOUR (p. 201)

FIG. 1.—The tumour was soft and fluctuating during rest, but became hard, tense, and larger in size if the child cried or exerted itself. It was impossible to diminish it by pressure sufficiently to discover the state of the underlying frontal region.

FIG. 2.—The surface is now absolutely flat; it is not so white as shown here.

PLATE XIV.—ERECTILE VASCULAR TUMOUR

Three months afterwards the tissues had an admirable appearance, much modification having taken place without surface inflammation.

This instance shows the use that can sometimes be made of flexible radiferous "toiles," and their value even when of weak radioactivity. It also proves the great advantage of radiumtherapy in cases of large extent, which could not have been so easily reduced by any other treatment, without pain or inflammation.

2. PROMINENT VASCULAR TUMOURS

Our "cross-fire" method finds its most frequent use in the treatment of this variety of tumour. The following case formed the substance of our communication of October 8th, 1907, to the Academy; and the facts which it gave us an opportunity of establishing were a revelation even to ourselves. It was then that we clearly grasped the idea of a specific selective action of radium, which our previous results had only foreshadowed. Since then many other cases of the same kind have been treated, and the reduction and absorption of the tumours have been obtained with almost mathematical regularity, confirming on every occasion the truly remarkable effect of radium. We will first select some examples of tumours with a port-wine coloured surface, situated on the face, and then give a few instances of subcutaneous vascular tumours, both on the face and on the body.

(1) **Deeply coloured angiomatous tumour projecting 2 cm., and measuring 2 cm. at base, in process of extension, situated on forehead of infant seven months old** (Plate XIV). Cure by simple, gradual, and regular absorption, without perceptible inflammatory reaction. First application of the "cross-fire" system.—On March 15th, 1907, Dr. Gastou brought to us an infant of seven months, from Dr. Artin's clinic. The child presented a reddish purple tumour in the middle of its forehead, soft and full of blood; it lost one-fifth of its size on pressure. The child cried during examination as if the pressure was painful. Crying caused the tumour to swell and become harder, and assume a darker colour. We were unable to ascertain the degree of soundness of the subjacent osseous tissue. It was important to act without much delay, for the growth was in process of extension. It was necessary to avoid ulceration for fear of hæmorrhage, and too energetic action from front to back, lest the brain, which might be exposed under the tumour, should be affected. We devised the method of "cross-fire" in order to satisfy these requirements. The cylindrical shape of the tumour enabled the apparatus to be applied on its peripheral surface, and the rays to be directed parallel to the anterior surface of the brain. To avoid any reaction which might be followed

by ulceration, it was sufficient to employ an instrument with very weak external radiation, so that, in a space of time short enough to be borne by the child, it was possible, by daily exposures of fifteen minutes, to keep below a dosage which would have injured the epidermis. But there was a danger that this action would prove too weak. We then thought of combining the activity of several applicators of equal value, placed at the same time on opposite points of this lateral surface. All difficulties were thus solved. We avoided the brain, and the skin was not too much affected, whilst the action of the convergent "surpénétrant" rays was multiplied in the depth of the tumour. By means of this "cross-fire," the tissues in the centre were subjected to an action four to five times stronger, without, however, causing any risk of surface inflammation.

Treatment was begun on March 22nd, with Nos. 8 and 9, applied simultaneously on two opposite points, for fifteen minutes, then for the same period on two more opposite points. A fifth separate place was also treated at the same time with another apparatus. By this method, therefore, in the course of the same sitting there was deep action of five times fifteen minutes, that is, an hour and a quarter, and only fifteen minutes on each point of the surface. Similar applications followed on March 25th, 27th, 28th, and 30th, and April 3rd, 5th, 8th, 10th, 12th, 13th, and 15th. On the last-mentioned date a slight crust was observed on the periphery of the tumour, which indicated increasing inflammatory reaction, and treatment—at least on the lateral surface of the angioma—was suspended. As the tissues evinced greater resistance than we had expected, we were not afraid to apply apparatus No. 7, which is more powerful, twice in half an hour, on the top, which had not yet been treated. The infant was then allowed to rest. On May 3rd, after seventeen days' interval, and on the forty-third day of treatment, we found that the angioma was reduced by at least one-half; its colour was only pale lilac, and it was covered by a scale which was easily detached. There was no sign of ulceration.

The resolution of the tumour allowed us to examine its base and ascertain the soundness of the underlying bone. We then felt justified in continuing the treatment and making simultaneous applications to the top and surface of the growth. From that time what remained of it seemed to melt away before our eyes. There were nine applications of apparatus Nos. 8 and 9, made for fifteen minutes on two places, from May 6th to 30th. On June 5th, 7th, and 17th the tumour was treated with No. 7, which corresponded to it in size, for fifteen minutes. On July 24th the small instrument, No. 8, used alone, entirely covered what was left; it was applied for thirty minutes on July 24th, 25th, 26th,

and 27th, then every three days only during the month of August, in order to avoid all reaction. On September 15th we saw the child again. Complete healing had taken place two or three weeks previously. Nothing remained of the tumour, and nothing could be felt by the hand when passed over the forehead. In its place there was skin, lighter than the healthy tissue; and even in the centre of this decolorised surface there was only a slightly red area. There was no change when the child cried. The tissues had absolutely no cicatricial character, and the skin was smoother and less granular than normal.

These new and surprising results were very important, since they proved the selective action of radium. We had observed the disappearance, by simple resolution, without pain or perceptible reaction, of a tumour in process of extension, which it was necessary to treat at once, and which it would have been most inconvenient to subject to electrolysis, surgery, or X-rays.

The technique of this remarkable case must not be taken as a model; instead of applying the apparatus unscreened, it would have been better to add the use of aluminium screens to the "cross-fire" method, and thus have allowed of longer applications on each occasion. The growth would then have disappeared much more rapidly.

(2) **Angiomatous tumour on forehead** (Dr. Lenglet's patient).—An infant, eleven months of age, presented, on the left side of the forehead, an angiomatous tumour with a base of 2 cm., about 1 cm. high. The whole surface was purple and crossed by a vascular network. It became slightly red and swollen when the child cried. This case was exactly like the one just mentioned, and we took advantage of this to treat it in the same way, and note the results, which were in all respects similar. A first series of applications with the same apparatus in "cross-fire" was made from January 17th to the 31st, in exposures of fifteen minutes, repeated every two days; and from the first month onwards there was considerable reduction of the growth. The second course was in March, and the third in May. At the beginning of the second series the tumour, which had required at first four applications of apparatus No. 6 to cover it, only took three. Finally, the instrument was applied flat to the surface. Five months sufficed for the disappearance of this growth. When seen again lately, nine months afterwards, it presented a flat, whitish surface, smooth and even, with a somewhat redder centre.

(3) **Angiomatous tumour.**—An infant, nine months of age, had a tumour in the middle of its forehead, 2 cm. wide by 1 cm. high. There were also scars resulting from previous treatment which made the surface less supple than normal. The tumour commenced at birth with a small red patch, which a week afterwards began to increase

gradually in size. When the child was four months old, vaccination was performed. This produced no result, but left an indelible scar. After the failure of this treatment the infant was taken to a surgeon, who applied the actual cautery. Five days afterwards there was rather severe hæmorrhage. The operation, although it produced a change in the colour—from red to purple—did not reduce the tumour, and left traces of scarring on the surface. The radium method employed was that of "cross-fire"; six applications of apparatus Nos. 7 and 8 were made on alternate days in four opposite places, a quarter of an hour on each. Five weeks afterwards the tumour only measured 4 mm. in height. It was now too small for the use of "cross-fire"; we therefore resorted to medium and "surpénétrant" rays, applying for five hours (an hour a day) apparatus No. 7, in $\frac{1}{10}$ mm. of lead. This treatment was repeated during each of the two following months. Five months after treatment was begun the tumour had disappeared, decolorisation was complete, and the scars left by the previous surgical operations were considerably improved.

We have hitherto only mentioned tumours of marked colour, in which the skin surface was affected; we will now consider a few cases of tumour of the face and body, in which the skin was intact, either completely or in part.

(4) **Angiomatous subcutaneous tumour of right parotid region.**—This was the case of a child a year old. At the age of two months a tumour appeared in front of the tragus, which at first remained stationary, and then, about the sixth month, gradually became larger. The growth occupied the parotid region, and was subcutaneous. The skin which covered it was not quite intact, for it showed an aggregation of small and very deeply coloured spots on the top of the growth. The aim of the treatment was first to decolorise them, and for this purpose two hours' application of apparatus No. 5 was sufficient. In order to act at a depth No. 17 was then applied for six hours, with the interposition of a lead sheet of $\frac{1}{10}$ mm. Two months after completion of this treatment the greater part of the growth had dispersed, and the red points had disappeared from the surface. A new series of applications was then made with No. 17, in $\frac{4}{100}$ mm. of aluminium only, for five hours, spread over three days, and then, one month afterwards, for four hours in three days. Six months later the mother wrote to us that the tumour had entirely disappeared.

(5) **Subcutaneous vascular tumour of right cheek.**—In a case of facial asymmetry in a girl of 15, consisting of extensive hypertrophy of the right cheek, the cheek was enlarged over its whole surface,

from the zygoma to the lower edge of the horizontal ramus of the lower maxilla. Under certain influences—such as heat, cold, or agitation—the tumour became congested. The skin was not absolutely normal, but showed a rather more brownish-red colour than the opposite side. The tint was more marked when the cheek was congested, and some bluish arborisations could be traced beneath the epidermis. There was a bluish zone, crossed by a large vein under the right commissure of the lips. The mucous membrane of the cheek was normal. When touched, it gave the sensation of a flabby tumour which could be partly emptied by pressure. This growth, which had begun in infancy, had gradually increased in size, and was still in process of evolution. It was, in fact, an enormous angioma, developed in the thickness of the cheek itself. The medical man consulted could suggest no treatment likely to be beneficial, and sent his patient to us in the hope that radium might be useful.

This tumour differed from those previously treated, but as we had already succeeded, in several cases, in getting rid of subcutaneous vascular tumours, and as the region was admirably adapted for "cross-fire," we consented to try the effect of radium, by employing "surpénétrant" radiations on the inside and outside of the cheek, being certain in any case of doing no harm. The treatment was divided into several courses. From May 11th to 26th, on the outside, half an hour each day of apparatus No. 1, in $\frac{5}{10}$ mm. of lead; on the inside, for the same length of time, No. 6, in 1 mm. of lead. From July 22nd to 29th, externally, No. 1, in 3 mm. of lead, applied every night, for twelve consecutive hours. On the inside, No. 4, with 1 mm. of lead, for one hour every day. In consequence of this treatment, inflammatory reaction was produced, lasting about twenty days. Then, in the course of October and November, not only was growth stopped, but the tumour diminished in size, and there was a marked decrease in the congestive symptoms. The sensation of a doughy mass on palpation gave place to a feeling of greater suppleness. A fresh series was carried out from November 16th to December 7th. Apparatus No. 1, with 3 mm. of lead, was used on the outside for twelve nights, with one night's interval, and we also applied No. 4, in 1 mm., for an hour every day, to the interior of the mouth, against the mucous membrane. Growth has now finally ceased, the asymmetry is certainly less marked, and the congestion is not so pronounced. In fact, radium has brought to this otherwise absolutely incurable case very definite though incomplete relief.*

* *Note by Dr. Wickham.*—At the present time (January 4th, 1910), the tumour has entirely disappeared.

(6) **Subcutaneous vascular tumour with cutaneous arborisations.**—An infant of sixteen months presented a large vascular tumour, situated in the angle formed by the right scapulo-humeral articulation and the clavicle. It was sent to us by Dr. Ménard. The appearance of this tumour dates almost from birth. A small red point showed itself in ten days, and gradually extended until it reached the size of a one-franc piece. The lesion was then vaccinated; but, contrary to expectation, from that moment it began to develop and become prominent. When the child was brought to us the growth was the size of a tangerine orange, 3 cm. high, 5 cm. from right to left, and 6 cm. from top to bottom. The surface presented reddish ridges, enclosing patches of white or normal skin. In consistency the tumour was very soft. The method of treatment employed was that of "cross-fire," with applicators Nos. 6 and 7 placed opposite each other for ten consecutive days, fifteen minutes to each area, with three changes of place at each exposure. In two months great improvement was perceptible. A new course was made with the same apparatus, but with $\frac{1}{10}$ mm. of lead, ten days in succession. Six places, two by two, were treated daily, each for thirty minutes. Two months afterwards the tumour had perceptibly diminished; it had subsided to such an extent that "cross-fire" could no longer be used. The treatment was continued with apparatus No. 2, in $\frac{1}{10}$ mm. of lead, applied for one hour each day, on ten successive days. At the end of six weeks the growth had almost disappeared, and what remained of it was more like an excess of normal tissue, resembling the walls of an empty sac. The purple vascular ramifications on the surface had become decolorised.

(7) **Subcutaneous angio-fibroma of arm** (Professor Gaucher's patient).—A girl of 13 presented a slight projection on the anterior surface of the right arm, at the junction of the middle and lower thirds. The skin in this part was bluish in places, with a yellowish circumference, and of ecchymotic appearance. On palpating it one could feel a deep-seated tumour of hard consistency, measuring 4 cm. from top to bottom, and 2 cm. across. Two instruments—Nos. 5 and 6—with $\frac{4}{10}$ mm. of lead, were placed opposite each other, on each side of the tumour, for three days running, an hour a day. On the three following days the same exposures were made, but arranged on different points. Finally, apparatus No. 7, unscreened, was placed for an hour on the coloured part at the top of the tumour. A month after the last application the growth had completely disappeared, and the surface had recovered its normal tint.

3. ANGIOMATA IN SPECIAL POSITIONS

In this section we group angiomata for which special treatment is indicated by their position.

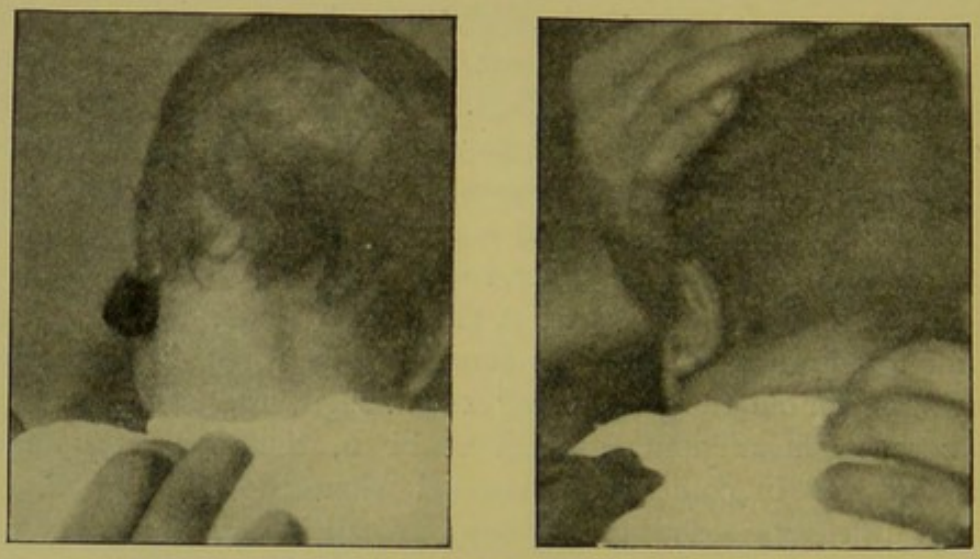
(1) **Angioma of scalp.**—A small pulsating, purple, angiomatous tumour the size of a large cherry was observed in a baby of six months, situated on the top of the head. In the course of a lecture at his polyclinic at the St. Louis Hospital, M. Gaucher, exhibiting this angioma before treatment, dwelt on the frequently malignant character of nævi in this region. He considered the area, situated above a horizontal line drawn through the eyebrows, dangerous. Three months after our radium treatment, the infant, cured of the angioma, was again shown to the students. There was nothing but a slightly reddened surface on the former site of the tumour. The treatment had consisted in the application, every other day, of instruments Nos. 7 and 8, for ten minutes, on two places opposite one another, and for the same length of time on two other places. After five exposures there was a month's rest, and the reduction was so marked that it was afterwards sufficient to repeat them three times a week, in order to complete the treatment.

(2) **Angioma of scalp** (Plate XVI, Figs. 1 and 2).—This case (that of an infant six months old) was similar to the preceding one, but the tumour was double the size, being 1 cm. high, and 2 cm. in diameter at its base. The angioma existed at birth, the size of a small pea. It was dark-red in colour, and swelled when the child cried. Treatment was urgently needed, for the tumour had increased rapidly of late. The technique employed was the same as for the preceding example. By the fifth month the projection had disappeared ; on passing the hand over the region nothing could be felt. The tissues were smooth, even, and whitish ; the region was devoid of hair, but this had been the case before treatment.

(3) **Prominent angioma on tip of nose.**—A child 2 years of age had, at the tip of the nose, a prominent purple angioma, which was a serious disfigurement. The growth was double the length of the lobe of the nose, and rather hard and tense. Apparatus No. 9 was applied direct, for an hour on three consecutive days. A month afterwards the tumour had decreased to one half its size. The same apparatus as in the first series was then used again. After another interval of a month No. 7 was applied. By the sixth month from commencement of treatment the nose had recovered its normal shape, though the skin was rather whiter than before.

(4) **Pulsating angioma of lobule of ear** (Figs. 51 and 52).—An infant of three months, sent to us by Dr. Müller, presented a pulsatile

angiomatous tumour on the lobule of the left ear, the lobule being hypertrophied throughout its extent, deviated from its normal axis, and to some extent folded. This deformity was due to the extreme length of the angiomatous lobule, which, from contact with the regions on which it rested, took an angular shape as it developed, standing up at right angles to its extremity. The retroauricular groove was occupied by a thick vascular ridge in its lower part. The growth was in process of extension towards the upper part, where the transition between the lobule and the rest of the ear was marked by a pale purple colour. It throbbed quite perceptibly, and became swollen when the child cried. The lower extremity of the angioma was covered with a large



Figs. 51 and 52.—Pulsating angioma of lobule of ear.

blood-stained crust, showing signs of recent hæmorrhage. It had bled copiously on several occasions. Treatment by the "cross-fire" method without a screen was here clearly indicated. Whilst the anterior surface allowed of the application of apparatus No. 5 in three places, the posterior surface was treated with No. 6. For ten consecutive days each place was rayed for fifteen minutes. Five weeks after cessation of treatment the lobule had recovered its normal aspect. There was very severe reaction, and yet no hæmorrhage was produced.

The extremely rapid cure of angiomata of the ear in infants justifies us in considering this region specially favourable for radium treatment.

(5) **Angiomatous tumour of upper eyelid relapsing after surgical operation** (Figs. 53 and 54).—A child 2 years of age had a tumour projecting 12 mm. above the surface, measuring 3 cm. from right to left, and 2.5 cm. from top to bottom. It occupied the external

three-fourths of the upper eyelid of the right eye, extended above the eyebrow, and lowered the eyelid by overhanging it in such a way that the sight was obstructed on that side. It was yellowish, in places slightly port-wine coloured, and of doughy consistency, the tissues appearing to be somewhat sclerotic. It could not be emptied by pressure, and its surface was studded with circular, slightly depressed scars. A cicatricial band traversed it from one side to the other. These scars and the sclerotic consistency had resulted from various attempts at healing. Total removal had been effected by a very skilful surgeon, and yet the operation, performed when the growth was the size of a nut, was followed by relapse, with gradual increase of the angioma.

Figs. 53 and 54.—Angiomatous tumour of upper eyelid, recurring after excision.

Electrolytic operations were afterwards undergone at the Trousseau Hospital, but effected little change. At length the child was entrusted to the care of Dr. Jacquet, at the St. Antoine Hospital, in January, 1907. From that time, by means of galvano-cauterisation every month, growth was stopped, and a certain amount of decolorisation brought about. But as, during the next sixteen months, progress was very slow, and the operations were painful, Dr. Jacquet thought of trying radium, and sent the child to us.

At this period, June 1st, 1908, the tumour was in a condition very unfavourable for treatment. It was difficult to foresee the action of the rays on sclerotic tissue studded with scars. Fortunately, the site of the growth was fairly well adapted to the "cross-fire" method. By placing applicators Nos. 6 and 7, with a screen of $\frac{8}{100}$ mm. of aluminium, opposite each other, above and below the tumour, it was possible, with comparatively short exposures, to act both on the

surface by rays of medium penetration, and at a depth by the accumulation and crossing of very penetrating rays. A first series of applications was made from June 1st to June 5th. Eight places were treated every day, two by two, for half an hour. A dry crust formed, which fell off of itself a month afterwards. The tumour was very soon reduced, and on July 17th only projected 7 mm. above the surface. On August 12th a fresh series was begun, similar to the first. On September 17th the growth was only 5 mm. thick, and a new course was undertaken. Since October 1st the lesion has been in the state shown in Fig. 54. The eye is free, and the eyelid only slightly depressed. The region is perceptibly flattened and decolorised; it still has traces of scars, resulting from previous traumatisms. No tendency to relapse can be perceived. The child was injured by a fall on the tumour, about the month of September, and this was followed by a large ecchymosis. We expected that this would cause relapse, but it disappeared in the usual manner, without altering the gradual improvement which the tumour was then undergoing.

(6) **Angioma of lower eyelid** (Plate XV, Figs. 3 and 4).—An infant of ten months was sent to us by Dr. Apert with a deeply coloured nævus, which occupied the external half of the lower eyelid of the left eye, and affected the ciliary margin. In order to preserve the eye, it was necessary to invert the apparatus, drawing down the eyelid. But since by this means the eye itself was left uncovered, the applications could only be very short. This disadvantage was, however, compensated by their frequency. The total duration was two hours, in periods of ten minutes, with apparatus Nos. 7 and 8. A month after this first course of treatment the nævus was reduced by one-quarter. The second series consisted of six applications, of ten minutes each. Four months after the commencement of treatment the child presented in the affected region a flat, smooth, and even surface, rather too much decolorised. The eye was not involved, and there was no retraction.

4. ANGIOMATA OF MUCOUS MEMBRANES

Angiomata of the mucous membranes are very easily reduced, as will appear from the instances given below.

(1) **Erectile angioma of lower lip** (Plate XV, Figs. 1 and 2) (Dr. Ertzbischoff's patient).—An infant of 3½ months had on the lower lip, near the left commissure, both on the skin surface and mucous membrane, a prominent angioma which swelled that portion of the lip and infiltrated the whole of the tissues. The tumour was the size of a small nut. A deep ulcer, towards the outer part, on the side

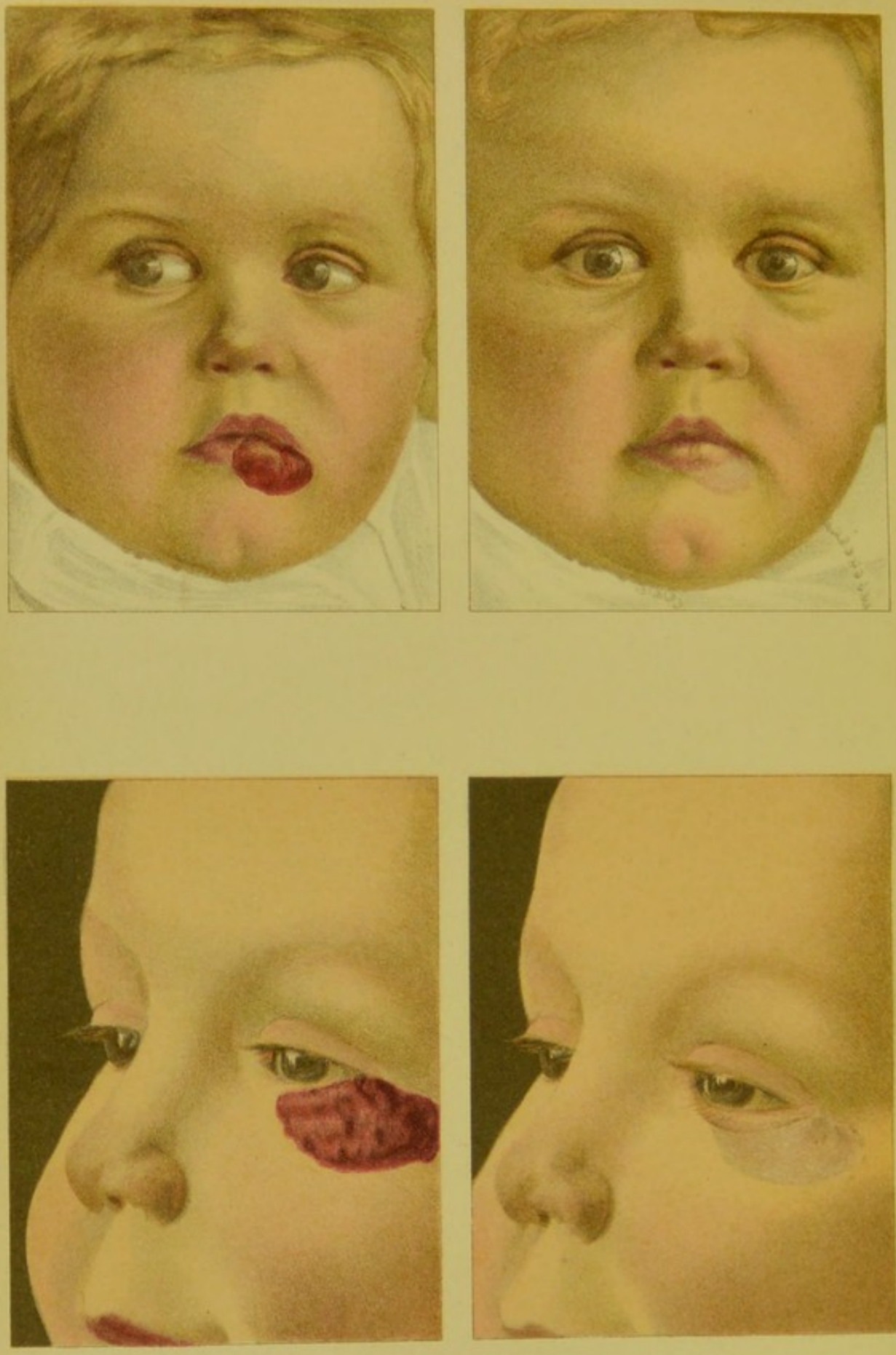


PLATE XV.—ERECTILE ANGIOMA OF LOWER LIP AND OF LOWER EYELID

PLATE XV

ERECTILE ANGIOMA OF LOWER LIP (p. 210)

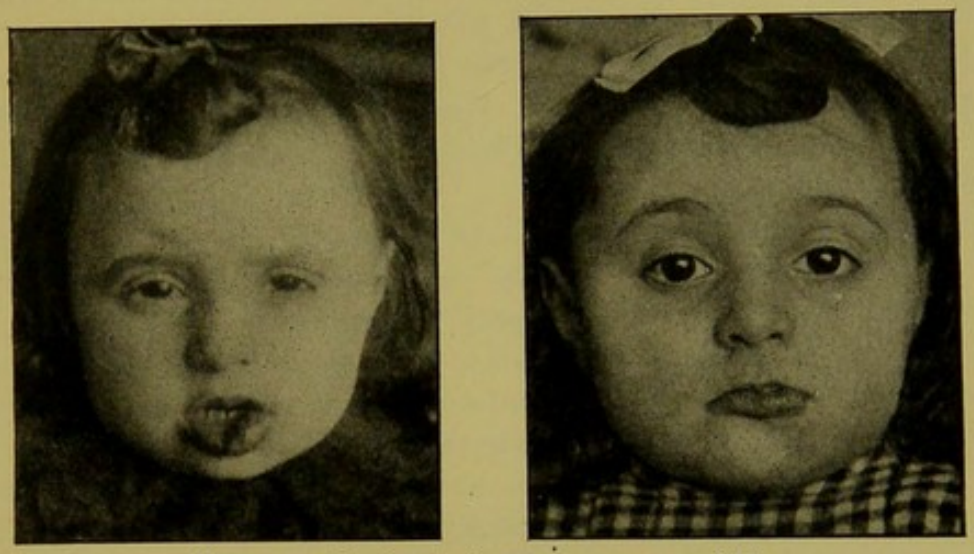
FIG. 1.—This prominent angioma affected the entire thickness of the lip, and projected from the mucous membrane as much as it did externally.

FIG. 2.—The cicatrix which remains is hardly visible, and has since been still more reduced.

ERECTILE ANGIOMA OF LOWER EYELID (p. 210)

FIGS. 3 AND 4.—The angioma affects the ciliary margin. No retraction of the eyelid occurred after treatment.

of the mucous membrane, sharply divided the lesion. Hæmorrhage had taken place on several occasions, and the colour was that of port wine, with a deep-red background. The region was suitable for the "cross-fire" method. Instruments Nos. 5 and 6 were applied simultaneously, one outside, the other inside, covered with aluminium of 0·02 mm., and rubber tissue. The exposures were made in three series, each spread over a month, and consisted of six applications of twenty minutes each, with an interval of one day. The whole treatment lasted eight months. The lip now (fifteen months afterwards) appears almost normal, both outside and inside. A slight depression persists, corresponding to the original



Figs. 55 and 56.—Angiomatous tumour of lip.

crevice. The skin is decolorised, and somewhat lighter than normal. The mucous membrane has remained slightly redder, but there is no longer any swelling, and on touching it scarcely any specially soft tissue can be felt in this region. This very remarkable result was confirmed by several other cases. In children, angiomata of the mucous membranes are easily reduced, and there is no occasion to resort to strong doses.

