*THE PHARMACOLOGY AND THERAPEUTICS OF RADIATION.

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INTRODUCTION.

I have purposely chosen a title for this paper which some of you may perhaps think would be suitable only if used in connection with what are popularly known as "drugs." The standard dictionary in which I recently looked up the word "drug" defines it as "any substance used in medicine." The same dictionary defines substance as, (1) "The material of which a thing is made"; (2) "the elemental part of that which is immaterial." Now, if I were dialectically inclined, I might say that radiation falls within this second definition of substance; and that, as it is certainly used in medicine, it may be classified as a drug. However, I do not wish to be accused of sophistry, which my dictionary tells me is subtly fallacious reasoning, sound in appearance only.

I will therefore devote a few minutes to showing that the word "substance" has come to have little meaning, except in a popular sense. When the older physicians prescribed a drug, they had in mind something they could see, handle and weigh. For example, calomel or rhubarb powder. But many of our modern drugs are never seen by those who administer them. They see solutions only, and take on trust the properties of these solutions from other people. And so long as physiological standardization is necessary, it is obvious that in certain cases no one has seen, handled or weighed the "elemental part"—to quote the dictionary once again—which is responsible for the effect desired.

Let us be frank, and admit that we know nothing of matter or substance except by its effects. The learned Dr. Johnson is said to have banged the table when asked for his definition of matter. But what he experienced was merely a sensation of resistance, possibly of a pain like that of a blow. Now, I will undertake by means of a suitably controlled electric shock to give any of you a sensation which you will not be able to distinguish from that of a blow; and if you try to push an aluminium plate on to the poles of a powerful electro-magnet, you will experience resistance, although there is no "substance" between the plate and the magnet. Or, conversely, if you try to pull an iron plate away from its poles, you will be unable to say, if you experience resistance, whether the magnet is being excited by an electric current, or whether the plate is attached to the poles by material bolts.

I quote these examples to show that the senses of touch and resistance are quite valueless in enabling us to arrive at any scientific distinction between substance and force, or matter and energy.

If it be argued that substance is that which can be weighed, the reply is that light, and, of course, all other electro-magnetic waves, have mass and weight and therefore by this test cannot be distinguished from matter.

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It is an observed fact of nature that matter, as we know it, **can and does** change into energy—that of radiation. The converse has not yet been observed; but to the philosophically minded, it would seem almost a certainty that this re-conversion is occurring in some remote corner of the universe, or that in future it will take place. In the words of scripture, “that which was in beginning, is now, and ever more shall be.”

I have put these somewhat metaphysical considerations before you, not out of sheer wanton inhumanity, but because it is necessary to combat the point of view which looks upon radiation therapy as something outside the ægis of an orthodox pharmacopœia—as something alien, tinged with an empiricism which does not attach to such things as insulin and atropine. It is so comforting to read in the text books the nicely tabulated pharmacology and therapeutics of these drugs, and to think that one can really put something comfortably *material* inside a patient's body by the aid of a nice little syringe, which can be felt in the hand, and which the patient can feel in another sense when the needle goes into him. The water which fills the barrel can actually be seen and measured in c.cs. and the whole procedure is highly scientific and satisfactory to the mind!

Although my student days coincided with the therapeutic nihilism which was so prevalent in the early years of the century, you must not think I am being mildly satirical at the expense of drug treatment. I have always been a firm believer in skilfully applied drug medication. What I am jibing at is the attitude of mind which regards medication by *substance*, so-called, as essentially more scientific than medication by *energy*. I have tried to show you that there is no real difference between the two, and that we are entitled to treat radiation as a drug with an established pharmacology and therapeutics, just as we deal in the arsenic or strychnine.

PHARMACOLOGY OF RADIATION.

Pharmacology is generally taken to mean the action of a drug on normal tissues as determined by observation and experiment. In considering the pharmacology of radiation, one is bound to include the whole electro-magnetic spectrum. Rays are named, somewhat arbitrarily, cosmic rays, gamma rays, X-rays, ultra-violet rays, light rays and infra-red rays. Nothing is as yet known as to the biological effects of cosmic rays—whose wave-length is the shortest of the series, and I do not intend to touch on the medical uses of wireless waves—the longest known as to wave-length—as this form of therapy is still in the experimental stage. One must, however, consider the gamma rays of radium, X-rays and ultra-violet rays as a whole, because they have many effects in common.

