

Indian Journal of
Radiology

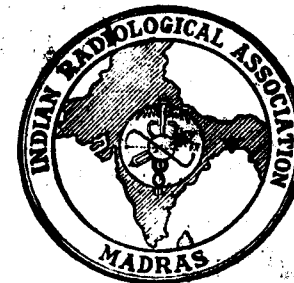
Nov. 1949



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The
Indian Journal of Radiology

A quarterly Journal
devoted to Clinical
Radiology and allied
Sciences



Owned and published
as its Official organ by
the Indian Radiological
Association

VOLUME 3

NOVEMBER 1949

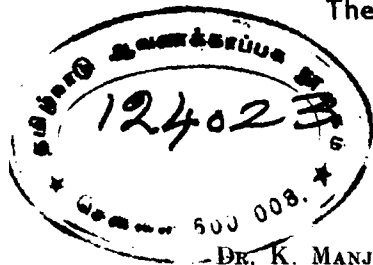
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THE INDIAN JOURNAL OF RADIOLOGY (QUARTERLY)

Owned and Published as its Official Organ by
The Indian Radiological Association



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All matters concerning advertisements in this Journal should also be addressed to the Editor-in-Chief.

Subscription: Rs. 12 per annum. Single Copy Rs. 3.

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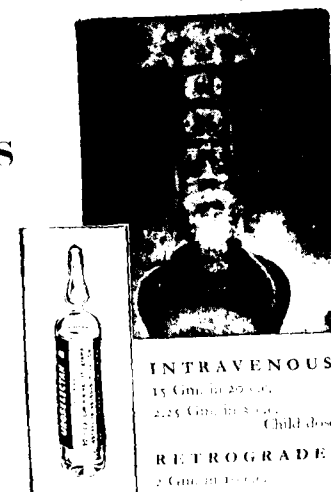
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The Indian Journal of Radiology

Vol. III.

NOVEMBER, 1949

No. 4.

It is with great regret that we record the death of **Dr. A. E. Barclay** on April 26, 1949. It is indeed an irreparable loss to the science of Radiology to which he made very important contributions.

We can pay no better tribute than that of **Brigadier McGrigor** which we reproduce by the kind courtesy of the "British Journal of Radiology" in the following pages.

He was one of the Honorary Members of our Association and evinced a keen interest in its inception and progress. Not a few of its members were either his students or have passed through his hands.

Though sick and infirm during his last days he very readily consented to deliver the First Jagadish Memorial Lecture of our Association.

Our heart felt sympathies go to Mrs. Barclay and other members of his family. May his soul rest in peace.

EDITOR-IN-CHIEF.

DR. A. E. BARCLAY

A PERSONAL TRIBUTE

“UNCLE B”, as all his friends referred to him, has gone, and all radiologists, other scientists and friends, at home and abroad, will hear the sad news with a feeling of great sorrow and personal loss. He had been with us so long, so regularly and so intimately, his personality had charmed members at so many meetings and he was so much a part of all these that his absence now is grievous and his front seat in radiological science empty.

I had the honour of being accepted by him as one of his close friends for many years. Our association, especially during the war, when he formed an integral part of a consultative team that correlated the needs of the civil and military services, was a happy and collaborative one. He was ever ready to help the war effort in any way within his power and his support and advocacy during these years were edifying and buoyant. Elsewhere will be recorded the fatiguing amount of travel and work he did up and down England many times, in all weathers, in his capacity as Consulting Adviser in Radiology to the Emergency Medical Service. This was an appointment that I think only he, with his charm, could have handled so successfully.

His life was marked by outstanding scientific achievements interspersed with technical and classical accomplishments, while his pen recorded and disseminated these with rare integrity.

The record of his works, ranging from his “Early days of Radiology at the London Hospital”, “Early days of Radiology at Manchester”, “Early Observations” in Bythell and Barclay’s “X-ray Diagnosis and Treatment” and “Radiology of the Digestive Tract”, up to his more recent researches on the foetal circulation, ductus arteriosus, kidney cortex, stomach mucosa, the envisaged micro-radiography of the brain cortex (not completed), and his latest book embodying most of this recent work, just about to be published although too late for him to see its success, shows how continuously he had planned and advanced scientific radiological problems throughout his life.

