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on

PERSONAL EXPERIENCES OF THE CLINICAL VALUE OF RADIUM.

by

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I N T R O D U C T I O N.

Radium as a new therapeutic agent has of late loomed large in both the medical and public view. In giving my experiences of its clinical value I have thought it well to preface my remarks with a short account of the science of radio-activity, and of the spontaneous disintegration of elements which the study of radio-activity has revealed to us.

The science of radio-activity is a new science, and is concerned with a knowledge of the elementary atoms, to which the old laws of physics and chemistry do not apply, as they concerned themselves almost wholly with external relationships. If someone twenty years ago had ventured to predict the advent of radium, he would not only have been told that it was wildly improbable, but actually opposed to all the established principles of the science of matter and energy. But radium to-day is an undisputed fact, rendered so by the work of Mme. Curie who has proved its existence beyond doubt by carefully analysing and defining its spectrum, and by working out/

heat as does coal or any other substance burning. These effects of radio-activity have been demonstrated by experiment to be due to the fact that radio-active substances emit rays. There are three different kinds of rays, known respectively as alpha beta, and gamma rays. Each will receive future detailed consideration in this thesis. But the distinctive feature of radio-activity lies not so much in the rays, the radio-active substances emit; the main interest of the new property consists in the spontaneous and continuous emission of energy of which the rays are but one manifestation. Heat and light may be obtained in numerous ways but it is a new thing to find them being given out by a substance as they are by radium year after year, without apparent intermission or diminution and without the substance being in any apparent way consumed or altered.

The law of the conservation of energy states that energy is a new entity, and has a real existence no less than matter. Now matter cannot be destroyed, no more can energy though the forms it may assume are legion. Energy, as is known, is only available for useful work once, and ultimately it is dissipated in heat. If one wants energy, one must pay/

pay for it, as for any other commodity, and the value of the energy, though not the energy itself, is destroyed by use. This fact was looked upon as truth itself until radium was discovered.

Nothing goes by itself in nature except apparently radium and the radio-active processes. Energy can be measured exactly, and though it exists in many forms it can be readily and completely converted into heat, and measured as such. The energy given out by radium is no exception to this rule and exact experiments have proved that the amount of heat given out by one gram (= 15·4 grains) of radium is 133 calories per hour. This is many times the energy obtainable from the combustion of the same weight of coal. And it must be remembered coal is no longer coal, when it is burnt and consumed, but radium after evolving energy is as active as ever.

These are some of the facts that scientists were asked to accept for the first time, towards the end of last century, and the realisation of which has rudely shaken all our ideas of chemical principles. Thus radium has a deep interest for physicists, and it holds no less an interest for medical men for besides the above phenomena observed radium is possessed of strong/

strong biological properties.

When carrying out experiments to find out all its properties and characteristics, it was discovered that radium acted on the human tissues in a remarkable manner though as in the case of some other great discoveries, this action was only found out by accident. ARCHIMEDES is said to have formulated his theory of specific gravity and the buoyancy of bodies from an accidental observation while taking a bath. NEWTON first thought of the law of gravity from idly observing an apple fall from a tree, and M. BECQUEREL happened to be using a tube containing pure radium and put it into his waistcoat pocket. Though warned of the imprudence of such an action he took no notice and carried the tube about with him for several hours. A fortnight afterwards a severe inflammation appeared in the skin immediately below the pocket which could only be attributed to the action of the radium. This has become known and is referred to as the BECQUEREL burn. Soon afterwards PROFESSOR CURIE having made a conclusive experiment on himself, advocated its use for medical purposes. Once this fact was made known great progress was made in the study/

study of radium therapy, and it soon became evident that it had a definite therapeutic value and would become a valuable resource in the treatment of various diseases in the field of medical and surgical pathology. The first effect obtained was the resolution of certain neoplasms without the slightest surface irritation, and afterwards the cure of various growths by destroying them by strong radiation leading to the production of a sore which later on heals like a simple ulcer, leaving a small cicatrix. The third effect observed was the production of analgesia without surface reaction. Complete analgesia was obtained in the treatment of such conditions as cutaneous hyperaesthesia, neurodermatitis and pruritus. A fourth effect observed was that radiation in some cases had a marked bactericidal action.

Such were the conclusions first arrived at and since then much work has been accomplished that has justified the claim of radium to a scientific position in therapeutics.

About five years ago owing to the munificence of a benefactor the town of Hull came into the possession of over a thousand pounds worth of radium. It was one of the first places in the Kingdom to obtain/

obtain some radium in response to a public appeal. The radium purchased was handed over to the Health Committee of the Corporation and kept in the office of the Medical Officer of Health.

Immediately the radium arrived in the town a Radium Department was started in the Hull Royal Infirmary and for a period of sixteen months as a house surgeon in the Infirmary, I was associated with the working of the department.

In this thesis I purpose to give an account of the various conditions we treated during the period February 1912 to February 1913, of some of the difficulties we encountered, and the results attained by radium treatment. Before dealing with the subject proper, I shall give a short historical outline of the discovery of radium and radio-activity with some account of the preparation, and methods of using the applicators.

HISTORICAL OUTLINE.

The history of Radium is essentially modern, and no account of it would be complete without some short reference to the discovery of X-Rays, and/

and on which the discovery of Radium and radio-activity to a large extent depends. It was in October 1895 that PROFESSOR W.C.RÖNTGEN while experimenting with a Crookes' vacuum tube electrically excited and enveloped in a black covering observed that some rays, proceeding from the tube passed through the black paper and affected a fluorescent screen. To these rays he gave the term X-Rays and this discovery familiarised scientific workers with a type of radiation able to traverse objects opaque to light.

The suggestion was made by POINCARÉ at this time that perhaps all fluorescent bodies could emit rays capable of passing through substances in the same manner as X-Rays and imprinting photographic plates. This led physicists to examine the bodies, which are phosphorescent after exposure to light, in order to ascertain whether they possessed these properties. In 1897 BECQUEREL acting on the suggestion put forward by POINCARÉ and being engaged in the study of the phosphorescence of the uranium salts was the first to prove that the visible spontaneous radiations emitted by phosphorescent uranic salts was also emitted by salts of uranium oxide and uranium protoxide/

protoxide, and even by the metal uranium itself all of which are non-phosphorescent substances. From this he came to the conclusion which in the light of further discoveries turned out to be premature that spontaneous radiation was independent of phosphorescent properties and was only produced by the uranium atom. In reality this action is to us an entirely new inherent property of the element uranium which it shares with several other new elements discovered shortly afterwards. BECQUEREL afterwards found that this invisible radiation not only acted on photographic plates after passing through opaque bodies but was also capable of discharging electrified bodies i.e. that it had the power of ionisation. It was this new phenomenon which differs from phosphorescence and fluorescence and which we now call radio-activity that the name "BECQUEREL rays" was given.

In 1898 these BECQUEREL rays or properly radio-activity was the subject of study on the part of two workers, Mme. CURIE and M.SCHMIDT and who carrying out experiments quite independent of each other, proved the existence of these rays in thorium, a metal long known to physicists. Thus the question as/

as to whether uranium alone of all the eighty elements known, possessed radio-activity and which BECQUEREL had proved to be an intrinsic property of the element uranium was answered by this latest discovery which showed thorium to be radio-active. Mme. CURIE now took up the investigation of the activity of the rays of metallic uranium and succeeded in ascertaining and formulating the degree of this activity. But further investigation showed that pitch-blende (the mineral from which uranium is extracted), was more active in the above respect than could be accounted for by its uranium content, some pitch-blendes in fact, are from three to four times as radio-active as pure uranium oxide[1] and this led her to the conclusion that the radio-activity of uranium oxide ore (pitch-blende) was due to some substance or substances present in minute quantity, to which the phenomenon was due. There are a great number of elements in pitch-blende though most of them are present in very small amount. After long and laborious research Mme. CURIE in 1900, found that of the elements so separated, two in particular the bismuth and the barium were strongly radio-active. Now ordinary bismuth and barium are not at all radio-active/

radio-active and the radio-activity of these elements when separated from pitch-blende is really due to the presence of two new elements in minute amount mixed with them. The one associated with bismuth was discovered first by Mme. CURIE and named Polonium after her native country Poland. The other which was discovered very soon afterwards is associated with barium, is, very much more active than the first named, and is called Radium. Investigation of the residue of the ore after extraction of these bodies still continued and in the same year, DEBIERNE discovered a third radio-active body namely Actinium, but so far the difficulty of extraction of this substance has been an insuperable obstacle to its being utlised up to the present time. At the present stage of our knowledge actinium seems to be found only in the uranium metals and this fact would point to its being a product of uranium, though, on the other hand it is possible it is an independent primary radio-element.

In 1904 RAMSAY and HAHN discovered radio-thorium and two years later BOLTWOOD of America discovered Ionium thus completing, as far as our knowledge at the present time goes, this class of the newer metals. Ionium chemically resembles thorium so/

so completely that if the two are mixed they cannot be separated.[2] This chemical resemblance is analagous, to that between radium and barium or polonium and bismuth referred to above, and does not signify any genetic connection between the substances.

Having considered somewhat in detail the history of the discovery of Radium and its associated metals we must now direct our inquiries to one special portion of the subject namely the nature of the rays emitted by the radio-active elements, by means of which, or rather of the effects of which the property was first discovered.

GENERAL/

GENERAL OBSERVATIONS ON RADIUM AND RADIO-ACTIVITY.