Ultra-Violet Rays.

We will begin with the ultra-violet rays, because they alone produce effects under normal conditions. Radiations of shorter wave-length do, of course, exist in nature, but not in sufficient concentration for us to be certain that they influence the human body. On the other hand, the effects of sunlight, especially in high altitudes, are well-known. These are both local and general. Locally, excessive exposure causes acute inflammatory reaction, and even though there is no erythema, lassitude and exhaustion follow. This may be taken as summing up the pharmacology of ultra-violet light. Pharmacology, being by definition the study of the effects of drugs on healthy organisms, is essentially toxicology, as any observed effect must be a departure from the normal.

The therapeutic value of sunlight—which is chiefly, but not wholly due to its ultra-violet content, was known to the ancient Greeks, but was for all practical purposes lost, and only rediscovered towards the end of last century. The invention of lamps capable of a heavy output of ultra-violet rays has enabled us to determine local and general reactions to measured doses.

Locally, most chronic skin troubles, ulceration, etc., may be benefited by doses capable of producing a sharp erythema; but on the whole, ultra-violet light is much less efficient in such cases than small doses of X-rays. It is the effects of general irradiation by ultra-violet rays which are the most important. Graded doses will, in most patients, ultimately produce pigmentation over the whole body, but such pigmentation is not, in my experience, essential for successful therapy.

Chemical changes occur in the skin, some of which have been worked out. The production of activated ergosterol, the parent of vitamin D, which was worked out some years ago, led to a sort of boom in ultra violet light therapy. The history of this boom threw a somewhat lurid light upon the false value which is placed upon laboratory work as opposed to clinical observation. A lady worker stated that not only were her laboratory rats benefited by ultra-violet exposures, but if their cages were irradiated during their temporary absence, the same result was attained! This story was looked upon as being on all fours with the type of mediæval medicine which considered that swallowing a piece of parchment on which was written the name of a drug had the same effect as taking the drug itself. This was no doubt often true, but scarcely in the way the leech intended! However, as I say, the lady was laughed at until someone else discovered that not only was vitamin D formed in the living body under the influence of light, but that fats could be activated *in vitro*. Hence the mystery of the rats' cages was explained; fragments of food were acted on, which they subsequently ate.

Now there was abundant clinical evidence of the value of general light treatment before ever it was known that vitamin D was formed; but as soon as people knew that something was produced which they conceived of as a substance, and which was already known to be the vitamin lacking in rickets, they began to believe in the value of light. The manufacturers descended on the scene with bottled vitamins, and it was soon being said that light was no longer necessary. But it is still going **strong**.

Light, applied to the body, will ultimately cure lupus of the face, even although the face be kept covered. It appears to arrest Paget's disease, but only for so long as it is kept up. In simple anæmia the number of red corpuscles and the percentage of hæmoglobin rises rapidly week by week; and it will even help patients in an advanced stage of breast cancer, with metastases, to fight the disease for long periods. I made this statement several years ago at a discussion at the Royal Society of Medicine; and one member reproved the president for having permitted me to waste the time of a learned body by talking unmitigated nonsense. Now, I am glad to say, there are very few cancer clinics in which light is not used as an adjunct to other treatment.

The probability is that the constitutional action of light and other forms of radiation is brought about by altering the chemistry of the body. In the case of rickets we happen to know, in part, what does happen. This discovery should warn us not to disbelieve clinical evidence of benefit in other diseases because the bio-chemical side of the matter has not yet been elucidated.

I have devoted some little time to discussing the action of ultra-violet rays, because it is, as a rule, wise to proceed from what occurs normally in nature to phenomena of an allied but more recondite character.

X-rays.

Coming now to the pharmacology of locally applied X-rays, we find that local action on the normal body is not unlike that of ultra-violet rays. We should, however, on purely physical grounds, expect their effects to range over a much wider field, in view of the difference in penetrating power. For whereas ultra-violet rays may penetrate perhaps a millimeter beneath the skin surface, X-rays, by reason of their shorter wave-length, produce local effects at various depths below the surface, or even through the whole thickness of the body.

