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PART I.

ORIGINAL COMMUNICATIONS.

ART. XIV.—*Radium*.^a By J. JOLY, Sc.D., F.R.S.;
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It has been unfortunate for the progress of the radio-active treatment of disease that its methods and claims involve much of the marvellous. Up till recently, indeed, a large part of radio-active therapeutics could only be described as bordering on the occult. It is not to be wondered at that when, in addition to its occult and marvellous characters, claims were made on its behalf which in many cases could not be supported, many medical men came to regard it with a certain amount of suspicion.

To-day, I believe, we are in a better position. I think it is possible to ascribe a rational scientific basis to its legitimate claims, and to show that in fact, in radio-active treatment we are pursuing methods which have been already tried extensively and found to be of definite value; and that new methods differ from the old mainly in their power and availability and little, or not at all, in kind.

A Lecture to Post-graduate Students of Medicine delivered in the School of Physic in Ireland, Trinity College, Dublin, on Friday, October 2nd, 1914.

I shall rapidly review the basis of the science. Radium is a metallic element chemically resembling barium. It possesses, however, a remarkable property which barium does not. Its atoms are not equally stable. In a given quantity of radium a certain very small percentage of the total number of atoms present break up per second. By breaking up we mean their transmutation to another element. Radium, which is a solid element under ordinary conditions, gives rise by transmutation to a gaseous element—the emanation of radium. The new element is a heavy gas at ordinary temperatures and, like other gases, can be liquified by extreme cold. The extraordinary property of transmutation is entirely automatic. No influence which chemist or physicist can apply can affect the rate of transformation.

The emanation inherits the property of instability, but in its case the instability is more pronounced. A relatively large fraction of its atoms transmute per second to a solid element designated Radium A. In turn this new generation of atoms breaks up—even faster than the emanation—becoming yet another element with specific chemical properties. And so on for a whole sequence of transmutations, till finally a stable substance is formed, identical with ordinary lead in chemical and physical properties but possessing a slightly lower atomic weight.

The genealogy (p. 323) of the radium series of elements (which is not complete) shows that radium is not the starting point. It possesses ancestors which have been traced back to the element uranium.

Now what bearing has this series of transmutations upon medical science? Radium or emanation, &c., are not in the Pharmacopœia as are, say, arsenic or bismuth. The whole medicinal value of these elements resides in the very wonderful phenomena of their radiations. They radiate in the process of transmuting.

The changing atom may radiate a part of its own mass. The “alpha” ray (α -ray) is such a material ray. It is an electrified helium atom cast out of the parent atom

with enormous velocity—such a velocity as would carry it, if not impeded, all round the earth in two seconds. All alpha rays are positively electrified atoms of the element helium, which thereby is shown to be an integral constituent of many elements. The alpha-ray is not of much

	<i>Period in which $\frac{1}{2}$ element is transformed</i>
URANIUM $\begin{smallmatrix} \nearrow \alpha \\ \searrow \alpha \end{smallmatrix}$	6×10^9 years
↓	
URANIUM X $\begin{smallmatrix} \nearrow \beta \\ \searrow \gamma \end{smallmatrix}$	24.6 days.
↓	
IONIUM $\rightarrow \alpha$	3×10^4 years
↓	
RADIUM $\begin{smallmatrix} \nearrow \alpha \\ \searrow \beta \end{smallmatrix}$	2×10^3 years
↓	
EMANATION $\rightarrow \alpha$	3.85 days
↓	
RADIUM A $\rightarrow \alpha$	3 minutes.
↓	
RADIUM B $\rightarrow \beta$	26.7 minutes.
↓	
RADIUM C $\begin{smallmatrix} \nearrow \alpha \\ \searrow \beta \\ \searrow \gamma \end{smallmatrix}$	19.5 minutes.
↓	
RADIUM D	15 years.
↓	
RADIUM E $\rightarrow \beta$	4.8 days.
↓	
RADIUM F $\rightarrow \alpha$ (Polonium)	140 days

value to medical science, for in spite of its great velocity it is soon stopped by encounter with other atoms. It can penetrate only a minute fraction of a millimetre into ordinary soft tissues. We shall not further consider it.

Transmuting atoms give out also material rays of

another kind : the β -rays. The β -ray is in mass but a very small fraction of, even, a hydrogen atom. Its speed may approach that of light. As cast out by radio-active elements it starts with speeds which vary with the element, and may be from $\frac{1}{3}$ rd to $\frac{9}{10}$ th the velocity of light. The β -ray is negatively electrified. It has long been known to science as the electron. It is also identical with the cathode ray of the vacuum tube.