As has been stated above, radium ore exists in all the uranium compounds, with one exception, namely an ore called Pyromorphite. These uranium ores are found in different countries and are known by different names. The principal workings are those of the St. Joachimstal mine in Bohemia but to-day the Austrian Government who hold the monopoly of this mine, do not allow the ore to be exported, and in consequence there is a great dearth of the raw material. Besides the pure uranium oxide ore designated as pitch-blende or pitch uranium, there are others in which the uranium is found in association with various other metals, and to each of which a distinctive name has been given. The double phosphate of uranium and calcium is known as uranite or autunite which takes its name from the locality of Autun (Auvergne) in the neighbourhood of which it is found in considerable quantities. Autunite has also been found in Portugal and Tonquin. Chalcolite is a double phosphate of uranium and copper, which has been met with mixed with autunite in France, Saxony, and/

and Portugal. Carnotite or vandate of uranium has been found in the plains of Utah U.S.A. The uranium and thorianite oxide is known as thorianite in which form it is found in Ceylon as crystallised cubes. Pyromorphite referred to above has been met with in France. This is the only instance of a radium ore free from uranium. It is a phosphate of lead and is no new discovery, as it has been worked and in commercial use for some time. Besides the St.Joachimstal mine mentioned above there are many other pitch-blende workings, the most important being in Bohemia, Hungary, Saxony, Turkey, Sweden, Canada, Colorado and Cornwall. One of the chief difficulties to be overcome in radium therapy is the enormous cost of radium. But radium is at all times a rare metal, added to which there is the expensive process of extracting it from its ores, the operations necessary for such treatment are invariably long, numerous and difficult of execution. The cost of radium can be understood when one takes into consideration the fact that one ton of pitch-blende must be worked up to produce two grains 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 the chemical composition. As the simplest/

simplest treatment is that employed for pitch-blende the following may be taken as a short account of how the process is carried out. The mechanical preparation of the ore is the first process, and this involves a series of different operations. The ore is first ground into lumps about the size of a nut, after which it is pulverised into a fine powder by means of a hammer-crusher. This powder which contains many foreign substances is now enriched as regards its radium content, by dressing in the way most suitable for each substance by means of percussion tables, or washing, followed by separation according to the varying degrees of density.

In the residue thus obtained the radium exists in an insoluble state, being blended or combined with earthy silicates or alkaline earths. The ore having gone through the above processes is now treated with repeated washings of hydrochloric acid and water and thus the inactive material is removed and the insoluble part containing the radium is left; it is now subjected to prolonged boiling with carbonate of soda which brings about the transformation, of the insoluble radium salts unchangeable by acids, into salts equally unchangeable but capable of being affected by acids. The slime thus produced is

treated/

treated with hydrochloric acid which dissolves the radium with a large quantity of impurities. This solution is afterwards purified by precipitation of the sulphides in the acidified liquid and afterwards of the oxides in the same liquid rendered alkaline. Thus a solution is obtained containing only barium and radium.

The next process carried out is described as fractionisation. This in essence consists of concentrating the liquid obtained by the last process in a receiver and after cooling, crystals are deposited on the sides and bottom of the vessel. The liquid is now decanted into a second receiver, water is added to the first and both solutions are concentrated. When cool the water from the second receiver is decanted into a third receiver while the water from the first is poured on to the crystals, deposited in the second, and more water is added to the first receiver to redissolve the crystals. The solutions are again concentrated and allowed to cool and another receiver is added to the series. This is carried out until only a small quantity of a very active salt, remains at the beginning of the series, and after a final very careful purification is made pure radium bromide is produced.

Needless to say radio-activity and radium were/

were discovered long before this complete process for the extraction of the latter was evolved and perfected, but once the preparation of radium could be carried out in a small way in the laboratory the nature and analysis of the radiation began to be enquired into. I have in a previous section described the discovery of radio-activity and given some account of its main effects e.g. photographic, fluorescent, electrical and thermal. These effects are due to definite radiations emitted by the radio elements and the first analysis of the complete radiations emitted by each of the radio-elements - uranium, thorium and radium - was done by RUTHERFORD.(3) He classed the rays into three main types the alpha beta, and gamma distinguished from one another by enormous differences in their power of penetrating matter. All these rays like the new X-Rays, and unlike light, are absorbed by matter, roughly in proportion to the density of the matter.

Alpha rays are very easily absorbed, and only slightly penetrating. They are completely absorbed by very thin screens - even by a sheet of thin paper, or by a few centimetres of ordinary gaseous air. But the energy possessed by these feebly penetrating rays/

rays which at first sight are of comparatively little importance is always immensely greater than that of the other two types taken together.[4] The alpha particles produce very intense ionisation along their path in a gas, and thereby soon lose their energy and after traversing a few centimetres their velocity falls below the power, at which they can ionise.[5] The extreme distance which the particles travel before being stopped is known as their range and for a particular product the ranges of all alpha particles are the same; but particles of different products have different ranges, which varies from 2·5 centimetres in the case of uranium to 8·6 cms. for thorium C,[6] at atmospheric pressure and ordinary temperature. A point to be remembered with regard to alpha rays is that they are deviated by a magnet, in the opposite direction to beta rays. I have said that alpha rays are only feebly penetrating and here it is necessary to mention a fact, which comes into play on account of this easy absorption of alpha rays in passing through matter. In the first place the radio-activity of a radium salt is given off from every portion of a salt, not the surface only. And as radium salts are dense and heavy these rays are absorbed/

absorbed by the salt itself to some extent. But this absorption does not affect the more penetrating rays nearly so much as the feebly penetrating alpha rays. In fact those alpha rays generated inside the salt, do not escape at all, The consequence is that whereas when working with small quantities of radium the strength of the penetrating rays is more or less proportioned to the quantity of radium employed, with the alpha rays this is no longer the case. The weight of the substance is less important than the amount of surface exposed. A very small quantity, say a milligrame of radium bromide spread out as a thin film, on a large plate, will give out immensely more alpha rays than the same quantity in the form of a small crystal. This point is of importance since, as will be explained later the different rays whether slightly penetrating, of medium penetration "surpénétrant" or "ultrapénétrant", produce different reactions.

Beta rays are similar to the cathode rays emitted from a Crookes' tube, but about five hundred times more penetrating. They form a heterogeneous group and exist in the proportion of about nine per cent in the radiation from naked radium. They vary among/

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 beta rays are comparable to the alpha rays, and are described as soft beta rays. Hard beta rays are composed of particles of extreme tenuity and are animated by great velocity akin to that of light. Between these two extremes, soft beta and hard beta, come the intermediate rays called medium beta. These three varieties of rays, of the beta type, have great powers of penetration and easily traverse substances, but they do so unequally and with more and more ease in an ascending scale from soft to hard beta. A fourth variety of rays is the secondary beta rays, which result from the action of gamma rays on encountering matter but they do not call for consideration at the present stage.

Beta rays are strongly deflected by a powerful magnet and if they are caused to traverse the space between the poles of a magnet they may be completely coiled up into closed circles or spirals. This is exactly what would happen to a current of electricity if it were made to flow between the poles of a strong electro-magnet. This behaviour of the beta rays in a magnetic field associates them at once with/

with some previously known radiations from the Crookes' tube and experiment has proved that the beta particle is identical with that of the cathode ray particle of vacuum tubes, but the velocity of the beta particle as I have previously mentioned is far higher than that of the fastest known cathode ray. From this it will be seen that the beta particle ejected from the radium atom was already known - it is the same particle as Sir Wm. CROOKES dealt with in his vacuum tube thirty years ago.

Gamma rays are a pulsation of the ether and similar to X-Rays. Unlike alpha rays and beta rays they are not deviated by a magnet. They have a velocity equal to that of light and their origin has been accounted for in the disturbance produced by the disintegration of radium into alpha and beta atoms. Gamma rays are extremely penetrating (in nature) being able to traverse as much as ten centimetres of lead, and indeed in a laboratory it is very difficult to get rid of them. In this their power exceeds that of X-Rays which is limited by one or two millimetres of lead, in fact the chief interest in gamma rays, lies in the fact that they are by far the most penetrating type of radiation at present known. These/

These gamma rays will take a radiograph of the kind produced by X-Rays though they are not well adapted for it, as they are far too penetrating so that objects of the density of the bones of the hand hardly cast a shadow on the plate at all.

Radium in process of disintegration not only sets free energy in the form of the rays which I have just described but also gives off continuously a radio-active gas called the emanation. Again we owe a debt of gratitude to Professor RUTHERFORD for the greater part of our knowledge of this new gas, and to which he gave its special name. Similar new gases or emanation are given by two other of the radio-active elements, namely thorium and actinium. This discovery of emanation has been and will be of priceless benefit to radium therapy, as by this means we have what is practically an inexhaustible store of radio-activity. For this gas is intensely radio-active on its own account, that is to say, it gives out rays very similar in character to those given by other radio-active bodies and capable of producing the same effects. The activity of all radium salts or solutions depends principally upon the emanation they contain. If they are heated or subjected/

subjected to a vacuum they lose nearly all their activity which may be collected in the form of gas by suitable means. The activity of the gas, at first about nine per cent of the total activity of the original salts or solutions, decays gradually, falling to half value in 3·85 days ceasing to be active in a month and finally yielding helium, an inert gas. Conversely the salts or solutions regain their lost activity at the same rate as the activity of the emanation obtained from them has decayed. It was obvious that this emanation could be of therapeutic use for not only is it possible to make applicators or tubes for special cases, and impart to them either a high or a low activity but these applicators could be sent long distances while the parent stock of radium remained to furnish in a short while emanation for further needs. This regeneration of emanation is a fundamental law of universal application to all radio-active bodies and it has been called the Law of the Conservation of Radio-activity. Thus radium is a powerful source of energy manifested in the form of emanation and rays and now that the demand for radium has become so great, emanation has a future before it, as definite and encouraging results have been obtained by those who have worked with it.