Where the skin is concerned, there is close parallelism in the phenomena produced. A dose of X-rays of a certain intensity results in the production of an erythema, but this erythema does not appear until ten days to three weeks after the skin dose has been given, instead of the twelve hours' latent period after a dose of ultra-violet light. Higher dosage results in blistering, or even ulceration. The latter sometimes appears months after the application, or the skin may develop telangiectasis years later. Such doses are not, of course, used in skin therapy.

Erythema is not necessary to produce effects, as the phenomena of X-ray epilation prove. Here a dose which produces no redness or visible reaction, nevertheless causes the hair to fall out about the eighteenth day. The effect is only temporary. However, a dose sufficient to produce a smart erythema may result in permanent loss of hair, and later, telangiectasis.

This epilative effect is not observed even with severe doses of ultra-violet light, as the latter does not penetrate to the roots of the hair.

Whereas the pharmacology of locally applied ultra-violet rays begins and ends with the skin, that of X-rays may be discussed with regard to almost any organ in the body. I shall have to confine myself to a brief description of some effects which are of practical interest—phenomena of the same order, and the same medical importance, as, for example, the slowing and strengthening of the normal heart-beat by the exhibition of digitalis.

Sterilization. To take first the generative system. In the male, temporary sterilization is readily produced, but very large doses are required to destroy the spermatogenic function of the testis. Cases are on record of the begetting of children after twenty years of azoospermia, followed by three years of efficient protection. Sex desire and potency remain unaffected in such cases.

In the female, the phenomena are different. Exposure of the ovaries to a sufficient dose of X-rays results in an artificial menopause—and the sex desire may soon be lost, or it may persist for many years, just as is the case after a natural "change of life."

Effect on Bowels. Severe irradiation of the bowels will produce an enteritis; the salivary glands are put out of action permanently by large doses.

Effect on Lungs and Spleen. Heavy doses involving the lungs may result in pneumonic consolidation; and degenerative changes can be produced in the follicles of the spleen.

Constitutional Effects. Text books on pharmacology are accustomed to divide the action of certain drugs such as arsenic, into local and constitutional. A similar treatment is desirable in the case of X-rays. Small repeated doses over wide areas produce the same effects as ultra-violet light. There is slight increase of hæmoglobin, a feeling of well-being and ultimately a general pigmentation. Excessive general exposure to ultra-violet light causes lassitude and sickness, but it is perhaps not a fair analogy to compare this with X-ray sickness. X-ray sickness is most likely to occur after irradiation of the upper abdomen. The saline content of the plasma is diminished, and intra-venous saline injection often relieves the symptoms. Some authors hold that the splanchnic ganglia and the pancreas are affected.

As regards the blood, the first effect is to produce a leucopoemia; later, there is loss of hæmoglobin and degeneration of the red cells. There have been numerous experiments on animals which show the sensitivity of the white cells, but the fatal effects of prolonged exposure on the mammalian body have unfortunately been proved by the fate of some X-ray workers, and many of those who have handled radium for long periods.

A very large dosage over practically the whole body, of such a nature as to produce deep pigmentation of the whole skin of the trunk and thighs, can apparently be given without ill effect upon the health of the patient. Dr. Gilbert Scott showed some years ago several cases from the London Hospital, which he had treated over a period of months, by what he called an X-ray bath—that is, two tubes, one placed on either side of the body, and at a considerable distance. The immunity of these patients may seem to conflict with what I have said as to the evil effects of small doses of X-rays on the blood of those exposed to them over long periods; but there is a very important point of difference. The body has defensive powers against most things that can hurt it, and pigmentation may represent a defence against radiation. However, *if the dosage is below the threshold of stimulation, it may endanger the organism so insidiously that no resistance is aroused.*

Radium.

The pharmacology of radium, local and general, is so much like that of X-rays that little need be said of it. Locally, changes in the blood vessels are perhaps more pronounced; rupture of capillaries occurs, and, ultimately, changes resembling obliterative endarteritis. It is perhaps wise to mention that while radium gives off three kinds of rays—alpha rays and beta rays (both of which are material particles) and gamma rays—only the latter rays are to-day used in medicine. The others are cut off by heavy metallic screening, and the escaping radiations are neither more nor less than X-rays of extremely short wave-length and high penetrating power. Gamma rays are not homogeneous, but their average wave-length is that of X-rays generated at about one million volts.

