X-RAYS AND THEIR BIOLOGICAL EFFECTS.

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X-RAYS were discovered by the celebrated Bavarian physicist Wilhelm Röntgen in November, 1895. During the few years following the discovery there was considerable speculation as to the nature of the rays, but an intensive study of their main physical properties soon showed them to be similar to ordinary light in all respects except that the wavelength was very much smaller. In fact, we now know that the recently discovered cosmic rays, which probably have their origin in the depths of space, the gamma rays from radium, X-rays, ultra-violet light, visible light, infra red rays and radio waves are all electro-magnetic or æther waves, travelling in straight lines through space with a velocity of 3×10^{10} cms./sec.* Since the velocity is the same for all these types of radiations it is to the values of the wavelengths that we turn in order to explain the differences between them, and it is indeed here that they lie. From the cosmic rays whose wavelengths are of the order 10^{-11} cms. †we observe a continuous range of increasing wavelengths right up to the radio waves, where the wavelength may reach a mile or more. This extended and continuous band of wavelengths forms what is referred to as the electro-magnetic spectrum, diagrammatically represented in Fig. I, in which the wavelengths are expressed also in terms of the Ångstrom unit, which is 10^{-8} cms. The cosmic rays have a wavelength of about 10^{-11} cms., are able to penetrate fifteen feet of lead before they are absorbed, and so far as we know are unproducible on this planet. Next in order of increasing wavelength come the gamma rays of radium and radio active substances, decreasing in their penetrating power as their wavelengths increase, until we pass into the X-ray region, where the penetration continues to decrease with increasing wavelength.

The properties of an æther vibration thus vary with the wavelength or the frequency of the vibration ; they all transmit energy and require particular methods for their generation and detection. Given a suitable detector the electro-magnetic energy may be transformed into the

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* 30,000,000,000 cms. per sec.

† 0·00000000001.

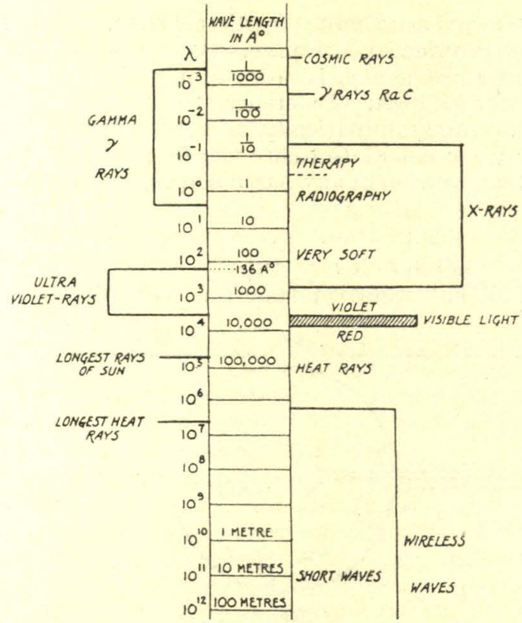

Figure I.

equivalent amount of heat energy. There is little need from our standpoint to travel further ; but before passing on to a consideration of the production of X-rays, we must mention an important relationship between certain characteristics of a wave motion. If we stand at one place and watch waves travel past us, the velocity with which the disturbance travels may evidently be found by counting the number of wave crests passing in one second (call this n) and multiplying by the distance between successive crests, (λ). Thus the velocity of propagation c, which is equal to the distance travelled by a wave in one second, is given by

$$c = n\lambda$$

in which n is known as the frequency and λ the wavelength of the vibration. This relationship holds for all wave motions. The constant c (*i.e.*, the velocity of the wave) is the same for all electro-magnetic or æther vibrations, and is equal nearly to $3 \cdot 0 \times 10^{10}$ cms./sec. Thus, for the electro-magnetic spectrum we write

$$c = n\lambda = 3 \cdot 0 \times 10^{10} \text{ cms./sec.}$$

Amongst other things, this formula enables us to calculate the frequency of the vibration in terms of the velocity and the wavelength of the disturbance. The frequency and the wavelength are inversely proportional; for long waves the frequency is low; for the short waves the frequency is high. Reference to the electro-magnetic spectrum (diagrammatically represented in Fig. I) thus enables us to calculate easily the frequency of an electro-magnetic vibration in any particular region of the spectrum.