(2) **Angiomatous tumour of lip** (Figs. 55 and 56).—A child of 3 had a large angiomatous tumour on the left half of the lower lip, the weight of which prevented it from closing its mouth. The growth was so large that the left half of the lip was pushed forward, forming a sort of lateral beak. That part of the chin which was situated below the left commissure had increased in size, and was crossed by large veins. When the lip was everted the surface of the mucous membrane was shown to be deep purple, and the site of numerous vascular

dilatations. The growth was not confined to the lip, being continuous with a large angiomatous mass, occupying the internal surface of the cheek thoughout its width. It was, in fact, a huge vascular tumour, which did not appear adapted to surgical treatment, and for which electrolysis, performed a year before at the Hospital for Sick Children, had given no result. Radium treatment could not be pursued with the necessary method and energy, for the mother was nursing a young baby, and only brought the sick child at very irregular intervals. Apparatus No. 17, covered by $\frac{1}{10}$ mm. of lead, was applied for two hours on the skin; on the mucous membrane No. 7, wrapped in 0·4 mm. of aluminium, was used for ten minutes, on four opposite places, with the apparatus in contact with the skin. These exposures were renewed nine times during one month, at irregular intervals. The child was brought to us three months after the last application, and we observed very great reduction in the lip. The same treatment was continued, and two months afterwards the child could keep its mouth closed, as shown in Fig. 56.

(3) **Angioma of lower lip.**—An angioma of the mucous membrane of the lower lip, strongly coloured, and slightly raised, encroaching a little on the skin, and in process of development, had made its appearance in an infant of five and a half months. The size was that of a 50-centime piece. Dr. Druelle entrusted the treatment to us. The parents lived in the country, and could only bring the child once a week. There were four visits, and at each we applied apparatus No. 8, with 0·1 mm. of aluminium, for half an hour. After the first two applications there was a gradual reduction in colour. Six months after treatment the condition was very satisfactory, scarcely any trace of the growth remaining.

(4) **Angioma of upper lip.**—A small angioma on the left side of the nose, in an infant a fortnight old, was healed quite easily, by half an hour's application of apparatus No. 6. During the reaction we observed the surprisingly rapid development of an angioma of the mucous membrane of the upper lip. At the first visit it was only a small, red point; a fortnight afterwards this point was the size of a pea. It was one of those malignant growths which in a few months give rise to angiomata of the kind indicated in our fifth section. The treatment adopted in this case, which was in full process of development, very quickly arrested the growth.

We have now under treatment an enormous angiomatous tumour of the tongue, which is diminishing rapidly under the influence of weak doses employed by "cross-fire."

PLATE XVI.—ANGIOMATA

PLATE XVI

ANGIOMA OF SCALP (p. 207)

FIGS. 1 AND 2.—The angioma healed very easily. The centre of the region where it was situated remained slightly red, but there was no projection. The surface was glabrous before treatment.

ANGIOMATOUS TUMOUR (p. 213)

FIG. 3.—The photograph was taken before the end of treatment, to allow comparison to be made with the parts not yet subjected to radium. A rounded, rose-coloured surface may be seen on the cheek, which exactly reproduces the shape of the apparatus employed. Before treatment, this place was as prominent and deeply coloured as the rest.

5. ENORMOUS ANGIOMATA OF MANY FORMS AND IN VARIOUS POSITIONS IN THE SAME PATIENT, PRODUCING MARKED DISFIGUREMENT

The action of radium on this group of angiomata is very remarkable. We are here concerned with the unsightly and multiple deformities, which sometimes endanger the lives of infants, and which have been to a great extent successfully modified. The example illustrated in Figs. 57 and 58 is particularly striking. The infant was considered to be in an almost hopeless condition by the medical men consulted. It could not take the breast, nor could it breathe without difficulty. Its general state of health was miserable, and it was becoming gradually weaker. There was no possibility of relief from any therapeutic measures, since chloroform, or painful or fatiguing operations likely to produce hæmorrhage, might have been fatal. Since the application of radium—very slowly, it is true, but with a minimum of pain and fatigue—the lesions have gradually become flattened and reduced; the orifices have been freed, and the child has regained a normal appearance. As we shall see, this is not an isolated case. The great surprise of our colleagues, and the gratitude of the parents, show the value of radium treatment for these otherwise incurable growths.

(1) **Prominent angioma covering half of head** (Plate XVI, Fig. 3).—An infant of eighteen months presented an enormous angiomatous mass, situated on the left cheek, left side of nose, and temporal region, and encroaching largely on the fronto-parietal region. The appearance of this angiomatous area was very peculiar. It was a mass of doughy consistency, non-fluctuating, resembling sclerotic tissue, and presenting a purple surface, intermingled with yellowish patches. The aspect of the child was positively hideous. Various operations (electrolysis and cauterisation) had only exaggerated the unsightliness of the lesions, by covering them with disfiguring scars. The lids of the right eye, in particular, were drawn and retracted by fibrous cicatricial bands. There were deep, depressed scars in the lower half of the affected part. The mother, who lived in the south, could only devote a limited time to the treatment. As the absence of fluctuation permitted us to act vigorously without fear of hæmorrhage, we applied apparatus No. 2 to the cheek, for four days in succession, an hour a day. Two months afterwards we were surprised to find that, in consequence of moderate inflammatory reaction, less marked than we had expected, the surface scarcely showed any difference from the healthy skin surrounding it. It was merely somewhat

redder ; the vascular arborisations had disappeared, and there was no longer any trace of the scars, which had been very deep in this part. It is at this stage of treatment that the infant is shown in Plate XVI (Fig. 3). The lower part treated, which had the rounded shape of the apparatus, can be distinguished from the upper part, which has not yet undergone treatment, the contrast between the two regions being very striking. Similar doses were afterwards used for the other parts of the nævus, with the same result.

(2) **Tumour occupying half of head** (Plate XVII) (patient of Dr. Delporte).—An infant of three months had an absolutely repulsive appearance. Almost the whole parietal region and all the temporal region, with the external third of the upper and lower eyelids, the zygomatic region, the parotid region, and the lower half of the ear, were covered by an angiomatous mass, 1 cm. thick in parts. The lobule of the ear had disappeared from sight in this huge mass. The consistency of the tumour was soft, and in places fluctuating, plainly indicating that an enormous blood-containing area rested on the underlying bony plate ; its surface was irregular, and its colour a deep purplish mauve. The cheek was studded with small raised nævi, and the whole lower lip covered with a large angiomatous tumour. The median region of the neck, situated between the thyroid cartilage and the upper part of the sternum, was the site of a rather swollen purple patch. Each of these growths was fluctuating, and of the same colour as the principal one, and they were all in process of extension. The child appeared to suffer as the result of these malformations ; it was puny, sickly, and badly developed.

The treatment consisted of a series of exposures of ten to fifteen minutes, repeated on each place, every week, for two months. The doses were weak, with the object of obtaining slow and gradual resolution of the tumour, avoiding, as far as possible, reaction severe enough to produce hæmorrhage. The instruments used were apparatus Nos. 1 and 3 (ten minutes), and Nos. 5, 8, 12, and 13 (fifteen minutes), according to the regions. The results were more rapid than we had expected, the growths subsiding with astonishing facility. After three months' rest we observed a very marked tendency to levelling and decolorisation of the nævus. Treatment was then pursued with apparatus Nos. 16 and 17, without a screen, for some of the areas, and No. 1, covered by $\frac{2}{10}$ mm. of lead, for the parotid region. An hour's application was made every week for five months. After this second course we obtained the results shown in Fig. 2 of the plate.

The angioma from which this child suffered was not amenable to any of the therapeutic methods usually employed. The tumour was

PLATE XVII.—ERECTILE ANGIOMATOUS TUMOUR

PLATE XVII

ERECTILE ANGIOMATOUS TUMOUR (p. 214)

FIG. 1.—The angioma was prominent, and formed an enormous thick and doughy mass.

FIG. 2.—In proportion to the reduction of the angioma, the child, who was in a bad state generally, manifestly improved in health. A considerable number of small rose-coloured spots remained on the surface, but there is no prominence.

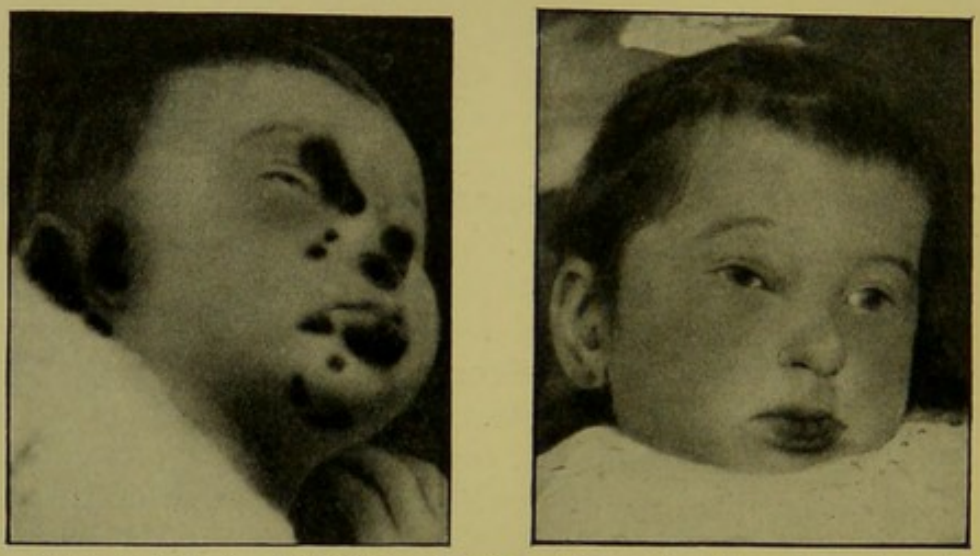
spreading rapidly, and prompt action was necessary, for the child's health was precarious. By means of the selective action of radium, applied in powerful and well-regulated doses, we were enabled to arrest the process of invasion, and to modify the growth so completely as to leave only some comparatively trifling remains of the old lesions. A point which it is important to note is the recovery of the child from its bad state of general health, in proportion to the applications of radium and the reduction of the tumours. This infant, which before treatment had been reared with difficulty, was badly nourished, and had bad nights, did not suffer at all from the many journeys necessitated by the treatment. Living in the country, where travelling facilities were defective, the child bore the fatigue without any difficulty, even in winter. The mother said there was greater vitality, and marked improvement in sleep and appetite. During our five months' care of this baby we were able to watch its gradual and rapid development.

(3) **Multiple prominent angiomata of face and buccal and conjunctival mucous membranes** (Figs. 57 and 58).—We present this case as our chief example of the application of radium to angiomata.

Those who had seen the child before treatment could not believe that it was the same afterwards shown to them. In a single year the alteration was radical and complete. Previously, the life of the infant had been seriously endangered. It could not suck, nor breathe through the nose; the sight and hearing on the right side were destroyed, and it was puny, sickly, and very miserable in appearance. Moreover, the poor little thing was repulsively ugly. After a year's treatment by radium, the transformation was complete; there was no longer any fear for its general health, and the orifices obstructed by the angioma were free, and had recovered their functions. The child had developed into a much better condition, similar to that of the previous case. The following is a *résumé* of its history.

The infant, eight months old, sent to us by Dr. Boutin, in October, 1907, had its right eye entirely closed; a vascular orbital tumour was pushing the eyeball forwards, downwards, and outwards. The two thickened eyelids were almost completely closed. On their surface, the skin was traversed by clearly perceptible veins. The canthus was the site of a slightly raised nævus, reddish purple in colour, which seemed to be an excrescence from the subpalpebral tumours. The cheek presented two small vascular patches, near the nasal groove. The tip of the nose was deformed by a prominent vascular tumour, and the median part of the upper lip was occupied by a purple angioma projecting 8 mm., which penetrated and obstructed the nostrils. The

lower lip, from one commissure to the other, was the site of a large reddish purple tumour with an irregular surface, which made it three times its usual size, everted it, and made it hang down so as to touch the chin. There was a huge prominent angioma, which the infant sometimes pinched between the two jaws, producing occasional hæmorrhage, on the internal surface of the right cheek. This was a continuation of the growth on the lip. On the cheek there was a small, slightly prominent nævus, also the source of frequent hæmorrhage. In the median suprahyoid region there was another, of 4 square cm. In front of the ear was a large tumour, raised at the centre, and projecting 2·5 cm. above the surface. The auricular canal was stopped up by



Figs. 57 and 58.—Multiple angiomata of face and of buccal, nasal and conjunctival mucous membranes.

several small vascular tumours. The retroauricular groove had a thick purple angiomatous edge.

It will be seen from this description how serious were the difficulties we had to overcome, and we must acknowledge that the result of the treatment we are about to describe would not have been so successful had not the mother of the child shown remarkable energy, patience, care, and medical intelligence. Thanks to her, the most minute and delicate operations—such as the introduction and maintenance of the apparatus under the eyelids—could be performed, and were followed by excellent results.

The treatment was varied according to the character of the tumours. In October and November the greater number of the lesions were treated by apparatus Nos. 6, 7, and 8, left on each day for a period not long enough to induce inflammation, very short applications being made of five to fifteen minutes, frequently repeated. In January,

1908, a marked improvement of the nævus regions could already be observed, and the treatment was continued in the same manner. The mucous membranes were more difficult to deal with systematically. The applications were arranged according to the child's sleep; we took advantage of the shortest sleep to operate at once, were it only for five minutes, with apparatus No. 13, on the conjunctival mucous membrane, by slightly opening the eyelids. On the buccal mucous membrane we used No. 7, covered with screens of 0·04 to 0·08 of aluminium. In the course of the first five months of 1908 we observed the gradual subsidence and decolorisation of the greater number of the angiomata. The nose and auricular canal regained their shape, and were freed from obstruction. All the nævi lost their colour, and most of them were levelled. The lower lip underwent a great transformation. It was still thickened, and projected beyond the upper lip, but it was no longer pendulous. The angioma of the buccal mucous membrane was very easily reduced, but treatment of the conjunctivæ was particularly delicate. As soon as the eyelids were half opened, the angiomatous mucous membrane projected, and the apparatus could only be applied on these points during sleep, for a very short time. The combined effect of these applications with those produced through the eyelids, and others on their outer surface, soon reduced the fungating and projecting tissue. The eyelids could then be opened more easily, although not everted. Apparatus No. 13 was first carefully slipped on to the caruncle, and then by degrees on to most of the other parts of the conjunctiva. On the external surface of the eyelids, we acted with No. 4, covered by 0·1 mm. of lead, and left in position four hours, thus using "cross-fire." By degrees, freedom from congestion and swelling was so effectively obtained, that at the present time the eyeball has recovered its shape; the child opens its eyelids of itself, and its sight on that side is gradually improving. At first the unused eye did not share in this recovery of sight; there was marked strabismus, but in time the child was able to make use of both eyes. A few points still remain to be completed and improved; but the total results obtained were astonishing, greatly exceeding anything we had ventured to expect.

(4) **Multiple angiomatous tumours.**—A child of 5 presented a huge prominent angiomatous area covering the frontal, temporal, and right parietal regions. In its lower part this mass overhung and dragged down the upper eyelid in such a way that the child was obliged to throw the head back in order to see with this eye. The eyebrow was obliterated, and the upper eyelid swollen, the ciliary margin itself

being affected. This huge tumour, which extended for some distance into the scalp, and on the surface of which no hair had grown, was of greyish colour, studded with purple protuberances. There was a rather sharp prominence of about 1 cm. in the frontal region. The parotid region was the site of a tumour raising the skin. The latter did not seem to be affected, except at a few points, where there were small purple patches. The tip of the nose was prolonged by a tumour of soft consistency, the surface of which was bluish.

The treatment may be divided into two stages. In the first we sought to produce rather severe reaction, in order to level the prominent portions of the tumours. It was composed of three sets of exposures, made at intervals of two months. Each series consisted in the application to the frontal and temporal regions of apparatus No. 1 for three hours, in divisions of fifteen minutes a day. No. 5 was used on the nose and parotid region. Each of these courses was followed by normal reaction, after which the levelling of the lesions became still more marked. The part overhanging the upper eyelid had gradually contracted, so that the sight was no longer interfered with, the eyelid scarcely descending lower than that on the healthy side. The second stage of treatment, after four months' rest, had for its object the modification of the deeper parts of the remaining lesions of the superciliary arch and the parotid region. We succeeded in this by applying apparatus No. 5, in 0·2 mm. of lead, on each of these places, left in position for twenty hours, in divisions of two hours.

(5) **Prominent angiomatous tumours in adult** (Plate XVIII) (patient of Dr. Macaigne).—A man of 55 presented, over three-quarters of the right cheek, lower eyelid, and right half of the upper lip, a succession of large angiomatous ridges, deep purple in colour, forming vermicular bands which in some places surrounded small portions of healthy skin. Their prominence varied, according to their situation, from 6 to 15 mm., nor was their consistency everywhere equal. In the lower portion of the cheek there was a thick mass 5 cm. in diameter, papillated, easily depressed, and somewhat fluctuating. Beginning at the external angle of the eye, and reaching the lip, there were four erectile angiomatous bands. The two upper ones were sclerotic and of doughy consistency, their base being spread over a large area; the two lower showed an umbilicated centre. The tumour of the upper lip, which partly covered the lower, was harder than the others, because it had formerly been treated by electrolysis; this had decreased the size of the lip, which previously hung down to a greater extent, and had partly reduced its colour.

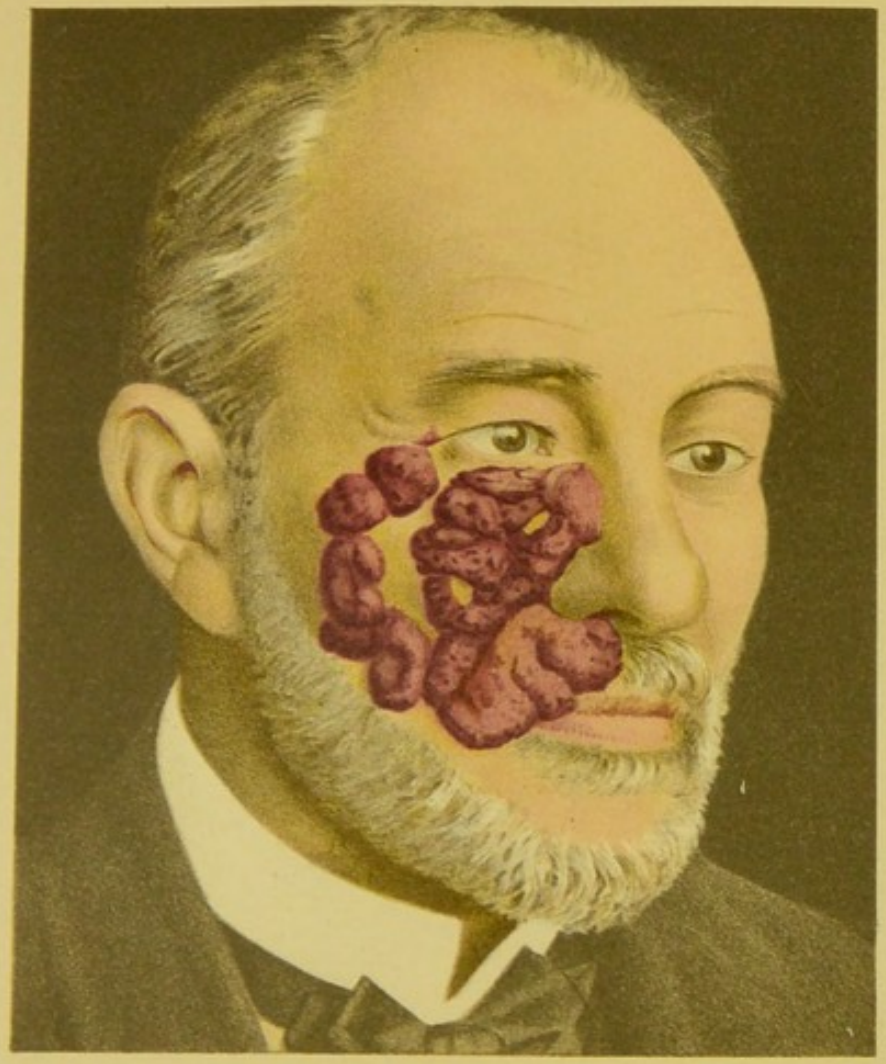
These angiomata are much more refractory in adults than in

PLATE XVIII

ANGIOMATOUS TUMOUR (p. 218)

FIG. 1.—The angiomatous serpentine bands were hard and prominent; palpation gave no sensation of fluctuation, and produced no diminution in size, except in the lower part of the cheek.

FIG. 2.—The edge of the angiomatous bands has remained slightly red. The spot under the nostril has not yet been treated.



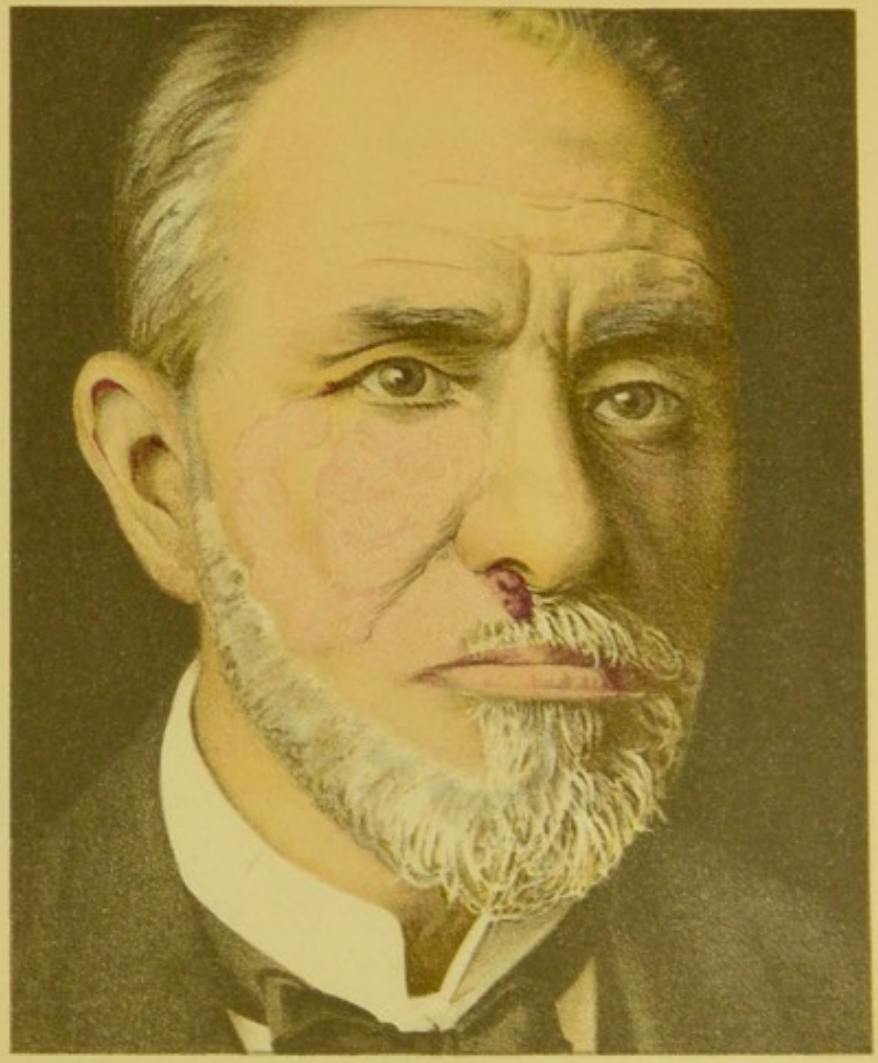


PLATE XVIII.—ANGIOMATOUS TUMOUR

children. Indeed, in the former they are fully organised tumours, and healing can only be obtained by combining the specific effects of radium with its destructive properties. Hæmorrhage need not be feared, and massive doses are permissible—at any rate at the beginning of treatment—in order to obtain levelling of the growths, without too great loss of time.

Apparatus No. 1 was used on the lip and lower half of the cheek for four hours, during three consecutive days. In spite of this strong dose, the reaction was slight. A month after the application, partial resolution and decolorisation took place, but the results were incomplete. On the upper regions of the angioma, below the external angle of the eye, apparatus No. 14 was placed for four hours, spread over two days. Two months after this first series the lesions as a whole were levelled, and allowed of fresh applications of No. 1 for two consecutive hours. Several more courses were undertaken, in order to make sure of all the points where resolution was slow in taking place. At present, except for one point under the nose which remains to be treated, decolorisation is almost complete. The tissues are smooth and even, but rather lighter and more like mother-of-pearl than normal skin, and a red edge still persists at the centre and periphery of the regions where the tumours had been. The improvement was so great that the patient was no longer recognisable. His occupation being that of a commercial traveller, he amused himself by puzzling people at the hotels, who had known him for many years, by his altered appearance.

ADVANTAGES OF RADIUMTHERAPY

In the preceding sections of this chapter, we have given the directions which we consider most important for the radium treatment of the various forms of angioma, and we shall not, therefore, return to this subject. It will be well, however, to sum up in a few words the chief benefits of the treatment. Electrolysis, surgery, and X-ray treatment were the principal means at our disposal before the use of radium, and they are still very useful in some cases.

Electrolysis is an excellent method for dealing with nævi of small extent, and it produces brilliant results. Until we took up our present system of treatment, we usually availed ourselves of it, and, thanks to the admirably precise method taught by Dr. Brocq, have always succeeded in obtaining very smooth and scarcely visible surfaces of repair. Unfortunately, the operations are painful, and this is a serious drawback, the more so because, as a rule, they have to be frequently repeated. Moreover, the pain produced—which, when

prolonged, is most exhausting—makes such treatment impracticable for nævi with a very extensive area, and it is not available, even in theory, for certain regions, *e.g.* the lips, eyelids, and nostrils; nor can it succeed when the infiltration extends deeply. It should also be added that electrolytic operations must be conducted with very great skill in order to obtain the admirable results indicated. We had not previously grasped the importance of this point, but we have learned it from our work with radium, since most of the patients who come to us suffering from nævi have formerly tried electrolysis. Some have been repelled by the pain and frequent disturbance produced, and many others, much to our surprise, have been further discouraged by the production of very conspicuous and disfiguring scars, prominent or depressed. In this connection we would recall the fact that in most of these cases radium has succeeded in partly improving the electrolytic scars as well as the nævi. Whatever be the place taken by this new healing agent in the treatment of vascular nævi, electrolysis will still be of use in the following cases:

1. Star-shaped telangiectases and small nævi, which can be easily cured by a few punctures.

2. The telangiectases which often surround nævi.

3. Small nævi produced by the union of telangiectases, which do not form uniform areas.

4. Lastly, it sometimes happens that fine telangiectases persist or are produced in the repaired tissues. Electrolysis will get rid of these.

Surgical measures may be employed with advantage, but only for prominent and sufficiently small angiomatous tumours—particularly those of the body and limbs. They are rapid, and obviate the inconvenience of lengthy treatment, but of course require chloroform. Radium seems a better method for tumours of the face, and for those which affect young children, and we cannot too strongly insist on its special value in growths of this kind. Very large tumours cannot be treated by surgery. They are usually very troublesome, but they can now be healed by radium.

Cauterisation can only be used successfully on very small lesions, and in this case electrolysis is to be preferred; on more extensive surfaces it sometimes leaves unsightly scars, which we have often had occasion to reduce when treating angioma.

As to **X-ray treatment,** it sometimes gives very satisfactory results. Drs. Gastou, Barjon, and others have employed it successfully. But it seems difficult to ascertain the exact dosage, and X-ray operators are afraid of producing radiodermatitis, for up to the present time,

although it is the older method, and numerous experiments have been made with it, there is no systematic work dealing with the action of X-rays on all the different kinds of vascular nævi. Moreover, we are met by the difficulty of acting at a depth without injury to the surface, so that no comparison can as yet be made. But when this problem is solved, it will be very interesting to compare the results, and to ascertain the differences—for we are convinced that radium rays are not identical with X-rays—both in curative action and in the value of the tissues of repair.

It will be seen that these methods are very limited in their scope. This is not the case with **radium,** which shows a degree of usefulness which may vary according to individual cases, but which is incontestable in the treatment of the great majority of nævi, even for very extensive forms and enormous tumours, which no previously known therapeutic treatment could have hoped to alleviate even under favourable conditions. This superiority is due to the specific, selective action which radium exercises on angiomata; *and this is the fundamental truth which our researches have brought to light.* Some angiomatous tissues can, under its influence, be decolorised, reduced, and to some extent absorbed, without the production of destructive inflammation. All the rays—even those of weak penetration—possess this selective property, if they are administered systematically according to the method chosen. "Surpénétrant" radiations employed alone also bring about curative effects in the depth of the angioma without affecting its surface too strongly. In addition to this selective action, with which, in practice, we must often combine destructive action, two very important advantages should be mentioned, viz. the painless character of the applications, and the convenience with which they can be made.