The harmful constitutional effects of daily exposure to radiation have been more strikingly demonstrated in the case of gamma rays than in that of X-rays. Whether this is due to the nature of the rays, or merely to the fact that protection is so much more difficult to achieve, is a matter not as yet settled.

THE THERAPEUTICS OF RADIATION.

So much for the pharmacology of radiations. I now come to therapeutics. As is so often the case with potent drugs, pharmacology gives only a very partial indication as to what may be expected from a therapeutic point of view. A study of any text book on materia medica will prove this. Strychnine, with its irritant effect on the spinal cord, might be expected to act as a nerve stimulant; and it might be inferred from laboratory experiments that digitalis would be useful in certain forms of heart disease. But the pharmacology of quinine, mercury and potassium iodide gives no hint as to their value in those diseases for which they are in some sense specifics.

Ultra-violet rays, X-rays and gamma rays all produce inflammatory reactions in the skin; this points the way to their trial in skin diseases. The value of ultra-violet light in rickets was, in fact, well-known before the discovery that it produced vitamin D in the skin, but had this fact been previously known from pharmacological experiment, it would have pointed the way to a therapeutic application. As to X-rays, their effect on white blood cells points to a trial in leucæmia; and their power of destroying ovarian function suggests their use to determine an artificial menopause. To those who believe that the cells of malignant growths are embryonic in type, the destructive effect of X-rays on germ cells might seem an indication for the exhibition of radiation in cancer.

X-rays.

The actual therapeutic range of X-rays—and this term includes gamma rays where local treatment is under consideration—is, however, far wider than anything which could be inferred from their pharmacology.

Warts. I shall not attempt to deal with diseases of the skin, except to point out that fortnightly or three-weekly "reactive doses" exclusively favoured by dermatologists are not always the best practice. To take a simple example, such as warts and corns. I have seen cases in which sharp reactions have resulted in permanent telangiectasis, though the original wart remained. Apart from this, it is inconvenient for a person with a corn, or infected wart on the sole of the foot to be taken off his feet even for a day or two by reaction. In my experience the worst cases can be satisfactorily dealt with by small doses twice weekly with no visible re-action and relief of pain within a few days. Five or six weeks may, however, be needed before the condition is finally cured. As the patients have often been in the hands of a chiropodist for long periods, to attend twice a week for a month or so cannot be considered any great hardship. Again, some widespread condition such as lichen planus are better treated by X-rays to the back alone: that is, by indirect action.

Epilation. Then there is the eternal problem of superfluous hair in women. It is often more a psychological than a physical one, some of the patients with the least to see being the most distressed. Such hair can be removed permanently by X-rays, and without immediate reaction; but a large percentage of the cases will show telangiectasis a year or so later. By this time the

company dealing in "a new and perfectly harmless way of treatment for superfluous hair" has probably dissolved and sprung up elsewhere under a new name; and so actions for damages are defeated. This sort of thing is impossible within the area governed by the London County Council, but such establishments flourish just beyond its borders.

Can anything be safely done for these people, apart from electrolytic epilation hair by hair? I have for some years used a method which gives reasonable satisfaction in many cases. It is well known that prolonged friction causes hair to fall off—and ultimately weakens the actual growth. If one epilates by X-rays as for ringworm—that is, by a dose the effects of which are temporary only, and subsequently gets the patient to use friction with a fine pumice stone 'against the grain,' night and morning, quite a good result is obtained, and after some months the amount of rubbing may be diminished. The method is successful in the milder cases only, but these are often the patients most concerned mentally about their condition. It is well to realize that with some women the thing becomes an obsession, and I have had such people come to me, after what I considered a very good result, saying that they could still see hair against the light when they used two mirrors to get a profile view. In one instance of this kind the girl threatened suicide, and it would not surprise me at all if she took her life. Of course, in such cases, the hair may be merely a point on which to focus some deep dissatisfaction with life.