THE PRODUCTION OF X-RAYS.[1]

The Coolidge X-ray tube is shown in Fig. II. *F* is a small flat spiral of tungsten wire (filament), and *T* is a solid block of tungsten, known as the target, both of which are suitably supported and fused into the glass bulb *E*, which is freed of air as completely as possible. To operate the tube the filament is heated to incandescence by a battery *B* of some 4 to 6 volts and a potential difference *V* of many thousands of volts is applied between the filament and target. Under these conditions X-rays are given off from the target in all directions. It is found in practice that the target becomes extremely hot, and it may therefore be necessary to arrange to cool it by the simple process of allowing a constant stream of water to flow down through the supporting piece T_1.

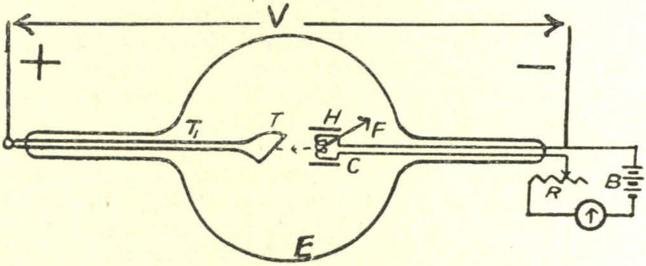

Figure II.

Let us now consider the mode of action of an X-ray tube. It is known that a heated metal gives off a copious supply of small negatively charged particles known as electrons, and these electrons are whisked from the heated filament towards the target, in virtue of the high potential difference applied to the tube. Just before they make impact with the target they attain kinetic energy equal to $\frac{1}{2}mv^2$ where m is the mass of the electron and v is the velocity with which it is moving. On striking the target it is clear

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[1] See also "Physics: Fundamental Laws and Principles," Booth and Nicol, Australasian Medical Publishing Co. Ltd.

that this kinetic energy must suffer transformation more or less rapidly, according as to whether or not the electrons penetrate the material of the target. Actually the kinetic energy $\frac{1}{2}mv^2$ is transformed partly into X-radiation and partly into heat, and the target itself becomes very hot because, in general, the greater part of the arrival energy ($\frac{1}{2}mv^2$) is transformed into heat. The transformation of the kinetic energy of the electrons into X-radiation is a very inefficient process, and most of the difficulties encountered in the construction of very powerful X-ray tubes centre around the provision of adequate cooling devices.

When an electron with a charge e moves down a tube having a potential difference V between its ends, it is accelerated, and finally attains a kinetic energy of eV (from the physical definition of V). Hence we must have

$$\tfrac{1}{2}mv^2 = eV.$$

When the electron strikes the target it will give up this kinetic energy on being brought to rest, the energy of motion being partially or completely turned into X-ray energy, which is radiated. Obviously, the maximum amount of energy available for radiation is $\frac{1}{2}mv^2$, or eV, a quantity which increases with voltage.

Now it is known that, under such circumstances, a radiation of frequency n will be emitted in accordance with the following equation

$$eV = hn$$

$$\text{or } n = \frac{eV}{h}$$

in which h is a constant known as Planck's quantum of action. Thus we see that the highest frequency emitted by an X-ray tube is directly proportional to the voltage V, which is employed to excite the tube.

Hence the ideas of "hard" and "soft" X-rays. A hard or penetrating X-ray is one produced under a potential difference of some 200,000 volts. A soft X-ray may correspond to a potential difference of some 10,000 to 20,000 volts only. The penetrating power of the radiation depends only upon the voltage applied across the X-ray bulb.