Another and quite different kind of radiation is given out by many of the transmuting elements :—the γ -ray.—This is not material, it is æthereal. It is known now with certainty that the γ -ray is in kind identical with light, but of very much shorter wave length than even the extreme ultra-violet light of the solar spectrum. The γ -ray is flashed from the transmuting atom along with the β -ray. It is identical in character with the x -ray but of even still shorter wave length.

There is a very interesting connection between the γ -ray and the β -ray which it is important for the medical man to understand—as far as it is practicable on our present knowledge.

When γ -rays or x -rays fall on matter they give rise to β -rays. The mechanism involved is not known but it is possibly a result of the resonance of the atom, or of parts of it, to the short light waves. And it is remarkable that the γ -waves which, as we have seen, are shorter and more penetrating waves than the x -rays, give rise to β -rays possessed of greater velocity and penetration than β -rays excited by the x -rays. Indeed the β -rays originated by γ -rays may attain a velocity nearly approaching that of light and as great as that of any β -rays emitted by transmuting atoms. Again there is demonstrable evidence that β -rays impinging on matter may give rise to γ -rays. The most remarkable demonstration of this is seen in the x -ray tube. Here the x -rays originate where the stream of β - or cathode- rays are arrested on the anode. But the first relation is at present of most importance to us—i.e., that the γ - or x - rays give rise to β -rays.

This relation gives us additional evidence of the identity of the physical effects of γ , x , and light rays—using the term light rays in the usual sense of spectral rays. For it has long been known that light waves liberate electrons from atoms. It has been found that these electrons possess a certain initial velocity which is the greater the shorter the wave length of the light concerned in their liberation. The whole science of “photo-electricity” centres round this phenomenon. The action of light on the photographic plate, as well as many other physical and chemical phenomena, find an explanation in this liberation of the electron by the light wave.

Here, then, we have spectral light waves liberating electrons—*i.e.*, very minute negatively-charged particles, and we find that as we use shorter light waves the initial velocity of these particles increases. Again, we have x -rays which are far smaller in wave length than spectral light, liberating much faster negative electrified particles. Finally we have γ -rays—the shortest æther waves of all—liberating negative particles of the highest velocity known. Plainly the whole series of phenomena are continuous.

We can now look closer at the actions involved in the therapeutic influence of the several rays and in this way, also, see further the correlation between what may be called photo-therapeutics and radio-active therapeutics.

The β -ray, whether we obtain it directly from the transforming radio-active atom or whether we obtain it as a result of the effects of the γ - or x - rays upon the atom, is an ionising agent of wonderful power. What is meant by this? In its physical aspect this means that the atoms through which it passes acquire free electric charges: some becoming positive, some negative. This can only be due to the loss of an electron by the affected atom. The loss of the small negative charge carried in the electron leaves the atom positively electrified or creates a positive ion. The fixing of the wandering electron to a neutral atom creates a negative ion. Before further consideration of the importance of the phenomenon of

ionisation we must fix in our minds that the agent which brings this about is the β -rays. There is little evidence that the γ -ray can directly create ions to any large extent. But the action of liberating high-speed β -rays results in the creation of many thousands of ions by each β -ray liberated. As an agent in the hands of the medical man we must regard the γ -ray as a light wave of extremely penetrating character, which creates high-speed β -rays at every point in the body to which it penetrates, these β -rays being most potent ionising agents. The β -rays directly obtained from radio-active atoms assist in the work of ionisation. β -rays do not penetrate far from their source. The fastest of them would not probably penetrate one centimetre in soft tissues.

We must now return to the phenomenon of ionisation. Ionisation is revealed to observation most conspicuously when it takes place in a gas. The + and - electric charges on the gas particles endow it with the properties of a conductor of electricity, the + ions moving freely in one direction and the - ions in the opposite direction under an electric potential. But there are effects brought about by ionisation of more importance to the medical man than this. The chemist has long come to recognise in the ion that he is concerned with the inner mechanism of a large number of chemical phenomena. For with the electrification of the atom attractive and repulsive forces arise. We can directly show the chemical effects of the ionising β -rays. Water exposed to their bombardment splits up into hydrogen and oxygen. And, again, the separated atoms may be in part recombined under the influence of the radiation. Ammonia splits up into hydrogen and nitrogen. Carbon dioxide forms carbon, carbon monoxide, and oxygen; hydrochloric acid forms chlorine and hydrogen. In these days recombination can also be partially effected by the rays.

We can be quite sure that within the complex structure of the living cell the ionising effects which everywhere accompany the β -rays must exert a profound influence.