He was much sought after on his travels, which included Australia, New Zealand, Canada and America and his daily mail from friends abroad was remarkable in amount.

He was most regular in his attendance at Council meetings and over a longer period than any other

officer. He had a unique and unbroken attendance at all the past five International Congresses of Radiology. His correspondents were not confined to radiologist, but included physicists, gastro-enterologists and physiologists. The latter were so much impressed by his recent successes in research that they accepted his micro-radiographic work as providing a new outlook on physiology of certain organs and termed it “Barclay’s Physiology”.

He was invited to give the MacKenzie Davidson Memorial Lecture in March, on these researches and their effect on Physiology, but unfortunately his health prevented him from delivering the lecture. Nevertheless, the Council of the B.I.R. did not invite anyone to take his place and the medal was presented to him at Oxford by the President. This graceful tribute was one which gave him much pleasure.

He received many honours and gave many memorial and other lectures at home and abroad. Among his latest honours, the most valued were the awards of the Hon. D.Sc. by both Oxford and Manchester Universities. He also received in March the Bose Memorial Gold Medal as the first Lecturer (in absentia) in memory of that outstanding Indian scientist Sir Jagadish Bose.

Outside medicine he had many other interests and artistic talents.

For example, he was a great lover of classical music and had a magnificent collection of records of the Masters and many of his friends have enjoyed a real treat at his home sitting by the fire exchanging thoughts, listening to superb music in quiet contemplation.

His workshop was the craftsman’s dream where by his skill he could forge, cast, turn, produce or repair any piece of apparatus or gadget in metal or wood that he thought of for his many inventions. He was a keen sportsman and fisherman and spent many happy days fishing in Scotland.

He always attributed his success to the help and ability of Mrs. Barclay in looking after everything in his life outside his speciality, thus leaving him entirely free to direct his creative ability. The Barclays as hosts were charming, generous and homely, and the many American Army Medical Officers that were stationed round Oxford during the war appreciated this to the full, many lasting friendships were thus made and international links were so forged.

In the last year or so, and especially in the last few months, he displayed a fortitude and courage such as I have never seen. His last words to me a few days before his death were “It’s time for me to go now, Mac, I am of no further use to

any one", and so passed Uncle B, "The Grand Old Man of British Radiology"—a wonderful friend, a very brave and gallant gentleman, calm and serene to the end.

A typical illustration of how he was appreciated everywhere occurred the other day when several of the staff in his Club in London, knowing I was a friend, came to me and said how much they missed him, as he was so kind and nice to them all.

At the last I quote a moving eulogy written recently by a well-known colleague in America, "I am sure that each of his many friends feels the richer for having come to know him. It is only now and again

that a bright light like Barclay's traverses the human and intellectual sky and we, the ordinary folk, can look up in wonderment and be glad and inspired by his brilliancy performed with no thought of personal gain or fame. He had imperturbable belief in his own convictions, unafraid in standing up and upholding the truth, that which was good, just and right, with steadfastness and perseverance. His life was a full, replete, exemplary and active one. He has shown the way, we shall follow as best we can."

—D. B. McGRIGOR.

(By courtesy of the *British Journal of Radiology*).

Dr. Barclay's letter to the President, Indian Radiological Association a few days before his death.

*The Cobden
South West Morning
Paper
15.3.46*

Dear Dr. Raw!

The lovely gold medal has just come. It is a thing of beauty and I shall prize it greatly. But how I wish I had been able to express my ardent wishes to help you all in your uphill struggle by coming over, seeing you all & delivering the lecture in person.

Please think all my good friends & give them the greetings of one who, in the serene & yellow leaf, looks back on a long life of intense happiness in the radiology that has filled the whole of my life this last half century.

Yours sincerely

A. S. Barclay

Look forward to seeing the I. R. A. & to having reprints.