1. **Absence of pain.**—The apparatus produces no painful sensation when placed on the tissues. For timid persons, in the treatment of large surfaces, and for infants who can be operated on during their sleep, this is an inestimable advantage. But although the applications themselves do not cause pain, is this the case when inflammation is subsequently produced? Slight inflammatory reaction certainly causes a "sensation," but it is very insignificant, and consists of a slight tickling feeling, which lasts about a day, before the formation of the crust. If the latter covers an ulcerated surface, everything depends on the adherence of this crust. So long as it remains in place there is no disagreeable sensation, but if it is torn off by accident it gives the patient the sensation of a burn. It is, however, very seldom necessary to produce such inflammation.

2. **Convenience of application.**—The apparatus can be left in position for many hours, which is a great advantage when dealing, as is usually the case, with very young children. It is a fortunate and somewhat curious coincidence that this new therapeutic agent, which is specially adapted for removing angiomatous growths in children, should present precisely those conditions of painlessness and simplicity which are best suited to their great sensitiveness.

To sum up, we consider radium an excellent means of treating all kinds of angiomata, more particularly in young children.*

* We desire to thank Professor Gaucher for having introduced a *résumé* of our studies of angiomata into his recent work on "Diseases of the Skin" (No. XIV of the "Nouveau Traité de Médecine et de Thérapeutique," by Brouardel, Gilbert, and Thoinot).

CHAPTER VI

THERAPEUTIC RESULTS (Continued)

IV. PIGMENTARY NÆVI*

Our first radium experiments on pigmentary nævi (1905) were not very satisfactory. We treated a flat "beauty-spot" of small size, which, in consequence of rather severe reaction, was completely obliterated, only to reappear some months later. We had also a case of a small lobulated pigmentary nævus, which was very slowly reduced, and lost its colour only to a slight extent. These first attempts led us to suppose † that radium had no very beneficial action on these growths; but failure may have been due to the method of operating, and alterations in the technique employed might have produced different results. Our more recent investigations have confirmed these suppositions, and, by means of intense doses applied to nævi of larger size, we have ascertained that radium is capable of rendering valuable service in the treatment of such cutaneous malformations, provided that the pigmentary layers be destroyed.

These circumstances led us to recognise that pigmentary nævi were not a specially favourable ground for this treatment, and to consider the exact meaning which we intended to give to the word "specific" when applying it to the action of radium. Although not beyond criticism, this term expresses fairly well the special selectivity which radium possesses with regard to certain pathological tissues. We have seen, in the preceding chapters, that such tissues could become modified and repaired under the influence of radium treatment, without undergoing the slightest visible reaction. Certain kinds of subcutaneous neoplasms can be successfully modified, without injury to the overlying skin; in this case we should say that radium had a specific action. On healthy skin, on the contrary, it only brings about visible modification when visible reaction is produced, and this seems to apply also to pigmentary nævi, since, in order to obliterate them, it appears to be indispensable to disorganise the pigmentary layers.

* This chapter was written in collaboration with M. Combres, House Physician at St. Lazare.

† *Ann. de Derm.*, October, 1906.

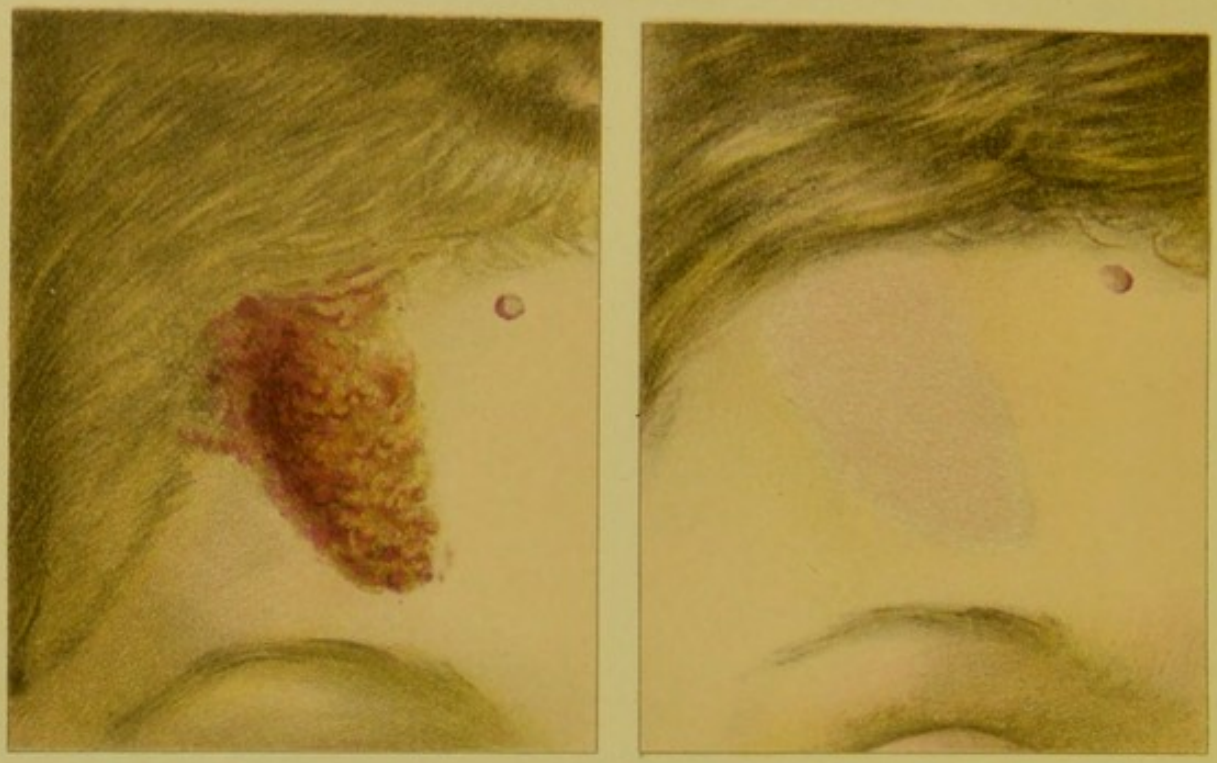
It is true that we have certainly observed modification without perceptible irritation in a few cases, but such instances are rare, and the change is not very marked. We therefore conclude that radium is not specific for these growths. Our friend Dr. Abbé, of New York, who is a great authority on radiumtherapy, is of the opinion that pigmentary nævi are amenable to the "specific action" of radium, and in support of this opinion he quotes a case* in which the nævus was replaced by tissue similar to that of healthy skin; but we learn from this paper that a sharp reaction, with blistering, was produced, after the application of radium, and we therefore think that the term "specific" is not here correctly employed. The distinction is an important one in practice, for the technique will differ, according to whether we are dealing with a lesion which is or is not amenable to specific action. In the first case, weak doses will sometimes be sufficient. In the second, the doses should always be fairly strong and capable of producing destruction, as in the case of pigmentary nævi.

But of course non-specificity does not imply inefficiency. Destruction is a very frequent means of healing in therapeutics. Now radium, regarded as a destructive agent, combines absence of pain with action at a depth, which is followed by favourable repair of a special character. We have laid stress on these qualities in the chapter on reaction. Radium therefore represents a valuable therapeutic asset, even when it cannot act specifically. Various conclusions may be deduced from these results with regard to the line of treatment to be pursued, both in the choice of the technique and the selection of suitable cases.

What kinds of pigmentary nævi should be treated? Hairless, slightly *café-au-lait* patches, which are quite superficial, and those with a very extensive area, should not be subjected to the rays. They are not conspicuous, and we should incur a risk of replacing the nævus by a very white or unevenly coloured cicatricial surface, owing to the recurrence of pigmented points, and the appearance of telangiectases, which might be worse than the original patch. On the other hand, radiumtherapy is clearly indicated for hairy and deeply coloured prominent tumours. It is obvious that in such cases the patient will receive great benefit from the treatment, even if the resulting scars are visible or even conspicuous.

Pigmentary tumour.—Fig. 3 of Plate XIX shows an enormous and most unsightly pigmentary tumour, developed in a child of 11. Its mass not only filled the entire nasal cavity, but also overhung the nose by about 1 cm. The growth had an irregular surface, was

* Robert Abbé: "The Specific Action of Radium as a Unique Force in Therapeutics." *Med. Record*, Oct. 12, 1908.



PIGMENTARY NÆVUS

PIGMENTARY TUMOUR

PLATE XIX

PLATE XIX

PIGMENTARY NÆVUS (p. 226)

FIG. 1.—The nævus was slightly prominent, with a shagreen-like surface, and of a doughy consistency.

FIG. 2.—The surface is smooth and uniform after treatment; it has remained in this state for a year.

PIGMENTARY TUMOUR (p. 224)

FIG. 3.—The tumour is papillated, and extremely prominent.

FIG. 4.—The reduction of the tumour has continued for eighteen months. A little pigmentation remains in some places; in others there is too marked an absence of colour.

yellowish brown, and in some places slightly green in colour, and gave the face a repulsive appearance. Apparatus No. 14, in rubber, was applied to each place for five hours, distributed over three days. Ulcerative reaction occurred, which lessened the size of the tumour by one half, and took two months to become cicatrised. No. 3 was then applied for seven hours spread over three days; the reaction was very sharp, but did not last long. While waiting until the tissues had acquired a certain amount of stability, we also subjected the various points of the periphery, which had only been partially treated, to destructive doses. No. 14 was applied on these for four hours, distributed over two days. The child was brought to us again three months after the completion of treatment. The tumour had completely disappeared; the left nostril had gradually recovered its normal size, and the surface was level. The colour which remains is very slight, resembling that of *café au lait*, and whitish cicatricial tissue exists at two points (Fig. 4, Plate XIX). The treatment took place more than fifteen months ago, and neither the pigmentation nor the tumour has recurred. The tissues are perfectly supple, and there is no retraction, either of the nose or of the lower eyelid. It is again easy to recognise here the special qualities of the repaired tissue following destruction by radium.

These results may therefore be considered very successful. We have had to treat several pigmentary nævi which had formed tumours, and on each occasion the benefit has been marked. When the nævoid masses are fibrotic and of hard consistency, the cure is easier and more rapid. Between the two extreme classes of nævi—those which are flat and superficial and have little colour, and the prominent and deeply coloured variety—there is a whole series of intermediate forms, from which those that are amenable to radium treatment must be selected. The existence of more or less marked development of hair should influence our choice.

Depilatory action.—Radium treatment not only succeeds in levelling projections and removing colour; it also has a very definite action on pilosebaceous glands. Therefore a superficial, slightly coloured pigmentary nævus, of the kind that we should reject without hesitation if it were only a matter of decolorisation, should be treated when the development of hair is marked, as in the following example.

A child two and a half years of age presented on the right temporal region a superficial pigmentary nævus, which was hairy but not projecting. It was circular in shape, light in colour, measured 4 cm. in diameter, and was covered with fine hairs, 5 to 6 cm. long. Apparatus No. 1 was applied, in $\frac{1}{100}$ mm. of aluminium, for four

days, an hour a day, then in 1 mm. of lead, for two days, an hour a day. The object was to act at first specially on the pigmentation, and afterwards, by using "surpénétrant" rays, to act deeply on the pilosebaceous glands. The result perfectly answered our expectations. The hairs have not reappeared since treatment, which took place twelve months ago; the repaired surface produced after very severe reaction being smooth and brilliant, although it has lost rather too much colour.

Pigmentary and hairy nævi of doughy consistency with rough surface.—One frequently meets with slightly raised growths of this kind, somewhat doughy in consistency, and with a rough verrucous surface, rather highly coloured, and covered with hairs. They are perfectly amenable to the action of the rays, but although reduction, and destruction of the hairs, may be promised, no such certainty can be felt with regard to the entire decolorisation and æsthetic appearance of the tissues of repair. They can be ensured to a great extent, but it often happens that the surface is too light, nacreous, or marbled, or the pigmentation may relapse in course of time. It is true that, in the majority of cases, relapse only means the recurrence of a light coffee-coloured shade, so that the benefit of the treatment is often retained, even as regards decolorisation. In some cases this may be complete, as in the following example.

A child had a pigmentary nævus on the right half of the forehead (Plate XIX, Figs. 1 and 2). The growth combined the various conditions which seem to us suitable for the use of radium: fairly dark colour, sufficient size (it measured about 6 to 8 square cm.; small nævi are more difficult to treat), projecting 3 to 4 mm., an irregular and slightly verrucous surface, and slight downy growth. After rather pronounced ulcerative reaction, the tissues of repair resulted in a smooth, even, hairless surface, level with the skin. During the first few months it was rather too light and cicatricial in appearance, but in course of time the tints became mingled; and now, eighteen months after treatment, the healed surface is still intact. The treatment consisted in three applications, without a screen, of apparatus No. 1, with a week's interval, the first being for thirty minutes, the two next for an hour and a half each.

In the following instances, which refer to precisely similar nævi, pigmentation recurred six months after treatment ceased, but only in part.

A girl of 10 had a pigmentary nævus on the external surface of the middle of the right forearm. This growth, of a dark chestnut colour,

was fairly thick, projected 3 mm., and had a granular surface. It measured about 5 cm. wide, and had formerly been covered with hairs, but very vigorous X-ray treatment had finally destroyed them. The pigmentation, the doughy consistency, the prominence, and the general appearance of the nævus had not, however, been altered in any way. Apparatus No. 1 was applied for half an hour every day, for ten days. Severe inflammatory reaction ensued, which required six weeks for complete healing. The girl returned six months afterwards and showed the following results: levelling, smooth and even surface, decolorisation, normal consistency of tissues, and diminution in size. We learned five or six months afterwards that the pigmentation had unfortunately reappeared. A new series of applications was made for two hours with apparatus No. 2. At the present time, eight months after the completion of this second course, the nævus surface has not recovered its normal tint, being slightly coffee-coloured, and presenting a few traces of telangiectasis. The edges are retracted, and the surface diminished in size, but without the smallest band or puckering at the periphery. The tissues are supple, having lost the doughy character that they had originally, and the surface itself is smooth. In fact, the benefit of the treatment is quite evident, although incomplete. The relapse, which appeared six months afterwards, shows how careful one should be before exhibiting patients who have suffered from these growths to the learned societies, as instances of complete cure. As the nævus which we have just mentioned was situated on the forearm, on tissue which was very supple and loose, surgical removal might have been thought of. In our opinion this would have been a mistake, for the surface was too extensive, and the post-operative scar would have produced a retracting cicatrix inferior in appearance to that which we obtained.

We will now mention a case of a very large pigmentary nævus. The growth extended in height from the horizontal branch of the maxilla to the temporal region, measuring 10 cm. in length; in width, it began at 1 cm. in front of the ear, and reached to the malar apophysis, measuring 7 cm. at the upper part, and diminishing slightly at the lower part. It projected above the level of the skin by about 2 mm.; it was of extremely firm consistency, covered with very coarse hairs, growing close together, and it was almost black. Apparatus No. 1 was applied for six hours, on as many places as were necessary to cover the nævus, the small intervening points being treated for ten hours with Nos. 7 and 8. Reaction was produced fifteen days after the first application, and at the end of three months the nævus was flat, depilated, and partly decolorised. The skin is supple, whereas before

treatment it had the roughness of leather. The surface of repair, without being positively cicatricial, is smooth, glossy, and very slightly pigmented.

Pigmentary nævi known as "beauty-spots."—We have already said that the variety known as "beauty-spots" had misled us at the beginning of our researches, and caused us to form conclusions about pigmentary nævi which were not quite accurate. Circumstances had led us to begin with these small growths, and we did not then know the great importance of the size of the surface of an apparatus in the technique. Even with pure radium, an instrument with a small surface has a comparatively weak radiation, and this weakness must be compensated by the length of the exposures. In this way alone can we obtain destruction, but even then the flat superficial marks frequently relapse; therefore radium should not be applied to them. On the other hand, the treatment is very successful for thick, coloured spots covered with hairs, for even if partial relapse of the pigmentation takes place, the levelling and depilation are appreciable results. Sometimes, as in the following cases, pigmentation does not recur, and if it reappears, it is never so marked as before.

A patient presented a pigmentary hairy nævus of the right cheek, coming under the category of "beauty-spots." It was raised 3 mm., of a blackish tint, and studded with very coarse hairs. Apparatus No. 8, which covered it almost completely, was applied without a screen for eleven hours, distributed over eighteen days, in exposures lasting one hour. After inflammatory reaction, which was long in healing (about six weeks), levelling, decolorisation, and depilation ensued, and these results have been maintained for two years.

A lady, aged 50, consulted us for a large hairy pigmentary "beauty-spot," measuring 1 cm. in diameter, and projecting 6 to 7 mm. beyond the skin. It was nearly black, the surface being covered with numerous hairs. Application of apparatus No. 7 was made for nine hours, spread over three days. A month later we observed a great decrease in size, and the colour had disappeared, though some of the hairs still resisted treatment. Three months afterwards we applied No. 7 for four hours, in order to get rid of a slight prominence which still persisted, and a faint pigmentation which had reappeared. The lesion has entirely disappeared since this last treatment.

Technique.—The destructive doses which must be used—care being always taken not to overdo them—may proceed either from total radiations which allow of great intensity, or from "surpénétrant" rays. The total radiation (apparatus without a screen) is the best for superficial nævi with but little development of hair. For

instance, three hours of apparatus No. 1, unscreened, if its whole surface be used, will suffice for a first course of treatment. Two months later it will probably be necessary to make a second series of applications, but only for two hours. The "surpénétrant" radiations, which contain a majority of β rays, are indicated for very thick nævi covered with a number of large hairs. Twenty-four hours of apparatus No. 1, used over its entire surface, with $\frac{1}{10}$ to $\frac{3}{10}$ mm. of lead, will allow the "surpénétrant" rays to act destructively, and at a rather greater depth. These two methods can sometimes be used with advantage in combination. In treating small pigmentary growths (prominent "beauty-spots"), it will be necessary to bear in mind the importance of the size of the apparatus, and to increase the length of application in inverse proportion to the amount of radioactive intensity. A small apparatus must therefore be left in position for a comparatively long period.

Results.—Radiumtherapy applied to pigmentary nævi plays a much less important part than in the diseases dealt with in preceding chapters; nevertheless, the results obtained, though limited to depilation, levelling of projections, and a decolorisation which is always considerable, though often incomplete, would seem to place it in the first rank in comparison with other methods of treatment, which are never quite satisfactory. It renders valuable service in cases in which we were formerly helpless, except, indeed, as regards the depilation and surgical removal of small hypertrophied nævi. We have notes of several cases in which the use of X-rays, even in the most skilful hands, had only brought about depilation, whilst with radium the improvement was more marked.

A child of 4 was sent to us by M. Brocq. It had been treated by X-rays (twenty-four exposures), under the best possible conditions, for a pigmentary, hairy nævus of the left cheek. This growth covered an area of about 16 square cm., and showed two distinct portions, one in the centre, projecting 5 to 6 mm., and deeply coloured, and one at the circumference, superficial and slightly coloured, level with the neighbouring skin. Depilation resulted from the treatment, but the prominence and pigmentation were not modified. Radiumtherapy was then tried. The whole growth was treated with apparatus No. 1 for two hours, divided into equal parts, and distributed over six days. We also applied No. 8 for three hours in the centre, on the prominent thick part. The reaction which followed was very acute, particularly at the centre, where repair did not take place for two months. The child was seen again six months afterwards, when the central tumour had disappeared, and the surface was perfectly level,

the decolorisation also being almost complete. A red angiomatous patch had developed on one of the points at the edge of the central portion. This red point disappeared after application of No. 7, for three hours, one hour a day. A year later the child was brought to us again. The pigmentation had recurred to some extent, for the surface in the centre presented a slight brownish tint, but the levelling had been perfectly maintained. In spite of the slight relapse, the benefit derived from the use of radium in this case was quite appreciable.

We may sum up our remarks by saying that radium is specially suited to hairy nævi which are thick and deeply coloured and have a rugose surface, and also to pigmentary tumours. Flat, slightly coloured, hairless nævi, those of large extent, or formed of scattered growths, and nævi with a small surface, do not benefit by the action of the rays. As regards the line of treatment to be pursued for pigmentary nævi in new-born children, we must repeat what we have said about vascular nævi—namely, that these growths often show a tendency to spontaneous improvement during the first two months. It is therefore necessary to watch them, and postpone the treatment of those which are stationary, dealing at once with those which continue to increase.

CHAPTER VII

THERAPEUTIC RESULTS (Continued)

V. TUBERCULOSIS OF SKIN AND MUCOUS MEMBRANES*

THE first experiments in radiumtherapy concerned cutaneous tuberculosis almost as much as benign cancroids, and many authors—especially Danlos, Blandamour, Follard, Davidson, and Shober—concluded that radium was equally useful in both these diseases. The results which they published referred to lesions of small extent, and only dealt with a few of the many forms of cutaneous tuberculosis. Our own experience during the last five years has included a great variety of serious cases, and has led us to somewhat different conclusions. It has confirmed the facts stated with regard to epitheliomata, but in the case of cutaneous tuberculosis, in spite of results which justify us in devoting a separate chapter to this subject, it has shown that radium has a less constant, as well as a different action. The specific effect produced on certain neoplasms by this new agent did not seem to occur with the same certainty in cutaneous tuberculosis, especially in lupus vulgaris and in lupus erythematosus. Radium appears to give the best results in this disease when used as a destructive agent. The advantages of radiumtherapy here consist chiefly in the ease with which destruction can be accomplished, and in the satisfactory appearance of the repaired tissues. We shall see, however, that in some cases the rays also partly act by relieving congestion. The following is a brief summary of the essential points of treatment for the principal forms of local tuberculosis.

1. **Ulcerative and non-ulcerative lupus vulgaris.**—From the beginning of our investigations we had noticed that lupous ulcers, treated with doses of comparatively weak radioactivity, sometimes became rapidly cicatrised, but that newly formed nodules subsequently recurred in the scar. We therefore concluded that the treatment was not sufficiently strong, and that it was necessary, for greater security, to resort to vigorous doses in all cases of ulcerating or hypertrophic lupus vulgaris. We therefore preferred to use instruments of great radioactive power—

* This chapter was written in collaboration with M. Combres, House Physician a St. Lazare.

e.g. Nos. 1, 2, and 3, applying them for three and four hours at a time. Although several series of applications may sometimes be required, a single course will often give remarkable results. This was the case (Figs. 59 and 60) with one of our patients, aged 26, who was affected by a lupus which invaded almost the whole of the face, especially the cheeks and nose. The condition had existed for eleven years, and had been treated several times by curetting and the actual cautery without much benefit. When he came to consult us he presented a number of tuberculous ulcers, large aggregations of ulcerating tubercles covered with crusts, and small nodules embedded in cicatricial tissue. The whole of the tissues were much congested.

Figs. 59 and 60.—Lupus vulgaris.

Most of these lesions, especially those on the nose and cheeks, were treated by No. 1 apparatus, applied without a screen, for two hours on each. Very severe reaction ensued, and the inflammation on the nose took a long time to subside. Some months afterwards the lesions were replaced by good scars, which were smooth, even, not depressed, and in every respect satisfactory. Some active nodules, however, remained at the root of the nose, the internal angles of both eyes, the left malar region and the left ala nasi, for which very strong doses were given with applicators of a size appropriate to the regions. A few months afterwards the patient was in an excellent condition ; but some lupous nodules had reappeared in the centre of the scar, which were then destroyed by electro-cautery, and afterwards treated by radium. At the present time—two years after treatment—the local improvement has been well maintained. The patient has grown stouter and looks better, as shown by the photograph (Fig. 60), which

was taken recently. Similar results have been obtained in several other patients.

We will now describe how lupous tissues are modified by the action of strong doses of radioactivity. The vegetations covering the ulcers subside quickly, and the base—as often happens in the case of other lupous lesions, with or without ulcerating vegetations, when subjected to similar doses of radium—then becomes the site of a somewhat severe ulcerative inflammatory reaction. When this ceases, cicatrisation gradually begins, and usually terminates in the formation of a tissue distinctly differing from the normal skin by its white, smooth, and shiny appearance, a few telangiectases being sometimes formed on the surface at a later stage. The scars have the advantage of being seldom depressed and irregular, and they never cause retraction, or become the source of fibro-sclerotic cicatricial bands or cheloids. One to three months is a sufficient time to obtain this result. It is sometimes necessary, as we have seen, to make a second series of exposures after the first course of treatment. If care is taken to act extensively, both on the surface and at a depth, the result may sometimes be permanent; but the scar must be watched with the greatest attention, for, in spite of every precaution, it is not unusual for lupous nodules to recur.

We must here digress for a moment, in order to lay stress on the treatment of isolated lupous nodules, the first stage of common lupus. These may be more or less deep-seated. They are situated sometimes in the scars of ordinary lupus, which have been treated in the manner just described, sometimes in the healthy skin. They seldom occur singly, several being usually scattered around the lupous patches. When the nodules are sufficiently near each other, they must be treated as a single infiltrated patch, and the method previously indicated should be followed. In the case of definitely isolated nodules, a screened apparatus can be used, so as to intercept the slightly penetrating rays, leaving only those which are very penetrating. It will then be sufficient to leave the instrument in contact for a period long enough to produce severe inflammation of the tissues. Deep destruction will thus be brought about, and will influence all the nodules. But as this treatment is very slow and sometimes unsuccessful, it is much simpler to destroy these small foci by galvano-cautery, or, if they are larger, by curetting, afterwards applying radium. The double operation will considerably hasten the cure, and result in a satisfactory scar. This is the method we employed in the case of the patient just mentioned, and in a certain number of analogous cases. We consider this therapeutic combination very effective. Certainly Finsen treatment alone cures

these lesions very well, but it needs long and frequent exposures. Scarifications used alone are painful, the operation must be frequently repeated, and the treatment is protracted. Moreover, caustics and cauterisation sometimes give rise to disfiguring scars. In radium, applied after the galvano-cautery, it seems that we possess a more rapid method, which is followed by good cicatrisation. Generally speaking, radium holds an important place in the treatment of lupus vulgaris, notwithstanding the advantages, in individual cases, of cauterisation, scarification, Finsen treatment, X-rays, etc. It may also be very valuable when combined with other therapeutic agents. Of course one sometimes meets with refractory or relapsing cases, very extensive and grave in character, which no treatment would cure, and in face of which one is always more or less helpless. The latter observations also apply to other forms of cutaneous tuberculosis.

2. **Chronic lupus erythematosus.**—Radium has given some very satisfactory results in this exceedingly refractory disease, for which we possess scarcely any effective remedies. These can, however, only be obtained by means of fairly strong doses, especially when applied far beyond the limits of the lesions. This is a rule on which we cannot too strongly insist, since relapses or fresh outbreaks always occur at the periphery of the scars. It is advisable to warn the patient of these relapses, the commencement of which is shown by slight pruritus, as they should be treated as soon as possible. When the points which seem threatened with relapse are small, we usually destroy them by means of the galvano-cautery, and treat them afterwards with radium. The use of strong doses is undesirable, because the inflammatory reaction leaves rather marked scars, the appearance of which may be subsequently spoiled by telangiectases. Moreover, they are often very light, smooth, and shiny, and do not always satisfy the patients, who, not understanding the gravity of the lesion, only consider its appearance from an æsthetic point of view. From a purely medical standpoint, the results are often very satisfactory.

A patient, aged 34, was sent to us by Dr. de Beurmann for lupus erythematosus of the nose and ears following chilblains, which had existed for seven years. Scarifications had had no effect. We applied apparatus No. 6 for two hours on each place, and a month afterwards No. 15 for the same period. After the inflammatory reaction, which was rather severe, had subsided, the lupus erythematosus gave place to a healed cicatricial surface.

Another patient, aged 22, was attacked by chronic lupus erythematosus of the external half of the left eyebrow. A few points

still existed at the periphery of the scar following radium treatment. They were destroyed by galvano-cautery, and then again subjected to radium, and the cicatrix has since remained sound.

A young girl had several patches of fixed lupus erythematosus of the cheeks and nose, which were treated by radium from November 2nd to 14th, 1906, a different method being used for each side of the face. On the nose and left cheek we used applicator No. 14 for ten hours; for the right cheek, hypodermic injections of radiferous water. The injections were ten in number, the solution being 1 mg. of pure radium bromide to 1 litre of water; each cubic centimetre, therefore, containing a millionth of pure radium. The quantity injected was 8 to 10 drops on each occasion. On the left side there was very sharp reaction with destruction of the tissues, followed by gradual repair. On January 16th the scar was excellent, but on June 22nd a relapse occurred at the periphery of the lesions. There was no visible reaction on the right cheek, but diminution, followed by disappearance of the erythema of the patches, which was replaced by a white scar. When we saw the patient on June 22nd the healing on the right side was well maintained, whilst there was relapse on the left.

This is a particularly interesting case, since it seems to show the superiority of treatment by injection, but it can possess no value unless it is confirmed by other examples of the same kind.

We have only used radium for the chronic forms of lupus erythematosus; the aberrant forms should be treated with weak doses, with the object of relieving the congestion, and not of producing inflammatory reaction.

3. **Lupus vulgaris of mucous membranes.**—The treatment of lupus of the mucous membranes by radium deserves serious consideration, since they are difficult of access by other methods, especially in the case of the conjunctiva. Radium apparatus, on the contrary —and this is one of its principal advantages—can be adapted to the different shapes of the diseased areas; moreover, its use is valuable here on account of its property of neutralising congestion. We have been enabled to obtain satisfactory results in several cases of lupus of the conjunctiva, owing to this double advantage, sometimes even in spite of very weak doses. It is, however, necessary that the exposures be short, for the mucous membrane must not be too much irritated, and the region is one which would not bear prolonged applications. There are flat applicators, such as No. 13 in our table (pp. 46, 47), containing pure radium, which are suitable for the conjunctivæ; the exposures should be frequently repeated.