The woman with a man-like growth, who has to shave, is an unsuitable case for the exhibition of this treatment. After temporary epilation, the hair cannot be kept down by rubbing. Broster has treated some such cases by removal of an adrenal. I tried irradiating the adrenal area in one case, and some of the hair fell out; but as soon as I stopped, it grew again, so that one was not encouraged to experiment further.

Septic Conditions. The good effects of suitably applied X-rays in septic conditions is of special interest to the general practitioner. Sinuses, apart from faecal fistula, can usually be made to heal quickly, provided that drainage is satisfactory. A supra-pubic cystotomy wound, for instance, may be very obstinate in its "nearly healed" phase—irritating both patient and doctor by intermittent leaking. Two or three weeks' X-ray treatment will usually close it permanently. Obstinate whitlows and other septic conditions of the finger nails can be dealt with quickly. These small chronic ailments are the very ones which bring discredit on the practitioner if allowed to go on too long.

Less certain to cure, but nevertheless worth trying, is X-ray treatment in chronic infection of the sinuses of the skull. It is particularly indicated in frontal sinus trouble, when no one wishes to operate if it can possibly be avoided.

Before I leave this question of X-rays in septic conditions, I must mention the effects, often dramatic, of very small doses of X-rays in erysipelas of the head and neck. This is the one disease in which radiology ranks with operative surgery as an emergency life-saving agency. No one who has seen the clinical picture change within twelve hours in case after case dangerously ill with erysipelas, can doubt the efficacy of X-rays. The doses are extremely low and

easily obtained from a small portable machine. For some unknown reason, erysipelas in parts other than the head and neck does not show anything like the same response. To produce "limiting bands" of a sharp erythema in the path of the disease by means of ultra-violet light seems better practice in such cases.

Theories as to the mode of action of X-rays in septic conditions are somewhat vague. One thing, however, is certain: in view of the smallness of the doses required, the action must be indirect. It is true that, unlike ultra-violet rays, X-rays can penetrate deeply into the tissues; but doses of the order clinically employed have no effect whatever upon microbic cultures. We know, however, from the facts of X-ray epilation, that profound changes can be brought about without visible reaction; and one assumes that local defence mechanisms, including phagocytosis and antibody production, are stimulated by X-ray application; it is otherwise difficult to account for their remarkable therapeutic powers.

Stimulation of the body's capacity for defence and repair must, in fact, be the aim of most X-ray treatment. The production of an artificial menopause is the only certain example of the therapeutic use of X-rays exclusively for their destructive powers. The disappearance of a malignant growth under radiation is at most only partly due to direct action; local and general resistance come largely into the picture, and their absence defeats all attempts at amelioration, no matter what doses are used.

Malignant Disease. This is perhaps the best place to make a brief résumé of the uses of radiation in malignant disease. I do not intend to say much, because, in my opinion, excessive concentration on cancer has tended to obscure the very real value of radiation in numerous other maladies. Radiotherapy is not a cure for cancer any more than is surgery; but it has a much wider range as a palliative, and undoubtedly adds useful years to the life of the victim of malignant disease.

I will discuss here only breast cancer, as that is the form of the disease to which I have devoted most attention. There are certain facts about X-rays in breast cancer, which cannot be disputed. One is, that a comparatively mild course of pre-operative raying will often reduce the size of the primary growth by half. It is a logical deduction from this that the activity of the disease is reduced for the time, and that operation should be relatively safer. Another fact of a somewhat more recondite nature, is that X-ray treatment of a similar kind given at intervals after operation, helps to maintain a normal serological picture as shown by graphs of the differential sedimentation rate. This is found to be abnormal in patients with active carcinoma of the breast; it improves after operative removal but is very apt to relapse later. When it does so, it can be restored to normal, or near normal, by X-ray treatment so graduated as not in any way to upset the patient. Conversely, overdosage may swing the serum graph in the wrong direction either temporarily or permanently. The sedimentation charts are no more specific than temperature charts, where we have to decide on one of several likely causes. It is usually possible, however, by a

process of elimination, to determine the real reason for variations shown in a temperature chart. In any case, the important thing is to get the temperature back to normal. Neither the reduction in the primary growth, nor the power to turn an abnormal serum graph into a normal one, is positive proof of the value of X-rays in improving the results of surgery. I can only say that in my own experience over a great number of years I am convinced that the expectation of life is improved, and that I have converted more than one surgeon in this district to the same view.