Therapeutic Possibilities of Radio-phosphorus and other New Radioactive Materials

A. G. S. COOPER,
QUEENSLAND RADIUM INSTITUTE, BRISBANE, AUSTRALIA.

THE discovery by Joliot and Curie in 1934 of artificial radio-activity opened up new vistas in the field of therapeutic radiology. At first, however, the preparation of therapeutically useful quantities of any required product was impracticable. As larger cyclotrons were constructed radioactive materials became available in some centres for medical research. The internal administration of radioactive material was tried quite early in the century, using various members of the radium series, but this type of treatment failed owing to the long life of these products. Artificial isotopes are only applicable in therapy because of their shorter life which permits control of dosage. It appears from the literature that P^{32} was first administered to a large series of patients by Low-Beer, Lawrence and Stone at the Croker Laboratory, California, in 1937, but the results of this work were not published until 1942⁽¹⁾. Soon after the entry of the United States of America into the War supplies of isotopes were curtailed owing to the use of cyclotrons for a military purpose, which we may now presume was the preparation of fissionable products. More recently the discovery and

development of the plutonium pile or neutron reactor promises to step up by several hundred times the cyclotron production of various radioactive isotopes including that of phosphorus. The secrecy attached to the preparation of plutonium, and the high priority accorded to the development of commercial atomic energy, have up to the present restricted the preparation and issue of radio-isotopes in the countries operating piles. When these difficulties and the problems of transportation can be overcome there is reason to believe that liberal supplies of these materials should be available in Australia. If it is permitted to look still further ahead, it is possible to envisage the installation in this country of a cyclotron and small plutonium pile from which the products could be distributed by air to all States of the Commonwealth.

Radioactive Phosphorus P^{32}

Before proceeding further it is desirable to answer the question "What is P^{32} and how is it prepared?" Natural phosphorus has a nuclear constitution denoted $^{15}P^{31}$, which implies an atomic number of 15 and atomic weight equivalent to 31. In other words there are 15

protons in the nucleus balanced by a similar number of negatively charged electrons outside the nucleus. The remaining 16 units of atomic weight are provided by neutrons within the nucleus. This element is bombarded in a cyclotron by a stream of deuterons and when a deuteron makes a close collision with the phosphorus nucleus a reaction occurs resulting in the transfer of a neutron from the deuteron to the P^{31} nucleus. (Fig. 1).

chemical treatment, as it is most conveniently employed in therapy as the soluble salt, di-sodium hydrogen phosphate. To obtain an isotonic solution, the salt is usually employed as a 1.5% solution in water. It is of interest to note that the ratio of phosphorus atoms which are radioactive to the unchanged atoms is of the order of 1:10⁷. Under these conditions the radioactivity of the solution will be equivalent to approximately 750 microcuries

(27.75rd) per millilitre. Solutions of higher concentration are obtainable from the pile.

Physical properties of P^{32} .—

(1) Half life period is 14.3 days. From this value a table of decay is computed.—Table 1 (vide page 148).

(2) Beta-rays only are emitted. Average energy about 0.6 Mev

(million electron volts). Maximum energy 1.8 Mev.