In the case of one of our patients, aged 18, treated in Dr. de

Beurmann's clinic for a lupus of the upper and lower palpebral conjunctivæ, a total application of half an hour was sufficient to bring about a cure. Apparatus No. 13, covered with rubber, was applied for three days in succession, to three places of the upper eyelid, and two of the lower, ten minutes on each place. Slight inflammation of the conjunctiva followed, and then very marked alleviation, with great improvement of the palpebral swelling which had previously existed. Three weeks afterwards we made a second course of applications similar to the first, and the cure then obtained has been maintained for a year.

Another of our patients had a scrofulous cicatrix which radium succeeded in levelling, and also a lupus erythematosus of the lower eyelid, with chronic inflammation of the conjunctiva. The lupus was treated with the same apparatus, and for the same length of time, as in the foregoing example. The healing of the conjunctiva, which was obtained without difficulty, has lasted for eighteen months. These instances have been confirmed by a sufficient number of other cases to enable us to state that radium treatment seems superior to other therapeutic agents in the case of the conjunctival mucous membranes.

4. **Lupus verrucosus.**—The action of the rays is here very marked. In this form, as in ordinary lupus, it is necessary to act energetically, after having removed the crust covering the lesion by scraping, or by fomentations. Verrucous lupus is somewhat refractory to treatment, and often requires several courses of applications. The resulting scar should be carefully watched, for we have several times seen lupous nodules appear in the sclerotic tissue. In such cases the destruction of the nodules by electro-cautery, followed by fresh radium exposures, has brought about a permanent cure.

Amongst the many patients we have treated, we will cite the case of a man who presented a patch of warty lupus on the dorsal surface of the right hand. Apparatus No. 7 was applied on two occasions, for two hours and a half each time. Normal reaction ensued, only lasting a short time; the lesion, however, still had a verrucous character which necessitated a second series of applications of one hour on five consecutive days. After this it disappeared almost entirely. Three months later, however, the skin assumed a slightly thickened, reddish appearance, which indicated a relapse. Apparatus No. 1 was then applied for three hours, distributed over three days. The cure is now complete, and has lasted for a year.

We also treated with the same success a patient who presented a verrucous lupus of the metacarpo-phalangeal joint of the left thumb. This had been treated by galvano-cautery and scarification, but without

permanent benefit. We applied No. 7 for three days, an hour a day. Very severe reaction ensued, followed by a crust, then by a fissure, and finally by a small scab in the centre. Six weeks after the beginning of treatment, there was a surface of excellent appearance, on which we thought it well, by way of precaution, to apply the same apparatus for a second series of two hours.

Another case, no less interesting, was that of a baby of thirteen months, whom Dr. Tansard sent to us for verrucous tuberculosis of the internal border of the left foot, which had made its appearance at the age of three months. The general health of the child was bad. Apparatus No. 7, enveloped in rubber, was applied for ten hours, distributed over ten days. Fifteen days after the last application the warty appearance was gone and the reactive stage had set in. We now observed a slight, whitish scab, with œdema of the tibio-tarsal articulation. As this swelling was slow in disappearing, and caused us some anxiety, we advised the parents to take the child into the country. Its general health then improved, the infiltration disappeared, and the cicatrised surface looked very satisfactory. Verrucous lupus often requires stronger doses than ordinary lupus. More or less penetrating rays should be used, according to the degree of infiltration, but always in sufficiently large doses to produce very marked destruction of the tissues.

5. **Scrofulodermia.**—Radium may be of great service in this condition, but only in certain forms, which must be carefully selected. Subcutaneous lymphatic glands, isolated, or, still better, aggregated, can be treated by "surpénétrant" rays, emitted from a very powerful radioactive source. For instance, an apparatus giving a "surpénétrant" radiation of 4,000 to 5,000, through a screen of 2 mm. of lead, will be sufficient to relieve the congestion of lymphatic glands, to a certain extent, without irritating the surface, if the time of exposure is not too long. If the glandular masses affect the derma, and are ulcerated (ulcerating scrofula), or if there are indolent ulcers, with detached peripheral edges, isolated or aggregated, attached to each other by bridges of epidermis, and presenting sinuses and pockets, the surfaces must first be cleaned up; it will then be necessary to open the abscesses and to empty and curette them; to remove the detached edges and the bridges of epidermis; to open the sinuses—in short, to lay everything bare; and this first operation, facilitated by cocaine, need not be very painful. Applications of radium should then be made on the surface thus prepared, according to the methods previously described for ordinary ulcerating lupus. If the tissues are deeply infiltrated and ulcerated, radiations of great intensity, without screens, should be used with the object of destruction, after which recourse may be had to

" surpénétrant " rays, in order to relieve the deep-seated inflammatory congestion. The reaction produced will often be followed by satisfactory repair. There should be further courses at widely spaced intervals, according to the gravity of the lesions and the results that are obtained.

Scrofulodermia frequently gives rise, by its own evolution, to cheloidal scars and prominent fibro-sclerotic bands. The power of reducing and partly softening these irregularities of the surface is another advantage possessed by radium, of which we have spoken at length in a special chapter. The rays produce this result by acting on the tuberculous tissue.

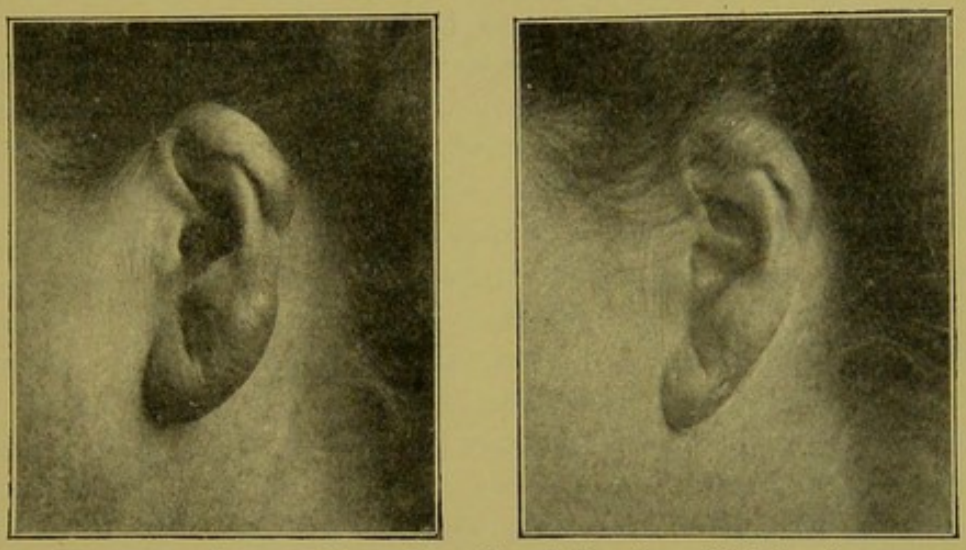
In May, 1905, we treated a patient, aged 25, who presented a bilateral cervical adenopathy with suppuration. He had also a somewhat extensive nodular lupus of the left foot, and a tubercular infiltration with an ulcerated centre below the knee. The lupous patch on the foot covered the whole upper surface of the great toe, and extended to the anterior internal portion of the metatarsus. This red, crusted surface presented ulcers, detached portions with bridges, prominent nodules, and brownish lupous infiltrations.

Exposures of thirty minutes, with the interposition of cotton-wool 1 cm. thick, were made three times a week, with applicators Nos. 2 and 3 (p. 7). Each place was treated for about three hours in all. After reaction, with crust formation and partial cicatrisation, fresh applications were made, and in about eight months the scar seemed permanent. The patch of tuberculous infiltration on the knee was the size of a five-franc piece; it was purple in colour, of thick and doughy consistency, and presented a rather deep sanious crusted ulceration in the centre, over a surface about 2 square cm. With this exception, there was no solution of continuity. Apparatus No. 2 was applied for five hours on the ulcerated portion, after the interposition of a cotton-wool pad, half an hour at a time, every other day. This dose produced violent inflammatory reaction, from which at one time another ulcer resulted, deeper and larger than the first. The treatment of the non-ulcerated peripheral parts was to be undertaken after cicatrisation of the centre. But, to our surprise, very perceptible improvement occurred at the periphery, at the same time as the repair of the centre; and this was so complete that the whole patch—the peripheral as well as the directly affected parts—was transformed into cicatricial tissue, which has not since relapsed.

This result shows that the rays can act by peripheral diffusion, and that in some cases—although they are rare, it is true—they reduce the tuberculous infiltrations to a certain extent, without producing

any visible destruction. It would seem, indeed, that while in ordinary lupous lesions it is absolutely necessary to destroy the granuloma, for forms of tuberculosis where congestion seems to be the predominant feature, the special properties of radium may have some action on the vascular system. We have already seen that it can relieve inflammatory lupus of the mucous membranes, and the foregoing example is another instance of this. The next case is no less interesting in this connection.

A lady, aged 47, was sent to us by Dr. Bernheim for diffuse tuberculous infiltration of the lobule of the ear (Figs. 61 and 62). The lobule had increased in size in every direction ; it was elongated, almost doubled up, shiny, and œdematous. Both surfaces had a reddish-purple



Figs. 61 and 62.—Diffuse tuberculous infiltration of lobule of ear.

inflammatory aspect. The growth had appeared thirteen years previously, and since then the lobule had continued to enlarge. A diagnosis of a tuberculous infiltration was inevitable, and, by a process of exclusion, this had also been made in a clinic at the St. Louis Hospital. Applicators Nos. 3 and 6, screened by $\frac{6}{10}$ mm. of lead, were used by " cross-fire " for six hours ; one on the anterior and the other on the posterior surface of the ear. As the result of this exposure the congestion was relieved and the lobule became much smaller.

6. **General indications.**—We cannot indicate the action of radium on all forms of local tuberculosis, or attempt to state any definite conclusions. We have confined our investigations to a few types ; moreover, in so difficult a subject, many years of study would be required in order to establish permanent results. We have, however, been able to formulate from our own experience some general indications, the principal of which are as follows :

The treatment of tuberculous lesions chiefly requires powerful action, both wide and deep, and long-continued and careful supervision of the resulting scars. There does not appear to be any special selective action in these cases which would permit of weak doses, as in the radium treatment of other neoplasms. Tuberculosis of the mucous membranes, and certain infiltrations where congestion is very marked, can, however, be improved by the influence of radium in relieving congestion, without any very perceptible inflammatory reaction. In most cases the applications need include only a short period of treatment (two or three days), which would be possible even for patients living at a distance. The subsequent therapeutic reaction can be easily kept under supervision. The shape of the apparatus may correspond to that of the parts treated, and this is a very material advantage. As to the permanent value of the results obtained, time alone can show this, on account of the possibility of relapse; but they are inferior in every respect to those which we have mentioned in the case of carcinomata, cheloids, and angiomata. But, considering the numerous drawbacks which so often accompany the methods at present in use, and the particularly refractory and even incurable character of certain clinical forms of lupus, the results which we have so far obtained certainly give radium a place among the most valuable therapeutic agents, in spite of the reservations mentioned. It would be premature to try to establish any comparison between radiumtherapy and other therapeutic measures. We meet with advantages and drawbacks, according to the particular case, whether we resort to dermatological surgery on a small scale, to caustics, or to larger surgical operations under chloroform, to X-rays, radium, or the Finsen treatment. Moreover, most of these methods are in a transition period of development, and have not yet reached maturity. It would seem, however, that some of them are suitable for certain forms of cutaneous tuberculosis, and that the combination which we have employed is, in the majority of cases, the best line to pursue.

Lastly, it is our opinion, after the observation of 150 cases (the older cases dating back four years), that while radium can render good service, in varying degrees, in all forms of cutaneous tuberculosis, it holds a place of its own in the treatment of vegetating lupus, tuberculous ulcerations, lupus of the conjunctiva, chronic lupus erythematosus, lupus verrucosus, and certain infiltrations and prominent disfiguring cicatrices following scrofula.

We cannot conclude this chapter without laying stress on some experiments of another kind which have been already mentioned—those relating to the action of radium in radiferous or radioactive

solutions injected into lupous tissues. We have tried this new plan in several cases. The doses are very weak, and the liquid is probably very quickly absorbed, but they contain an element which is wanting in radiations of the ordinary apparatus—namely, the emanation. Now this has an action which possesses definite bactericidal properties. As we have already said in a general way, and with reference to other diseases, by injecting certain insoluble radium salts in emulsion in substances which are only slightly absorbed, it is possible to obtain longer contact of the salt with the lupous tissues, and more powerful action both from the radiation and from the emanation itself. Our clinical experiments with radiferous and radioactive solutions have given us encouraging results. In a case of lupus vulgaris with nodules, a certain amount of improvement took place. In another instance of chronic erythematous lupus, with multiple foci, we observed that the patches treated by injection had disappeared without relapsing, while the others, for which the ordinary method was used at the same time, had recurred. There is here an opening for new methods, which will be found useful when the raw material has become more plentiful.

CHAPTER VIII

THERAPEUTIC RESULTS (Continued)

VI. ANALGESIC ACTION OF RADIUM PRURITUS, NEURODERMATITIS, ECZEMAS

In this part of our work we shall deal with some forms of pruriginous inflammatory affections of the skin; a subject which had been but little studied before we began our researches. Radium was considered useful only for lesions of small extent, and therefore the idea of employing it for dermatoses on a large scale had hardly been thought of. Some small isolated patches of psoriasis and eczema had been successfully removed under its influence; but operators were still far from regarding it as useful for general therapeutic purposes. Indeed, in 1905, radiumtherapy could scarcely have been put forward as a means for treating the whole of an eczema, for instance. Even if the theory of the improvement of these dermatoses by radiumtherapy had been admitted, the imperfection of the instruments available at that time would have rendered the application of the theory to current practice impossible for large lesions. This is why, after the early communications of Lassar and Blaschko, this branch of the science remained in the background. At the present time, after having treated 160 cases coming under this category in the course of about four years, we think that it may render very appreciable service in clinical practice. Amongst the causes which lead to improvement, the alterative properties and power of relieving congestion possessed by radium may again be mentioned; but its analgesic action seems to play the chief part. It is therefore important in the first place to make the reality of this property clear, by showing the action of radium in pruriginous and painful diseases into which the inflammatory element only enters to a small extent. We shall therefore divide this chapter into two sections:

1. Pruritus, neuritis, neuralgias.
2. Inflammatory pruriginous dermatoses.

I. LOCALISED PRURITUS, HYPERÆSTHESIAS, NEURITIS, NEURALGIAS

In previous chapters we have had occasion to lay stress on the analgesic effect of radium. One of the first results obtained in painful epitheliomata and cheloids is relief of pain. The present chapter will

deal more fully with this property of the rays. With local pruritus and cutaneous hyperæsthesia we have grouped neuralgic and other pains which are beyond the general scope of our division, but which are amenable to this analgesic action. The results obtained by one of us (1905–6) on neuralgias, neuritis, painful attacks of acute gastritis, gonorrhœal and rheumatic arthropathies, as well as similar results recorded by others, led us to investigate this question of analgesia. Some of these have since been published by us, particularly in a communication made to the 9th Congress of Medicine (Paris, October 16th, 1907), in collaboration with Dr. de Beurmann. Moreover, many cases were found in the literature of the subject which corroborated our statements. A. Darier, in 1903, mentioned the relief of pain in cases of subacute iritis, irido-cyclitis, and orbital neuralgia. Foveau de Courmelles presented a case of rapid cure of refractory facial neuralgia at the Congress of Pau in 1904, and had previously, in 1902 and 1903, shown the alleviation of pain produced by the use of radium. Raymond and Zimmern, at the Académie de Médecine in 1904, showed four tabetics in whom there had been definite relief of girdle pain, gastric crises, and lightning pains. Soupault, on November 11th, 1904, at the Société Médicale des Hôpitaux, showed not only the power of relieving congestion, but also the analgesic effects of radium in articular rheumatism and various other articular diseases. H. Dominici, in 1907, working with Dr. Ertzbischoff, noted in Professor Albarran's clinic three out of five cases of painful tuberculous cystitis which showed marked improvement, lasting several weeks. He also recorded the cure of two cases of intercostal neuralgia and two of sciatic neuralgia, and, with Gy, confirmed and amplified the investigations of Soupault in chronic articular rheumatism and gonorrhœal arthritis. Bongiovanni in 1907 published four cases of neuralgia and two of facial paralysis, successfully treated. Besides these positive cases, which incontestably prove the analgesic action of radium, there are a certain number giving negative results, especially with regard to deep-seated pain. We agree with the very sensible conclusion of Barcat and Delamarre, in their paper on the radium treatment of neuralgia and neuritis, read at the 1st French Congress of Physiotherapy (April 22nd, 1908), that improvement of the technique will give more numerous positive results. Our own cases amount to about thirty. We will only give one example of each kind of disease.

1. **Pruritus ani.**—It is well known that localised pruritus of the anus and vulva is often very severe and refractory. In this affection we have several times obtained very successful results with radium.

A patient, aged 36, was sent to us by Dr. Hallopeau with an anal pruritus which had begun twelve years before. All the methods of treatment previously tried had failed. The anus and perineum, in consequence of scratching, were the site of slight transitory inflammation, but there was no lichenification. The pruritus was slightly external to the anal orifice. Apparatus No. 16, simply enveloped in rubber tissue, was applied for a quarter of an hour to each side of the anus and the perineal region. This application reduced the inflammation. Eight days afterwards No. 1 (with $\frac{1}{100}$ mm. of aluminium) was applied for ten minutes to the anus, the buttocks having been previously firmly drawn back. The itching diminished, and disappeared within a fortnight. The patient having felt a slight return of the trouble in the course of the following month, apparatus No. 2 was applied for fifteen minutes, wrapped in $\frac{1}{100}$ mm. of aluminium. The itching was permanently allayed, and has not since returned, although the treatment took place fifteen months ago.

2. **Pruritus and hæmorrhoids.**—Anal pruritus often has a hæmorrhoidal origin, and the action of radium on the blood-vessels can be made use of for the hæmorrhoids, whilst the analgesic action is exercised on the pruritus and accompanying pain.

A man, aged 48, was attacked by very severe pruritus ani at periods corresponding to the hæmorrhoidal congestion. He had been suffering from attacks of internal hæmorrhoids for about twenty years, and pruritus was always excited on these occasions. For several years it did not entirely disappear between the attacks, so that scratching, unconscious during the night, led to frequent waking and insomnia, with excoriation and anal fissures.

The radio-uterine apparatus, described further on, was well adapted to this region, since, by means of its stem, it could be made to act upon the whole mucous membrane of the anus, and by its cup it could be applied flat on the radiating muco-cutaneous folds of the anal orifice. This apparatus, after being wrapped in a lead sheath of $\frac{5}{10}$ mm., which was itself covered with rubber, in order to intercept the secondary rays, was introduced high up into the anus, in such a way that the cup was adapted to the orifice. It contained 9 cg. of radium sulphate, with an activity of 500,000, and was left in place for fifteen minutes, ten days in succession. Thus the entire pruriginous hæmorrhoidal region was affected by rays which were at once sufficiently penetrating —since hardly any but "surpénétrant" rays were emitted by the apparatus—and sufficiently active, since the thickness of 0·5 mm. of lead allowed hard β rays to pass in large numbers. The itching was considerably relieved in the course of the following month. No super-

added inflammation of the surface was produced. A second series of applications was made a month later in the same way, but the instrument was left in place twenty minutes instead of fifteen. The pruritus then disappeared. The case is too recent for any final conclusion to be drawn as regards the hæmorrhoids; but the attacks, which used to occur at least once a month, have ceased for the last three months. The double action of radium, at once decongestive and analgesic, seems admirably suited to the treatment of these lesions, especially those accompanied by pruritus. This example also shows the various uses to which the radio-uterine apparatus may be put, although it was originally intended for the uterus only.

3. **Pruritus vulvæ.**—A lady of '72 had suffered for ten years from pruritus of the perineum and vulva, which nothing would alleviate. She could not bear a sitting position for long, and her nights were broken by wakefulness caused by the intense desire to scratch. There was no vaginal discharge. The labia majora and surrounding regions were thickened, and the perineum and ano-perineal region red and inflamed. An application of apparatus No. 2, three minutes on each place, repeated for three consecutive days, relieved the painful sensations, and especially the nocturnal itching. Eight days afterwards a second course of applications, similar to the first, was followed by remarkable, though gradual, improvement. The patient could remain seated for a longer period without feeling pain, and the itching at night had disappeared. By degrees the improvement became more marked, and ended in the disappearance of all the symptoms. This cure took place a twelvemonth ago. The extreme simplicity of the treatment, compared with the importance of the results obtained, shows plainly the services which radium is capable of rendering in such cases. It meant new life to the patient, whose old age was made miserable by the pruritus, as well as recovery of her general health, which was giving way.

4. **Hyperæsthesia following herpes zoster.**—The hypersensibility being superficial in these cases, it would appear especially necessary to have recourse to very weak rays; but, while avoiding the least inflammation, it is advisable to make the action of the rays last as long as possible. It will be found better, in practice, to suppress the α and some of the β rays. We have several cases in which this mode of treatment has been very successful.

A lady, aged 35, came to consult Dr. Wickham, in April, 1905, at the medical and surgical clinic of Drs. Cazin and Banzet. She was in a curious state; her eyes were dilated by pain, she was holding her collar away from her neck, could hardly speak, and

came in supported by two persons. It was a case of hyperæsthesia of the whole cervical region, following herpes zoster. The cutaneous elements of the zoster had almost completely disappeared. There remained, however, an aggregation of reddish zones. Breathing on the region was sufficient to excite a burning sensation, and the light contact of a finger was unbearable, but pressure did not produce deep-seated pain.

Apparatus No. 4 (p. 7) was applied, not without difficulty, for ten minutes in six different places, an hour in all. After this treatment the patient no longer felt anything unusual. She seemed much astonished, and could hardly believe that such a result had been obtained. This sudden cessation of pain was very remarkable, and it seemed at first that it must be attributed to suggestion. However that may be, the patient dressed without difficulty and walked away by herself, without dragging at her collar, or being supported by her friends. Two days afterwards the lady returned, lamenting the recurrence of her trouble. There had been twenty-four hours of almost complete relief, after which the hyperæsthesia had returned again. It was, however, much less severe, and the sensations now experienced were those of tingling rather than burning. Another course, identical with the first, was followed by rapid alleviation, which lasted for twenty-four hours. Then the hyperæsthesia reappeared, but this time was still less marked than before, and this occurred after each series of applications until the cure was complete. There were in all eight exposures, with intervals of two days between them. There was no return of the symptoms after the fifth, and those which followed were made by way of precaution. Since then the patient has been completely free from trouble. It should be noted that there was not the slightest surface inflammation, during treatment or afterwards.

In this case it would be difficult to overlook the analgesic effect produced by radium, and it cannot be attributed to suggestion, since the repetition of the same applications led to the same results on each occasion. The apparatus, selected intentionally, had a screen of $\frac{1}{10}$ mm. of aluminium. A layer of cotton-wool was also interposed, so that the radiation was composed of medium rays, and was well suited to the treatment of the condition. Moreover, the application in six different places gave a sufficiently extensive total action. This is an unusual form of hyperæsthesia, on which the rays had a very soothing effect.

5. **Frontal dermatalgia.**—A lady came to consult us on July 6th, 1908, with the following diagnosis from Dr. Brocq: "Patches of frontal dermatalgia without definite cutaneous lesions, with slight chloasma

of forehead, and some foci of telangiectasis, strongly marked in a neuro-arthritic subject, for several months pregnant, in whom the patellar reflexes are very slightly increased." The hyperæsthesia affected the whole of the frontal region. Pressure provoked momentary increase of the pain, which, however, arose spontaneously, had the character of a burn, and lasted for whole days. The suffering was very severe and, indeed, almost intolerable. It had commenced about two months previously.

Apparatus No. 2, with $\frac{1}{100}$ mm. of aluminium, ten sheets of paper and one of rubber, was applied for five minutes on each place, for six consecutive days. On August 15th, the patient, who had returned to her home in the country, wrote to us as follows :

"During the first four days after treatment, from July 12th to 16th, there was slight improvement, for the pain in the forehead did not last the whole day, as before, and was less severe. From the 17th to the 20th acute pain occurred, which made me fear a return of the long and severe attacks, but it disappeared instantaneously. There seemed to be a struggle between the disease and the stored-up rays. The pain has not returned since that date, and I think that the rays have at last triumphed."

Six months afterwards we again asked for news of the patient. This was her second letter :—

"On August 16th a fresh outbreak occurred [there had therefore been complete freedom from July 20th to August 16th], but the pain was only intermittent. In any case it had never been so severe or lasting as before treatment, which certainly brought great relief. It would, perhaps, have been desirable to make a fresh application of radium in August, but we feared the fatigue of the journey. The confinement took place normally on October 30th. The pain has not recurred since that time, and the brown spot on the middle of the forehead has almost entirely disappeared."

In this case the effect of pregnancy must be taken into account. Nevertheless, in spite of the share which must be attributed to parturition in bringing about this cure, which at present appears to be permanent, we can hardly fail to recognise the analgesic action of the radium, which was partial for a time, complete for nearly a month, and was produced immediately after treatment and before the confinement. Moreover, the treatment was insufficient, and at least two more series of applications should have been made. It must be remarked that no surface reaction was produced, and no additional pigmentation occurred. On the contrary, the chloasma disappeared.

6. **Leprous neuritis.**—In the clinic of Dr. de Beurmann, at the St. Louis Hospital, Dr. Degrais has had the opportunity of treating several cases of leprous neuritis. This disease appears to be specially

suited to radium treatment, for in each of the cases undertaken the results have been similar to those obtained in the following case:

A man, aged 21, had been suffering from leprosy for four years; he complained of pains on the external surface of the thighs, tibia, and feet. They continued night and day, but were worse at night, being so severe that the patient could not sleep. He also suffered from severe pain in the back of the hand and lower half of the forearm. Application was made of apparatus No. 1 ($\frac{4}{100}$ mm. of aluminium) for ten minutes, on as many places as were necessary in order to cover the whole of the parts affected. So marked was the diminution of pain that the patient was able to sleep the first night after the applications, and by degrees the pain entirely ceased, and has not recurred during the last year and a half.

Our investigations, however, have not been confined to such manifestations of leprosy as these. We have treated visible lesions, and the results obtained in the reduction of lepromata, although recent, lead us to hope that radium may afford valuable help in getting rid of the characteristic disfigurement of the face.

7. **Intercostal neuralgia.**—This affection involves more deeply seated pain, and the results of radium treatment, although generally successful, have been found less constant and less complete than those mentioned above. A lady was suffering from extremely painful neuralgia of the submammary intercostal region. The respiratory movements were very painful, and coughing or sneezing occasioned acute twinges. Apparatus No. 1, with a screen of $\frac{8}{100}$ mm. of aluminium, was applied for ten minutes, on as many of the places as seemed necessary. The relief was very marked. Three days afterwards treatment was resumed with the same apparatus and length of exposure, and repeated once more three days later. The last application was followed by complete and final disappearance of the pain.

8. **Sciatic neuralgia.**—Two patients suffering from sciatic neuralgia, treated in 1905, were considerably relieved by radium. One of these cases deserves special notice, for the technique adopted served as the basis for our invention of the "cross-fire" system. It was that of a workman who could only come three times a week to undergo treatment. He came from a great distance, partly on foot, and partly by omnibus, and was much fatigued by the journey. The conditions under which the treatment was carried out were therefore quite unfavourable, and yet decided improvement was obtained. The patient —who at the time of his first visits was hardly able to walk—certainly had much greater freedom of movement after twelve applications. Feeling better, he gave up coming on account of the loss of time. The

neuralgia had continued for two years, and was aggravated by standing or walking. The difficulty was therefore to obtain deep action with sufficiently numerous and penetrating rays, without irritating the skin. We adopted the following technique :—

(1) Interposition of a pad of compressed absorbent cotton-wool, wrapped in a double layer of gold-beater's skin, and forming a screen 1 cm. thick. By this means the α and soft and medium β rays were intercepted, and the apparatus could be left longer in position.

(2) Simultaneous application of several instruments (Nos. 1, 2, and 3, p. 7).

(3) Application of each apparatus for a time less than that sufficient to produce surface reaction—*e.g.* five minutes for No. 1.

(4) Change of position of each apparatus, with the double object, first, of covering the largest possible surface of the painful region, particularly at the special neuralgic points ; and then of concentrating at a depth, by means of very penetrating rays, an action corresponding to the whole length of application of several instruments.