But/

But at present the practice of radium therapy almost entirely consists of the use of rays without the emanation and this brings us to the consideration of how it is applied for clinical use. Radium applicators are of many forms and sizes and with the growth in popularity of this branch of therapeutics there has been a corresponding growth in the improvement of the appliances. Certain qualities are indispensable in these applicators and I propose to enumerate briefly what qualities the ideal applicator should possess. Efficient protection to prevent any loss of the material is a matter of great importance in the construction of apparatus especially in that form of applicator which is used for external application, with the radium on the outer surface. The radium in an applicator of this kind is usually fixed to a metallic base with varnish which is especially chosen for its resistance to the wear and tear of the surface of application. The varnish while exercising strong fixative power on the radium salt, must at the same time be of a nature and be so applied as to allow the greatest permeability to the most easily absorbed rays. Added to this the surface should be smooth and even. A second consideration in the/

the manufacture of these applicators is to arrange that the output of radio-activity should be homogeneous i.e. that any portion of the surface of the apparatus considered separately ought to have the same radio-active strength as any other part. In this way the therapeutic effects will be uniform and identical at every point. The value of an applicator from a therapeutic standpoint is not so much the quantity of salt contained as the quantity of radio-activity liberated;thus the output should be the maximum possible. This is secured by using the thinnest varnish possible to contain and enclose the particles at the same time keeping in view the previous conditionsI have mentioned. Bearing this fact in mind it is possible to utilise not only the gamma and beta rays, but also a certain quantity of the soft penetrating alpha rays.

All the above conditions are present in the applicator which has found greatest acceptance amongst different workers. The appliance is commonly described as the flat varnished type of applicator, and consists of a metallic base coated with varnish in the substance of which the radium salt is imbedded. On account of its great adaptibility and suitability for most cases, this is probably the most commonly used/

used applicator for both superficial lesions and deep growths; though for the latter condition the silver tube variety is reaching great prominence. In this type of applicator the grains of the radium salt are packed in a glass tube, which is hermetically sealed and enclosed for the sake of protection in a silver tube, to which is attached a long pliable wire handle. Our equipment in Hull, contained only these two types of applicators, but no description of these appliances would be complete without a passing reference to what is known as the "Toile" applicator or shortly "Toiles". These applicators are made by spreading varnish impregnated with radium over cloth in a manner very similar to an ordinary plaster. In this case a very thin coating of varnish suffices to hold the grains of radium in position thus the rays collectively form radiations of great intensity. The proportion of alpha rays especially is increased compared with the output of an applicator furnished with a metallic base. Another great advantage is their flexibility which enables them to be adjusted accurately to any part. These toile applicators however, are very fragile and must be handled with great care; in practically all cases they have to be used/

used with protecting screens, and this results in a great loss of radio-activity. This can be counteracted to some extent by superimposing one toile applicator on another, and thus increasing the radiation to a considerable extent. On account of the thinness of the cloth base, the radio-activity is exercised almost equally on either side of the toile, a fact which can be taken advantage of in the treatment of such regions as the vagina or rectum, where the lesions affect the periphery of the canal. I simply mention the toile to show what an ideal applicator it makes and though we were possessed of several such in Hull, I have no experience of working with them, as those in question were old and somewhat damaged, and we had no data regarding their strength or radio-activity.

Our armament in Hull consisted of fourteen applicators. They all came from the Armet de Lisle works in France, and on the metallic base, or silver tube each had marked the quantity of salt (radium sulphate) contained in the applicator, and its radio-activity tested after manufacture. The following is a list of our applicators.

LIST/

L I S T.

No.1	contained	3	centigrammes	of	salt	with	activity	of 500,000
" 2	"	2	"	"	"	"	"	" 500,000
" 3	"	5	Milligrammes	"	"	"	"	" 1800,000
" 4a	"	2	"	"	"	"	"	" 1000,000
" 4b	"	$\frac{1}{2}$	milligramme	"	"	"	"	" 1800,000
" 4c	"	$\frac{1}{2}$	"	"	"	"	"	" 1800,000
"4d	"	2	centigrammes	"	"	"	"	" 1800,000
" 5b	"	1	milligramme	"	"	"	"	" 2000,000
" 5c	"	1	"	"	"	"	"	" 2000,000
" 5d	"	3	milligrammes	"	"	"	"	" 2000,000
" 6	"	4	centigrammes	"	"	"	"	" 250, 000
" 7	"	3	"	"	"	"	"	" 500,000

* Later/

Later our store of applicators was increased by the addition of two small silver tubes variety of strong activity, which we found eminently suitable for burying in tumours. As regards the applicators details of which are given above Nos. 1,2,6,and 7, are of the flat varnished variety, Nos. 1,and 7, being square having a superficial area of 4 sq. cms., Nos 2 and 6 being rectangular and have a superficial area of 3·75 sq.cms., Nos 3,4a,5b,5c, and 5d are silver tubes with wire handle attached. 4b.and 4c are concave applicators mounted on detachable holders. This form was specially designed for application to the eyelids, cheekbones or any convex surface. No.4d is an applicator devised for uterine work but could also be used for application in various regions as occasion might suggest.

The last consideration in the "modus operandi" of radium therapy is the question of screens. Screens have been used from the outset of radium treatment at first simply for the protection of the apparatus, but afterwards, with the growth in knowledge of the action of the rays with a view to modifying the radiation emitted by the applicator. Varnished applicators have always to be covered with a thin layer of rubber sheeting to effectively protect/

protect them from contact with any secretions or moisture and to avoid the necessity of repeatedly cleansing the apparatus. This sort of screen is at all times waterproof, it is easily adjusted to the applicator and can be used for each case or application. Silver tubes do not require this protection, as the silver acts as sufficient screen to the glass tube inside. Screens of other material have to be used occasionally and are made from aluminium, lead, and tin foil among other substances. When we come to consider the action of radium on the tissues, something more will be said, as to when these denser screens are called for, let it suffice to say, that not only is the quantity of the radiation diminished by the thickness of the screen, but also the quality by filtration in fact it is impossible to diminish the total amount of radiation, without altering its composition.

Aluminium as a screen possesses many advantages. It can be rolled out into thin sheets down to 1/100 millimetre, though for practical purposes a thickness varying from ·01mm. to ·08mm. is found most generally useful. These screens are very light, and easily worn by the patient.

Lead/

Lead can be rolled to $^{1}/_{10}$ mm. and its great pliability makes it adaptable to all shapes. Screens of this material vary from 1mm. to 2mm. in thickness those of the latter thickness being used when it is desired to employ hard beta or gamma rays only or to give prolonged applications without causing surface irritation. The weight of these screens, however, is a drawback.

The lesion to be treated is gently cleaned and dried and all crusts or flakes of secretion are removed.

THERAPEUTIC/

THERAPEUTIC APPLICATIONS.

(a) REACTION.

The various ways in which morbid tissues respond to the action of radium may be divided into two classes, the inflammatory reaction and the non-inflammatory reaction. At the beginning of this thesis I have referred to the famous BECQUEREL burn; this was the first example of inflammatory reaction, due to an overdose; but since then it has been found possible to obtain cellular modification and clinical results without producing inflammation. The first named reaction is produced when the doses have caused an inflammation, followed by ulceration and the formation of crusts. This ulceration takes place on the surface of the tissues operated on; it is generally painless, and when the crust is not interfered with, it comes off sooner or later, and the tissues underneath are found to be healed. Constant interference with the crust formed, however, may mar the aesthetic appearance afterwards by producing a depressed scar. Either of these two reactions I have mentioned may be brought about by the careful application of radium by an experienced worker/

worker, but occasionally factors are present which may alter the effect desired. Thus personal idiosyncrasy or susceptibility must always be taken into account, when considering the effect of any application, and the site of the lesion, whether situated upon skin, bone or mucous membrane, plays an important part in the reaction obtained. I shall refer to this again in the part dealing with my clinical experiences. Some tissues can be influenced very easily; they are susceptible and easily acted upon by the rays; other tissues are more refractory, but the resistance they offer is never quite complete, and a time always comes when the cell undergoes a certain degree of degeneration, and is destroyed. This destructive action is very valuable in the treatment of certain lesions.

But besides this action a certain number of diseased tissues can be modified without being subjected to any inflammatory reaction, and herein lies one of the principle interests in the use of radium. These tissues seem to possess a special receptivity to the rays, and respond most easily to their influence. To this action the description 'selective' or 'specific' has been applied, though some authorities are not inclined to grant this claim.

KNOX/

KNOX [7] in his paper on the results of his experience at the Cancer Hospital thinks the description is bad and maintains that radium simply acts on all living cells, according to the resistance of the particular cell in question; young and actively growing cells are more readily influenced than mature cells, and the cells of a new growth, approximating in structure and resisting power to those, are so much the more readily subject to the action of radium. WICKHAM [8] on the other hand thinks the expressions are perfectly appropriate to the action produced. Whatever be the opinion held in those cases, the tissues undergo retrogressive changes, and are modified without the production of a visible inflammatory stage. WICKHAM'S opinion is borne out to some extent by the fact that this retrogression may be obtained either by comparatively weak doses, or by strong doses, and with rays of strong or weak penetration. This sensitiveness is often greater than that found in normal tissue, and in these cases the normal tissues surrounding the diseased cells, although subjected to the same doses, remain unaffected in outward appearances. From this it is argued/

argued that sensitive tissues deep-seated under the skin can be modified without any visible change of the cutaneous tissue. The subjacent tissues act as filters modfying the quantitative and qualitative value of the radiation, whichreaches the deep parts under treatment. In support of this statement, and of the claim of radium to a selective action on certain tissues, the action of extremely penetrating rays on glandular masses infiltrated by a new growth is pointed out. From the practical point of view, this non-inflammatory reaction must never be lost sight of, as it is of the utmost importance when aesthetic results are desired. Some lesions can only be treated by destructive action, others are amenable to specific action, but only after a long period, so that it is sometimes useful to proceed partly by destruction in these latter cases, and thus combine the two methods.