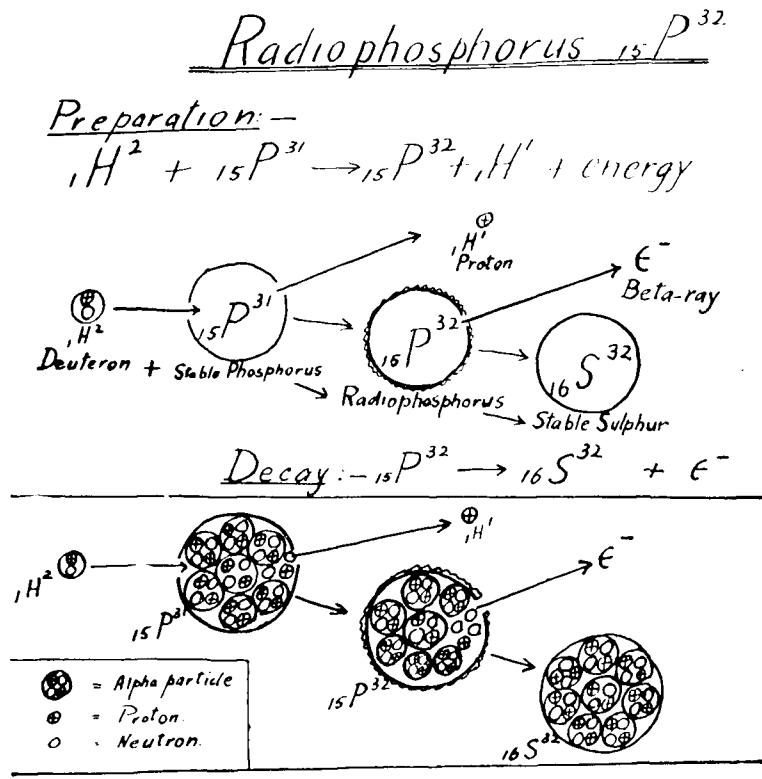


FIG. 1. Symbolical Atomic Transformation.

TABLE I.
Decay of Radioactive Phosphorus (P^{32}). Half-value Period, 14.3 days.

Time in days	Fraction remaining	Time in days	Fraction remaining	Time in days	Fraction remaining	Time in days	Fraction remaining
0	1.000	8.0	0.678	22.0	0.344	46.0	0.107
0.5	0.975	9.0	0.655	23.0	0.328	48.0	0.097
1.0	0.953	10.0	0.616	24.0	0.312	52.0	0.080
1.5	0.930	11.0	0.586	25.0	0.297	56.0	0.066
2.0	0.902	12.0	0.559	26.0	0.283	60.0	0.054
2.5	0.886	13.0	0.532	28.0	0.257	64.0	0.045
3.0	0.865	14.0	0.507	30.0	0.233	68.0	0.037
3.5	0.844	15.0	0.483	32.0	0.212	72.0	0.030
4.0	0.824	16.0	0.460	34.0	0.192	76.0	0.025
4.5	0.804	17.0	0.438	36.0	0.174	80.0	0.021
5.0	0.785	18.0	0.417	38.0	0.158	90.0	0.013
5.5	0.766	19.0	0.398	40.0	0.144	100.0	0.008
6.0	0.747	20.0	0.379	42.0	0.130	120.0	0.003
6.5	0.730	21.0	0.361	44.0	0.119	140.0	0.001
7.0	0.712						

Average penetration in tissue 2 mm.
Maximum " " " 7 mm.

(3) Radiation effects will be local only, in keeping with the limited range in tissue.

(4) All chemical reactions are exactly identical to those of the naturally found isotope. This means that the material is ideal for tracer experiments.

Methods of detection and measurements.—Most of the artificially prepared radioactive isotopes emit Beta or Gamma rays, or both types of radiation simultaneously. These materials are detected, by virtue of the radiations given off, with the aid of an ionisation chamber or a Geiger counter.

This instrument consists of a sealed glass tube containing a suitable

gas at a pressure of 5 to 10 cms. of mercury. Mounted within the tube is an axial wire at positive potential relative to a surrounding hollow conducting cylinder. A single Beta-particle entering the tube can produce a burst of ionisation great enough to operate an electrical circuit which will count the number of bursts.

It has been the practice to express the strength of radioactive isotopes in terms of the curie or part thereof. The curie was originally defined at Brussels Congress in 1910 as "the amount of radon in equilibrium with one gram of radium". It has since come to mean the amount of any radioactive substance of which 3.7×10^{10} atoms disintegrate per second.



FIG. 3. Autoradiograph of thin slices of a tomato showing differential uptake of P^{32} by the seeds. [Vide page 149.]



FIG. 2. Leaf the stem of which had been allowed to remain in a dilute solution containing P^{32} for 24 hours. The autoradiograph shows an even distribution of radioactive material. [Vide page 149.]