The sequence of chemical events which as yet seem beyond the ken of science and which are involved in metabolism cannot fail to be affected. And it is not to be wondered at that as the result of experiment it is found that the radiations are agents which may be used either for the stimulation of the natural events of growth or used for the actual destruction of the cell. It is easy to see that the feeble radiation should produce the one effect, the strong the other. In a similar way by a moderate light stimulus we create the latent image in the photographic plate; by an intense light we again destroy this image. The inner mechanism in this last case can be quite logically stated.

There is plainly a true physical basis here for the efficacy of radio-active treatment and, what is more, we find when we examine it that it is in kind not different from that underlying treatment by special radiations. But in degree it is very different and here is the reason for the special importance of radio-activity as a therapeutic agent. The Finsen light is capable of influencing the soft tissues to but a short depth. The reason is that the wave length of the light used is too great to pass without rapid absorption through the tissues; and, further, the electrons it gives rise to—*i.e.*, the β -rays it liberates—are too slow-moving to be very efficient ionisers. X-rays penetrate in some cases quite freely and give rise to much faster and more powerful β -rays than can the Finsen light. But far more penetrating than x-rays are the γ -rays emitted in certain of the radio-active changes. These give rise to β -rays having a velocity nearly approximative to that of light.

The γ -rays are, therefore, very penetrative and powerful ionising light waves. Light waves which are quite invisible to the eye can beam right through the tissues of the body. To the mind's eye only are they visible. And a very wonderful picture they make. We see the transmuting atom flashing out this light for an inconceivably short instant as it throws off the β -ray. And : "How

far this little candle throws its beams"! Everywhere in the complex systems of the cells, atoms shaken by the rays send out β -rays; these in turn are hurled (like those dreadful war missiles we read about in our daily papers, but thousands of times faster) against other atomic systems. Fresh separations of electrons arise and new attractions and repulsions spring up and the most important chemical changes are brought about. Our mental picture can claim to be no more than diagrammatic of the reality. Still we are here dealing with recognised physical and chemical phenomena, and their description as "occult" in the derogatory sense is certainly not justifiable.

Having now briefly reviewed the nature of the rays arising in radio-active substances and the *rationale* of their influence we must turn to more especially practical considerations.

The Table given above shows that radium itself is responsible for α - and β -rays only. It happens that the β -rays emitted by radium are very "soft"—i.e., slow and easily absorbed. The α -ray is in no case of more than mere surface application. Hence we see that, contrary to what is generally believed, radium itself is of little or no direct therapeutic value. Nor is the next body in succession—the emanation, for it gives only α -rays. In fact, to be brief, it is not till we come to Ra B that β -rays of a relatively high penetrative quality are reached; and it is not till we come to Ra C that γ -rays are obtained.

It is around this element, Ra C, that the chief medical importance of radio-active treatment by this family of radio-active bodies centres. Not only are β -rays of Ra C very penetrating but the γ -rays are perhaps the most energetic rays of the kind known. Further in the list there is no very special medical interest.

Now, how can we get a supply of this valuable element Ra C? We can obtain it from radium itself. For even if radium has been deprived of its emanation (which is easily done by heating it or bringing it into solution) in a

few weeks we get back the Ra C. One thing here we must be clear about. With a given quantity of Ra only a certain definitely limited amount of Ra C, or of emanation, or any other of the derived bodies, will be associated. Why is this? The answer is because the several successive elements are themselves decaying—*i.e.*, changing one into the other. The atomic percentage of each which decays in a second is a fixed quantity which we cannot alter. Now if we picture radium which has been completely deprived of its emanation, again accumulating by automatic transmutation a fresh store of this element, we have to remember :—(1) That the rate of creation of emanation by the radium is practically constant; and (2) that the absolute amount of the emanation decaying per second increases as the stock of emanation increases. Finally, when the amount of accumulated emanation has increased to such an extent that the number of emanation atoms transmuting per second becomes exactly equal to the number being generated per second, the amount of emanation present cannot increase. This is called the equilibrium amount. If fifteen members are elected steadily each year into a newly-founded society the number of members will increase for the first few years; finally, when the losses by death of the members equal about fifteen per annum the society can get no bigger. They have attained the equilibrium number of members.

This applies to every one of the successive elements. It takes twenty-one days for the equilibrium quantity of emanation to be formed in radium which has been completely de-emanated; and it takes 3.8 days for half the equilibrium amount to be formed. Again, if we start with a stock of emanation it takes just three hours for the equilibrium amount of Ra C to be formed.

We can evidently grow Ra C either from radium itself or from the emanation of radium. If we use a tube of radium we have an almost perfectly constant quantity of Ra C present, for as fast as the Ra C and intervening elements decay the Ra, which only diminishes very

slowly, in amount makes up the loss. But if we start off with a tube of emanation we do not possess a constant supply of Ra C because the emanation is decaying fairly rapidly and there is no radium to make good its loss. In 3.8 days about one half the emanation is transmuted and the Ra C decreases proportionately and, of course, with the Ra C the valuable radiations also decrease. In another 3.8 days—that is in about a week from the start—the radio-active value of the tube has fallen to one-fourth of its original value.