In order to make this clearer, let us suppose a painful region of 70 square cm., which can be covered by three or four applicators. Each instrument, being left in place for only five minutes, will only act on the surface of the skin for this short period, whilst at a depth the length of action of very penetrating rays will be equivalent to five times the number of the instruments—that is, fifteen to twenty minutes. An exactly similar process enabled one of us, at the same date, to arrest very painful attacks of chronic gastritis. An application of one hour was distributed over the whole of the epigastric region, in such a way that the radiation came in contact with each place for five minutes only. These cases clearly show that Dr. Wickham's researches were already (in 1905) leading to the use of very penetrating rays, and the interception of weak rays, and that he had put into practice the idea of filtration, obtaining it both by means of screens and by the use of the tissues themselves as filters. It was with this idea that we afterwards studied together the action of filters, especially those of rubber-covered lead,* and established the method of "cross-fire." At the present time, for various regions which allow the instruments to be applied opposite each other, and which are the site of deep-seated pain, we use medium screens of $\frac{1}{10}$ to $\frac{5}{10}$ mm. of lead, changing the place of the apparatus when continuance of the exposure would be likely to produce inflammation. We think that very penetrating radiations, composed of a majority of γ rays, may be used with advantage when the painful parts have a limited surface, but the

* *See* "Glaucoma," p. 277.

treatment is less practicable when it is necessary to cover a large surface, the length of application for each instrument being necessarily greater.

9. **Articular pains.**—These often respond well to radium treatment. Soupault had grasped the value of radium in articular inflammation when, at the Société Médicale des Hôpitaux, in 1904, speaking of the analgesic properties of radium, he said that articular affections having a chronic or subacute course, such as gonorrhœal arthritis, seemed to benefit greatly by radium treatment. We have ourselves collected several cases which confirm this statement. One, which dates back to June 17th, 1905, is of special interest.

A working painter, aged 40, presented a gonorrhœal arthritis of the left index finger, of the spindle-shaped type of Professor Fournier. The patient could not bend the finger, and the arthritis caused him great pain. He also suffered from chronic gonorrhœa. Apparatus No. 3 (p. 7) was applied for three minutes, on four different places around the inflamed joint. The patient said that he felt relief from the time of this first application. There were afterwards nine similar exposures, distributed over three weeks. These only produced slight cutaneous reaction. The swelling perceptibly decreased from the second week onwards; the patient no longer felt pain, and could bend the finger slightly. Since then, the interesting works of Gy and Dominici have furnished a large number of instances in which the analgesic action of radium on articular pains has been abundantly proved.

The foregoing facts clearly show the benefit which can be derived from this property of radium. Owing to the improved instruments and technique now in use, radium can be used to relieve pruritus and accessible local pains, whether superficial or deep-seated, provided that they are not produced by general or central causes, and that total radiations of great intensity or very penetrating rays are used. The choice of technique must always depend on the depth to which it is necessary to penetrate, the care that must be taken not to injure the skin in any way, and the extent of the surface to be treated. It is better to select large apparatus of great activity, making short and frequent exposures without a screen, if the lesions are superficial and extensive; longer applications with a medium screen if they are deeper and extensive; and, lastly, very long exposures, with extremely dense filtering, for deep-seated localised lesions. However, in some cases, appreciable benefit may be obtained from instruments or "toiles" of weak activity, left in position for long periods with light screens.*

* *Note by Dr. Wickham.*—MM. Teulière and O. Claude have recently obtained good results in gonorrhœal arthritis by enveloping the joint in radioactive mud. This mud is the residuum of non-silicious uranium ores. It has very little radioactivity.

II. NEURODERMATITIS, LICHENIFICATION, ECZEMA

This section is of special interest, since it proves, contrary to the opinions of the earlier observers, that radiumtherapy can be employed for surfaces of large extent. It indicates a new and very appropriate method of using total radiations of great quantitative value, particularly when composed of weak and medium rays; and, lastly, it shows that, by means of special methods, these rays may be used effectively without producing the slightest surface reaction, even on inflamed tissues, which are particularly irritable and sensitive. These are the chief points brought out by our investigations. We will now choose one or two cases out of each group. For the sake of keeping to the order in which we undertook these studies, we shall speak first of neurodermatitis, then of chronic lichenified eczemas, and lastly of acute eczematous eruptions.

1. NEURODERMATITIS

We first began to study the action of radium in pruriginous inflammatory dermatoses on patches of localised lichenoid eczema (the circumscribed neurodermatitis of Brocq). In all the cases which we have treated, the results have been clearly marked from the time of the first applications. Some of them have not relapsed after healing, in spite of the distant date of their treatment; others, eight months to a year afterwards, have shown some points of relapse, which have quickly disappeared when again subjected to radium. Sometimes, however, this recurrence is very refractory, as the following instance will show.

A man of about 70 had suffered for many years from itching in the fold of the right buttock, at the junction of the posterior surface of the right thigh with the buttock, a region exposed to friction in the sitting position. Various methods of treatment had been tried, with no result beyond transitory improvement. This was a patch of circumscribed neurodermatitis without perceptible thickening of the skin, but extremely pruriginous. The surface was brownish red, and slightly quadrillated.

Apparatus No. 17 was applied, without a screen, four times for twenty minutes, in the course of fourteen days. The pruritus soon ceased, and shortly afterwards all traces of inflammation had disappeared, the skin only remaining rather more deeply coloured than normal. The cure was maintained for about nine months, and this result is most remarkable when compared with the inefficiency of the therapeutic methods employed during the previous eight years. After this long period of freedom from itching, a slight relapse occurred in the

centre of the former lesion. The patient consulted a specialist, and after the application of various ointments and plasters the relapse became aggravated, and the old patch formed again. Radium treatment was then resumed, with a screen of $\frac{8}{100}$ mm. of aluminium. The inflammation disappeared by degrees, and for two months no further recurrence has taken place.

We will choose from among our most striking cases two of typical neurodermatitis; one situated on the nape of the neck, the other on the upper internal surface of the thigh.

(1) **Neurodermatitis of nape of neck** (Plate XX).—A girl of 25, sent to us by Dr. Triboulet, had suffered from a neurodermatitis for six years. It occupied the whole region of the nape of the neck, and extended to the scalp, where there were numerous pruriginous papules. This patch, with its clearly marked limits, its thickening, quadrillated surface, and papules excoriated by scratching, was absolutely typical. The itching was very severe. In the lower part of the neck, on the left side, there was another small isolated patch. The treatment was exceedingly simple. Apparatus No. 2 was applied for ten minutes on the large plaque on the nape of the neck, then, after an interval of five days, No. 7 was used twice for three minutes. No. 7 was applied to the small isolated spot for three minutes on three consecutive days, and once only for five minutes to the papules on the scalp. Immediately after the first applications the patient experienced considerable alleviation of the itching. The pruritus then completely disappeared. The whole diseased surface underwent modification, as shown by the lessening of the characteristic symptoms. The skin became softer, the quadrillation less marked, and the shiny appearance disappeared. The lesions continued to improve, so that at the present time, twenty months after treatment, it is impossible to find the slightest trace of the former eruption on the skin.

(2) **Neurodermatitis of thigh.**—A lady, aged 40, suffered from very severe itching on the upper and inner surface of the left thigh. This was a case of the well-known dermatitis of the thigh. No treatment—not even that of X-rays—had effected any permanent alleviation. The diseased surface was very extensive. Apparatus No. 1 was applied for two minutes, six times on each spot, with one day's interval, and there was very marked improvement for five or six months. A relapse was treated by the same method, and the disease appeared to be permanently cured. It should, however, be noted that very pronounced pigmentation, which faded away by degrees, was produced at first.

PLATE XX.—NEURODERMATITIS

PLATE XX

NEURODERMATITIS (p. 252)

FIG. 1.—The various characters of the inflammation are typical, and the chromo-lithograph represents the lesion very accurately.

FIG. 2.—Nothing remains of the neurodermatitis. The skin is absolutely normal.

2. ECZEMA

The reason why radiumtherapy is practicable for eczemas of large extent is because these cutaneous affections may be modified by doses with a weak total radiation, and a very powerful apparatus will furnish them in sufficient quantities in quite a short time—one to five minutes. The following case was easily treated and healed, in spite of its size.

(1) **Chronic lichenified eczema affecting entire surface of both lower limbs.**—A patient, aged 53, was suffering from lichenified eczema of the lower limbs. It began on the right calf, four months previously, with a small patch, which gradually spread until it covered both legs and thighs. The skin formed a thick fold when taken between two fingers; its surface was dry, red, roughened, and quadrillated. It was the site of very severe itching, which prevented the patient from sleeping.

Apparatus No. 1, with a screen of $\frac{1}{100}$ mm. of aluminium, was applied for ten minutes on each place, on two occasions. Very soon afterwards the itching ceased, and the lichenification, which had been maintained and aggravated by scratching, was improved. We had entrusted the use of the apparatus to the patient himself, advising him not to let the applications overlap. Being circular, the instrument left triangular spaces between every three applications. An interesting result was obtained. The diminution of swelling, and depression of each area treated, could be observed by comparison with the intermediate areas, which remained unaltered, and continued to be affected by pruritus. This example undoubtedly demonstrates the value of radium. The places treated were free from congestion, and did not show the least trace of surface inflammation. The treatment was then completed with apparatus No. 4, applied for ten minutes on each area, and the lesions have not reappeared.

We have obtained very successful results in cases in which lichenification had existed for several years. It is well to call attention to this possibility of treating large surfaces, since it has always been thought that the action of radium was very limited, on account of the comparatively small size of the apparatus. This would be true if it were necessary to use very long exposures, but since these need not last more than one to ten minutes, twenty applications will cover very large surfaces, if the instruments are of 20 to 30 square cm. The foregoing case clearly shows this, since two mornings were sufficient for the covering of all the affected parts, and as the apparatus is very easy to handle, the patient was able to treat himself. Moreover, the use of

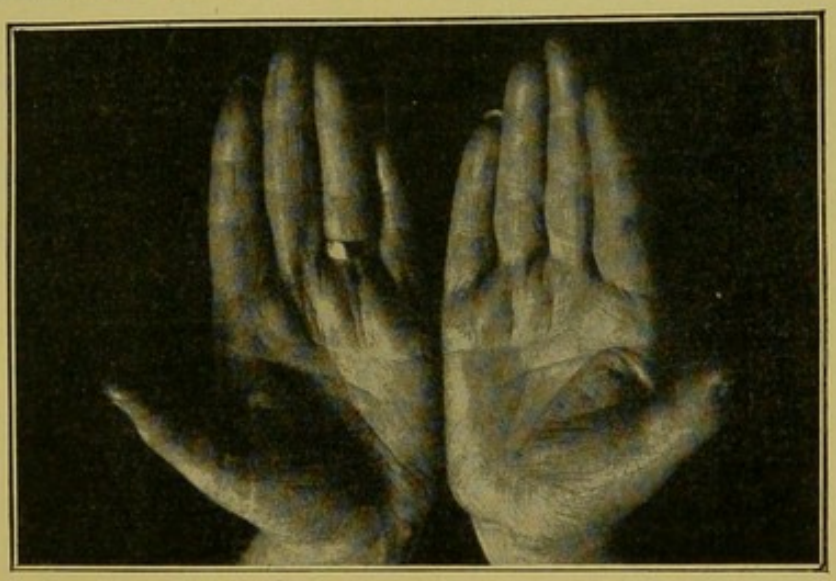
two instruments at once would have enabled us to reduce the total length of the exposures, and the same object could have been attained quite as well by adopting our usual plan, which consists of applying powerful apparatus for three minutes, three days in succession, and making three series, each at an interval of a week. Thus each application would be comparatively short. When the lichenification is very deep, it is advisable, as we shall see, to complete the treatment by one or more series of applications with instruments covered with $\frac{1}{10}$ mm. of lead. The most penetrating rays will influence the deep tissues, their object being to prevent any risk of relapse.

(2) **Chronic eczema of upper limbs.**—Permanent results, and even continuous relief, are generally more difficult to obtain on the hands, and yet in the case of many of our patients occupied in manual work, whose treatment was completed long ago, there has been no relapse. The following are some examples:—

i. A hairdresser came to us with a lichenified eczema of the back of the hands. The eczema had existed for about ten years, and for the last two had been treated at the St. Louis Hospital, but without success. The patient did not conceal his incredulity as to the efficacy of the treatment. He said that nothing could cure him, and that he only allowed himself to be treated because he had a little time to spare. Apparatus No. 1 ($\frac{1}{100}$ mm. of aluminium and a sheet of rubber) was used on each place, for four minutes the first day, three the second, and two the third. The following week there was a second series of three applications, three minutes on each place, with the same apparatus, on alternate days. A month afterwards nothing remained but a little redness of the external surface of the left middle finger, with slight itching. The square apparatus No. 3 was applied for three minutes on the reddest point, and for one minute on some small isolated spots. From that time (March, 1908) the patient resumed his occupation, and although his work necessitates frequent washing of the hands, the cure has been maintained.

ii. A patient, aged 52, suffered from eczema of the palmar surface of both hands, accompanied by severe itching (Figs. 63 and 64). On the right hand the eczema had been present for eight years; on the left the lesions had only appeared a year before. The skin on the right was hard, red, and cracked, and in places covered with scales. There were several painful fissures, so that the patient could not close his hands, and only used them with difficulty. On washing them, the itching and burning sensations were very severe. Various methods of treatment tried at the St. Louis Hospital had failed to relieve his complaint, which made him to some extent helpless.

The radium treatment consisted in two courses of applications with an interval of eight days, for six minutes on each place, three days in succession, of No. 1 apparatus, with an aluminium screen $\frac{4}{100}$ mm. thick, covered with rubber. The object of this light screen was to reduce the number of very weak rays, and to allow of rather longer



Figs. 63 and 64.—Chronic eczema.

action. After the first series, improvement was shown by diminution of the itching and greater softness of the skin in the palmar region; the fissures began to heal, and the fingers to bend more easily. We had decided to undertake a third series, in order to follow up this improvement, but the patient—who was living in the country—informed us that, to his great regret, he could not continue the treatment, on account of an attack of shingles. Having been

cured of this, he wrote to us two months afterwards that the improvement in the eczema had become more and more marked, and that the itching had disappeared. The skin of the palmar region had recovered its normal aspect, and the fingers could be bent freely.

(3) **Chronic eczema of face.**—Eczema in this position is perhaps the most inconvenient and difficult of all to cure by the ordinary dermatological methods, but we shall see that obstinate lesions of long standing yield to radium treatment with extraordinary rapidity, without dressings or any special precautions. One of the most convincing cases which we have had formed the subject of a paper by M. P. Combres * (Figs. 65 and 66).

"On April 8th, 1908, a man, aged 50, came to Dr. Wickham's clinic at the Laboratoire Biologique du Radium, with chronic eczema of the face, from which he had been suffering for twelve years. On examination, deep inflammatory infiltration of the tissues was observed, showing very intense redness and œdema on the surface of the superciliary, palpebral, malar, nasal, and labial regions; similar lesions being also present on the back of the right hand, the surface of the metacarpo-phalangeal articulations, and the dorsal surface of the left ring finger. This was a lichenified eczema, the frequent acute outbreaks of which produced very severe itching. The patient had tried various kinds of treatment, which had only given him slight temporary relief. This failure had induced him to try radium.

"Apparatus No. 1, which is very powerful, was applied without a screen, and the whole radiation was used, with a majority of weak and medium rays. The applications were made on the face and hands of the patient, for three minutes on each place affected by the eczema, during three consecutive days. In this short period, the rays which chiefly acted were α and soft and medium β; *i.e.* those of weak and medium penetration; the 'surpénétrant' radiation, composed of hard β rays and γ rays, scarcely needed to be considered, owing to its weak quantitative value, which requires very long exposures in order to take effect. One might have thought that these weak and medium rays would produce inflammation, but this is the case only when the doses are wrongly proportioned. In this particular instance, on the contrary, the eczematous tissues, which are so fragile and sensitive, were improved and freed from congestion without the least surface reaction. On the twelfth day the pruritus and fissures had disappeared, and the lichenification was considerably reduced. The patient, acting against our advice, returned to his home at Grenoble before a more permanent result could be obtained. The cure, however, remained complete for six months.

"On November 25th, 1908, he returned to Paris for treatment, the eczema having relapsed a month before on the same parts of the face, although this time the hands were intact. The supervision of the treatment was

* Combres: *La Clinique*, March, 1909.

entrusted to us. We operated with the same apparatus and technique as in April, by a course of applications for three minutes, three days in succession. Between the fourth and ninth days we were surprised to notice the gradual disappearance, first of the pruritus, and then of most of the inflammatory symptoms. The deep-seated infiltration still remained. The two sketches (Figs. 65, 66) show the condition of the face, with an interval of nine days between them. The patient believed himself completely cured, but we succeeded in convincing him of the need of further treatment. Three supplementary series of exposures were then made : the first two according to the method previously described, with an interval of one week, and the third with the same apparatus, but covered with 1 mm. of lead, five rounds of black paper, and a sheet of rubber. By means of this screening, the available radioactivity was reduced to

Figs. 65 and 66.—Chronic lichenified eczema.

about 7,500, and composed only of hard β rays to the amount of 30 per cent., and 70 per cent. of γ rays. We left the apparatus for fifteen minutes on each place, and repeated the applications for eight days in succession, so as to act on the deepest portion of the tissues. When the patient left us his face no longer showed any sign of the former lesions, and the skin had recovered its normal appearance and suppleness. This typical case confirmed similar results which had already been observed by Drs. Wickham and Degrais. It was, indeed, astonishing to see lesions which are usually refractory to dermatological methods yield so rapidly and easily to treatment. No other medicament was given, and the patient took no special precautions. He was merely recommended not to use soap when washing."

This result, if it had been a solitary instance, would have been of little importance ; but it has been confirmed by others.

A printer, aged 27, had had chronic lichenified eczema of the face for seven years. It improved regularly in the spring, and reappeared at the beginning of each winter. The last eruption, about

which the patient consulted us in February, 1907, dated from October, 1906, and was particularly severe and irritable. Up to that time no treatment had relieved it. The whole face—particularly the eyelids—was affected by severe inflammation; the skin was thickened, brownish red, and lichenified.

Apparatus No. 1 was used for three minutes on each place, for three successive days, except on the eyelids, where the applications were only given for two minutes. After this first treatment the patient noticed great improvement; the relief was so great that, after weeks of insomnia, he was at length able to sleep all night. Eight days later a new series was given similar to the first, and this time it was followed by complete healing. In June, 1907, a few points of relapse on the upper lip, the labial commissures and forehead, led us to undertake a repetition of the treatment. In December, 1907, a much later date than usual, the patient began to feel slight tingling, which increased every day. He complained of pruritus, affecting the whole face, but much less severe than that of his former winter attacks. The face was slightly erythematous. Treatment was again instituted as at first; that is to say, two series at intervals of eight days, three minutes on three consecutive days. From that time the cure seemed to be permanent, for the patient passed the winter of 1908 without suffering from any eruption.

(4) **Eczema in young children.**—We must now mention a remarkable effect of radium. We have hitherto spoken of chronic eczemas in adults only, but radium has been successfully employed even for infants, whose tissues are extremely sensitive. Moreover, scratching and the friction of the clothing are apt to interfere with any therapeutic measures, and maintain the refractory character of the disease. In March, 1907, a child of eight months was brought to us with extremely pruriginous eczema, covering the whole face (ears, eyelids, nose, and lips) as well as the scalp. It was in a deplorable state, such as is often seen in the clinics of the St. Louis Hospital. The pruritus occasioned constant scratching. The lesions were oozing and bleeding, and in parts covered with crusts. The general health was impaired by loss of sleep and appetite, owing to constant irritation of the nervous system. Various methods of treatment had had no effect. As we had not yet ventured, in the case of infants, to apply radium to such acute and sensitive lesions, we tried in succession, for six months, the ordinary therapeutic methods, special diet, very careful hygienic measures, Langlebert's ouataplasm, wet compresses, marsh-mallow, elder, sweet almond oil, casein, vaseline, zinc oxide, and various powders. These were applied regularly and systematically, but were all quite useless.

Short periods of improvement were always succeeded by acute relapse. In October the use of radium was decided upon. We then knew that the most powerful apparatus, applied without screens, could act without producing surface inflammation, if the length of application was judged rightly, but we certainly did not suspect that this formula would apply even to the most fragile and sensitive tissues. For the right appreciation of the following result it must be remembered that this eczema was of the kind which is so sensitive that an inert and usually inoffensive powder, used in place of a greasy substance, or *vice versâ*, may produce sudden inflammation. Dermatologists know the extreme difficulty and delicacy of treatment in such cases. It would, therefore, have seemed rash in the extreme to use an apparatus of such activity, five minutes' application of which would produce erythema on healthy skin. The instrument chosen was the most powerful of those which we then possessed—No. 1 of our table. It was simply covered with rubber, and left for one minute and a half on each of the places on the face and scalp, not excepting the more delicate regions, the eyelids, ears, etc. The next morning a similar application of one minute and a half was made. The child then was taken home to the country, and a fortnight afterwards the mother wrote that there was now nothing the matter with her baby. A few more applications were, however, necessary, in order to obtain a complete cure. A year afterwards a letter from the doctor in attendance spoke highly of this remarkable result, and stated that there had been no trace of eczema since the radium treatment. Possibly this was an exceptionally successful instance, but since then we have observed almost exactly the same thing in infants in eczemas of the scalp, face, limbs, and body.

(5) **Peri-oral eczema.**—This condition is particularly obstinate, especially when situated on the mucocutaneous portion of the lips, and generally resists the usual methods of treatment. The following is a case selected from several others, in which the results were very successful. A patient, aged 17, was suffering from chronic peri-oral eczema of the lips, for which he could find no cure. It had appeared six years previously, and since that time, in spite of various kinds of treatment, followed by temporary relief, the lesions had continually grown worse. The circumference of the lips was the site sometimes of cracks, sometimes of scales. The labial commissures were cracked, and speech was hindered, for the slightest movement opened up the fissures, and produced very severe pain. Their bluish-red colour gave the lesions an unsightly appearance. The patient was much disturbed by them, and almost in a state of neurasthenia, for it was most distressing to him to be obliged to appear among his fellow-students in this condition.

Apparatus No. 1 was applied for three minutes on each place, three days in succession. Two months afterwards there was no longer itching or scaling. Two fissures, one at each commissure, had just reappeared; but the circumference of the lips remained in good condition. Apparatus No. 9 was applied to each fissure for five minutes on each place, in four exposures, with one day's interval. Rather severe inflammatory reaction of the surface was produced, and the unfortunate patient feared that the whole eczema would return. But the inflammation subsided a fortnight afterwards, and then disappeared, leaving very supple tissues, and in a month the labial commissures were completely healed. The lips had recovered their normal appearance, and the fissures had disappeared, the brownish colour of the circumference of the lips having given place to a normal tint. The patient, when seen again recently, remained well.

(6) **Refractory seborrhœic eczema of retro-auricular grooves.**—A patient was attacked several years ago by a refractory seborrhœic eczema of the retro-auricular groove on both sides. This lady had come from the country several times to undergo X-ray treatment, but the results had not been entirely satisfactory. A fresh eruption, with abundant oozing and very severe itching, brought her to Paris, and radium treatment was suggested. Apparatus No. 7, covered with rubber, was applied for three minutes on each place, three days in succession. The patient could not devote more time to treatment, and we considered these doses quite insufficient. She wrote, however, several months afterwards to say that the itching had ceased since her return home, and that the eczema was, in fact, healed or cured for the time, which had not been the case for many years.

(7) **Indolent non-pruriginous eczema in scrofulous subject.**—A patient, aged 19, had suffered in early childhood from suppurating adenitis, which had left a chain of enlarged cervical lymphatic glands. The condition of the left apex was suspected. In winter he constantly caught colds, which lasted several weeks. During the previous three years peculiarly indolent non-pruriginous eczematoid patches had slowly developed on the back of his hands. There were three on each hand, the size of a two-franc piece. His mother, a midwife, had used various kinds of treatment without success, and he was advised to try radium. Apparatus No. 4, enveloped in $\frac{8}{100}$ mm. of aluminium, and in a sheet of rubber tissue, was applied for half an hour on each place, three times in three weeks. A stronger dose than usual was chosen, on account of the indolence of the lesions, which, in this case, required considerable modification. The object of the screen was to procure a little more action on the deeper portion of the derma, with-

out irritating the surface too much. A slight superficial inflammatory effect was produced, which lasted for a fortnight, after which the skin gradually recovered its normal appearance. There has been no recurrence during the two years which have elapsed since the cure was obtained.

(8) **Acute eczema.**—We now use radium for acute eczemas, having recently ascertained the remarkable and special action of weak rays on the acute eruptions occurring in the course of chronic eczemas, and on the eczemas of young children. We cannot yet form any definite conclusions on this subject, but the two following instances will be of interest.

i. A patient, aged 60, came to us on November 10th, 1908, for acute eczema on both hands, with vesicles and papular elements. This lady had had slight attacks of eczema from time to time, but the present eruption was not concurrent with chronic inflammation. Applicators Nos. 1 and 2 were used on each hand for ten minutes, in five different places. From the following day remarkable improvement took place, but ten days afterwards slight relapse occurred. We have often noticed some such recrudescence ten to fifteen days after the applications, and its character should be recognised. It is not a fresh eruption of eczema, but merely slight superficial reaction due to radium. It indicates, however, that the dose was rather strong, and it is better avoided. An exposure of our No. 1 apparatus for ten minutes at a time seems to us to give an inferior result to one of the same duration divided into three separate periods. In the present case the inflammation disappeared in a few days without further complications. On December 2nd and 9th No. 2 was applied for five minutes on each place, in order to make the cure certain. On December 16th No. 4 was placed between the fingers, where some traces of eczema still remained. The patient is still in a satisfactory condition.

ii. A man, aged 35, had suffered for six years from paroxysmal eczema during the summer, but was completely free from it in winter. For the last few years the eruption, which was almost intolerable on account of the severe itching, had begun regularly in the spring, and had only diminished about the end of October. Its dysidrotic origin was quite clear. The patient had abundant hyperidrosis, chiefly of the feet, with dysidrotic vesicles on the lateral surfaces of the toes and fingers. The eczema was situated on the lower half of both legs, and the dorsal surfaces of the feet. No treatment had succeeded in relieving him, and, tired out, he had at length resigned himself to awaiting the return of the cold weather. Circumstances led him to consult us in May, at the time of a fresh eruption, which was particularly acute and

irritable. After radium treatment it rapidly subsided, and the eczema did not reappear in the course of the summer. At our first examination, the legs presented, in their lower half, an eruption of small vesicles and papules excoriated by scratching, which was the only thing that afforded relief to the very severe itching. During the examination we saw that the dorsal surfaces of the feet and great toes were covered with small drops of sweat, which were easily distinguished from the oozing due to the eczema.

Apparatus No. 1 was applied, for three minutes, on as many places as were necessary to treat all the affected parts, an hour being sufficient to cover the whole of the lesions. An aluminium sheet of $\frac{1}{100}$ mm. was interposed between the instrument and the skin. These applications were renewed three days in succession, making a total of nine minutes on each place in three days. From the time of the third, the itching ceased, and the oozing appeared to have decreased. On the eighth day the lesions were much improved, and freer from congestion. A similar series of applications, made twelve days afterwards, gradually brought about the disappearance of the eczema. The object of a third course, after another interval of twelve days, was to make the cure permanent. This technique has given us the best and most rapid results.

GENERAL CONCLUSIONS

Our cases have enabled us to formulate a few general indications, the chief of which are as follows :—

Rays of weak and medium penetration have a favourable selective action on certain inflammatory pruriginous dermatoses of the eczematoid type, which may heal without the production of reaction. This latter consideration should be emphasised, since, contrary to expectation, not only do extremely sensitive pathological tissues bear the action of the rays without becoming more inflamed, but inflammation in them is even allayed. This fact negatives the exclusively destructive *rôle* to which one might be tempted to limit the action of weak and medium rays. We cannot too often repeat that it is the dosage alone which regulates the production of superficial inflammation ; and in this group of eczemas, in order to avoid reaction, it will be sufficient to reduce the length of the applications in inverse proportion to their total radioactive intensity. The possibility of applying radium-therapy to large surfaces has just been shown. By employing several large varnish or " toile " instruments simultaneously, a whole arm or leg, for instance, can be covered in one or two hours, thanks to the brevity and convenience of the applications. After studying various

methods, we have recognised the importance, except in the case of small areas—

(1) Of using large apparatus with powerful radioactivity.

(2) Of making short exposures, with intervals between them.

(3) Of using weak and medium rays in as large numbers as possible, and for this purpose interposing no screen, or only one with small powers of absorption (1 per cent. to 8 per cent. of aluminium), except in the case of deep infiltrations.

(4) Of avoiding superadded inflammation.

These are the reasons which have hitherto generally led us to use apparatus Nos. 1 and 2 in superficial inflammatory conditions, adopting an average plan of operation; namely, three minutes' exposure on each area, three days in succession, the series of applications being renewed three times, at intervals of a week. In cases where the infiltration is deeper, it will be necessary to use more penetrating rays, and to interpose medium screens, $\frac{1}{10}$ mm. of aluminium, or even of lead, lined with discs of paper, the whole being covered with rubber. The length and number of the exposures can then be increased. The results have been rapid and successful in cases which had been for years refractory to the ordinary dermatological methods (greasy substances, powders, lotions, wrappings, cataplasms, etc.). As a rule, the patients have not been obliged to give up their ordinary occupations during the course of treatment, and improvement has taken place while they were still at work, without the necessity of using disagreeable and inconvenient dressings. This convenience of operation is of great value, the advantages which it offers being specially marked in the case of very young children.