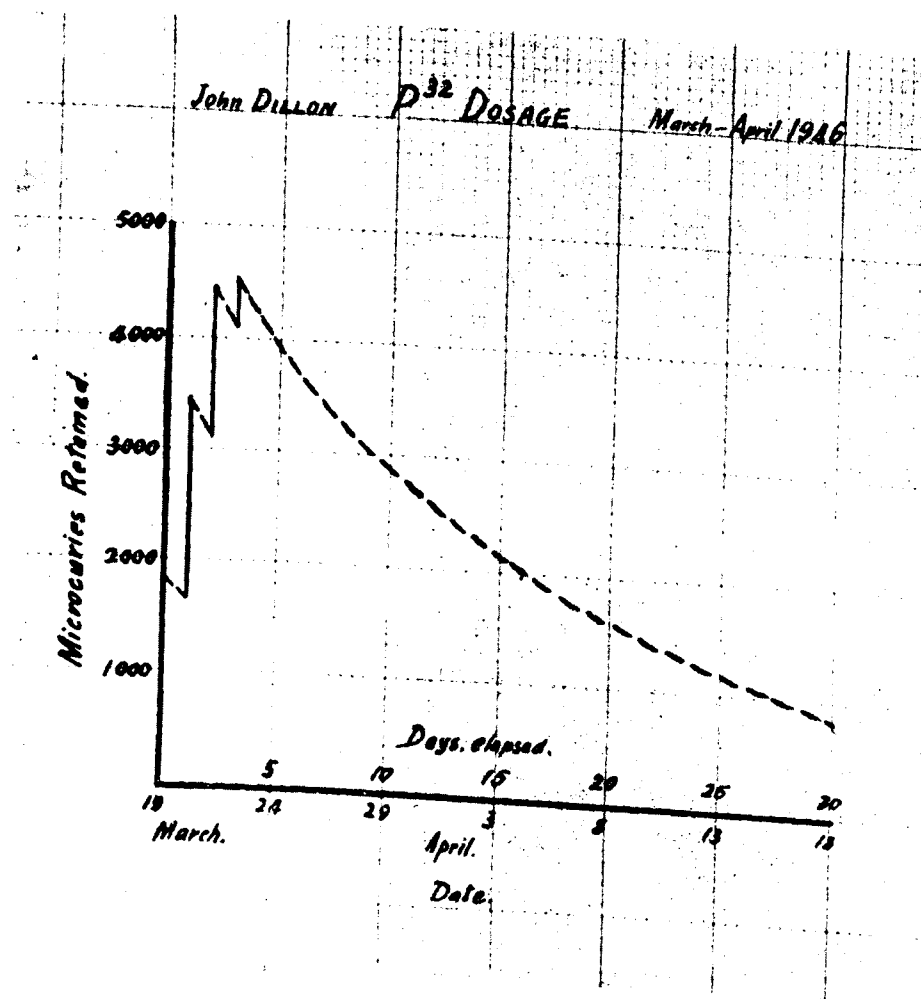


FIG. 4. Graph illustrating typical treatment of polycythemia vera with P³².
[Vide page 152.]

In 1946 Condon and Curtis⁽²⁾ suggested the application of a new unit, the rutherford, to represent that amount of material producing 10^6 disintegrations per second. The appropriate abbreviation becomes "rd". It is anticipated that the new unit will be widely used and it should be remembered that the conversion factor is 37rd per millicurie. The rutherford is a quantitative unit of activity and does not imply dosage in a radiotherapeutic sense.

We are informed that the energy absorbed from 1 microcurie of P³² in 24 hrs. is 3550 ergs. If a patient receives a quantity of P³² equivalent to 0.1 microcurie per gram of tissue, the energy absorbed in 24 hrs. should be 355 ergs per gram. The energy absorbed from 1r of X-rays in one gram of tissue is 83 ergs. From this we assume that a concentration of activity equal to 0.1 microcurie per gram gives a dose equivalent to 4.2r in 24 hrs. This concentration, taken arbitrarily for purposes of illustration, represents an unusually high dose in practice. It is of interest to note that, under the conditions stated, the integral dose in a patient of 60 kilograms bodyweight, would be approximately 0.25 equivalent megagram roentgen in 24 hrs.