I am going to voice another opinion. If there are no palpable glands in the axilla, no attempt should be made to clear it. The lymph glands form a natural barrier against the spread of cancer. Their resistance is usually overcome, but it may be stimulated by radiation, as has been shown by Nakahara and by Ewing. And this stimulation is accompanied by actual necrosis of carcinoma cells. Therefore, when invasion, if present, is still microscopic, radiation of the lymph glands is the treatment of choice. By this means the risk of what is sometimes called a "surgical arm" is avoided. I shall be interested to hear the views of the surgeons present, but some surgeons, at least, claim that a swollen arm is a sign of a thorough operation. I am myself convinced that many swollen arms are post-operative: they may go on indefinitely without any other sign of trouble. Although the surgical arm never reaches the proportions of one in which the cause is malignant invasion, it can be very distressing to the patient.

In a paper read at the Annual Meeting of the British Medical Association at Melbourne, and recently published in the British Medical Journal, the author deals at length with the question of radiation in breast cancer. He advocates pre-operative raying, in which I agree with him; but he states that any growth which is considered inoperable before it is irradiated should never be touched by the surgeon. This dictum, to my mind, is wholly unjustified, and compliance with it would result in much unnecessary suffering. If by surgical interference radical operation is meant, then it is true that only harm can result; but removal of a quite extensive nature is often imperative as a palliative measure. X-rays alone will often render a local or "toilet" operation safe; but if a case responds well to Todd's sulpho-selenium injections combined with X-rays, surgical procedures which would otherwise result in rapid spread of the disease may be safely performed. In January of this year I showed at the Clinical Section of the Royal Society of Medicine, a case of acute carcinoma of the breast, with skin of peau d'orange type, which has been quieted down by Todd's method. The opinions expressed at the Section were all to the effect that operation would be fatal. Nevertheless, trusting in Todd's statement, I recommended removal of the breast and partial clearance of the axilla. Mr. E. M. Cowell operated in March, and last month I showed the patient again, with the wound healed. Cervical glands remain; but the patient has at least been saved a fungating breast.

A year ago, with the co-operation of the governors and staff of the Croydon General Hospital, I was able to establish a clinic for the after-care of breast cancer. We have had about sixty cases in the clinic, which is increasing. My chief disappointment is that I have not been able to get hold of more cases for

irradiation *before* operation. The point about this clinic is that it is a clinic for a certain type of case, and not for one particular method of treatment. It so happens that radiation is the mainstay in dealing with cancer of the breast; but we are always on the lookout for anything which may bring relief, and are, in fact, trying out forms of injection treatment other than Todd's. My own position, as physician-in-charge of the clinic, would not be affected even if radiation came to play only a subordinate part. It seems to me this is a sound principle and must make it easier to keep an open mind.

In closing my remarks on malignant disease, I should like to point out that statements quoted by Stanford Cade, surgeon to the Westminster Hospital, show that breast cases treated by post-operative radiation at Stockholm have a five year survival rate double that of those treated by surgery alone; and that Phaler's statistics of over a thousand cases at the Philadelphia General Hospital show about the same relative percentages.

Sterilization. I will now pass on to other uses of radio-therapy. I have purposely sandwiched my remarks on malignant disease between references to non-malignant conditions, as it is necessary to combat the idea that the radio-therapist is a mere cancerologist—a hideous term, but one which seems to be coming into use. So far as radium is concerned, its applications are indeed, mostly to cancer, if we except its use for sterilization. In my opinion, the latter use is not often justifiable. It is now admitted that an artificial menopause is brought about by the action of radiation on the ovaries; and this action can be attained with much less disturbance by X-rays than by radium. No hospital is necessary and there is little or no discomfort for the patient. The excuse usually made for using radium—namely, that scrapings can be made at the same time and the possibility of cancer eliminated—is not a valid one. Apart from the fact that it is very doubtful if one can eliminate cancer by examining scrapings, it is wrong in principle to mix up the question of diagnosis and treatment. If X-rays are less upsetting to the patient they should be used. If it is necessary to make an examination under an anæsthetic for diagnostic purposes, let this be done on its merits. One cannot sterilize by radium without permanently damaging the uterine mucosa—and this damage is, in the circumstances, unnecessary. I do not know to what degree sexual relations are affected after radium sterilization, but in my own experience of X-ray sterilization, backed by careful follow-up of cases, I am sure that sex desire is no more affected than after a natural menopause—which is to say that sometimes it fades away quickly, and, in other instances, continues little altered for many years.