It is quite clear that radium has only a local effect, and that the treatment of general causes must be carefully carried out. Since only palliative treatment can be used, relapse is always to be feared. The influence of radioactivity, however, sometimes seems quite decisive. We have noticed that the relief lasted longer after the cure than could have been expected, and in several cases in which relapse took place it occurred outside the parts treated. In a case of eczema of the back of the hands, a recurrence a year later did not attack the parts which had formerly been subjected to radium. Most of the forms of chronic lichenified eczema and neurodermatitis have been greatly benefited by its action, the results being very remarkable, and confirmed by the large number of cases. The more the eczematoid elements form patches, the more suitable are they for this treatment. Isolated papules, scattered over large surfaces and forming acute eruptions, are unsuitable. In a case of congestive gouty eczema, one of the true forms of *noli-me-*

tangere, we did not obtain good results. It is true that we have not yet studied the technique of the frankly acute varieties sufficiently to allow us to formulate any conclusions in this respect. The isolated elements of prurigo, if not too numerous, may be treated with advantage. In three cases in which they were aggregated, we were very successful in alleviating the itching.

The chief factor in the cure is certainly the suppression of the pruritus. The analgesic action mentioned in the previous section first comes into play. This explains the remarkable action of the rays on neurodermatitis. The eczematoid tissues are then no longer exposed to the perpetual scratching which keeps up inflammation, so that when once this analgesic effect has been obtained, there are several reasons which explain the rapidity with which the eczema sometimes disappears; namely, the cessation of scratching, the special modifying action of the rays, and their power of freeing the infiltrated cells from congestion.

We have never had reason to regret the use of radium, and this is due, we think, to our constant care to avoid any superadded inflammation of the surface. In spite of this line of action, which should be considered a general rule, we have sometimes unintentionally given excessive doses, and produced secondary reaction, ten to fifteen days after the applications. This has had no unpleasant consequences, but it is necessary to recognise it, and not to mistake it for relapse. It can be allayed by the use of emollients. In individual cases of neurodermatitis, and in some instances of lichenified eczema, pigmentation, which is sometimes rather marked, follows the treatment, but disappears in course of time. This complication may generally be avoided by carefully keeping below irritative doses, and by working slowly and patiently.*

* We desire to offer our special thanks to Dr. de Beurmann for the large number of cases from his own clinic which he has entrusted to us.

CHAPTER IX

THERAPEUTIC RESULTS (Continued)

VII. VARIOUS DISEASES

In the present chapter we have collected some notes on the effect produced by radium on lesions which were more or less refractory to the action of the usual therapeutic agents. Some of these form part of a sufficiently large number of cases to justify us in drawing inferences from them ; others will be given without comment.

Psoriasis.—Radium can be advantageously employed in the pruriginous forms of psoriasis, and when there are local indolent patches, such as are met with on the scalp, fingers, palmar and plantar surfaces, side of scalp, etc., and it is specially indicated when the nails are affected. Very extensive, congestive, or irritable forms, and those of small size, with many scattered elements, as well as the varieties with subintrant recurrence, are beyond the scope of its action. As to the methods, they vary according to whether it is necessary to act superficially or on deep-seated tissue ; and—except in some special cases which we shall indicate—all inflammation must be avoided. Screens of $\frac{3}{100}$ to $\frac{8}{100}$ mm. of aluminium, covered with ten discs of paper, and a layer of rubber, will form good average filters for the type of pruriginous psoriasis in which inflammatory reaction would be dangerous. When psoriasis is complicated by lichenification, the analgesic action first comes into play, as in the case of lichenified eczemas. From our cases, thirty-two in number, we will select a few examples.

A patient, aged 87, had suffered for more than twenty years from inveterate psoriasis of the whole body, except the face and hands. For the last five or six years it had become exceedingly pruriginous. After having tried several kinds of treatment without success, the patient, being unwilling to submit to the fatigue and inconvenience caused by baths, the application of ointments, etc., agreed to try radium. The upper limbs were the site of intolerable itching. On waking in the morning, and undressing at night, he felt an intense desire to scratch, which he satisfied by using a hard brush. The right arm was treated with apparatus Nos. 1 and 2, applied at the same time, five minutes on each place, on three occasions, with one day's interval, covered by

$\frac{3}{100}$ mm. of aluminium, and by rubber tissue. A fortnight afterwards a new series, similar to the first, was begun. The itching ceased after the first series; then the scales, which had been abundant, no longer appeared, the redness diminished, and in about two months the skin recovered its flexibility and an almost normal appearance.

Action on the scalp must be quite superficial, for fear of causing permanent depilation.

A patient suffered from inveterate psoriasis of the scalp. It was no sooner removed by various kinds of ointment than it reappeared. With radium, recurrence did not take place until more than six months afterwards. Apparatus No. 1 was applied ten times, for three minutes each day, wrapped in $\frac{8}{100}$ mm. of aluminium. Rather too strong inflammatory reaction was produced. It showed itself in the form of slight œdema, erythema, and a tingling sensation; but it was not followed by a crust, and it disappeared in a few days. The psoriasis did not at first seem to improve in proportion to the radioactivity used. However, favourable modification was gradually brought about, and it finally disappeared. The hair, which had partly fallen off in consequence of the applications, grew again.

For the treatment of psoriasis of the nails, as Blaschko has clearly shown, radium is specially useful, and will be found superior to other therapeutic agents. Its power of penetration enables it to act through the nail on the subjacent keratosis. A patient had succeeded in healing without difficulty, by the ordinary methods, various eruptions of psoriasis, from time to time developed on the arms, but for several years scaly patches scattered over the fingers, and psoriasis of the thumb-nails, were absolutely refractory, and could not be relieved in any way. Instruments Nos. 5 and 6, with the interposition of $\frac{1}{10}$ mm. of lead, were applied on each nail, for a total of five hours, divided into equal periods, in the course of ten days. The keratosis was modified without visible reaction, and the patient, when seen again a long time afterwards, could be considered free from ungual psoriasis.

For psoriasis with marked keratosis on the hands and feet, elbows, and knees, doses which affect the tissues more powerfully need not be feared, slight inflammatory reaction being sometimes followed by good results. If the keratosis is still more pronounced it will be possible to operate through lead screens, $\frac{1}{10}$ to $\frac{5}{10}$ mm., and to leave the instruments in place for the required time, three to five hours, for instance, for apparatus No. 1, in fractions of half an hour daily.

A patient suffering from psoriasiform parakeratosis had a round patch on the left thigh, the size of a one-franc piece, with a reddish base, covered with small scales. This was the only cutaneous lesion

which existed, or had ever existed, on any part of his body; he had never had eczema, nor any other eruption. There was no itching. When the scales were removed by scratching they were reproduced again within forty-eight hours. The lesion had begun with quite a small point, which had very slowly and gradually developed during the last ten years.

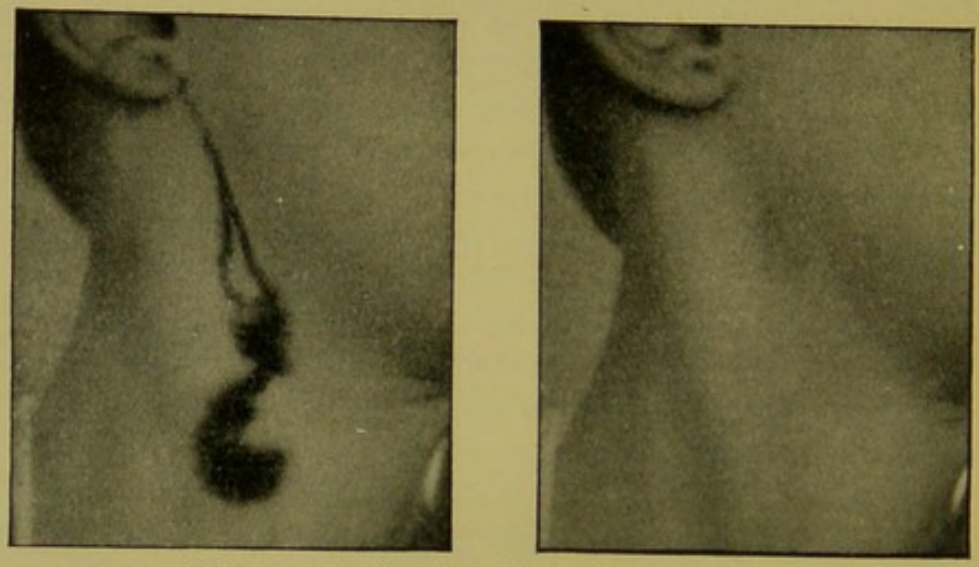
Apparatus No. 6 was used for fifteen minutes, once only. Slight reaction occurred, lasting for three or four days; the scaling ceased, and the erythematous base disappeared. This was nearly four years ago, and the lesion has not relapsed.

Congenital trophoneurotic dyskeratosis.—A girl of $11\frac{1}{2}$ years was sent to us by Dr. Hallopeau with a diagnosis of trophoneurotic dyskeratosis of congenital origin. At the birth of the child the parents noticed a small desquamating patch on the middle finger of the left hand, near the nail; this lesion gradually increased, and spread towards the articulation. Four years ago a fresh lesion of the same kind appeared on the left index finger, and then keratosis developed on the palmar surface. A year afterwards, in consequence of a burn, three small psoriasiform patches appeared on the anterior surface of the wrist, where the skin was desquamating and slightly red. There were similar lesions on the anterior surface of the axilla and the anterior surface of the thorax, the scapular region being also studded with small keratotic points. All these lesions were developed on the left side; there was nothing of the kind on the right. When the child was brought to us the lateral surface of the middle finger was fissured in the direction of its length, and when the two edges were drawn back warty growths were seen to spring from them, projecting 3 to 4 mm. above the surface of the skin. The left index finger presented the same appearance. The palm showed a similar vegetating fissure between the thenar and hypothenar eminences. The wrist and anterior surface of the axilla appeared to have recently been the site of vesicles. These lesions were not spontaneously painful, but they became so in the middle and index fingers, owing to the cracks produced by the movement of flexion. Many therapeutic measures had been tried, but without success.

We applied apparatus No. 1 on the middle finger, in $\frac{1}{100}$ mm. of aluminium and in rubber tissue, for two consecutive hours; on the palm, apparatus No. 6, with $\frac{1}{100}$ mm. On the index finger, Nos. 3 and 7, with $\frac{1}{100}$ mm., for two hours and a half in succession. On the lesions of the wrist, No. 3 for an hour. The inflammatory reaction, which had been produced intentionally, was not too severe; it was well borne, and did not cause pain. A month after the restoration of the tissues, no vegetations nor signs of keratosis were visible. In their place there

was smooth and even skin, rather more shiny than usual. There seemed to be no fear of relapse.

Angiokeratoma.—A girl of 21, one of Dr. de Beurmann's patients, showed patches of angiokeratoma on the right hand. The back of the hand was studded with small lesions, and we treated these points in succession by applying instruments Nos. 5 and 12 to each of them, after surrounding them by our special protective "caches." They were left in position for three hours. This seems a long time, but it should be noticed that only a small part of the surface of each of the instruments was used; and, moreover, we desired to produce a certain amount of inflammation. Reaction occurred in due time,



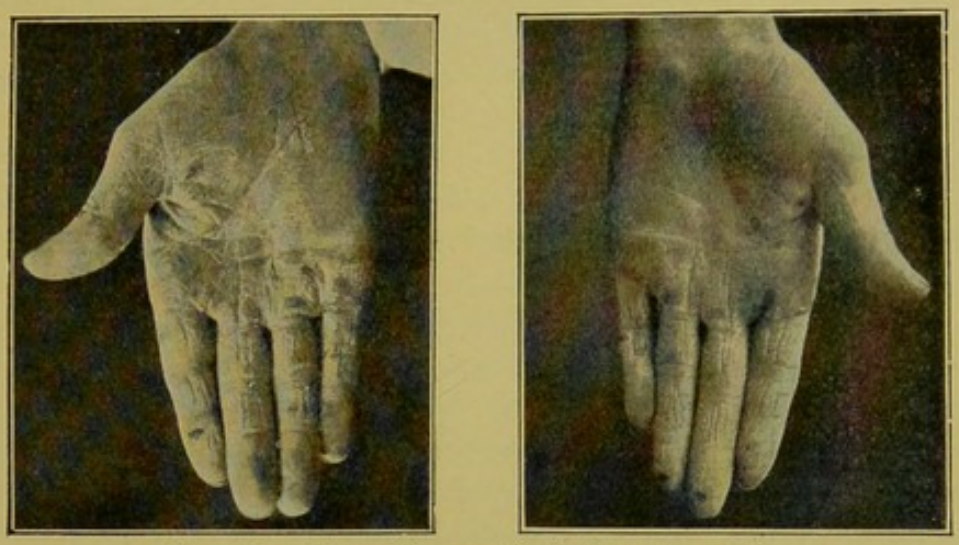
Figs. 67 and 68.—Zosteriform linear ichthyosis.

fifteen days after the applications, and was shown by slight ulceration followed by a serous discharge. Six weeks afterwards the angiokeratomatous lesions were replaced by small smooth surfaces, very slightly scarred, and scarcely visible.

Zosteriform linear ichthyosis (Figs. 67 and 68).—A child of 7 presented, on the right side of the neck, a lesion of congenital keratodermia, taking the shape of a long serpentine band, beginning below the lobule of the ear, on which there were also some small isolated lesions. When it reached the level of the angle of the inferior maxilla, this band divided into two branches, which afterwards met again, enclosing a lozenge-shaped area of healthy skin. The point of union of the two bands was a mass of about 1 square cm., to which another and more extended mass in the shape of a comma was appended. This lesion was dark-grey in colour and was formed by the juxtaposition of small keratotic elements, measuring about 3 cubic mm.

It was evident that the destructive power of radium was required in this case.

Applicators Nos. 7 and 16 were left in position for four hours on each place, being provided with " caches " which exactly fitted the shape



Figs. 69 and 70.—Symmetrical palmar keratosis.

of the serpentine bands. Inflammatory reaction occurred, followed by cure in some parts, but only improvement in others. Two months and a half afterwards apparatus No. 16 was applied for the same period

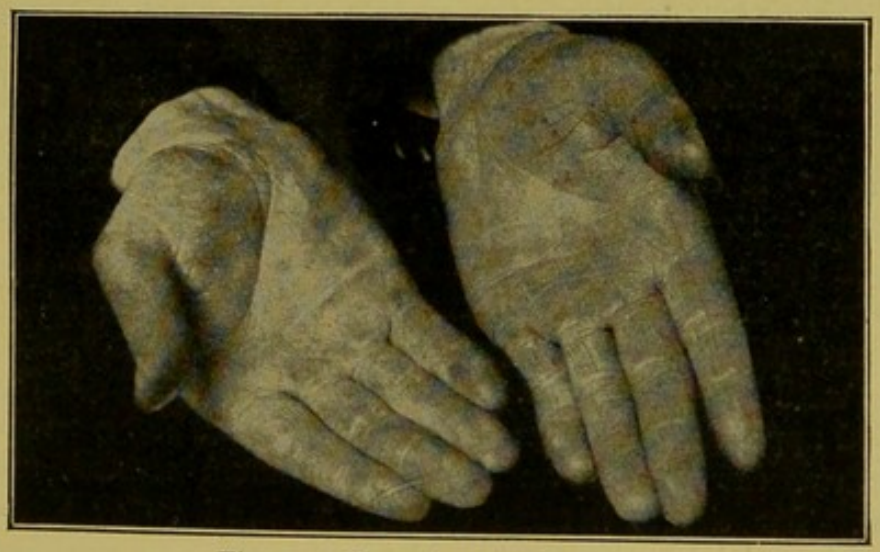


Fig. 71.—Cure of palmar keratosis.

on the few small points which still persisted. The present state of the lesion is very satisfactory, as only a few whitish marks remain.

We have had to treat several similar cases, and have always done so with successful results.

Symmetrical palmar keratosis (Figs. 69 and 70).—A man of 29 had suffered for several years from numerous crusts on the palmar surface of the hands. The skin was thickened, and presented deep cracks on the right side, particularly on the surface of the metacarpo-phalangeal articulations. On the left there were similar lesions, but with fewer fissures. The patient could neither open nor close the hands completely, on account of the pain caused by such movements.

Apparatus No. 1, with $\frac{1}{10}$ mm. of lead, was applied for twenty minutes on each place, five days running. On the fifteenth day it was possible to extend the fingers without great pain, and it therefore seemed desirable to try another series, but only for fifteen minutes in each place. This second course was sufficient to bring about such healing as is shown in the photograph (Fig. 71). The patient resumed work, and, as he was obliged to put his hands frequently into water, some cracks reappeared. We then made applications of three minutes, with apparatus No. 1, in five places, on each hand, for three successive days, repeating this course of treatment eight days afterwards. From that time the cure seemed permanent; a return to the normal condition was observed, and during the several months that have since elapsed there has been no recurrence.

Localised lichen ruber planus.— In consequence of the results which we had obtained in various chronic skin affections, Dr. Milian, who was taking Dr. de Beurmann's place at his clinic at the St. Louis Hospital, entrusted to us the treatment of a young girl suffering from several patches of lichen planus on the back of the right hand. Being obliged to do manual work, she was very anxious to get rid of the eruption. It consisted of one large patch and three smaller ones, with the typical objective characters of lichen planus. There was no eruption on any other part of the body. This localisation was curious; it is, however, met with occasionally, and is very refractory.

Radium applications were begun on December 14th, 1906, and renewed every day until December 20th. Each of them lasted forty-five minutes. We applied apparatus No. 4 on the large patch and No. 9 on the others. These instruments were covered with aluminium screens, and sheets of rubber. The tissues became quickly modified under the influence of the rays, and an erosion, covered by a crust, was produced on the surface of the patches. On January 15th complete healing was obtained, but with some whitish discoloration of the skin, indicating slightly cicatricial tissue. Urged by the patient, we had hurried on the treatment rather too much, and considerably weaker doses would have been quite sufficient. Nevertheless she and her parents were satisfied with

the results we were able to obtain. Further experience has taught us that four applications of twenty minutes each would have been sufficient with the most powerful apparatus, or six applications of twenty minutes with the weakest. We should have effected the cure equally well in this way, and the tissues would have been kept intact.

Lichen ruber planus in scattered zosteriform patches.—Dermatoses with scattered patches are usually unsuitable for treatment by radium. The following case shows, however, that this rule is not absolute.

A young English girl was sent to us by Dr. Robinson for a zosteriform lichen planus occupying the whole length of the forearm and the lower fourth of the left arm. Typical elementary lesions which justified this diagnosis were present in the neighbourhood of the wrist; everywhere else there were less characteristic small red blotches, with a flat surface. These regions were not the site of ordinary itching, but of a painful sensation of formication. We applied apparatus No. 1 for four minutes on each place, four days running. Eight days after the last application there was slight erythematous reaction, and a month later very great improvement, the crawling sensation only remaining to a small extent in the lower part of the forearm. Six weeks after treatment no trace of the old lesions existed. This case dates from June, 1907, and Dr. Robinson informed us quite recently that the cure had been maintained.

Action on pilosebaceous system.—Several of the factors in the healing influence of radium rays will be found to fulfil the conditions necessary for the modification of inflammatory lesions of the sebaceous glands. Their depilatory, decongestive, and atrophic action is very well suited to folliculitis and the acnes. The depilating effect is particularly marked, as we have already shown in the case of hairy and pigmentary nævi. In some instances, by the use of penetrating rays alone, obtained by means of screens of $\frac{1}{10}$ mm. of lead, a destructive action can be obtained which only affects the roots of the hair, without inflammatory reaction. This is an admirable method of acting on some kinds of local hypertrichosis. In treating acne cheloids we have been able to watch the disappearance of the acne lesions. In cases of eczema of the face we have often observed the removal of secondary folliculitis as well as decongestive action on the inflamed tissues. The special action on the blood-vessels, and even the sterilisation to some extent of the staphylococcal foci, not by direct bactericidal action, but by modification of the soil,* justify the trial of radiumtherapy in pilosebaceous inflammation. Moreover, X-ray treatment has been found

* *See* page 12.

successful in similar cases, for which, in the general estimation, it was necessary to produce slight irritation, in order to cause slight contraction of the vessels. By a similar astringent process, frequently renewed, but using the slightly penetrating α rays and soft and medium β, we have also obtained important results; but we think that a small number of medium β, freed from the α, and from a portion of the soft β, and, on the other hand, reinforced by the action of the γ and hard β, represents the best combination for the treatment of these lesions. Although it is advisable to avoid too much irritation—and it is known how irritable such tissues sometimes are—and not to act too energetically, it is necessary, on the other hand, to act at a depth of half a centimetre. This is the best means of acting effectively on the base of sebaceous lesions. For astringent action applicators Nos. 1 and 2—which are very powerful and have a large surface—should be used, either uncovered or covered with light aluminium screens, from $\frac{1}{100}$ to $\frac{1}{10}$ mm. thick. It is necessary to intercept carefully all the secondary rays by adding, in the usual way, discs of paper and fine rubber. This is the best method of lessening any risk of inflammation and consecutive pigmentation. The exposures should be short ones of three to fifteen minutes each, renewed at intervals of one day. After five or six applications there must be an interval of ten to twelve days before resuming treatment. When inflammation occurs, all treatment should be stopped until ten to fifteen days after its cessation. In order to act at somewhat greater depth without causing revulsion, by means of a larger proportion of hard and medium β rays, and by reducing the total intensity, we advise lead filters of $\frac{1}{10}$ to $\frac{3}{10}$ mm.; apparatus No. 1 would then be left in position, according to the thickness of the screens, either for fifteen minutes every day, for five or six days, or for thirty minutes every three days, five or six times for each series, and in several courses.

Acne rosacea.—A girl of 16 came to consult us about an obstinate acne of the face. It had begun four years before, and during this time none of the measures adopted at the St. Louis Hospital had proved satisfactory. It covered almost the whole of the face, with confluent inflamed and pustular acne lesions on the chin, left half of forehead, and upper half of the cheeks. We first expressed some of the comedones and opened the pustules. This preliminary cleansing was necessary, since the rays act better on areas infected by the staphylococcus if the areas are exposed. The right malar region, where the eruption of pustules and indurated elements was constantly occurring, was the first part subjected to treatment.

On May 29th, 1908, apparatus No. 1, in $\frac{4}{10}$ mm. of lead, and five sheets of black paper, the whole kept in place by the rubber covering, was applied for one hour every other day for a week. No secondary inflammation was produced in the course of the next twenty days; on the contrary, a diminution of the congestive element was apparent. A second series was made on the same area with No. 2, and the same filtering, but in exposures of six hours, one hour every alternate day. There was still no secondary inflammatory reaction, which shows that our dosage was quite appropriate. The inflammation again diminished, and improvement was evidently taking place. No fresh pustules had formed at this spot since the beginning of treatment, whilst around it new aggregations had appeared several times. About the thirty-fifth day the part treated showed clearly against the surrounding skin, owing to its lighter colour, smooth surface, and absence of pustules. The forehead and left cheek were then operated on, according to the plan adopted in the second series for the right cheek, the same results being obtained. The completion of the treatment is still too recent to justify definite conclusions, but the case seems so far entirely successful. We have also obtained good results in other instances, by leaving apparatus No. 1 in place for several whole nights, after covering it with 2 mm. of lead. γ rays would be in the proportion of 90 per cent., and hard β of 10 per cent., in this "surpénétrant" radiation of weak quantitative intensity.

Sycosis.—In sycosis, after very carefully evacuating and cleansing the abscesses, doses must be adopted which will bring about depilation. In one case, where the patient was not particular about keeping his beard, we obtained a very satisfactory result by increasing the doses to the point of permanently destroying the hair.

Rhinophyma, or hypertrophic acne.—In a case of rhinophyma in a negro, sent to us by Dr. Hallopeau, very appreciable reduction and levelling of the multiple protuberances covering the lobe and ala nasi took place after fairly strong doses of radium. For each place, apparatus No. 6, with $\frac{4}{100}$ mm. of aluminium, was applied for five hours in ten days, half an hour every day; in two series of two hours and a half each, with a week's interval. In the case of another patient we operated on a small tumour of the ala nasi by "surpénétrant" radiations, leaving apparatus No. 9 (with 1 mm. of lead) in place for three consecutive nights; and the result, after a short and slight inflammatory reaction, was quite satisfactory. In a third case, No. 7 left on for one night, with 1 mm. of lead, brought about freedom from congestion, and diminution of the hypertrophied lobe, after a slight reaction with crust formation. Some regions, such as the margin of the eyelids,

lend themselves very well to the application of the laminated apparatus. Several cases of chronic blepharitis have thus been rapidly improved.*

Syphilis.—Radium seems able to render good service in the local treatment of refractory syphilitic lesions. Syphilides are occasionally met with which, for various reasons, resist ordinary treatment, and, in some cases of this kind, radium has appeared to promote and accelerate healing.

In May, 1905, a patient was attacked by syphilis of malignant appearance, in relapsing eruptions which resisted general treatment. He presented on the forearms some large papular lesions, which still persisted after six weeks of mercurial treatment, with doses which could hardly have been exceeded. Local treatment by radium was proposed, and every growth had disappeared five or six days after being irradiated by apparatus No. 3 (p. 7), applied directly for fifteen minutes.

A woman presented herself at Dr. Wickham's clinic in October, 1906, having on each buttock, in the neighbourhood of the anus, large masses of vegetating papulo-hypertrophic syphilides, which, in spite of local and general treatment, were very slow in disappearing. Radium was tried, and the right buttock treated; eight days afterwards the syphilides had completely disappeared. Those situated on the opposite side, which had not altered during this time, were in their turn treated and healed during the following week.

A patient came to Dr. Wickham in April, 1905, who had been regularly treated with injections of grey oil, without success, for an ulcer of about 1 square cm., situated on the penis, which had at once been diagnosed as an ulcerating syphilide. The lesion was comparatively indolent, and on account of the resistance to treatment, we began to doubt the correctness of the diagnosis. Two months had passed since the last mercurial injection, and no alteration had taken place in the ulcer. A small radiferous "toile," about 1 square cm., with an activity of 8,000, was fixed in place, and left on for forty-eight hours, above a dressing of cotton-wool 1 cm. thick. In the course of the next fifteen days, the ulcer became modified, scarred over, and finally disappeared. The diagnosis of syphilis was afterwards confirmed, the patient returning some months later, suffering from further syphilitic lesions.

A man was suffering from peribuccal, serpiginous, ulcerating relapsing syphilides (October, 1906). We commenced general treatment. Radium

* *Note by Dr. Wickham.*—Since this was written we have had good results in cases of acne rosacea, and confluent and hypertrophic acne, and, in my opinion, radium is more beneficial in such cases than other methods of treatment.

was used locally, but at first only on the left half of the lesion, in order to make comparison possible. Apparatus No. 6 was applied on each place for about twenty minutes, on five occasions, equally divided over a period of seventeen days. As usual, these ulcers healed easily under the influence of grey oil, but the cure on the left side was rather more rapid, and the cicatrisation more smooth and regular than that on the right.

A lady came to consult us for an ulcer of considerable size and depth, occupying the anterior half of the left leg. As in the preceding case, this proved to be syphilis insontium. Local treatment was undertaken with radium, mercurial injections being made at the same time. The surface was acted on by several instruments at once (Nos. 4, 5, 6, and 7), and a radiferous tube was introduced into several fissures and excavations which reached a depth of 5 cm. These were confluent ulcerated gummatous infiltrations. The appearance of the lesions was speedily improved, and large fragments of slough came away. A fortnight afterwards the lesion was in process of rapid repair. It was difficult, in this case, to ascertain accurately the part played by local treatment, but it seemed evident that radium had had a large share in the rapidity with which the tissues were relieved of their scabs and offensiveness, and then repaired.

The following, however, is a case of ulcerating syphilis in which, owing to an error of diagnosis, local treatment by radium was employed alone. The ulcers, in a young woman, were situated near the top of the buttock; they were large, crusted, deeply excavated, and filled with pus. When the crusts were removed, the pain of the exposed lesions became intolerable. Moreover, the crusts soon formed again, even when the patient cleansed the wounds with antiseptics. The action of radium was tried on one of the ulcers, with apparatus No. 4. Two days afterwards the crust had not re-formed, the patient felt no pain, and the base of the wound was scarcely moist. Three other applications were made in the same manner every other day. After the third, the base became dry, and rapidly cicatrised, like an ordinary aseptic wound. On the twelfth day cicatrisation was complete. Three other ulcers of the same kind, treated in the same way, reacted in similar fashion. It was not a case of tuberculosis, as we had at first wrongly supposed, and as it had been diagnosed at the St. Louis Hospital, but one of ulcerating syphilides, for a month afterwards fresh eruptions, this time typical, showed the true character of the disease.

All these cases, selected from those which were most striking, agree in showing the use which can be made of radium locally. We will not repeat here what was said on page 34 about the injections of a solution

of biniodide and radioactive grey oil, which we have used for about thirty patients.*

Varicose ulcers.—We commenced the treatment of varicose ulcers by radium with the easy and rapid cure of a case which had previously proved refractory.† But in this instance the ulcer was small. In other lesions of the same nature, occupying larger surfaces, the results have been variable. In two painful cases the burning sensations were allayed, but the ulcers only healed over very slowly. In the others there was improvement, and cicatrisation up to a certain point, which, however, never resulted in complete healing. For extensive ulcers with thick walls and a varicose base, it is well to use medium rays, with a screen of $\frac{1}{10}$ mm. of aluminium to $\frac{1}{10}$ mm. of lead, without any hesitation as to the production of a certain amount of inflammation. This may even be beneficial, by stimulating the sluggish nature of the lesions.