WICKHAM and DEGRAIS[9] come to the following conclusions:-

(1) Reaction does not necessarily imply a destructive effect: there may be strong reaction without inflammation or destruction.

(2) Destructive inflammatory reaction is sometimes/

times useful and even necessary.

(3) All reaction of whatever kind is determined as much by the dosage adopted, as by the nature of the tissues.

To each type of ray - alpha, beta, and gamma - there is attached a certain reaction, thus each has its own individual value. As the alpha rays are most easily absorbed, it is probable, that the reaction which they produce is exercised only on the most superficial layers of tissue. This is the type of radiation most important in the 'toile' apparatus, and has been used with great advantage in the treatment of chronic superficial inflammatory disease.

Beta rays are present in large numbers in the most effective and most frequently used radiations being found as primary, and again as the secondary rays of Sagnac. The primary rays predominate largely, and possess amongst themselves different qualities of penetration; thus they can penetrate the whole thickness of the tissues at various levels. It has been proved that the beta rays have a real action, which may be selective or inflammatory.

Gamma/

Gamma rays form a low proportion of the radiation from an unscreened apparatus, and their action need hardly be taken into account in exposures lasting a short time. But the radiations composed of hard beta and gamma rays have a special clinical significance. They are described as surpénétrant rays, and they produce special reactions of great importance. They are obtained by interposition of lead screens of from 1 mm. to 2 or 3 mm. in thickness, and they form radiations of weak quantitative value. This can be compensated for, however, by the total length of the application, either by continuing them for some hours in succession, or by making them shorter, but frequently repeated.

Such long applications are borne easily by most parts of the body, excepting the buccal mucous membrane, where the exposures must be short and frequently repeated. These surpénétrant rays cause little surface irritation, and are valuable when one wants to work at a great depth, without causing superficial inflammation.

Many workers have studied the effects of radium on plants, and animals, and on human tissues. ABBÉ/

ABBE[10] of New York read a paper at the International Congress of Medicine in which he detailed results of this experiment on plant growth, after the seeds had been exposed to larger or smaller doses of radium, and the conclusions that he came to were, that according to the dosage, the growth of the seeds was stimulated or retarded, and secondly that the distance of the radium without filtration, from the parts exposed, had a marked result upon the effects produced. The first of these findings has an important bearing on the suggestion that has been advanced that some cases of malignant disease have taken on a more rapid growth after exposure to radium, a fact to which I shall draw attention in another part of this thesis.

DANYZS has inserted a tube of radium under the skin near the spine, and OBERSTEINER has immobilized animals in a box in the top of which and corresponding to the cranium was placed some radium. Both observers have found that the animals have quickly died from paralysis or tonic convulsions. Post mortem they found minute haemorrhages in the brain and cord, and degeneration of the endothelium of the/

the capillaries. These results have been confirmed by the experiments of SIR VICTOR HORSLEY and Dr. FINZI[11] who applied tubes of radium through a trephine hole on the pia mater over the pre and post-central gyri of three monkeys. HERTWIG[12] (Berlin) has ascertained that radio-active bodies have a powerful influence on vital processes in plants and animals. The endocellular ferments of the body are always stimulated, never inhibited by radiation. Lower plant growths (bacteria, etc.) are inhibited and even killed by large doses of the rays. The development of plants and animal ova is stimulated by small doses but definitely inhibited by large ones. On the animal organism there is stimulation of the respiratory metabolism, and insignificant increase in the protein exchange. As regards purin metabolism there is a limited increase in the excretion of uric acid, this increase is small and transient.

The chief diseases in which radium has proved of service are as follows: - Rodent ulcer, malignant growths, angiomas, lupus erythematosus, lupus vulgaris, keloids, Grave's disease and pruritus. In rodent ulcer radium has succeeded and produced remarkably/

remarkably good results, where other methods of treatment have failed. Opinion may vary as to the method of treatment to be applied to small rodent ulcers, which are evidently curable by various other therapeutic agents, but there seems to be no doubt that nothing is so effectual as radium in the large and inoperable ones. As a rule for a small ulcer, the application should consist of a short unscreened exposure of a full strength applicator. If the ulcer occupy a large superficial area, an unscreened application over the whole area at the same time, is apt to give rise to a severe systemic disturbance therefore, successive applications must be made in different places until the whole area has had a sufficient dose. Rodent ulcers affecting the nasal or buccal mucous membrane are not nearly so amenable to the action of radium, and in case of over exposure a painful reaction may be produced. HAYWARD PINCH in his Annual Report[13] of the Radium Institute, points out that many of those rodent ulcers which have received treatment for a long time with X Rays zinc ionization and carbonic snow respond badly to radium treatment, and thus the prognosis is rendered uncertain. Several of our cases of rodent ulcers had been/

been previously treated by some of these methods.

As regards other carcinomata promising results have been obtained in malignant disease of the breast and rectum. Radium seems to be our best palliative agent in carcinoma of the uterus by relieving pain, arresting haemorrhage, diminishing discharge and healing ulceration, also several inoperable cases have been rendered operable. Opinion to-day seems to be unanimous in answer to the question whether radium treatment is preferable to surgical removal, that operative treatment if possible should come first. ABBÉ (14) endorses the opinion of WICKHAM, that malignant tumours must first be excised as thoroughly as possible, and radium then used upon the bed of the disease. He has come to the following conclusions:

(1) That an undoubted retrograde degeneration of malignant cells occurs under correct dosage of gamma radiation.

(2) Effective use of radium lies in the application/

application of a large enough quantity to avoid the stimulating action of little doses at short range.

(3) The utilization of gamma radiation with its deep penetration can be made by the removal of alpha and short beta rays, by filtration through lead.

(4) Such filtration requires many times as long for a sufficient amount of gamma rays to act, as when other rays are eliminated by what may be called 'distance filtration'. One and a half inches or 4 cms., seems in practice to exclude most of these, and gives free and instant play of the entire gamma range, without delay of passage through lead.

(5) Cross-firing of several specimens simultaneously, or of one large specimen moved successively/

successively to several neighbouring places, is necessary for the best work.

(6) Normal tissue resists many times as large doses of gamma rays as are required to check and dissipate growths.

KNOX[15] is also of opinion that in early cases of malignant disease, operative measures should come first but states conditions under which radium should be second choice. Thus the patient may refuse operation, and thorough treatment by radium in early cases, may lead to a disappearance of the growth. The risk of operation may be too great. Inoperable cases are many of them hopeless from a curative point of view, but radium may cause marked relief to suffering. BARLING[16] would not take the responsibility of advising radium as a substitute for excision, in cases of malignant growths.

Next/

Next to Rodent Ulcer radium has been found most beneficial in Naevus. HAYWARD PINCH[17] in his Report regards flat superficial naevi, commonly called 'Port wine' stains, as being the most difficult of all naevi to cure. Great caution has to be exercised in applying the radium as personal idiosyncrasy is always a prominent factor. The best results can be looked for when the naevus is quite superficial and shows no tendency to infiltration. Cavernous naevi lend themselves more to treatment by radium than does the capillary variety. When the 'cross-fire' method can be applied, good results can be generally expected. DAWSON TURNER[18] draws attention to the destructive action of radium on the hair follicles, and questions whether this agent should be used, in the treatment of naevi on the scalp, as a bald spot is apt to be left. Pigmentary naevi can only be removed by the destructive action of radium as it is necessary to destroy the pigmented skin, and the hairs that are commonly present. As regards personal idiosyncrasy WICKHAM[19] found that the results of applying radium, may vary in different places/

places, and that doses sufficient for one subject produce scarcely any effect in another. He counsels operating on a single area by way of trial, the result obtained being an indication to the subsequent line of treatment. Inequality of action he explains as being due to differences in the types of skin e.g. dry or greasy skin, fair or dark in colour, and its delicacy. As most naevi occur in sites where an aesthetic result is the aim of treatment, in the use of radium inflammatory reaction must be avoided as far as possible.

Radium has proved of great value in the treatment of Keloids, a condition with which surgeons have had great difficulty in successfully dealing, due to the tendency to recur and increase on the slightest excitation. Radium correctly applied causes this type of growth to shrink up and disappear leaving a smooth supple cicatrix, though the degree of success in treatment depends much on the age of the keloid. This applies to true keloids of fibromatous material, but where hard fibrosclerotic bands are present, the tumour is more refractory to deal with, and one must have recourse to the selective method of reaction. Radium is of double value in/

in the treatment of contracting keloids, in securing an aesthetic result and in restoring elasticity to tissues, which may have been limiting movement, or causing deformity. WICKHAM[20] admits that in some of his cases he has found it expedient to combine surgery with radium. MASOTTI recommends a combination of scarification and of radium applications as it shortens the duration of treatment.