Biological factors.—The most important biological property of P³² is the selective uptake of phosphorus in certain tissues; for instance, lymph

glands, spleen, bone and bone marrow, and in most rapidly growing tissues. This point can be illustrated by autoradiographs. (Figs. 2 and 3, vide picture).

The effect of P³² on tissues will be comparable to the action of X-rays or Gamma-rays in that the charges are brought about by ionisation. It is obvious, as the average range of the Beta-particles emitted is of the order of 2 mm, that noticeable tissue destruction will be confined, apart from a small margin, to regions where the concentration of P³² is high. Methods available for detection and estimation of radioactive isotopes are now so sensitive that quantities of these elements, too small to produce appreciable radiation effect in animal tissues, can still be detected. The chemical and physiological behaviour being the same as that of the stable isotope, it is possible to "tag" a certain proportion of the atoms and trace their subsequent distribution and behaviour.

As an example of a tracer study thiamine (Vitamin B) has been tagged by synthetic preparation from radio-sulphur. The fate of this product in the body can then be traced by measurements of activity in various tissues and excreta. Hevesy studied the absorption of phosphates from the alimentary tracts of animals and man, finding that 25% of orally administered inorganic phosphates were

evacuated in the faeces. When the material was injected intravenously retention was much more effective. Uptake in normal adult tissues per unit weight varied in the following decreasing order:—bone, liver, stomach, heart, kidneys, lungs, blood, muscle, skin and brain. Lawrence compared the phosphorus metabolism of the tissue of normal mice and leukæmic mice. He demonstrated striking increases in the retention of P^{32} in leukæmic lymph glands and spleens as compared to normal glands and splenic tissue.

The preferential accumulation of P^{32} in certain body tissues, particularly in diseased tissues, can be expressed as the Differential Absorption Ratio (D.A.R.) which is obtained by dividing the amount of P^{32} absorbed per gram of a tissue by the amount of isotope administered per gram of the whole body. This ratio in a lymphosarcomatous lymph node shows an average value of 3.5 with a range of 2.2 to 12.0⁽³⁾. It has also been shown that if one microcurie of P^{32} is destroyed per gram of tissue the resulting dosage is 880 equivalent r⁽⁴⁾, in other words 100 microcuries per Kg, which is within the scope of practical treatment, yields 88 e. r. Assuming a D.A.R. of 3.5, the total theoretical dosage becomes approximately 300 e. r. in a region of preferential absorption.

Clinical factors.—The relative concentration of P^{32} in bone marrow

imposes a limiting factor in the use of this substance in the treatment of disease. Dosage calculations suggest that its sphere of usefulness would hardly be expected to extend beyond those conditions which are favourably influenced by X-ray skin doses of the order of 1000 r spread over several weeks. This deduction is confirmed in practice and it would appear illogical to attempt the treatment of bone metastases, primary tumours of bone, or multiple myeloma for the requisite effective dose would be damaging to the hæmopoietic system. The use of P^{32} as a so-called prophylactic against blood stream metastases at the time of surgery for malignant conditions is not recommended for the same reason; moreover, it has been pointed out that any radioactive material contained in a small mass of average diameter 200 microns, which is given as the average size of blood stream metastases⁽⁵⁾, would exert its maximum ionisation effects outside the tumour embolus⁽⁶⁾.

It is desirable to administer P^{32} intravenously rather than orally—

(a) to avoid the high initial loss in the faeces, and

(b) because it has been proved that uptake by diseased tissue is higher.

Values of average retained activity are shown (Tables II-a and II-b, vide page 151).

TABLE II-A.

Radioactive Phosphorus. Calculation of Retained Activity following Intravenous Administration of Radiophosphorus. (After Low-Beer, Lawrence and Stone.⁽⁵⁾)¹

Days	Percentage of Administered Dose
1	90
2	83
3	77

¹ For the first three days the activity on each day is calculated as a percentage of the administered dose; for each day after the third day the activity is calculated as a percentage of the activity retained on the third day.