Papillomata, warts, vegetations.—Several papillomata of the scalp have been healed by two applications, lasting thirty minutes each, with apparatus No. 7. A papilloma of the tongue, also treated in 1905, was reduced, but more slowly. When warts are small, numerous, and scattered, this treatment is scarcely practicable, for the instruments have a weak output on account of their small surface, and the exposures required would be too long. Moreover, it is rather difficult to surround such small growths. Radium would seem to be particularly useful for aggregations of vegetations requiring surgical operations. It is superior to other methods, patients having been freed from these growths quite easily and without pain.‡

A man, aged 25, in November, 1906, had on the penis, at the base of the glans and along the frænum, a series of confluent vegetations. Various measures had been tried for a year—scraping, galvanocauterisation, and various ointments; but relapse had always occurred in a very short time. Complete removal might have been effected, but the patient was unwilling to submit to an anæsthetic. We applied instruments Nos. 7, 8, and 9 to the vegetations, after isolating them by making windows in a protective "cache." The exposures were for two hours and a half in all, divided into three, with a day's interval. An average reaction was produced, and a month afterwards the growths had disappeared. They have not recurred since.

* *Note by Dr. Wickham.*—We have tried radium on "primary sores," which seem to heal more rapidly, and the secondary symptoms are less marked.

† Wickham and Degrais, Société Française de Dermatologie, July, 1907.

‡ *Note by Dr. Wickham.*—We have obtained excellent results in the case of a thick, deep-seated and painful wart of the sole of the foot, for which no treatment but free surgical removal would have been of any use. This was treated by strong doses of "surpénétrant" rays, followed by somewhat painful inflammatory reaction.

The confluent masses which sometimes surround the cervix uteri are quite easily absorbed. This point will be discussed in the chapter on gynæcology. Easy and rapid results have likewise been obtained in several cases of confluent vegetations of the vulva.

A young woman, suffering from vegetations of the vulva, was sent to us by Dr. Camescasse. The patient was pregnant, and at the commencement of pregnancy a patch of vegetations had appeared on the labia minora and the vestibule. Amongst them there was one which had increased to such an extent that its size caused inconvenience. It was important to remove this large growth, or at least to prevent its development, and yet any surgical operation had to be avoided, since it might have been injurious to the pregnancy.

Apparatus No. 3, enveloped in rubber, was applied for three quarters of an hour on the large vegetation, when it had been carefully freed, and surrounded by an opening made in a protective "cache." By the fifteenth day the small tumour had begun to be absorbed, without the slightest discomfort having been caused. A month later a fresh application was made, which was followed by almost complete disappearance of the large growth. As the smaller ones were of little importance, and did not increase in size, they were not treated by radium.

Ocular affections; case of glaucoma.—Radium treatment for various ocular affections has been mentioned by several authors, especially the ophthalmic surgeon, Dr. A. Darier; it seems to have given good results in nerve troubles, and has evidently cured cases of trachoma. We have ourselves tried it in a case of glaucoma, which we quote here, not on account of the result obtained, which was in no way remarkable, but because of the technique. In the latter part of December, 1906, a patient suffering from glaucoma, in the hospital of the Brotherhood of St. Jean de Dieu at St. Barthélemy, near Marseilles, was sent to us by M. de M——, who was well acquainted with the recent work in radiumtherapy. He was anxious that we should try the effect of radium; but, before sending his patient on the long journey from Marseilles to Paris, he inquired what methods would be used to avoid any inflammatory complication. We replied that the process would consist in interposing a rubber-covered sheet of lead between the instrument and the points of application. So far as we knew, this method of filtering by lead had not been used before; it gave us an opportunity of acting at a great depth, with—so we thought—a minimum of danger to the surface. The patient was completely blind in the left eye, and partially blind in the right. The eye on this side could distinguish some shadows. The diagnosis of the ophthalmologist at the institution was "inoperable glaucoma," of several years' standing.

The treatment, commenced on January 23rd, 1907, was repeated every day until February 5th, inclusive. It lasted twenty days, and consisted in the application of apparatus No. 1, for twenty minutes on each place, with the interposition of a rubber-covered lead sheet, 1½ mm. in thickness. The instrument was applied on the right and left fronto-superciliary region, exactly above the eyeball, and on the temporal region. The operation was simple, and was entrusted to the laboratory nurse. As we had hitherto only used these rubber-covered lead sheets as protective "caches," by making openings in them, those about us were surprised to see us direct the rays through the thickness of the sheets themselves. Our object was to lessen the total intensity, to avoid surface action, and to act very deeply. Moreover, the double action on the forehead and temple proceeded from the idea, which had already occurred to us at that time, of the importance of crossing the radiations as much as possible, in order to multiply the intensity of the most penetrating rays at a depth. These rubber-covered lead sheets were similar to those which serve as protectors in X-ray treatment. In this technique, we had, however, made the mistake of allowing the secondary rays of Sagnac to act. These rays are produced, after the passage of the radiation through metals, in sufficiently large quantities to inflame the surface, and there followed a slight, very superficial erythema. M. Beaudoin has since taught us a method of intercepting these secondary rays, which we at once adopted for our protective "caches."

The patient returned to Marseilles on February 12th. During the course of treatment he seemed to see unaccustomed lights, and felt much encouraged. On March 26th M. de M—— wrote to us that there seemed to be improvement; but since then the patient's condition has become the same as before treatment. We give this instance only because it marks our first attempt at filtering radium rays through a lead sheet. Before this, since the beginning of 1905, we had only used pads of cotton-wool, and aluminium sheets, as screens. Our second trial, under absolutely similar conditions, took place on November 6th, 1907, in a case of cancer of the breast sent to us by Dr. Triboulet, for which we wished to avoid all surface reaction (*see* p. 146).

Exophthalmic goitre.—In March, 1905, our friend Dr. Abbé, of New York, successfully applied his method of introducing cylindrical radiferous tubes into tumours * in a case of exophthalmic goitre. After the use of cocaine an incision was made in the median line, and then the opening was enlarged by dissection, avoiding the large veins. The tube could thus be introduced deeply into the central lobe, and left in

* *See* p. 40.

position for twenty-four hours. Eight weeks afterwards the goitre had considerably diminished, without injury to the general health. We have succeeded in obtaining a similar result—the first obtained in France—by applying our method of "cross-fire" on the skin surface of the tumour.

A patient, aged 40, was sent to us on November 6th, 1906, with goitre. The exophthalmos and cardiac lesions were not very marked, but the nervous troubles were pronounced. The tumour was the size of a tangerine orange, and was bounded on the right by the sterno-cleido-mastoid, extending beyond the median line on the left. It was formed of several lobes, and had an irregular surface. Instruments No. 4, 5, and 6 were applied simultaneously, on different points, opposite each other, and on each occasion the places selected were varied as much as possible. Thus the surface of the skin only received weak radiations, but the action of the "surpénétrant" rays was combined and concentrated at a depth. None of the exposures exceeded five minutes in length. The treatment was pursued every day for a month, and the tumour was slowly reduced. After a month's rest, a similar series was followed by retrogressive changes, and the nervous troubles improved. We should now choose the "cross-fire" method for the treatment of a case of this kind, combined with screens of $\frac{1}{10}$ to $\frac{5}{10}$ mm. of lead, using a very powerful radioactive source.

CHAPTER X

THERAPEUTIC RESULTS (Concluded)

VIII. APPLICATION OF RADIUM TO GYNÆCOLOGY

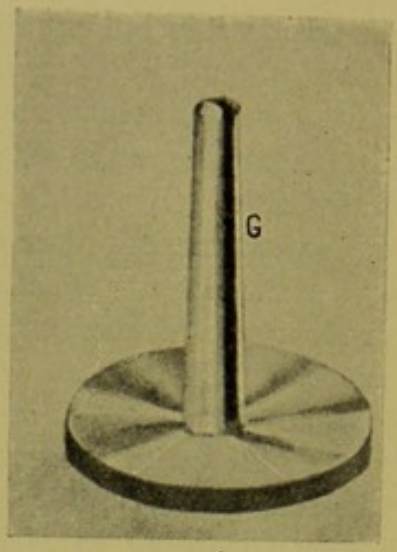
RADIUM is of great service in various affections of the uterus. This has been clearly shown from the results obtained by other investigators, as well as those which we have ourselves noted since the beginning of 1905, with regard to metritis, fibromata, and carcinomata. Owing to improvements in the technique, which enable us to make use of the various healing qualities peculiar to this metal, gynæcology certainly possesses in radium a new therapeutic agent of the highest value. It was natural that radiumtherapy should be specially directed to the uterus, for the properties of the rays are well adapted to the requirements of uterine lesions. Its analgesic, hæmostatic, and decongestive properties; the action—destructive or simply alterative—of the rays on diseased cells, according to the methods and dosage adopted; and the possibility of acting either on the surface or at a great depth, without producing superficial inflammatory reaction, are all qualities which, employed separately or in combination, should find frequent use in gynæcology. Moreover, the instruments themselves are admirably adapted to the uterine regions, since apparatus can be devised of any shape, and capable of carrying the rays into any part. When once an instrument is in position, a tampon will easily fix it, and keep it there for hours together, or even for whole days and nights. This therapeutic measure seemed likely to prove superior to other methods of physiotherapy, both in technique and radioactive energy. However, until the appearance of the very remarkable communication made to the Académie des Sciences, in 1906, by our friends Drs. Oudin and Verchère, on the action of radium in uterine fibromata, metritis, and gonorrhœal urethritis, the only paper of any importance which had been published on the subject of gynæcological radiumtherapy was a note by Dr. Abbé (1905) on carcinoma of the uterus. The former was reproduced and amplified in a paper by the same authors,* and in another on uterine hæmorrhage by M. Oudin alone.† Lastly, some interesting experiments have recently been made in Dr. Tuffier's clinic.‡

* Oudin and Verchère, *Ann. d'électrobiol.*, Oct. 31st, 1906.
† Oudin, *ibid.*, October, 1907.
‡ Tuffier, Congrès International de Chirurgie, Brussels, October, 1908.

Instruments.—Cylindrical and flat applicators are equally useful in gynæcology, but it is necessary that they should be of special shapes and sizes, according to the purpose for which they are intended. Cylindrical applicators are of two kinds. Some have the radium inside, and in that case silver tubes are generally used. The others are stems, the surface of which is covered with radiferous varnish, after the pattern of No. 15 of our table, but varying in diameter. The glass tubes simply enclosed in a metallic sheath are very small, and can seldom be used, except in the cervix, and for cancer of that region. In order to make them penetrate further, they must be placed at the extremity of a long, hollow catheter, the form of which allows of easy introduction into the uterus, or they may be mounted on a handle of suitable length. The filtering, of course, will vary according to the nature of the sheath or the catheter. The stems may be of different lengths. They can be used simply wrapped in a sheet of rubber, and will emit rays of greater total intensity. They can also be covered with screens of various kinds and thicknesses. When employing apparatus with a flat surface, it is better to select " toiles " of strong radioactivity, which, when covered by the lead or aluminium screen, may be moulded more or less to the cervix on account of their flexibility, and facilitate operation by their comparative thinness. These " toiles " should seldom be more than 12 square cm., so that they can be introduced into the vagina. Large instruments will also be useful, but only on the abdominal wall. It seemed important to combine the flat and cylindrical shapes in the same apparatus, and to construct an instrument capable of answering several purposes, according to whether it was used entire or in its separate parts. It was with this idea that one of us devised the above-mentioned radio-uterine apparatus. The illustration (Fig. 72) needs no further explanation. Apparatus should be selected containing salts of suitable radioactive quality and quantity, according to the effect desired, the requirements of the region, and the appropriate length of application. The therapeutic value and method of using these instruments should conform in all respects to the general rules concerning technique and filtration laid down in the first part of our work. All these applicators, stems, and radio-uterine plates must be carefully protected, at any rate by a sheet of rubber; and when they are enclosed in metallic sheaths, the latter must fit them exactly. The method of keeping them in place is quite simple, and consists of a tampon made with absorbent cotton-wool or sterilised gauze.

The operative procedure includes—

(1) Very thorough cleansing of the vaginal cavity.



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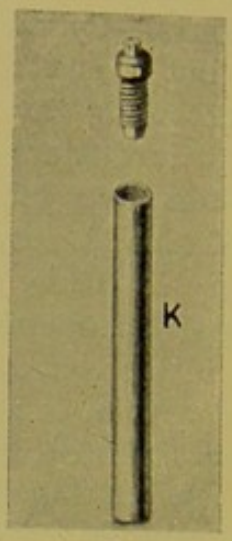

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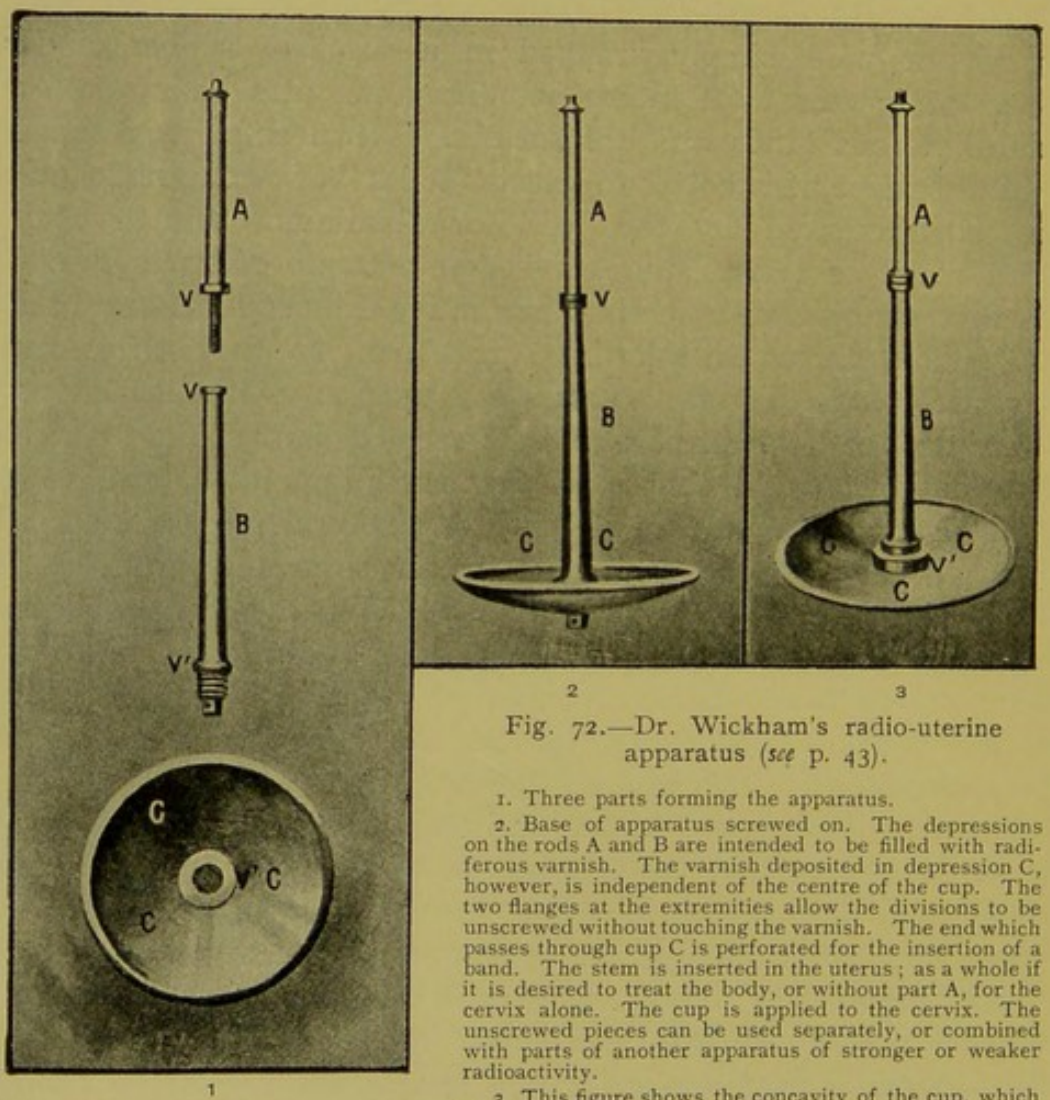

1 2 3

Fig. 72.—Dr. Wickham's radio-uterine apparatus (*see* p. 43).

1. Three parts forming the apparatus.

2. Base of apparatus screwed on. The depressions on the rods A and B are intended to be filled with radiferous varnish. The varnish deposited in depression C, however, is independent of the centre of the cup. The two flanges at the extremities allow the divisions to be unscrewed without touching the varnish. The end which passes through cup C is perforated for the insertion of a band. The stem is inserted in the uterus; as a whole if it is desired to treat the body, or without part A, for the cervix alone. The cup is applied to the cervix. The unscrewed pieces can be used separately, or combined with parts of another apparatus of stronger or weaker radioactivity.

3. This figure shows the concavity of the cup, which may be used alone, like the ordinary flat instruments.

4. Lead or silver screen, which fits on the stem and cup.

5. Screen-tube serving for the whole stem, or one of its parts.

This radio-uterine apparatus may be used for other treatment than that of the uterus, either entire or in its different parts.

(2) Perfect sterilisation of the screen or "toile" which comes in contact with the mucous membranes.

(3) Insertion of the apparatus.

(4) Fixing of the tampon.

Methods of a somewhat special kind should be used, according to the nature of the lesions; we shall mention the details of operation when we are dealing with the results.

In the following section we shall sum up the effects of radiumtherapy in gynæcology.

Carcinomata.—The two following cases were treated by Dr. Lacapère, under the supervision of Dr. Tuffier, in his clinic at the Beaujon Hospital.

"The first patient was a lady of 56, who had been suffering for several months from epithelioma of the uterus. She complained of a feeling of weight in the abdomen, especially on the right side, and said that there was frequent discharge of a blood-stained fluid, often reddish in colour, but no loss of pure blood. Vegetations of the surface had already been treated by curetting. Cancerous growths were observed, forming two principal groups situated on the anterior and posterior lips of the cervix, which they covered like two cauliflowers, separated by a horizontal fissure; and these vegetations bled at the slightest touch. There were no enlarged inguinal glands. The uterus was very big, firm, and painful, and the case was considered by Dr. Tuffier to be inoperable. On May 29th, 1908, the radiferous 'toile' (apparatus No. 15), enclosed in a lead sheet 1 mm. thick, and in rubber tissue, was applied for the first time.* This apparatus was placed exactly over the vegetations of the cervix uteri, which it covered. It was fixed with tampons, and left in position for thirteen hours. The applications were repeated for thirteen hours, on June 2nd, 11th, 19th, and 30th. By this time all the neoplastic growths at the base of the vagina were entirely removed. Dr. Tuffier found that the uterus was much softer, and was no longer immovable in the pelvic cavity; the loss of blood had ceased, but the patient still complained of a sanguinolent discharge. The action on the cauliflower growths of the cervix uteri appearing to be sufficient, we then placed a cylindrical stem, covered with radium salt having an activity of 500,000, and wrapped in three layers of rubber, in the uterine canal. It was left in position for sixteen hours, and the application was renewed from July 6th to 7th. The vault of the vagina at this time was red, and the cancer was entirely obliterated. A small cancerous growth, the size of a lentil, was observed on the anterior wall of the cervix. The patient was seen again at the beginning of October, and the tumour having continued to shrink, Dr. Tuffier considered operation possible, and performed a total hysterectomy. The histological examination made by Dr. Mauté, the head of the laboratory, showed that

* This apparatus came from Dr. Wickham's clinic at the Laboratoire Biologique du Radium. The first application was made with the assistance of Dr. Degrais.

it was a case of carcinoma of the cervix uteri, without invasion of the whole of the organ. The wound united admirably. It is now completely cicatrised, and nothing remains at the top and to the right of the vagina, except a kind of diverticulum, where some small red vegetations still exist. The application, therefore, caused very rapid reduction of the tumour, and allowed of a radical operation previously considered impossible.

"The second patient, aged 48, discovered for the first time in March, 1907, that she was suffering from an affection of the uterus. There was then a red circular erosion on the cervix, which was not painful, but oozed slightly, particularly when she was tired. Its existence had been discovered by a midwife. The patient was examined six months afterwards, at Nice, by Dr. Prat, who removed a small part of the tumour, and found that it was a case of a uterine neoplasm. The cancer was operated on in Paris, in December of the same year, by Dr. Tuffier. In June, 1908, a slight relapse was observed, for which radium treatment was suggested. When the patient was examined on June 19th, 1908, she complained of oozing whenever she walked for any considerable time, and vaginal injections brought away puriform flakes. Examination with the speculum showed that the vault of the vagina terminated in a cul-de-sac, on the left side of which there remained the cicatrix of the hysterectomy performed in December. This scar was thick and slightly infiltrated, presenting small recurrent vegetations. On June 26th, 1908, the same apparatus was applied as in the preceding case, and was arranged in the same way. It was left *in situ* for fifteen hours. As a result of the treatment, abdominal pains and uterine colic were produced, and there was also a discharge of some non-sanious substance which the patient compared to glue. On June 29th, the discharge was much less abundant, but had not entirely ceased on July 1st. On July 10th, the presence of some carcinomatous vegetations was observed on another point at the vault of the vagina, and dilatation with the speculum appeared difficult and painful. The same apparatus was then applied a second time in the same way, and left in place for sixteen hours, the application being repeated for the third time on July 28th. At this time the patient continued to suffer from discharges, but they were chiefly watery; she complained of a feeling of weight in the left adnexa. Some of the vegetations in the vagina were clearly removed, but others still persisted. During August, nine applications were made with the same apparatus, but for a period of twenty-four hours. The patient having left the hospital, she came every evening to have the instrument applied, and returned the next morning to have it removed. In September, improvement was already very marked; almost the whole cicatrix had become soft, the growths were much flattened, and the hæmorrhage entirely arrested. At the beginning of October, Dr. Tuffier had intended to employ curetting for the few remaining vegetations, but finding, on the 26th of that month, that improvement was taking place to a remarkable extent, he finally abandoned all idea of operating. Two applications were again made in December, which brought the total number up to twenty-three. The patient,

when seen again recently, no longer felt any fatigue; the loss of blood and mucus had permanently ceased, and local examination showed such improvement in the flexibility of the tissues that a complete cure seemed possible."

We have just (April 8th, 1909) seen this patient ourselves, and her condition was quite satisfactory.

These two cases are interesting for many reasons, and show the marked effect of radium. Our own experiments have led us to the same conclusions. Improvement usually begins with the disappearance of the offensive odour. In two cases the odour ceased from the fifth or sixth day, and then the sanguinolent and purulent discharges dried up. We have also met with the same succession of events in extensive carcinomatous ulceration of the skin. In certain operable cases, where the vegetations are exuberant and appear to affect the cervix only, curetting can be performed first and radium used afterwards. In inoperable cancers, radium is always indicated, and, indeed, it seems to be, in some cases, the most efficacious means of relieving the patients and prolonging life. In one case the improvement and increase of mobility were so great that the carcinoma, previously considered inoperable, could be operated on under almost normal conditions. In serious or hopeless cases the patients can, however, sometimes be relieved, for diminution, and occasionally even disappearance, of the pain may be obtained. Relapses, when inoperable, can also be subjected to radium. The nodules are often thick and submucous, and the use of "surpénétrant" radiations seems superior to other methods.

Technique.—The technique will differ according to the case; if the epithelial vegetation is fairly well limited to the cervix, and frankly fungating, it will be possible to begin—as we did in one case—with a very active apparatus, covered by a screen of average density, *e.g.* $\frac{1}{10}$ mm. of lead, used for twelve hours, in such a way as quickly to destroy the vegetating portions, and then in many cases to follow up this exposure by a series of applications, every night if possible, with an apparatus arranged like that which we recommended to Dr. Lacapère, but, when practicable, of even greater radioactivity. We have for this purpose an instrument measuring 3 cm. by 4 cm., which, by the intensity of the "surpénétrant" bundle it emits, gives considerable radioactive power for deep treatment. If the vegetations do not prevent penetration into the cervix, the radio-uterine apparatus (the cup and first portion of the stem being covered with a silver screen of the required thickness) should be introduced into the cervix in such a way that it entirely covers the outer surface, so as to act on the epithelioma in different places at the same time. As a rule, it will be found of

great benefit to advise curetting in the first place, before applying the instruments.

In May, 1907, we had to treat an inoperable epithelioma, which was extremely vegetative and hæmorrhagic. The slightest touch produced considerable loss of blood. In such a case, even when inoperable, curetting is certainly indicated in the first place. The instruments applied immediately afterwards, well secured by a plug of cotton-wool, and left in place for twenty-four hours, will then be able to arrest the hæmorrhage, for the hæmostatic action of radium is very marked. We have observed this in many instances. As regards carcinomata of the body, or the whole of the uterus, a tube or the terminal stem of the applicator should be introduced. This apparatus will be covered by a screen, so as to give out only "surpénétrant" rays, and may be left in place for several hours every day; it should be as active as possible. In inoperable carcinomata with invasion of the neighbouring organs, the "cross-fire" method should be used by applying concurrently to the abdominal wall instruments having a flat surface and great intensity, covered with 1 mm. of lead, and by frequently changing their place, before the skin has absorbed too large a number of rays. In some cases it will also be possible to act by way of the rectum.

If relapse occurs, the apparatus just mentioned may be applied on the new growths, always using filters of about 2 mm. of lead. It can then be left in position for several nights without inconveniencing the patient, or causing much irritation of the mucous membrane.

To sum up, we think that radium, on account of the convenience of operation, and great penetration of the rays, may be of the greatest service in cancer of the uterus. It combines the following advantages:—

1. It can assist surgery, either after curetting, or shortly after a radical operation performed as a preventive measure, or in the relapses following hysterectomy.

2. It can act by its specific reducing action in cases where a cancer, operable in itself, cannot be removed for other reasons, *e.g.* age, weakness, heart disease, etc.

3. Lastly, it can diminish the pain, secretion, and hæmorrhage, and, to a certain extent, relieve patients in inoperable and hopeless cases. Its use has sometimes even rendered carcinoma operable.

Fibromata and uterine hæmorrhage.—MM. Oudin and Verchère, in their interesting work, mention the cessation of hæmorrhage and of long-standing and refractory discharges, and the partial reduction of tumours,

and especially of the inflammatory swelling which accompanies them, from observation of several cases, from which we select the following :—

"Marie, aged 36, housekeeper. Nothing of special note as regards her antecedents. Menstruation difficult at nineteen. Sufficiently serious anæmic trouble at this time to necessitate a stay of three months at Laennec. Catamenia irregular, very scanty and painful. Married at twenty. Menstruation then became regular and painless. Has had six children in ten years. Pregnancies and confinements normal. For eighteen months the menses had increased in duration and abundance ; then there appeared in the intervals metrorrhagia, without pain, or symptoms of pressure ; the patient, however, felt the abdomen gradually increasing in size. Finally, during the previous six months, she had been losing continually. For some days it was only a slight oozing, and then the blood returned in large quantities, and the smallest effort or fatigue produced true hæmorrhage.

"May 19th.—Present state. Patient anæmic, with waxy complexion, discoloured and almost bloodless mucous membranes, cold extremities, and vertigo on the slightest movement. Œdema of the extremities and often of the eyelids. On palpation, the uterus is anteflexed, and markedly anteverted, the cervix being very high and difficult to reach, the orifice looking backwards. The fundus of the uterus is in contact with the abdominal wall, rising by four finger-breadths above the symphysis. In the two lateral culs-de-sac, masses can be felt the size of a tangerine orange, less hard than the central tumour, and not very painful ; the whole forming a mass, or immovable swelling, the upper edge of which is ill defined by palpation. When, on May 19th, we made our first application of fifteen minutes,* laparotomy was to have been performed on May 20th. Some loss continues during the day, but the discharge is very slight at night, and has completely disappeared the next morning.

"May 24th.—There is now no serous or sanguinolent discharge. To the touch the tumour seems to show considerable modification. The uterus is more movable, and the fundus appears to be further withdrawn from the abdominal wall, and less easily made out on palpation.

"May 28th and June 9th.—Further exposures of fifteen minutes.

"June 19th.—For three days slight sanious discharge, which ceased spontaneously during the night of the 18th to the 19th, and completely stopped in the morning. The patient drew our attention to the fact that, at the time when she dated the monthly periods, they occurred from the 15th to the 20th of the month. Application of fifteen minutes. Slight blood-stained oozing at first round the tube, but this ceased during the exposure. The patient was seen again for the last time on July 20th. There had been no further loss of blood since June 19th. The tumour is still much more mobile than

* The apparatus used was a glass tube 25 mm. in length and 2 mm. in diameter, containing 27 mg. of radium bromide, with 70 per cent. of the pure salt. This tube was fixed at the bottom of a long hollow aluminium rod, having the shape and size of a hysterometer of 3·5 mm. diameter. According to the inventors, the apparatus thus arranged radiated 920 units.

before treatment, and the tumours of the lateral culs-de-sac are scarcely perceptible. The diminution of the total size, and the mobility, seem to be due rather to the absorption of perimetritis and inflammatory swelling than to the disappearance of the fibroma. Her general condition is excellent. The patient, when seen again early in September, was in the same condition. Menstruation had taken place in August, and lasted five days."