THE INTENSITY OF A BEAM OF X-RAYS.

X-rays, we have seen, are a form of energy, just as heat, light, *et cetera*, and it is well known that all these forms of energy are mutually convertible into each other at a fixed rate of exchange. We must regard the energy as travelling outwards in all frontal directions from the target in the form of X-rays. In order to determine the intensity of the X-ray beam at a given point, we require information relating to the amount of energy falling on unit area placed perpendicular to the X-ray beam at the point considered, in unit time.

The radiologist, however, is more particularly concerned with the amount of X-radiation that is actually absorbed in the tissue which is being exposed to the action of the beam of X-rays than with the amount of energy falling on each square centimetre of the tissue. This brings us to the idea of X-ray " dose." The dose is the total quantity of X-radiation absorbed in each cubic centimetre of tissue, or other absorbing substance, and, obviously, the rate of absorption is directly proportional to the intensity. If all the energy were absorbed in one cubic centimetre of any material, then the dose for that cubic centimetre would be the total amount of energy poured in ; a body, however, only absorbs a fraction of the energy falling on it, this fraction varying with the penetration of the radiation.

THE LAW OF ABSORPTION OF X-RADIATION.

The intensity of a beam of X-rays is reduced by its passage through matter. This is in virtue of the facts that

(*a*) a certain amount of the X-ray energy is truly absorbed by the medium ;

(*b*) a certain amount of the X-ray energy is scattered in all directions by the medium, and is thereby lost to the main beam.

Quantitatively we may write

$$I = I_0 e^{-\mu d},$$

in which I_0 is the intensity of the beam falling on the substance (*e.g.*, living tissue), I is the intensity of the beam after passing through and emerging from a thickness d of the substance, and μ is a constant, known as the coefficient of absorbtion of the beam of X-rays in that particular substance. μ is obviously small for penetrating or hard radiation, and large for soft or easily absorbed radiation. The form of the absorbtion formula arises from the fact that the stoppage of X-radiation, when passing through a group of atoms, is a probability phenomenon. Thus, if a certain thickness of living tissue absorbs 1% of the radiation, it must necessarily transmit 99%, and a second thickness d will again absorb 1% of the 99%, and so on. Thus each succeeding thickness d absorbs 1% and transmits 99% of the radiation that falls on it. The values of $e^{-\mu d}$ in the formula may be obtained from tables, and we thus have a simple relation between I and I_0. The reader should bear in mind the all important fact that the biological effects of X-rays are related solely to the amount of radiation actually absorbed in the living tissue. The radiation that passes through the tissue exerts no effect on the biological mechanism.

THE QUANTUM THEORY.

According to the quantum theory a beam of X-radiation is to be regarded as a fusillade of radiation bullets or quanta which are indivisible and contain energy equal to hn (*i.e.*, the amount of energy in the quantum or elementary energy bundle, equal to the product of the frequency of the radiation and Planck's quantum of action). The quantum theory was introduced into physical science to explain certain phenomena which did not fall into line with the ordinary classical theory, and its introduction has been more than justified. To a certain and even fundamental extent this idea of the quantum is contrary to the ordinary wave theory, so we have to use which ever theory is best for the particular job in hand. Sir William Bragg has aptly remarked that we use the classical theory on Mondays, Wednesdays and Fridays, and the quantum theory on Tuesdays, Thursdays and Saturdays.

The quantum theory has definitely and successfully invaded the problem relating to the quantitative biological effects of X-radiations. The absorption of the energy of the beam by the living cell must be regarded in the more strictly accurate way of absorption by quanta. The cell may or may not be struck by a quantum, and a probability distribution is introduced.

THE MEASUREMENT OF THE INTENSITY OF A BEAM OF X-RAYS.

One of the most accurate methods by which the intensity of X-rays can be measured is by the ionisation produced in a gas.