As regards the therapeutic action of radium in tuberculosis, comprising surgical tuberculosis, lupus and scrofula, results have been varied, and in the main disappointing. SIMPSON[21] reports a series of cases of different nature treated by radium applications, which he extols in lupus vulgaris, and lupus erythematosus, among other conditions. DAWSON TURNER considers that radium is not specially indicated in lupus. He has seen improvement in localised cases, but not more than could be obtained by other means. HAYWARD PINCH[22] says that Finsen light is to be preferred to radium in cases of lupus vulgaris, and whenever possible it should always be adopted, though lupus erythematosus is usually benefited by radium. WICKHAM'S experience is that all tuberculous/

tuberculous conditions, can be influenced by radium, but the degree of receptivity differs according to the varied forms of tuberculosis, and subcutaneous tuberculous glandular enlargements are more amenable to the rays, than are the many varieties of lupus, and notably the nodules of lupus vulgaris. He concludes that it is better to destroy isolated lupus nodules and those recurring in the cicatrix, by the electro-cautery, and not with radium; and that ulcerated vegetating warts and erythematous forms yield the best results. In the treatment of tuberculosis of the skin, radium must be used for its destructive action, the advantage of radium therapy here lying in the satisfactory appearance of the repaired tissues. There can be no doubt, however, that in some cases the rays act by relieving congestion, and in lupus affecting mucous membrane, this is an especially valuable property. The chief drawback to the treatment is the tendency to recurrence which all these conditions manifest. The different experiences are summarised in the statement that the treatment of tuberculous lesions requires powerful action, both wide and deep and long

continued/

continued, with careful supervision of the resulting scar. Radium does not appear to have any selective action in lupus. A point one is apt to lose sight of, is that in the treatment of any tuberculous condition, by whatever means, attention must be paid to the general health and mode of living of the patient. In our cases latterly we started to carry out constitutional treatment allied with radium treatment, when we thought it was indicated.

Radium therapy has been tried in various other conditions, and has proved of value in pruritus, chronic eczema, and goitre. One of the first results obtained by the use of radium, was its analgesic effect, and many workers have laid stress on its property of relieving pain. SOUPAULT has shown the power of radium in relieving the pain of articular rheumatism, and DOMINICI has recorded the cure of two cases of intercostal neuralgia, and two of sciatic neuralgia. In pruritus many successful results have been obtained, chiefly when there has been an actual lesion to account for it. When the trouble is purely nervous in character, the results are not so satisfactory.

Chronic/

Chronic eczema yields readily to weak, unscreened exposures of radium. This exposure can be furnished by a powerful apparatus in a short time, and in this way large surfaces can be treated. WICKHAM[23] states that out of 300 cases treated during the course of eight years, he has met with almost invariable success.

Many favourable reports as to the action of X Rays in exophthalmic goitre have been published, and much that has been said could be applied to the action of radium in this condition. ABBE of New York was the first to introduce cylindrical radiferous tubes into an enlarged thyroid. He was successful in obtaining a reduction in the size of the gland with a corresponding subsidence in the other symptoms. WICKHAM has succeeded in obtaining a similar result, by his method of cross-fire applications. DAWSON TURNER has produced marked improvement in four cases, and points out that radium has two advantages over X Rays in the treatment of this condition: (1) a perfectly definite dose of it can be given and repeated as often as may be desired; (2) the radium can be applied without noise or excitement/

excitement, while the patient is at rest in bed, and owing to the nature of the disease this is an important advantage.

(b) HISTOLOGICAL CHANGES.

To come to the histological aspect of reaction, this has been experimentally studied in the guinea pig by DOMINICI and BARCAT, and proved to be the same, whether the condition of the tissues be normal or diseased. When the normal skin of a guinea pig is exposed to a series of radium applications, after a period it is found that 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 connective tissue, and from this a cicatrix is gradually produced, having neither the structure of the corium of normal skin, nor that of post-inflammatory sclerotic tissue. The same changes were found to take place, when radium was applied to experimental cutaneous tuberculosis. At first there is a diminution of the simple inflammatory/

inflammatory perituberculous reaction, the changes consisting of a disappearance of the polynuclears of macrophagocytosis, transformation of lymphatic cells into plasma cells, and development of nodules possessing a lymphoid structure. Then organisation of the vascular connective tissue stroma, which was the seat of this simple inflammatory process, is noticed. Finally there is an extension of this process to the tuberculous follicles themselves. The epithelioid cells lose their globular conformation, become elongated and anastomose in a network of fixed cells of an embryonic type. As a result of this, the epithelioid tissue of the tubercles is changed into embryonic myxomatous tissue. The cure is completed by the transformation of myxomatous into sclerotic tissue.

The retrogression of sarcomata takes place in the same manner. The size of the body and of the nucleus of its enormous cells gradually decreases. As they shrink the neoplastic elements elongate, the contour of their nuclei become regular, and they finally assume the form of large embryonic connective tissue cells anastomosing in a cell mass similar to that/

that of the myxomata. The tissue of the sarcoma is thus transformed into myxomatous tissue, which ultimately changes into tissue resembling that of a fibroma.

Under the influence of radium rays the cells of epitheliomata of the skin, or of the muco-cutaneous regions, gradually diminish in size. 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 as in the cases of cutaneous tuberculosis and sarcoma mentioned above. Thus it will be seen that 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, forming connective tissue bundles and elastic fibres.

A PLEA FOR A POSOLOGICAL STANDARD.

One of our chief difficulties was the question of dosage, what length of application to apply in any given case. To anyone with a knowledge of the wonderful physical properties of Radium, and with a recollection of some of the terrible results, that followed on the incautious use of X Ray treatment, at its inception a few years ago, the above question must be the cause of much serious consideration, followed by careful observation of results obtained. It is still too early in the history of the subject for anyone to dogmatise as to what is the correct length of an exposure in any given case, though experienced workers are now in a position to express an opinion as to what would be actually harmful.

Many things have to be taken into consideration, as for instance, the strength of the applicator, the quality and quantity of screens to be used, the depth and situation of the growth to be acted upon etc. Mucous membrane is especially sensitive to the action of radium, and drastic reaction usually follows an overdose, causing much pain to the patient/

patient, and even sloughing of tissues. A case in point - A male aet. 50 came to us suffering from a malignant growth of the right tonsil. We applied a silver tube applicator to one portion of the growth, the silver wire attached to the applicator, being brought through the mouth, and fixed to the side of the face with adhesive plaster. Due to the difficulty of application, the tube was kept in situ for six hours. Our experience had taught us, that, cancerous growths in other situations could bear this exposure easily, but in this case the patient afterwards suffered from pain, discharge, dysphagia, and a burning sensation in the throat, pointing to reaction in the growth and neighbouring parts, probably due to movement of the applicator. We had evidently given an overdose considering the situation of the growth. It is stated,(24) that unshielded radium, which gives remarkable results in cutaneous epitheliomas, is dangerous for cancers which encroach on the buccal mucous membrane, as it may stimulate rather then arrest their development. GAUCHER has pointed out that the same rate holds good for certain caustics.

The quantity of salt contained in the applicator though useful is not the main thing. The chief thing to know is the activity that can be utilized by the operator. In merely mentioning the quantity/

quantity of salt contained, the thickness of the walls of the applicator is not taken into account thus one is left in doubt about data, on which the value of the treatment depends. By this loose use of terms, a second observer cannot arrive at a corresponding therapeutic result as the first, since the radioactivity is not known. We must have useful measurements, and determine scientific doses and quantities. Until the recent preparation of International Radium Standards, various methods of determining the value of radium bromide were in use. But now the determination of the radioactivity of specimens of radium salts, is made by direct comparison with a standard specimen of radium chloride deposited in the Bureau International des Poids et Mésures in Paris. The standard was prepared by taking a known weight of radium chloride separated by Mme. Curie for determination of the atomic weight of radium. The comparison, whenever possible, is made by means of the gamma rays. This ensures that the strength of specimens is accurately known, and is of guidance to the operator. But this attained, we have not gone far enough, for we have no relation between the activity of the applicator and the length of application.

Radium/

Radium applicators differ as regards size i.e. surface area, shape and activity, and for one worker to state that he cured a rodent ulcer with an applicator containing 3 centigrammes of radium salt with an activity of 500,000, with an exposure of one, two, or three hours is of no help to a beginner in the science, if he has not a similar piece of exactly the same area, containing the same amount of salt, and with the same available activity. What is wanted is a certain definite standard of activity, working for a certain definite standard length of time, and thus the dose could be stated in terms of the activity of the applicator and the length of exposure combined, or as we did in Hull, express the dose simply in terms of time.

The above was one of the first difficulties we met with in our experience with radium, and we overcame it in a manner very similar to what workers have devised in other centres. The method I am about to describe has been in use in Hull for the last five years, and the fact that the necessity for some such system of dosage as ours has been recognised by other operators, bears out my point, that without it there can be no co-ordination or helpful comparison/

comparison of results.

DAWSON TURNER is the only authority I have met with who has advocated[25] what I have attempted to explain above, and before describing our system I shall give his suggestion in his own words[26]: " . . . . . the dose ought to be stated in terms of the product of the strength of the preparation and the length of the exposure - what would be termed in electrical measurement the "ampere hours". Thus a 10 millegramme specimen applied for one hour would be called 10 millegramme hours; applied for thirty minutes 5 millegramme hours. If 5 millegrammes were applied for 12 minutes, it would be one millegramme hour, and so on. Thus a dose of 10 millegramme hours could be given by 1 millegramme applied for 10 hours or 20 millegrammes applied for thirty minutes etc." In giving an account of his cases, DAWSON TURNER states his doses in this manner. Our method though substantially the same idea differed from the above, in that we did not express our doses in terms of the product of the strength of the applicator and the length of the exposure, but in terms of time only, by a calculation which I shall describe.

Our unit of measurement we selected as 1 centigramme/

centigramme of active salt with an activity of 500,000 curies, acting for 1 hour, and from this we worked out the strength of our applicators in terms of time. By our method each applicator had a standard time of its own, during which period it gave off a radiation equivalent to any other applicator in its respective standard time. This period of time we called a Standard Hour, or shortly S. H. At the beginning the standard hour for each applicator was worked out, and entered in the radium book. When a dose of so many standard hours was prescribed, I simply consulted this book, and gave the exposure with any applicator found suitable. The only drawback to this method, and one which applies also to DAWSON TURNER'S suggestion, is that it takes no cognisance of the superficial area of the piece. But granted that the quality and quantity of the screens is mentioned, our system comes nearer to giving an accurate account of what radiation was applied than any I have heard of.