The following is one of many cases of hæmorrhage without any fibrous tumour:

"Mme. G——, married, without children, was ill for the first time in May, 1905; she was sent to us by Dr. Barthélemy. Four years previously metrorrhagia had commenced; at first the courses gradually lasted longer and were more abundant, and then the sanious discharge became permanent, the patient having no longer any indication of the monthly periods. It is usually a slight oozing, which, at any moment, on the slightest fatigue, and often without any apparent cause, increases to such a degree that the patient uses five or six towels during the day, and is often obliged to lie down for twenty-four to forty-eight hours. Curetting was performed in 1902, and was followed for three weeks by a cessation of the discharge; after which it began again. She then underwent fifty applications of electrolysis, which, from what she tells us, must have been very strong. The discharge gradually diminished and then ceased, but reappeared fifteen days after the last application, as abundantly as before. For eighteen months the loss of blood did not cease for a single day, and the lumbar pains were almost constant. In spite of this the general state of health is not bad. The patient is stout, with a rather high colour. The uterus is slightly enlarged, but no induration can be felt, and there is no fibromatous mass. On the contrary, it is rather soft, and does not rise above the pubes. The cervix is enlarged, but only slightly, and is not ulcerated. There is no displacement.

"From May, 1905, to January, 1906, I made twenty applications of electrolysis of twenty minutes each, with 20 milliampères, in courses of three to seven applications, using the positive pole. There was improvement in so far that the profuse discharges were much diminished, but the oozing continued, and the patient at last got tired, and did not come again.

"In October, 1906, after the interesting results which we had obtained in metrorrhagias associated with fibrous growths, I wrote to her, and persuaded her to return. Since March the discharge had reappeared more abundantly than ever.

"On October 19th, 22nd, and 26th I made three radium applications of ten minutes each. After the first, the hæmorrhage was replaced by a reddish watery discharge, which became less and less coloured, and ceased on October 28th, but only to reappear on November 10th. On the 12th and 13th there was blood-stained discharge, which stopped completely and spontaneously on the 15th.

"On November 22nd fresh exposure of twenty minutes. From December

9th to 15th some spots of reddish watery discharge. Since that time there has been no further trouble. The patient had her periods on January 7th; they lasted five days, and were rather abundant. Since then, they have occurred normally every month for five days, without the least discharge in the intervals. The lumbar pains have disappeared. I saw her again recently, and she had remained perfectly well."

Technique.—The hollow stem containing radium in the free state in a glass tube is the form which seems best suited for the treatment of fibromata. We had had two indiarubber catheters constructed, covered with radiferous varnish at their extremities. They were flexible, and it seemed that introduction into the uterine passages, which are often very tortuous, would have been made easy. It was necessary, however, to cover the catheters with metallic sheaths, not only to protect them, but more particularly in order to obtain the "surpénétrant" rays as much isolated as possible, so that these instruments, though useful in other gynæcological diseases, did not fulfil the necessary conditions for the treatment of fibromata. The glass tube introduced into the catheter must have the smallest possible diameter, and should contain at least 1 cg. of pure radium. A larger quantity would be still better, and tubes with the highest radioactivity should be used. With the "cross-fire" system, which we are about to explain, this activity is greatly increased. The hollow stem should be of several different patterns, in order to facilitate operation. Some will be straight, others in the shape of a hysterometer, and in this case made to unscrew at their extremity, so as to allow the glass tube to be slid into the raised portion beyond the bend. These rods are made of aluminium, and vary in diameter, both as regards their hollow part and their external circumference, which will depend upon the thickness of the walls. It will thus be possible either to put the glass tube uncovered into a hollow tube with thick or thin walls, or previously to enclose it in a small lead tube of $\frac{1}{10}$ to $\frac{5}{10}$ mm. or more, if possible, introducing the whole into the hollow stem.

These directions are prompted by two considerations:

1. Great difficulty is often met with in passing a rod along the uterine canal. Fibromata frequently distort the organ, and the passages are very long and tortuous, measuring as much as 15 to 20 cm. In one of the cases under treatment at the beginning of our investigations, the hysterometer would not pass, but a soft catheter was able to traverse the 15 cm. of depth of the uterus, though with some difficulty. We were obliged to abandon the treatment, because the radiferous varnish, although wrapped in a rubber sheet, was injuriously affected by the friction, and also because the absence of metallic screens, in order to

avoid inflammation, necessitated too short and frequent exposures. It is therefore necessary to have various shapes at hand, so as to penetrate the passage in the best way.

2. The technique requires "surpénétrant" rays. The fibromatous tissues to be treated are thick and dense, and must therefore be permeated as thoroughly as possible with very hard rays. With an external radioactivity of 4,000, composed only of hard β rays and γ rays, if no colic is produced, the apparatus may be left in place every other night, in series of five or six exposures, repeated five or six times, at intervals of ten days. For large fibromata these doses are insufficient, but it is possible to act simultaneously through the abdominal wall as follows. A very powerful apparatus is covered by 2 mm. of lead, emitting a radiation of 4,000 to 6,000, and fixed each night on a different place. Thus there will be combination by "cross-fire" of the "surpénétrant" radiations, and great increase of their intensity at a depth.

On the whole, we consider that, if there is no special reason for a surgical operation, and the case is not very urgent, it will be right to try radium. Such attempts are nowhere more justifiable, since there is no risk, and the benefit may be great. In some cases, hæmorrhage and discharge are arrested, and the tumours are partly reduced, relieving the patients from some of their subjective symptoms. The growths become more mobile, being to some extent set free by the absorption of the surrounding inflammatory adhesions.

Metritis.—In chronic catarrhal metritis, the number of cases treated is sufficiently large to warrant some conclusions as to the value of radium-therapy, and different observers all agree on this point. In adding our own cases, which amount to twelve, to those of our colleagues, we find about thirty in which the result has been successful. Unfortunately, some of these have not been followed up or seen again. Many of them, however, were conclusive, and in these instances the symptoms of improvement have arisen in almost the same way. It would be difficult to overlook the unmistakably favourable action of radium on metritis. Under the influence of the rays, the eversion is lessened and the hæmorrhage diminished, and, as a rule, the pain is arrested. During the action of the rays—possibly owing to mechanical irritation from the pressure of the instrument in the uterus—uterine pains and colic are often produced, which compel modification of the technique, and the adoption of shorter applications. It is necessary carefully to distinguish these pains from those due to the metritis, which disappear altogether after the first applications. Several patients suffering from metritis have seemed to be completely cured, a month to six weeks after the end of

the exposures, and in these cases the hysterometer has shown that no atresia of the cervix had taken place. Amongst those which we have treated we will mention three in which the cure appears to be well established. The others have been reduced in almost the same way.

One of the former was an example of an extremely extensive case (body and cervix). It was refractory, hæmorrhagic, and purulent, with deep inflammatory infiltration, and considerable ectropion. We will take it as a type, for it presented a maximum grade of severity, and it happened that we were able to observe it for a long period.

A patient, aged 21, presented perivulvar vegetations, but we also found, on June 13th, 1906, a very pronounced metritis. The cervix was extremely swollen and indurated, and almost entirely covered by a red vegetating mass, hard at its base, which for a moment suggested chancre of the cervix. It was really an eversion, of considerable size. The whole mucous membrane bled easily, and there was also frequent hæmorrhage. The hysterometer penetrated to more than 7 cm. The vaginal culs-de-sac were bathed in muco-pus, and there was abundant glairy, bloodstained, and muco-purulent discharge from the uterine orifice. There were abdominal pains, and menstruation was extremely painful. The patient stated that these lesions dated back more than a year. This was one of those specially refractory and unfavourable cases in which curetting seems a necessity. We decided, however, to postpone surgical operation, and to try the effect of radium first.

We then possessed (it was before the opening of the Radium Laboratory) an instrument with a cylindrical stem of the same shape and pattern as No. 10 of our table (No. 6, p. 7), but its radiferous varnish contained pure salt over a length of 2 cm. This very active apparatus was introduced into the uterine canal to a sufficient depth to affect the inflamed mucous membrane throughout its extent. To act on the ectropion, we used apparatus No. 5 (p. 7), which also contained the pure salt. Its surface was much smaller than that of the ectropion, but, by holding it at a distance of a few millimetres, and slightly changing its place, we were able to treat the whole surface. On June 14th and 19th the stem apparatus was applied for twenty minutes. Applications of the instrument with a square surface, for twenty minutes, were begun on June 21st. The ectropion had already become paler. It was contracted and slightly reduced, and the appearance of the cervix was altered; it also bled much less. A certain amount of uterine colic was produced in the course of treatment. The double application, in the canal and on the cervix, was again made for twenty minutes, on June 21st and 26th. On June 28th there appeared on the surface of the ectropion, which was greatly reduced, a whitish false

membrane, which did not adhere firmly, and was easily removed with cotton-wool. On August 11th the vegetation on the anterior lip had completely disappeared, and the mucous membrane of the os uteri seemed healthy in this place. On the posterior lip the ectropion had perceptibly diminished, but a small red spot the size of a lentil still persisted in its middle portion, in connection with the uterine orifice. The hysterometer was easily introduced, without producing hæmorrhage. Moreover, the cervix was entirely altered in appearance, having almost recovered its normal shape and suppleness. There had been no hæmorrhage for a month; the discharge had not absolutely ceased, but had changed its character, being glairy, light in colour, and scanty. The patient, when seen again two months afterwards, was in an excellent condition. The appearance of the cervix was normal. The small erosion of the posterior lip persisted, but there was no longer any discharge. The pains and bearing-down had disappeared. We considered these results very remarkable, for many reasons. This length of application (eighty minutes in the vaginal passage and sixty minutes on the ectropion, spread over three or four sittings, with an average of three days' interval in the course of twelve days) represents an intensity of action which would have produced severe inflammation on healthy skin. Total radiations were used here, the weak rays not being intercepted. The uterine mucous membrane resisted perfectly. It was reduced without apparent ulcerative inflammation, and without subsequent contraction. In this particular case we desired to test the resistance of the mucous membrane, but in those previously treated we had interposed an aluminium sheet of $\frac{1}{100}$ mm., in a rubber covering, and since then we have always suppressed the α and soft β rays, even when total radiations have been used. The decongestive and hæmostatic action was very marked in all our cases. As to the subjective symptoms, although colic occurred during treatment and for some hours afterwards, rapid diminution of the abdominal bearing-down sensation took place. The next two cases confirm the preceding one.

A patient, aged 25, presented, in May, 1905, a chronic catarrhal metritis of the cervix, with considerable ectropion. The same apparatus was used as in the previous case, but wrapped in an aluminium sheet of $\frac{1}{100}$ mm. in three folds, making a thickness of $\frac{3}{100}$ mm., the whole being kept in place by a covering of rubber. For the ectropion we used the square apparatus No. 5 (p. 7) without a screen. In nineteen days there were six applications of twenty minutes in the cervix, and four on the ectropion for the same period. Improvement took place rapidly, and, a month after the last application, we observed the disappearance of the catarrh and the ectropion, except over a small

part of the surface of the posterior lip. The cervix had recovered its suppleness, and was in no way injured. The persistence of the small erosion on the lesser lip usually occurs in cases where the ectropion was originally large. It is a point where the resistance of the mucous membrane is weak, but the remainder is so perfect—at least in appearance—that this slight erosion is of no consequence.

The next of these cases was treated with a radio-uterine applicator, the varnish of which contained a total amount of 9 cg. of radium salt, with an original activity of 500,000. The hysterometer did not pass easily beyond the cervix. The ectropion involved the whole of the posterior lip, the cervix being hard and swollen. There was some abdominal bearing-down. The discharge of mucus was very abundant, but only slightly bloodstained.

We concluded that this was a metritis limited to the cervix. It was useless, in this case, to use the terminal portion of the stem. This was therefore unscrewed, and the cup and first part of the stem were used alone. After being wrapped in $\frac{3}{100}$ mm. of aluminium, and a covering of thick rubber, the apparatus was seized by means of a long forceps at the continuation of the rod which exists for this purpose at the back of the cup. It easily traversed the speculum, and was introduced into the cervix, the cup being applied to the os uteri. We placed on the cup, below the rubber, a thickness of $\frac{1}{10}$ mm. of lead, in the part corresponding to the anterior lip, which was not diseased, in order to protect it. Five applications of twenty minutes were made, with one day's interval. Six weeks afterwards it seemed that the metritis had disappeared. There were none of the symptoms observed before treatment, and retrogression took place without irritation, or apparent supplementary inflammation. The majority of our cases have confirmed these results. The following are those of Drs. Emery and Lacapère :—

"The patients suffering from metritis who were treated by radium at St. Lazare have always appeared to improve ; some of them, however, could not be kept at the clinic long enough to permit of sufficient observation of the results. In a general way, it would seem that this improvement became marked four to six weeks after treatment, and the patients whom we have seen subsequently have remained quite well. The apparatus used came from the Laboratoire Biologique du Radium."

A patient, aged 22, presented a glairy cervical metritis, with slight ulceration of the cervix.

"The first application was made on June 11th, 1908, with a radiferous rod 3 cm. long, covered with rubber, which reduced the activity of the radiation to about 4,000 (Beaudoin). The application lasted twenty-four hours ; there was concurrent treatment with injections of permanganate

of potash. Five other applications were made under the same conditions on the following days. By July 10th the metritis was much reduced.

"In a case of muco-purulent metritis in a patient, aged 25, the cervix was swollen and inflamed, and presented ectropion.

"Radium applications were begun on June 19th, 1908, with a cylindrical stem 2·5 cm. long, wrapped in rubber, and containing 2 cg. of radium sulphate, with an activity of 50,000. The rod was left in position for twenty-four hours. For the three following applications, an apparatus was used with an activity of 100,000. On July 20th the patient had only a very slight discharge; the lips of the cervix were still granular, but in better condition.

"For a purulent metritis, with abundant discharge, applications were made, on June 22nd, of the rod covered with thin rubber, with an activity of 100,000, and left in place for twenty-four hours. Four exposures were given at three days' interval, and then two at an interval of a week. By the end of the month the discharge had ceased.

"For a metritis of the neck with eversion and sero-purulent discharge, radium applications were commenced on June 19th. A rod with an activity of 500,000, covered with rubber, was left in place for twenty-four hours. Five applications were made, at intervals of three days. On July 10th there was marked improvement, the discharge being very scanty. The ulceration (eversion), which had not come into contact with the radiferous pencil, was not modified. On July 17th the patient was cured. Since then she has been seen again several times, and the disease has not relapsed."

Technique.—The radio-uterine apparatus fulfils the various conditions necessary for the treatment of metritis. It is easy to understand the many advantages of this instrument, and we need not stop to describe them. But the choice of suitable radioactive intensity is important, and difficult to formulate. As a rule, the best plan is to act with little or no irritation of the mucous membrane. Three methods may be used in order to arrive at this result:

1. Stems covered with weak radium salt may be employed (50,000 or even 30,000). These radioactivities, in which the α and soft β rays will be intercepted by coverings and light screens of 0·01 mm. to 0·05 mm. of aluminium, can be applied for four to six hours, spread over five days, with one day's interval.

2. Salts of very great intensity (500,000) may be selected, in which the α and soft β rays will also be suppressed, and the apparatus left in contact for five to ten minutes, on five or six occasions, with one day's interval.

3. These highly active salts, enveloped in sheaths of $\frac{1}{10}$ to $\frac{5}{10}$ mm. of lead or silver, may be left in place for five hours, on two different occasions, with an interval of two days.

These are the methods which seem to us to give the best results.

In conclusion, we think that the use of radium in metritis, an affection which is so refractory and difficult to treat, and in presence of which we too often feel ourselves helpless, is definitely indicated. In some cases it would even appear to be the most efficacious method which we possess.

Chronic urethritis.—The results obtained by MM. Oudin and Verchère in urethritis in women have been uncertain. To judge from our own experiments, we think that it is necessary to operate with very active rays, but to leave them on for a very short time, according to the plan adopted for eczemas. Long exposures produce mechanical irritation of the mucous membrane. A stem of great radioactive power, wrapped in rubber thick enough to intercept the α and soft β rays, and left in place for two or three minutes each day, five or six times, with one day's interval, will constitute good working conditions. Chronic urethritis is so obstinate and difficult of cure by ordinary therapeutic methods that experiments with radium are quite justifiable.

Interesting results have been obtained in other genito-urinary diseases in which we have used radium, but we do not wish to lay stress on isolated cases. Amongst others, there was one of the absorption of an aggrégation of vegetations situated in the inferior vaginal cul-de-sac (*see* remarks on Vegetations on p. 276); a case of esthiomène of the vulva which underwent very marked improvement, after having resisted several other methods of treatment; and a case of ordinary chronic ulceration, probably of gonorrhœal origin, which was also much improved.

From all these facts taken together we may infer that the use of radium in gynæcology, although as yet in its infancy, has sufficiently proved its value to be worthy of serious consideration. For our own part, we believe that it has a great future before it.

CHAPTER XI

PROPERTIES AND ADVANTAGES OF RADIUMTHERAPY

A NEW science can only be established when it is in possession of systematic methods of investigation, and no accurate conception can be formed of it without knowing the processes which it employs. It is precisely with the object of giving radiumtherapy a truly scientific character that from the very beginning of our researches we have always paid the greatest attention to methods and dosage. At the present time we may consider that this branch of physiotherapy has finally emerged from the empirical stage. From a physical point of view we are now in possession of known and analysed forces ; we know what therapeutic qualities are possessed by the rays. From a clinical standpoint, also, we have learned how to use the apparatus, and what doses are necessary to obtain certain results. These data, of course, are only definitely fixed as regards their main lines ; much must always be left to the experience, clinical acumen, and intelligence of the operator, especially in details ; and here, as in all other therapeutic methods, the individual qualities of the latter will determine the conditions of success, and bring about the best results from this new agent. In order better to emphasise them, we will now sum up in a final analysis the most important properties of radiumtherapy—those, in fact, which constitute its claim to originality.

1. **Selective action.**—Radium rays have a selective action on certain diseased tissues, including carcinomata, angiomata, cheloids, eczemas, and tuberculous glands ; they can modify such tissues without irritation, or the production of superadded inflammation, by diverting the pathological process towards a process of repair. This action may be exercised not only on easily accessible lesions, but also on those situated at considerable depth. A subcutaneous malignant neoplasm, for instance, may thus be favourably influenced, without any irritation of the skin.

2. **Destructive action from a therapeutic standpoint.**—By regulating the doses, it is possible to obtain, either on the surface, or at greater depth whilst affecting the surface, an inflammation of the tissues in varying degrees which may be carried to the point of destruction. This therapeutic action of the rays (obtained by screened or unscreened apparatus) is very useful in many cases, and has a special value for tissues

of repair. But it is necessary to know how to regulate it, for inflammation which might injure the æsthetic repair of the tissues and their subsequent evolution must be avoided.

3. **α and β rays.**—Radium is the only physical agent which at present gives us an opportunity of using these rays. The therapeutic part played by α and β rays is very clearly manifested in the treatment of certain surface lesions (eczema and flat angiomata). These rays, according to the dosage and the nature of the tissues, possess to some extent a selective property; they are not exclusively destructive.

4. **Penetrating power of hard β rays and γ rays.**—The hard β and the γ rays, isolated by filtering, like the α and soft and medium β, can produce either destructive action, or selective action independent of any superadded inflammation. As in the case of the α, and soft and medium β, this double effect depends directly on the dosage; in fact one dose, of whatever kind the rays may be, can have a destructive action on the tissues, and with another dose the same rays may have a selective action. If, then, the slightly penetrating rays are not necessarily destructive, the extremely penetrating rays, isolated by filtering, are not necessarily independent of the production of burns. The action of the very penetrating γ and hard β can be concentrated and utilised *without filtering*, by means of "cross-fire," or short and frequently repeated exposures, thus concentrating at a depth the action of rays with special properties, the less penetrating rays also being allowed to act in part. The action of the hard β and the γ rays may also be utilised by means of filtration. They have a very wide margin, corresponding to the great number of screens, forming a scale according to their thickness and density. The penetrating power of these γ and hard β rays is considerable. By the use of screens which intercept the slightly penetrating rays, it is possible to obtain deep action without irritating the surface; "cross-fire" combined with filtration increases this deep action still more.

5. **Convenience.**—The convenience of operation allows of long exposures. The facility with which the apparatus can be moved, and the absence of all constraint and of noise, are important in the treatment of very young children, old people, and timid or crippled patients.

6. **Adaptability.**—This quality includes the ease with which the apparatus can be adapted to different regions, and the great variety of operative methods and combinations. Whether radiferous "toiles," tubes, or metallic apparatus with varnish are employed, the power of each instrument can be varied *ad infinitum*, according to its shape, the weight of the salt used, and its proportion of pure radium. We will here summarise, by way of example, some possible combinations, taking No. 1 as a type. With this instrument, whether used uncovered or with a

series of screens, and whether left in contact with the tissues for a long or a short period, the following effects may be obtained :

(1) **Action on the surface, without inflammatory reaction.**—*a*. Superficial lesions (eczema, neurodermatitis, etc.). Apparatus applied uncovered, or wrapped in fine rubber tissue. Duration : one to three minutes, three days in succession, renewed three or four times, at a week's interval.

b. Lesions of rather greater thickness (thick lichenifications, etc.). Application of apparatus covered with $\frac{4}{100}$ to $\frac{8}{100}$ mm. of aluminium, five sheets of paper, and rubber tissue. Duration : three to six minutes, five days in succession, renewed at intervals of a week, more or less frequently, according to the thickness of the tissues treated.

c. Lesions on which it is necessary to act more deeply (superficial carcinoma, cheloids). Apparatus covered with $\frac{1}{10}$ mm. of lead, ten sheets of paper, and rubber tissue.* Duration : two hours distributed over eight days, renewed at intervals of a week.

(2) **Surface action with destruction (superficial carcinoma, pigmentary nævi, etc.).**—Application of apparatus uncovered, or with a screen of $\frac{1}{100}$ to $\frac{5}{100}$ mm. Duration : three consecutive hours, or four hours, an hour at a time, spread over four days.

(3) **Action at a depth without surface inflammation (cheloids, carcinoma, etc.).**—*a*. Screen of $\frac{3}{10}$ mm. of lead. Duration : one hour for three days in succession, the series being renewed a week later.

b. Screen of 1 mm. of lead. Duration : three hours, six days in succession, or twelve consecutive hours.

c. Screen of 2 mm. of lead (deep-seated carcinoma ; cancer of the breast, for instance). Duration : about seventy hours, in fractions of ten to twelve hours, every other day.

d. Screen of 3 mm. of lead. Duration : 150 hours, in divisions of ten hours, every other day.

(4) **Action at a depth with destruction (deep-seated carcinoma, affecting derma).**—Screen of 1 mm. of lead. Duration : seventy-two hours in succession.

These estimates, which show the multiplicity of uses to which one apparatus may be put, are far from exhausting the number of possible combinations, and are themselves only approximate, for they vary according to the nature of the lesions, and whether the whole or part of the surface of the instrument is used. If these many varieties are added to those resulting from combinations of

* We have often spoken of screens in the course of this work without referring to the addition of sheets of paper and rubber. These, however, are invariably used, but we have not mentioned them on each occasion in order to avoid repetition.

apparatus, in the " cross-fire " system, for instance, or that of introducing tubes or injections, it will be seen that the term " adaptability " attributed to radiumtherapeutic instruments is entirely justified.

7. **Introduction of radium into tissues.**—Lastly, owing to the solubility of radium, and the ease with which this substance, in the state of an impalpable powder, can be mixed with various other bodies, radioactive energy can be introduced into the interior of the tissues and the economy, not only in the form of rays, but also in that of emanation. A whole field of action is thus opened up to therapeutics which at present belongs to radium alone.

We see, in fine, the complexity of the new agent, and how many distinct methods it possesses ; we must learn how to use it in these different forms, and not limit it to any single one of them. In conclusion, we would say that we have been anxious to lay stress on these properties and advantages, because, taken collectively, they create for radiumtherapy an absolutely unique position, and give it a distinctive place in the therapeutic arsenal—a place which has already become one of the utmost importance.

THE RADIUM TREATMENT OF CANCER

(Addendum by Dr. Wickham to Chapter III, Part III)

THE MS. of the French edition of this work was sent to the publishers in March, 1909, but further investigation of the therapeutic action of radium on cancer has been made since that date. Many more cases have been treated, but my experience of the last nine months has not perceptibly modified the general trend of our conclusions. We could say more about cancer, but only by adding new cases to those already mentioned, and not stating fresh facts. It is true that a special chapter might be devoted to malignant tumours of the sarcomatous and lymphadenomatous type, but only on account of the large number treated during the past year. My present experience leads me to think that it is in these that radium treatment is most successful.

We need not retract our favourable verdict as regards pure epitheliomata. On the contrary, we have collected many new cases which confirm those already recorded; and, by the intervention of surgery, the deep action of radium has been successfully extended to regions hitherto considered inaccessible. I will give some examples.

We have treated cases of cancer of the neck of the bladder, with definite results, by the introduction into the urethra of a catheter containing a radium tube.

With the help of Dr. Cousteau, a distinguished laryngologist, we treated a case of cancer of the larynx by acting simultaneously on the pharynx above, and on the trachea below, through a tracheotomy wound.

In several cancers of the rectum and intestines (high up) we were able to introduce radium through the orifice of an artificial anus.

With the assistance of M. Gaultier and M. Labey, a surgeon of the Paris hospitals, we treated a cancer of the pylorus by our " cross-fire " method. A very powerful apparatus, with a thick screen, was placed externally on the abdominal wall, in the situation where the pyloric tumour could be felt, whilst a radium tube of great intensity was introduced, by means of a curved catheter, into the stomach itself, through an orifice made by M. Labey for gastro-enterostomy. The patient is now (ten months later) in good health.

In some cases we have had recourse to surgery, in order to make a wide opening in large tumours by incision, or to perforate them with the Delbet gimlet, radium applicators being introduced at the base of the opening.

In most of these instances we used radioactive energy of great strength (not less than 5 cg. of pure radium) and lead screens varying from $\frac{7}{10}$ mm. to

3 mm. in thickness, and the patients, as a rule, have certainly been benefited. All the instances just mentioned date back several months, and up to the present time we have observed a considerable degree of local improvement.

In another case, a very remarkable improvement must be recorded. A patient, after surgical removal of a sublingual carcinoma and submaxillary glands, had a serious recurrence in the submaxillary region. When I undertook the treatment, the tumour was enormous and very deep-seated, infiltrating the whole vascular and nervous tissues of the underlying part of the neck. It was absolutely inoperable, and its malignant evolution was rapid and very acute. I adopted a new method of procedure in this case, and requested Dr. Banzet, a surgeon, to remove as much of the tumour as possible by the bistoury. Excision could only be performed to a certain depth, on account of the large vessels. At the base of the enormous growth the greyish carcinomatous mass was seen, infiltrating the tissues still more deeply.

I introduced several radium tubes, placed close to each other, at the base of this gaping cavity, and put our most powerful flat instruments, covered with lead screens, on the edges of the lesion. These applications were made in series of 50 to 100 hours in length, with intervals for rest, according to our usual methods. On the 62nd day the lesion had undergone almost normal repair. At the present time (the 130th) there is apparently no fear of relapse. The growth left at the base of the lesion has not proliferated, and the skin is cicatrised. The carcinomatous tissues seem to have lost their malignant character and the appearance and all the signs are favourable. I consider this case very important, both as to technique and results.

Lastly, I would record a case in which a recurrent nodule of a carcinoma of the breast was removed by a new method devised by me: injections of an insoluble radium salt mixed with paraffin vaseline (the solution contained $\frac{1}{10}$ mg. of radium sulphate) *below* the nodule, and the simultaneous application of a flat radium instrument *above* the nodule. The object of this method was the establishment of "cross-fire" action, and we only mention the case in order to indicate this new technique.

Unfortunately we see no reason to modify the reservations we made (p. 157) with regard to carcinoma of the mouth. Except in a few rare cases, such as certain growths of the wall of the palate, tonsils and gums (osteosarcomata), the results have been very inferior to those obtained in other regions. We think that this is owing to the fact that sufficiently long exposures cannot be made, on account of the thickness of the screens required. Moreover, the great weight of the instruments themselves, especially when covered with thick lead screens, causes irritation in cancer, and it is difficult to fix them quite firmly, so as to avoid slight friction. When we possess apparatus containing 50 cg. to 1 grm. of pure radium, and can make short applications, even with very thick screens, radiumtherapy of the buccal cavity will have a better chance of success.

The foregoing remarks show how necessary it is to be circumspect in the radium treatment of cancer. Not only are there regions for which the technique is unsuitable, but, before undertaking the treatment of a patient,

it must always be remembered that radium only acts locally, and does not yet play any recognised part in general infections and in distant metastases. It must be used with caution for large carcinomata, even when they are localised, in order to avoid the production of toxic enzymes. It can have no value except in growths which are accessible, or have been made so, and the frequency of relapse must always be taken into account.

We desire definitely to dissociate ourselves from the exaggerated statements on this subject made by some workers; and although we have gradually become aware of the great value of radium in therapeutics, we have always taught that it is of the utmost importance, for the sake of the patients, to proceed with caution and discretion, lest they should be deprived of other methods of treatment, which may sometimes be of greater value.*

* Wickham, "Radium and Cancer," *Rev. gén. des Sci.*, Nov. 30, 1909. "Is Radium a Cure for Cancer?" *Brit. Med. Journ.*, Dec. 18, 1909.

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