But in spite of the inconstant character of the emanation tube there are many reasons for preferring its use to the use of the radium tube. Chief of these is the fact that we can keep the precious radium safely locked up in the laboratory and not exposed to the thousand-and-one risks of the hospital. Then, secondly, the emanation, being a gas, is very convenient for sub-division into a large number of very small tubes according to the dosage required.

In fact the volume of the emanation is exceedingly minute. The amount of emanation in equilibrium with one gramme of radium is called the curie, and with one milligramme the millicurie. Now, the volume of the curie is only a little more than one half a cubic millimetre. Hence in dealing with emanation from twenty or forty milligrammes of radium we are dealing with very small volumes.

How may the emanation be obtained? The process is an easy one in skilled and practised hands. The salt of radium—generally the bromide or chloride—is brought into acid solution. This causes the emanation to be freely given off as fast as it is formed. At intervals we pump it off by a mercury pump.

At the Royal Dublin Society this operation has now been systematically carried on for many months, thanks to the skill and care of Mr. R. J. Ross. The Society a few days ago received an addition of over 200 milligrammes of radium bromide purchased by a fund subscribed mainly

by Lord Iveagh, Sir John Griffith, and the Society itself; others also generously supporting it.

Let us see how many millicuries we will in future be able to turn out in the week. We shall have about 130 milligrammes of the element radium. In 3.8 days we get sixty-five millicuries from this—*i.e.*, half the equilibrium amount of 130 millicuries. Hence in the week, we shall, roughly speaking, have 130 millicuries.

This is not much.—Many experts consider this little enough for one tube. But we have here in Dublin been using the emanation in a more economical and effective manner than is the usage elsewhere, so far as I know. The economy is obtained by the very simple expedient of minutely sub-dividing the dose. The system in vogue, generally, is to treat the tumour by inserting in it one or two very active tubes, containing, perhaps, up to 200 millicuries, or even more, per tube. Now these very heavily charged tubes give a radiation so intense at points close to the tube, due to the greater density of the rays near the tube, and, also, to the action of the softer and more easily absorbable rays, that it has been found necessary to stop these softer rays—both the γ and β —by wrapping lead or platinum around the tube. In this lead or platinum some thirty per cent. or more of the rays is absorbed and, of course, wasted. But in the absence of the screen actual necrosis of the tissues near the tubes results.

If, however, in place of one or two such tubes we used ten or twenty containing $\frac{1}{10}$ th or $\frac{1}{20}$ th of the dose, we can avail ourselves of the softer rays around each tube with benefit. Thus a wasteful loss is avoided. Moreover a more uniform “illumination” of the tissues results, just as we can illuminate a hall more uniformly by the use of many lesser centres of light than by the use of one intense centre of radiation. Also we get what is called “cross-radiation,” which is found to be beneficial. The surgeon knows far better what he is doing by this method of uniform radiation, for the effects go on with approxi-

mate uniformity throughout the tumour instead of varying rapidly around a central point.

Finally, not the least of the benefit arises in the easy technique of this recent method. The quantities of emanation employed can fit in the finest capillary glass tubing and the hair-like tubes can in turn be placed in fine exploring needles. There is but little inconvenience to the patient in inserting these needles, and there is the most perfect control of the dosage in the number and strength of those tubes and the duration of exposure—facts connected with which Dr. Walter Stevenson is in a position to give you.

But, of course, applicators of various shapes and kinds are required for special purposes, and the medical man applying for emanation to the committee of the Royal Dublin Society will, doubtless, follow his own experience in the form selected and the mode of its application.

The interesting process of the extraction of the emanation from the Royal Dublin Society's stock of radium will, I am sure, be shown and explained more fully by Mr. Moss to any medical man desiring to see it. There are certain times in the week in which the operation is carried out. This—the first Radium Institute in Ireland—has already done good work for the relief of human suffering. It will have, I hope, a great future before it, for I venture, with diffidence, to hold the opinion that with increased study the applications and claims of radio-active treatment will increase.

ART. XV.—*Treatment of Graves's Disease by X-rays.*

By T. GILLMAN MOORHEAD, M.D., F.R.C.P.I., Physician to the Royal City of Dublin Hospital.

EXOPHTHALMIC GOITRE is a disease concerning which, owing to its tendency to run a chronic course, its liability to remissions, and its by no means infrequent tendency to spontaneous cure, one must necessarily feel somewhat diffident when speaking of the results of any method of