As I have mentioned, we took as our standard 1 centigramme with an activity of 500.000 acting for 1 hour, and from this we get the formula,

$$1 \text{ hour} \div \frac{\text{Activity of Piece} \times \text{Weight of Salt}}{\text{Standard Activity}} = 1 \text{ S.H.}$$

Standard hour.

Referring/

Referring to our list of applicators, the description of the first piece reads -
Applicator No. I. 3 centigrammes with activity of 500.000 and applying our formala

$$\frac{1 \text{ hour}}{\frac{A \times W}{S.A.}} = \frac{60 \text{ mins.}}{\frac{500.000 \times 3}{500.000}} = \frac{60}{3}$$

Where A equals activity of piece, W equals weight of contained salt, and S.A. equals our arbitrary standard activity, we find that 20 minutes is the standard hour for applicator No. I. In this way we worked out the value of all our applicators and I here append a list. It will be noticed how useful and speedy Nos.1, 2, 6 and 7 are, compared with the others.

No. I./

No.	1	contained	3	centigrammes	of	activity	500,000	∴	1 S.H.	= 20 mins.
"	2	"	2	"	"		500,000		"	= 30 mins.
"	3	"	5	milligrammes	"		1,800,000		"	= 33⅓ mins.
"	4a	"	2	"	"		1,000,000		"	= 2½ hours.
"	4b	"	½	milligramme	"		1,800,000		"	= 5½ hours (approx)
"	4c	"	½	"	"		1,800,000		"	= do.
"	4d	"	2	centigrammes	"		1,800,000		"	= 8⅓ mins.
"	5b	"	1	milligramme	"		2,000,000		"	= 2½ hours.
"	5c	"	1	"	"		2,000,000		"	= 2½ hours.
"	5d	"	3	milligrammes	"		2,000,000		"	= 50 mins.
"	6	"	4	centigrammes	"		250,000		"	= 30 mins.
"	7	"	3	"	"		500,000		"	= 20 mins.

In/

In giving this account of the results of radium therapy in the Hull Royal Infirmary, it must be remembered that the Infirmary possessed no radium of its own. There is no Radium Institute in Hull, and the town's radium is kept at the Guildhall, in the office of the Medical Officer of Health. It is lent as required to institutions or private practitioners by the Medical Officer of Health, and is supplied free for the treatment of any patient (private or institutional) whose income or that of the family does not exceed £2 a week, and a charge of one shilling is made for every pound or fraction of a pound over, that income.

The period of loan is forty eight hours, and a signed agreement is made between the borrowing practitioner or institution, and the corporation of the city, providing for indemnity in the event of damage or loss, and also for the furnishing of information as to the progress and result of treatment.

Contrary to expectations this free supply of radium was not taken advantage of by practitioners to the extent expected, and on many occasions we had no difficulty in prolonging the period of our loan. This was of great service, as it enabled us to/

to finish the application prescribed, saving waiting until next week. Every Wednesday night was Radium night at the Infirmary. Cases were sent to us from the out-patient department of the Infirmary, chiefly those cases that proved to be generally unamenable to ordinary medical or surgical treatment, such as naevi, lupus etc. Other cases were transferred from CO$_2$ snow, and X Ray treatment, to our care so that for the quantity of Radium we had a plethora of cases. Mr. HOWLETT, F.R.C.S., England, Senior Surgeon to the Infirmary, to whom I am indebted for the use of the case book for this thesis, was in charge of the department. Out of all the cases sent to us, we had to select carefully only those we thought would be benefited by the treatment, and it was often our sad duty to gently turn away a hopeless case of malignant disease, who had come with fresh hopes, having heard exaggerated accounts of the new treatment.

Each case was examined and the diagnosis confirmed or otherwise, as the case might be. Careful notes and diagrams were taken of the lesions, and every patient had to report himself from time to time, thus being kept under observation for many months/

months. Mr. HOWLETT in all cases prescribed the application of radium, and it was my duty to apply it. On many an occasion to apply and keep applied the applicators took considerable ingenuity and patience, as the lesions were often small, and in sites difficult of access e.g. the inner canthus of the eye, the tonsil, etc.

As regards screens we never used any, except rubber sheeting, and this was more for the protection of the radium, than to modify the radiation. On several occasions, notably in patients coming from the country, we kept the patient in bed for a couple of days and applied massive doses; this saved the patient trouble, and enabled us to make the best use of the radium during the short time it was at our disposal.

PERSONAL EXPERIENCES and NOTES of CASES.

The results of treatment of 71 cases are given in the following tables. The tables are followed by a general discussion in which typical cases of the various conditions are reported in detail.

Table/

TABLE I.

Summary of Cases.

Treated	71
Improving under treatment	25
Cured	12
Improved	5
Not improved	17
Abandoned treatment	8
Dead.	4
Total	71

I have included under heading 'Improving under treatment' those cases in which treatment was too recent to enable any conclusion as to the results to be stated. In table II. the cases are arranged according to the nature of the disease.

Disease	Cured.	Improving under treatment.	Improved.	Not improved.	Abandoned treatment.	Dead.	Total.
Epithelioma	1	1	2	4	3	2	13
Rodent Ulcer	7	6	-	-	2	-	15
Lupus	3	15	2	11	3	-	34
Naevus	1	2	-	-	-	-	3
Fibrona (Keloid)	-	-	-	1	-	-	1
Hairy Mole	-	1	-	-	-	-	1
Carcinoma	-	-	-	1	-	2	3
Papilloma Larynx	-	-	1	-	-	-	1
Totals	12	25	5	17	8	4	71

As/

As will be seen from the above table, a large proportion of our cases were suffering from lupus, almost 50% in fact. In these cases the lesion almost without exception was extensive, and our supply of suitable applicators was small, so that it took a long time to cover the area, and progress was necessarily slow. Some of our cases dropped treatment during the year, due to various reasons. Our cases of carcinoma occurred in old people, and death from adventitious disease, was the cause of treatment being stopped in a couple of cases. Other patients we found had removed from the district, and either could not afford or did not care to travel to the Infirmary. A few patients, chiefly those suffering from small epitheliomas, rodent ulcers, or small patches of lupus, grew discontented with the slow treatment and requested operation. In all cases the small supply of radium and the brief period of loan, rendered treatment as often as desired, impossible.

N O T E S/

NOTES OF CASES.

RODENT ULCER.

Our results exactly bore out what has been said by others. This, of all forms of malignant disease, is the most amenable to the action of Radium. To this I would add one qualification, by limiting the statement to ulcers not affecting mucous membrane or bone. Of the latter class, we had some terrible examples, and though in several cases we did much to ameliorate the condition in causing cessation of discharge and pain, after due trial we had to give up any attempt at a cure. For this type of case, the Paris school recommend a 'toile' or radium plaster, exactly covering the area of the ulcer, and applied for a long time. Out of our series of fifteen cases, seven were cured inasmuch, that after an interval of many months, we could find no evidence of a recurrence. Six cases were improving under treatment, some of which were very slow in healing. HAYWARD PINCH, F.R.C.S., in charge of the Radium Institute, points out in the Annual Report (27) of the Institute, that many of those rodent ulcers which have/

have received treatment for a long time with X-Rays, zinc ionization, carbonic snow etc., respond badly to radium treatment. Quite frequently the previously treated tissues break down to an extent which far exceeds the ~~re~~ resisting ulceration, and repair is very slow and imperfect. Not a few of our cases had had previous treatment by some of these means, and we found that the application of radium meant great destruction afterwards, from which recovery was slow and repair imperfect.

Small ulcers, situated on soft tissues, such as the nose or cheek, we found to disappear on one or two applications of an hour apiece. The larger ulcers we treated by several successive applications in different places, at intervals of two to three weeks, until the whole area was covered. Great care must be taken when there is involvement of bone or cartilage, that too great an exposure of an unshielded apparatus is not given, as this may cause a very acute, painful and prolonged inflammation. For these DOMINICI[28] recommends ultra-penetrating rays. The radium rays are filtred to the extent that only hard beta and gamma rays are allowed to get through, and very long exposures are required.

CASE/

CASE I.

A. M. B., male aet. 64, Hull, had for many years suffered from a rodent ulcer at inner angle of the left eye. He came first to the Infirmary on 20th March, 1912, and an application of 5 S.H. was prescribed. I applied our No. I. applicator for one hour and 40 minutes. Two months later he reported himself, when the ulcer was found to be much smaller. A similar dose was applied, and when seen one month later, the ulcer had totally disappeared, leaving a fine, white cicatrix.

CASE II.

W. H., male aet. 55, Hull. Rodent ulcer on tip of nose, about size of threepenny bit, which patient said had been coming on for several years. Two months ago had $\frac{3}{4}$ Pastille given, but no sign of healing taking place. On 21st June, 1912, he was seen first in the Radium Dept. and an application of 10 Standard Hours prescribed. No. 2 applicator was kept applied for 5 hours. He was seen again one month later when ulcer was found to be smaller and shallower. The same dose was repeated, and when one month later the patient reported himself, all trace of/

of the ulcer had disappeared. Several months later he was seen again, and there was no recurrence.

CASE III.

J. M., male, aet. 74, Hull, suffered from a rodent ulcer in the right malar region, about the size of a florin. He had been treated with repeated applications of C.O.2 snow. When seen first the ulcer was very excavated with prominent raised edges. The first application was 8 S.H. on 23th Aug. 1912. He was not seen again for 2 months, when ulcer was found to be smaller, with smooth, growing edges. In Nov. he again reported himself, no radium having been applied since the first dose. The ulcer had gone back to the status quo ante. Nov. 10th 1912 the original dose was repeated, and one month later, I entered him as being apparently cured. He reported himself in January 1913, when no recurrence was found.