Many substances, known as dielectrics, which are usually bad conductors of electricity, have appreciable electrical conductivity conferred upon them when subjected to the action of a beam of X-rays. Thus X-rays, in their passage through air, which ordinarily conducts electricity to an almost inappreciable extent, confer upon it a degree of conductivity which is very easily measured. The air is said to be ionised during the passage of the X-rays through it, and this phenomenon of ionisation involves the sudden liberation of one or more electrons from an electrically neutral molecule ; the electron, carrying away a negative charge, leaves the remainder of the molecule positively charged.

The end result is that positively and negatively charged clusters of molecules are formed in the gas in equal numbers, so that the gas has been rendered conducting, and the degree of electrical conductivity thus imparted is a measure of the intensity of the radiation.

The ionising action of X-rays is one which lends itself to exact measurement.

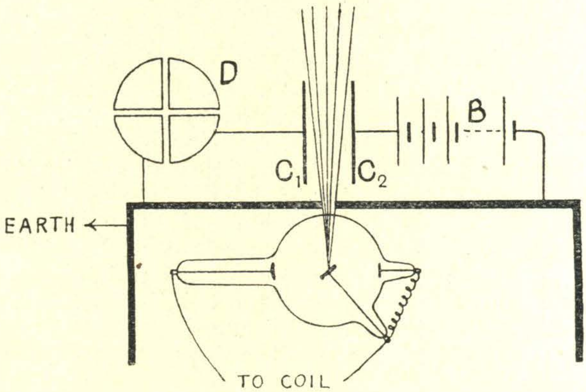

Figure III.

The beam of X-rays to be measured is caused to pass between two metal plates (C_1 and C_2, Fig. III) situated in air, the plates being connected to the terminals of a battery (*B*) of some hundreds of volts, in circuit with which is a current measuring instrument (*D*). The positive ions in the air between the plates are attracted to the negative plate, and the negative ions are attracted to the positive plate. The transport of these ions constitutes an electric current, which is measured by the instrument (*D*).

Care must always be taken to obtain the saturation current, that is to say, the voltage between the plates must be sufficient to ensure that the ions are removed from the gas at the same rate as they are being formed ; in this way re-combination of the ions with one another before reaching the plates is effectively prevented.

SECONDARY ELECTRONS.

We have just seen that a beam of X-rays when passing through air and other media liberates electrons from the electrically neutral molecules. Whenever X-rays strike an atom, ionisation occurs; high speed electrons are liberated, and one of the theories of the biological action of X-rays depends upon the bombardment of the cells by these secondary electrons. The maximum energy that these secondary electrons can possess must be given by

$$\tfrac{1}{2}mv^2 = hn,$$

because the energy imparted to the ejected electron cannot be greater than that in the radiation bullet or quantum that causes the ejection. Under the most favourable circumstances the above quantitative relation is an exact expression of the interchange of energy that takes place. Since the mass m of the electron is known, this equation enables us to calculate the maximum velocity of emission of electrons from substances bombarded with a beam of X-radiation of known frequency or wavelength. Having now completed a brief review of the main facts relating to the nature and production of X-rays, their measurement and interaction with matter, we are in a position to proceed to a consideration of the biological effects produced in living tissues when exposed to the action of a beam of X-rays.

Effect on Skin.

That X-rays are capable of producing very marked effects upon the skin was unfortunately soon made apparent to the pioneer workers in radiotherapy, many of whom paid for their experiences with their lives. Even today we have with us some of those original enthusiasts who did not realize the full significance of adequate protection against the radiations. The exposure of skin to X-rays produces reactions which vary from a simple reddening or inflammatory condition to a more profound ulceration, according to the dose of radiation absorbed by the skin. The ulcers may be deep, painful and slowly healing; and in the worst forms do not respond to any form of treatment.