Metrorrhagia. I feel sure that even to-day there are many women suffering from excessive pain and menstrual bleeding, whose lives are a nuisance to themselves and all about them, who could within three months be turned into normal human beings. In some instances I have come across, the patients had been urged to go into a nursing-home to have radium inserted, and had revolted at the idea. Yet they had not been told of any alternative. I have no hesitation in saying that the most grateful patients on the X-ray therapists list are those who have been relieved of the terrible curse of excessive menstrual bleeding.

Osteo-Arthritis. The subject just discussed is of interest, as I said before, because it is the only instance of the therapeutic use of radiation for its destructive effects upon particular cells. It is a pharmacological experiment lifted directly into the field of therapeutics. But in what I am about to discuss—the use of X-rays in osteo-arthritis—we are back in a region where pharmacology does not help. First, as to what I mean by osteo-arthritis. I mean the type of arthritis, usually symptom-free until middle age, which attacks one or more large joints—generally the hips, knees and lumbar spine. Radiographically it is marked by deformity of joints, loss of articular cartilage, and the presence of osteophytes. The X-ray appearances are not sharply related to the functional disturbances, except when they are very pronounced. This is fortunate, for it means that very few cases are not capable of improvement. Such improvement, amounting in some cases to a cure from the patient's standpoint, can and usually does occur without any change in the X-ray appearances. In the course of X-ray examination for other purposes, joints are often found showing pronounced osteo-arthritic changes, but not causing their owners any trouble. It is thus evident that those parts of the joints not shown radiographically, namely the soft tissues, are of primary importance as regards symptoms, and it is upon them that X-rays must exert their influence.

The action of X-rays upon osteo-arthritic joints is a local one—by this I mean that if a hip and knee are involved, both will require treatment. But it is a local treatment which will succeed over and over again when all other forms of physical treatment, baths, diathermy, etc., have failed. Strangely enough, in lectures by physicians on rheumatism, X-rays are often not mentioned. *One of the saddest things in the radiologist's life is the knowledge of the enormous amount of human suffering which could be relieved by radio-therapeutic methods, but which is not so relieved.*

If you ask me how X-rays exposures function in osteo-arthritic joints, I reply that they have an anti-inflammatory action. If you object that this is unscientific, I reply that medicine is full of similar terms—antipyretic is an instance. And though you may say that antipyretics act through the heat regulating centre, you have not really carried the matter much further.

Although there are many local uses of X-rays which I have not touched on, I must devote my remaining time to the very important subject of indirect therapeutic effect, or action through the constitution. There is an action similar, but more far reaching than that of ultra-violet rays, the value of which is well-known. The action of light is comparatively simple, as it must of necessity act through the skin. With X-rays the matter is unfortunately more complex; as owing to their penetrating properties there is no organ or tissue in the body which may not be concerned.

Asthma. The most striking instance of successful indirect therapy is to be found in the use of X-rays in asthma.

Dr Gilbert Scott made an interesting observation many years ago that the best results were obtained by treating the abdomen with the chest protected, not

by direct application of X-rays to the chest. Here we have a choice of action through the supra-renals, the solar plexus, or the digestive glands. Supra-renal regulation would seem the most popular hypothesis at present.

In asthma patients there is usually a profound change in the chemistry of the serum. This can be demonstrated by the differential sedimentation test previously referred to. The effect of suitable X-ray treatment is to swing the serum graph towards the normal, with corresponding improvement in symptoms. Overdosage produces a reverse effect. The test is thus very useful in deciding whether or not to go on with treatment in a symptom-free patient. If the serum graphs are normal in such a case, treatment may be suspended. If they are not, one should continue until they are normal, or as nearly normal as it is possible to bring them.