CASE IV.

M. L. female, aet. 70, Goole, suffered from a rodent ulcer on the tip of the nose for 6 years. The ulcer was small, and circular, with raised margins/

margins. As a first dose, 10 Standard Hours was prescribed. This I carried out, by applying No. 7 applicator for 3 hours, 20 mins. The patient was seen two weeks later, 15th April, 1912, when the report was, that it was much improved, the upper half looks active, with raised rolled edge. Three more applications of 2 S.H., were made at intervals of one month, and at the end of June 1912, nothing remained of the lesion, but a small white scar. There has been no trace of recurrence.

LUPUS/

LUPUS.

Our results in the treatment of Lupus, were disappointing. Out of a total of 34 cases treated, we could only claim 3 as being cured, or between 8 and 9%, this result is no better than what could be obtained by other methods of treatment. It would seem that Radium must be used for its destructive effect as it possesses no specific action on the tuberculous tissues, though here it is of value in securing a satisfactory appearance of the repaired tissues. Healing of small patches of Lupus vulgaris can often be obtained by comparatively small doses though recurrences are common. When seeking a destructive effect, severe reaction usually results in the ulcerated area, which sometimes ends in satisfactory repair after several months of slow healing. WICKHAM and DEGRAIS (29) recommend the use of the galvanocautery for recurrences, while HAYWARD PINCH in his report of the Radium Institute (30) says that treatment by Finsen light is to be preferred to radium in cases of this disease.

I would draw attention to Case 5, lupus erythematosus/

erythematosus affecting the columella of nose, and interior of nostril. This demonstrates one of the advantages of radium treatment, in that it can be adapted to sites difficult of access by other methods.

CASE V.

M.P. female aet. 24, Ferriby, suffering from lupus erythematosus of upper lip, columella, and introitus of nose. It had been coming on for nearly a year, and was painful, due to irritation. Just within the right nostril there was a small ulcerated area. An exposure of 3 S.H. was prescribed, 9th June 1912, which I effected by applying applicator No. 3 (silver tube) within the nostril for 1 hour 48 mins. Seen one month later the small ulcer had disappeared, and the hyperaemic character of the external lesion was much less. A similar dose was again applied, and when the patient reported herself in August 1912, there was remarkable improvement. No.I flat applicator was now applied to two small remaining patches on upper lip for 2 hours (6 S.H.) and when seen one month later, all trace of disease had disappeared. After an interval of several months there was no recurrence.

CASE VI.

E.K. female aet. 30, Hull, lupus erythematosus/

erythematosus covering whole of left cheek. Patient said she had had it all her life. At times it was painful and discharging. Six years ago she had been treated at Blackfriar's Hospital by Finsen Light and X Rays. When seen first by us, the diseased area, covered the whole of the left cheek. The upper half looked active, the lower half had a hard, keloid condition of the skin, but looked quiet. On 13th Nov. 1912 5 S.H. were applied by applicators Nos. I and 2 being kept in contact for 1 hour and 40 mins. and 2½ hours respectively. There was slight reaction afterwards and nothing was done for two months, when original dose was repeated. When seen later there was decided improvement in the upper half, the lower half still looked quiet. Treatment was still in progress when this report was made.

CASE VII.

J.H. male, aet. 26 Marfleet. For several years he had a painful, hard warty growth on chin, below lower lip. He first attended on 11th February 1912, and lupus verrucosus was diagnosed. He was treated by four short applications, at weekly intervals. As a result the skin became more supple and warty character less. On 10th March 1912 an application/

application of 5 S.H. (No.6 applicator for 2½ hours) was made, and this was repeated on the following Wednesday, one week later. Patient came for examination a month later, and no trace could be found.

EPITHELIOMA.

We were unfortunate in our experience of cases of this kind, as out of a total of 13 cases, 5 dropped treatment during the year Feb. 1912 to Feb. 1913, of the remaining 8 cases, we were allowed to carry treatment to the length we desired, but had finally to give up 4, as being beyond cure. This cannot be regarded as a good result, but we are not alone in our experience, as the views held by many as regards the curative powers of radium in advanced epithelioma are pessimistic. WICKHAM made the following remark at the July meeting of the British Medical Association, 1910 : "In the great majority of cases (i.e. epitheliomata) surgery should be associated with radium." CHEVRIER (31) questions the prudence of simple radium therapy as the only method of treatment of infiltrated cutaneous epitheliomata with glandular/

glandular involvement and pleads for the surgical removal of the tumor, and the use of radium to destroy the microscopical residue which usually causes relapse. Dr ROBERT KNOX, Director of Radium treatment of the Electro-Therapeutic Department at the Cancer Hospital admits (32) that in every early case of malignant disease operative measures should come first, giving at the same time a list of certain conditions when radium should be second choice. There can be no doubt that superficial cutaneous epitheliomata give way readily to radium, usually with an exposure that causes no inflammatory reaction and resulting in a fine white cicatrix. But for a larger growth, where ulceration has gone deeper than the skin, and the neighbouring glands are involved, the treatment must consist of heroic applications. A destructive reaction follows but many good results have been noted with very little cicatricial contraction. The results are disappointing when the mucous membrane is primarily affected, or is the seat of disease from a secondary invasion. I have referred to the difficulty of applying radium to the buccal mucous membrane (q.v. case of malignant tonsil) and to the danger of drastic reaction with subsequent congestion/

congestion of tissues. In fact, we had come to consider that the position of the growth plays an important part in the prognosis. Cancers in certain situations, readily lend themselves to the "cross fire" method of application, this bears out the statement just made.

CASE VIII.

M.W. male aet. 49: Hedon came to the Infirmary on Feb. 24th 1912, complaining of a lump in his lower lip, of about ten months duration. On examination a discrete swelling, about the size of a hazel nut could be seen and felt. The growth was immediately below the lip, and there was just a little commencing ulceration on the surface of the lip. There was no involvement of glands. We thought it an ideal case for radium treatment. An application of 6 S.H. was prescribed which I carried out by applying No.2 applicator for 3 hours. Patient reported himself three weeks later, when it was seen that the ulcerated patch had healed, the swelling was softer and patient thought it was a little smaller. A dose similar to the first was given again, and at the end of a month, a decided improvement was noticeable. The growth was only/

only about half the original size, and neighbouring tissues were soft and pliable. For the remaining part of the tumour, we decided to try the "cross fire" method, with a result very satisfactory. Applicators Nos. 1 and 2 were fixed on either side of the lip, and kept in position for two hours. When seen again in May 1912, three months from start of treatment, the lip was of normal size, and no trace of tumour could be made out. In August 1912, the patient reported himself again and said he thought it was coming back. There was undoubtedly a recurrence and as the man was a gardener, living outside the city, and found it difficult to attend for treatment, at his request, the growth was excised.

CASE IX.

A.L. female aet. 65. Hull. Epithelioma of malar region. Diagnosis confirmed by microscopical examination of part of growth. The floor of the growth covered the area of a florin, the base was ulcerated, and there were epitheliomotous nodules in the periphery. Patient said it was growing larger. All things considered, we thought it wiser to excise the growth, and apply radium to the edges of the wound/

wound. The patient was accordingly admitted to the Infirmary and on 23rd August, 1912, Mr HOWLETT operated. For some weeks afterwards the growing edges were dressed with a simple ointment, but soon little areas began to break down and several nodules formed. To each of these an application of 8 S.H. was given, and again the edges started to draw together. Two weeks later there was a recurrence in the upper margin, this was promptly treated with another 8 S.H. dose, and healing was completed under ointment. The patient reported herself at intervals of a month several times afterwards, when there was no sign of recurrence. Finally she failed to come back.

OTHER CARCINOMATA.

As will be seen from the table, with the results of treatment classified according to the disease, I have divided the cancer group into three sections, into which I think nearly all cancers could be put, excluding perhaps, Paget's disease. Of this third section we had only three cases during the year '12 - '13, and what I have said regarding the more serious/

serious and advanced type of epithelioma applies to these. In a case of operable malignant disease of any part radium is a more powerful factor in the after treatment to prevent recurrence, than X Rays. In a case of inoperable malignant disease, radium is a better palliative agent than any other known method. Haemorrhage can be arrested, discharge diminished, ulceration healed and pain greatly relieved by its use. All workers are unanimous that by its use a case previously declared inoperable may in some instances become operable. The exposures have to be prolonged, spread over a period of several days, and repeated at intervals of a month or six weeks.

CASE X.

J.L. aet. 54. Carcinoma of uterus (Recurrent) The patient had hysterectomy performed on May 7th 1912 for this condition, and made a good recovery. At the beginning of September she returned, complaining of a return of the pain. On examination it was found that there was a recurrence of the disease the left fornix being full and infiltrated. Applicator No. 3 (silver tube) was applied to the growth and kept/

kept in situ for 12 hours, and the following day this dose was repeated. As a result all pain ceased, and patient was allowed to go home. She came back for examination one month later, and the induration in left fornix was appreciably less. Several weeks later she was brought hurriedly to the Infirmary in great pain, the bleeding and pain had reappeared, and she was weak and cachectic. On examination it was found that the disease had spread rapidly, the anterior wall of the vagina was ulcerated, and there was implication of the bladder.

CASE XI.