It was in 1898 that Rodet drew attention to the very extensive skin lesions and wounds that may result from excessive exposure to X-rays. Experimental work had already been undertaken by Oudin who, in 1897, recorded the results obtained by exposing guinea-pigs to the rays; a marked dermatitis was produced, followed by the disappearance of hair and sweat glands. Similar experiments were reported by Unna (1897), Lion (1901) and Scholtz (1902).

It was also pointed out by Revillet and by other observers that the influence of the rays is not confined to that area of the skin upon which they impinge from the

X-ray tube, but in passing through the body they produce definite changes upon the skin of the opposite face.

LATENT PERIOD.

It is a noteworthy feature that these effects are never produced instantly : a period of time must elapse between irradiation of the skin and the production of any visible effect. The actual period may vary from a few days to a month or more, according to the initial dose of X-rays. This is an important consideration, because the essential physical change brought about by the radiation (*i.e.*, the emission of secondary electrons) is practically instantaneous. This latent period is observed in all biological reactions to X-rays, and its significance has been investigated by various workers.

THEORY OF ACTION OF X-RAYS ON LIVING MATTER.

It is certain that the initial change produced in living tissue by X-radiation is physical. This is undoubtedly followed by chemical changes, which are ultimately manifested as biological changes.

Any living structure is a complex involving a number of interdependent equilibria ; if one of these be upset, the others are immediately involved. Under normal conditions these equilibria are in a continual state of adjustment, and are capable of continual readjustment, provided they have not been subjected to too great changes, either by disease or by experimental intervention. Now in X-radiation it is clear that we have an agent which is capable of disturbing the normal equilibria in the parts irradiated. Irradiated matter is, as we have seen, to be regarded as the seat of intense electronic activity ; some electrons are torn from their staple positions and ejected by the rays with high velocities ; other electrons jump back into the positions thus left vacant. The biological effect appears to depend upon the transformation of the X-ray energy into kinetic energy of the electrons, which in some way disturbs the economy of the living cell.

Small doses of radiation, generally speaking, give rise to transient effects, while more intense radiation produces permanent damage, or complete destruction. In the former case the disturbance of the equilibrium has been so slight that a more or less complete restoration or repair is possible ; in the latter the alteration has been so profound as to prevent a return to normal conditions. It is also important to bear in mind the fact that we are concerned not only with the equilibria in the cell itself, but also with those existing between the cell and its surroundings. So much for a theory of action which has received the support of a number of investigators.

In the "point heat" theory of Dessauer, it is imagined that the tissues are locally heated to very high temperatures, the heated volume being, of course, very small compared to the total volume of tissue.

Other investigators are concentrating on the changes produced in the colloidal constituents of the cell; the time elapsing between irradiation and the appearance of any obvious changes in the colloids presents, at least, a suggestive parallel with the latent period already mentioned.

In discussing theories of action we must bear in mind the fact that there are grounds for considering that one single theory of action could hardly carry the full burden of experimental facts. Consider for a moment the well known fact that a cancerous growth, embedded in the tissues of the body, often disappears when suitably irradiated with X-rays. The main symptoms following such treatment are (*a*) inflammation in the skin, (*b*) diminution in the size of the tumour, (*c*) cessation of pain. It is hardly rational to ask for one single theory of action which will include such widely different effects. The animal itself provides a complex which refuses to be reduced to simple terms. We are, however, in possession of a great volume of precise information relating to the effects, both qualitative and quantitative, on living tissues, and particularly is this so when we consider the biological effects of X-radiation on the unit of living matter, *i.e.*, the cell.

(*Part II will follow in the next issue.*)

EDITORIAL NOTE

CERTAIN of the articles in the last issue were unsigned, as are some in this. Many correspondents and others, local or beyond the reach of direct retaliation, have intimated, courteously or otherwise, that the authorship is obvious. Some others whilst, naturally, admiring the matter and style, have not placed the authors, and think it would add to the interest if all articles were signed. So as to clear the matter up and avoid the responsibility being loaded on to the shoulders of innocent people, this definite announcement is now made.