Patients with marked abnormal graphs are very sensitive to radiation, and may be made ill by what would ordinarily be considered a very moderate dose. While it may be possible to arrive at a certain standardization for X-rays locally applied to small areas, it is actually dangerous to employ X-radiation in average dosage for its general effects without preliminary blood-tests. Failing blood tests, we can, of course, begin with nominal doses, gradually increasing them and watching the patient's response, but such a method is time-wasting and often entails unnecessary suffering on the part of the patient. I should not like to give the impression that in X-rays we have a cure for asthma, because we can never say when the trouble will return; but at least the method enables people who would otherwise be invalids to carry on their ordinary affairs for prolonged periods.

Spondylitis. I will now relieve your mind by telling you that I come to the last of the subjects on which I intend to make any remarks. A few words about a disease hitherto regarded as incurable—and, indeed still incurable in the later stages—namely, spondylitis in young people—or, as Dr. Gilbert Scott has called it, spondylitis adolescens. This is an entirely different complaint from the spondylitis of the elderly, which appears to be a degenerative disease, having relations with some forms of osteo-arthritis.

Dr. Gilbert Scott has shown by his researches at the British Red Cross Clinic for Rheumatism, and elsewhere, that in spondylitis adolescens there is a long prodromal stage in which there are no symptoms specially referable to the spine. The prodromal symptoms usually start in the early teens, and consist of pains in the back, shoulders and arms, often called "growing-pains". These come and go at first, with long free periods; sometimes there are acute attacks, with temperature, lasting a few weeks. These, however, may at first appear to be completely recovered from. Later on, they are associated with stiffness in the back, and mobility is not fully restored when the acute phase is over. X-ray examination at this stage shows no lesions in the spine, but the sacro-iliac joints present a characteristic abnormality. The sacro-iliac joints show signs of infection before there are any spinal symptoms at all; and this enables the cases of spondylitis adolescens to be separated at an early stage from those in which the pain is either unimportant or significant of some other kind of disease. In other words, any change in the radiographic appearance of the sacro-iliac joints in a young patient, irrespective of symptoms, must be looked upon as being of grave

importance. Whether or not sacro-iliac infection is the cause of spondylitis, it is at any rate the first radiographic sign. As it occurs before there is any permanent crippling, its detection is of the utmost importance. Left to itself, the disease does not always progress indefinitely; sometimes the sacro-iliac infection is overcome, and the joints ankylose, before the spine is injured. More often, spontaneous ankylosis occurs only after the disease has rendered the patient a permanent cripple. Contrary to what is usually taught, young females are attacked as well as males.

All the foregoing would be of purely academic interest if no means were known of checking the disease in its earlier stage. Such a means exists in X-ray treatment applied so as to obtain its constitutional effect. The differential sedimentation rate is altered in this disease. These patients are very sensitive to radiation and treatment must be checked from time to time by the test referred to. Several courses are required, and no patient should be accepted unless he is prepared to be under observation for a year. This does not mean he will be unable to follow any occupation—only that he must spare the necessary time to get in the X-ray treatment required. He cannot be considered reasonably safe until the sacro-iliac joints are ankylosed. The X-ray treatment appears to speed up the natural process of cure.

I make bold to say that if both general practitioners and radiologists became alive to the facts about spondylitis adolescents, no more cripples from this cause would be seen in our midst. It lies with the practitioner to recognize the symptoms which may represent the prodromal stage of the disease, and with the radiologist to detect the changes in the sacro-iliac joints. Once the diagnosis is made, and appropriate treatment initiated, there should be no fear of permanent disablement.

CONCLUSION.

In conclusion, I should like to emphasize the fact that while the local action of X-rays has been intensively studied for nearly forty years, scientific study of their constitutional effects has hardly begun. Many hundreds of observations with the differential sedimentation test have enabled us to show that the chemistry of the blood serum can be profoundly altered for good or ill by X-rays of medium wavelength distributed over a wide area of the body. The precise mechanism of these changes we do not know. In some cases effects may be produced through action of ductless glands; in others, through the sympathetic nervous system. At any rate, there is ample field for future clinical research in the pharmacology and therapeutics of X-rays regarded as a drug for internal administration.