L.Q. male aet. 43, Hull, gave the history that several years ago, he fell and struck his chin. Sometime afterwards a 'lump' grew, which gradually got worse. On examination the mental symphysis was unduly prominent due to a hard growth, fixed to the bone. There was much induration of the adjacent tissues, and the skin was pierced by several sinuses through which saliva constantly dribbled, there was a most offensive smell, and the patient's condition was pitiable. We started treatment in August 1912, by placing our two smallest silver tubes in two/

two of the sinuses for four hours. There was a marked reaction afterwards accompanied by pain and haemorrhage, but gradually it quietened down, and patient thought that the pain and discharge were less. It was six weeks before we ventured to give another dose, when the original dose was repeated. Again there was decided reaction, and from this onwards the growth seemed to take on a new activity, and patient rapidly went down hill, pneumonia finally supervening.

NAEVI.

We only treated three cases of neavus, of which one was cured, and two were improving under treatment, at the time, when this report was drawn up. In all our cases we used short exposures of our most powerful applicators, with nothing but a rubber screen. In one case we tried the cross-fire method, with a very satisfactory result, this was a cavernous naevus, with much infiltration. Our other two cases were small and superficial.

CASE/

CASE XII.

M.G. female child, 7 weeks old, residing in Hull, was brought to the Infirmary on 18th December, 1912. It had two small capillary naevi, each about the size of a threepenny bit, one on the back of the neck, the other on the back between the scapulae. On 18th December applicators 1 and 7 were applied to each respectively for 1 hour (3 standard hours). The child was seen a month later, when the upper naevus was much smaller, the lower was not appreciably changed. On 15th January 1913, the application was repeated, and one month afterwards the upper had disappeared, the lower was apparently shrinking. One month later (March) both had disappeared.

CASE XIII.

F.B. male child, three weeks old, Hull. This child had a large cavernous naevus at the inner angle of the left eye, spreading over the side of the nose, and extending on to the forehead. The swelling was bluish in colour, subcutaneous, very prominent and tense when the child cried. It covered an area about the size of a florin. Owing to the age and restlessness/

restlessness of the child we tried the cross fire method. This consisted of a series of short exposures of ten minutes, twice a week, of two applicators applied simultaneously to opposite sides of the tumour, so that the area between might be subjected to a powerful radiation, and the danger of surface reaction in the delicate infant skin reduced to a minimum.

Improvement was slow, but gradually the swelling grew less, and one month after treatment was stopped, it had shrunk to less than half its original size. The patient is still under treatment (12/2/13).

FIBROMA (KELOID).

It is said that keloidal conditions answer well to radium treatment. Applications have to be repeated at intervals, but improvement is steady, and usually results in a return to the normal without any surface irritation. We had only one case of this kind under our care, which I have included under the heading 'Fibroma', as, although the condition was keloidal, there were several soft fibromata projecting from the scar, and it was the presence of these that really/

really caused the patient to seek advice and treatment. We failed to affect any material improvement in the case, the condition remained unmodified after several applications, and the patient was advised to have the growths removed by operation.

CASE XIV.

B.L. male, aet. 42, Grimsby. Patient had undergone an operation four years ago for some growth on back of neck, and left shoulder, of what nature he could not tell us. On examination there was a large triangular scar, with its apex just below the occiput, and the sides of which outlined the upper half of the left trapezius. The whole scar was dense, red and elevated, but caused the patient no inconvenience, what really brought him for treatment was the presence of several nodules in the scar, varying in size from a berry to a grape. There were nine of these little tumours in all. On September 15th 1912 I excised one of the largest of these growths for examination, and the Clinical Research Association reported that it was an innocent fibroma.

One week afterwards the patient was admitted to hospital and a dose of 20 Standard Hours was applied/

applied, to the whole scar. The patient reported himself four weeks later, complained of no reaction, and we could find no appreciable difference in the condition. In October the exposure was repeated and we did not see the patient again for two months, as the condition was still unimproved, operative treatment was recommended.

HAIRY MOLE.

Radium applied to this type of growth, secures many desirable results, and although our experience only extended to one case, the progress made placed radium therapy in our estimation in a rank equal with any other method of treatment. The benefit derived from the use of radium in this case was quite appreciable, and the rapid depilatory action, and decolorisation that resulted, made us think that it was specially suited for this type of growth. At the time when this report was drawn up treatment was not finished, and the cure was far from complete.

CASE XV.

A.F. female aet. 16, Hull, had a large mole covering/

covering the right half of the upper lip. The growth projected somewhat, from the level of the skin, it was covered with a strong growth of coarse hair, and was nearly black in colour. The girl came first for treatment on 17th August, 1912, when an exposure of 8 S.H. was prescribed. Applicators Nos. 1 and 7 covered the whole area exactly, and were left in position for 2 hours and 40 mins. At the end of four weeks the patient reported herself, and it was seen that considerable depilation had taken place but there was no change in colour. On 22nd September the dose was repeated and one month later considerable improvement had taken place. The whole surface had become depilated, the growth was flatter and more on a level with the surface of the skin, and in the centre there was a considerable area decolorised. The patient was asked to report herself in two months' time.

PAPILLOMA.

CASE XVI.

A.C. male age 3½ years, New Holland, was brought to the out-patient Department of the Infirmary in/

in March 1912, complaining of difficulty in breathing, and at times when excited or agitated, crowing respiration. He was examined by Mr UPCOTT and admitted under his care as a case of papilloma of the larynx. In Mr UPCOTT'S absence, MR FRANCIS operated by performing thyrotomy , when he found multiple growths situated on the vocal cords, the ventricular bands, and the upper part of the trachea. These were removed as thoroughly as possible. The patient made a good recovery. Two months later the child was brought back, with a recurrence of the symptoms. MR UPCOTT operated again this time leaving in a tracheotomy tube. The patient wore the tube for several months with comfort, but was never able to do without it, and the occurrence of several accidents while the tube was being changed, led us to try radium. In November one of our smallest silver tube applicators was introduced through the tracheotomy tube and left in position for 20 hours. One week later the tracheotomy tube was withdrawn, and the child carefully watched. He still had some difficulty in breathing, but much less than before, and as the crowing respiration had ceased, the wound was allowed to close, and the patient discharged. As is well known/

known these growths sometimes spontaneously disappear and it may be argued that this, or the irritation of the tracheotomy tube may have brought about the improvement, but when the failure of the two operations to bring about a cure, first excision and curetting, second curetting and application of chromic acid, is considered, we were inclined to ascribe the improvement to the action of the radium.

SUMMARY/

SUMMARY AND CONCLUSIONS.

In conclusion to briefly summarise our results: out of 13 cases of epithelioma we only had one cure, or 7·6% of the total treated. We were unfortunate, however, in this category in having three abandoned treatment, and two dead as these combined made 38·4% of our total, in which we were not allowed to carry treatment to the extent we desired. Out of 15 cases of rodent ulcer we cured 7 or 46·8 %. It is noteworthy, that in this class in the table of results, none are entered under the heading 'not improved'. Our results in carcinomatous tumours, of the few cases treated were bad. We could not claim one as being improved, let alone cured, though looking back, I can realise that with a sounder technique of screens, and length of applications, several of our cases would have responded well to radium treatment.

Out of 34 cases of lupus we only succeeded in curing 3 or 8·8%. This result conforms somewhat to the experience of other workers, but in another part of this thesis, I have put forward reasons, why we effected so few cures, and why so many had to be entered/

entered under the heading 'improving under treatment'. Our results in naevus were satisfactory. Out of three cases treated one was cured and two improving under treatment. In our only case of hairy mole the first effects of treatment were encouraging: of fibroma (keloid) and papilloma, we had not sufficient cases to base any conclusions.

In bringing this account of one year's work in the Radium Department of the Hull Royal Infirmary to a close, I think I am justified in stating, that the cases I have been enabled to report from my own experience warrant me in saying that in radium we have an agent that, in many cases of disease, ordinarily unamenable to general methods of treatment, can be used with great hope of success.

As regards the question as to whether radium ought to be used as an alternative to operation in malignant disease, one is forced to admit, that with certain provisions already mentioned, the answer to the question is in the negative.
MORSON (33) in a paper read at a meeting of the Royal Society of Medicine dealing with the action of radium on metastases, states that with an experience of four cases, he found striking changes, the metastic growths being/

being obviously diminished in size. This result, however, is unconfirmed, and cannot be regarded as conclusive, and as experience has shown that even in a very early carcinoma there may be secondary growths commencing in the glands or lymphatics, a little remote from the primary growth, which cannot be detected by the most careful clinical examination, and knowing that a careful and wide operation affords a good prospect of a cure, in the light of our present knowledge of radium, one would feel bound to advise operative treatment first.

In summing up for and against radium therapy, both sides of the picture must be considered. Certain disadvantages are attached to its use. First the reaction in different people may vary, although the same dose of radium has been applied. I have seen cases that have remained quite unaltered after the application of radium, while others clinically indistinguishable from the first, have rapidly grown less under its influence. Another disadvantage is the danger of overdosage, and subsequent prolonged painful reaction, which may result in stimulation and acceleration of the original growth, or sloughing of neighbouring tissues. This is especially liable to/

to occur when the lesion affects the buccal mucous membrane, but its occurrence at any time must be regarded as a regrettable accident. Again thrombosis may be caused in neighbouring veins, or haemorrhage may be evoked from vascular tumours. Against all this, I have been strongly impressed by the following conclusions:

I. Radium correctly applied is a most efficacious remedy in many malignant conditions, especially rodent ulcer, and certain epitheliomata. It is also useful in the treatment of such conditions as naevus, keloids and lupus erythematosus.

II. It has a distinct palliative effect in ameliorating distressing symptoms in inoperable malignant disease.

III. It is undoubtedly of value in the post-operative prophylactic treatment, when it is impossible to do a wide enough operation.

IV. It is useful for aesthetic purposes to secure a good, and at times, almost invisible scar in lesions affecting the face, neck, hands etc.

V. At all times the ease of application, and accessibility to all sites, are distinct advantages in this method of treatment.

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