Treatment is always preceded by a preliminary study of the blood picture and, if practicable, of the bone marrow. In lymphosarcoma, and particularly in giant follicular lymphadenopathy, there is apt to be an infiltration of the bone marrow by cells which accumulate P^{32} readily. Over-irradiation of the already damaged marrow is said to result in a severe leukopænia. Cases with gross lymphadenopathy or massive tumour formation, are unsuitable for non-supplemented P^{32} therapy owing to the dispersal of the radioactive material and the resulting low concentration per unit volume of pathological tissue. It is appropriate to supplement the administration of P^{32} with deep X-ray therapy, and this may be necessary in the treatment of a large glandular mass or to reduce

TABLE II-B.

Radioactive Phosphorus. Calculation of Retained Activity following Intravenous Administration of Radiophosphorus. (After Low-Beer, Lawrence and Stone.⁽⁵⁾)¹

Days	Percentage of 3rd day activity	Days	Percentage of 3rd day activity
4	94	19	37
5	88	20	35
6	83	21	33
7	78	22	31
8	74	23	29
9	69	24	27
10	65	25	26
11	61	26	24
12	58	27	23
13	54	28	21
14	50	29	20
15	48	30	19
16	45	31	18
17	42	32	17
18	40	33	15

the size of a very large spleen. When this appears necessary it has been advised to deliver the deep therapy first, but one would expect previously irradiated tissue to show a lessened absorption ratio and the alternative sequence has been employed with gratifying response in Brisbane.

Radiation sickness is reported to be a very rare phenomenon in P^{32} therapy and has not been encountered in a small series of 25 cases treated.

Use of P^{32} in Treatment.

1. *Polycythaemia vera*—On theoretical grounds a good response

12402.5

would be expected in this disease on account of its origin in the bone marrow and the fact that P^{32} is selectively concentrated at this site. Moreover, it is well known that good remissions are obtainable in many cases by the use of wide field, whole body X-radiation. The X-ray dosage required is considerably higher than that needed for control of a chronic leukæmic condition (8). It is not surprising to find that a relatively large quantity of P^{32} must be administered. The initial dose usually advocated is from 5 to 7 millicuries but, unless the activity of P^{32} is 750 microcuries/cc or greater, it is wise to divide the dose into three or four daily fractions in order to encourage more complete absorption in the body. In patients who show evidence of involvement of the leucopoietic system, treatment by a fractional saturation method is desirable on account of an increased risk of a leukopaenic reaction. It is important to note that the red blood cell count and the hæmoglobin value are influenced slowly and do not reach a stable level for a period of about three months. In the event of an adequate response further administration of 2 to 3 millicuries is advised. (Fig. 4, vide picture).

2. *Treatment of leukaemia*:—Experience in the treatment of acute forms of the disease have been consistently disappointing and one is forced to the conclusion that it is

not possible to bring about any appreciable benefit to these unfortunate patients by the use of radioactive phosphorus.

3. *Chronic myeloid and chronic lymphatic leukaemia*:—Some American authorities advocate the administration of P^{32} in doses of 500 to 1000 microcuries weekly until the white cell count shows a satisfactory response. As some activity remains in the body for approximately 25 days, it is recommended that treatment be spaced out once the white cell count falls below 30,000 cells per cubic mm. This regime assumes that supplies of P^{32} will be available constantly and has not been practicable in my limited experience. The alternative method employed was to develop a total retained activity of 2,000 microcuries by a rapid fractionated technique and to maintain this level for 7 to 10 days whilst the blood count is watched closely. If an accompanying splenomegaly shows a slow response there is no objection to supplementary regional deep X-ray therapy. The first signs of overdosage by P^{32} are thrombocytopænia and a reduction in the reticulocyte count, followed by a leucopænia. (Figs. 5 and 6, vide picture).

4. *Treatment of lymphosarcoma*:—In the treatment of lymphosarcoma, American writers(3) describe several methods of administration.

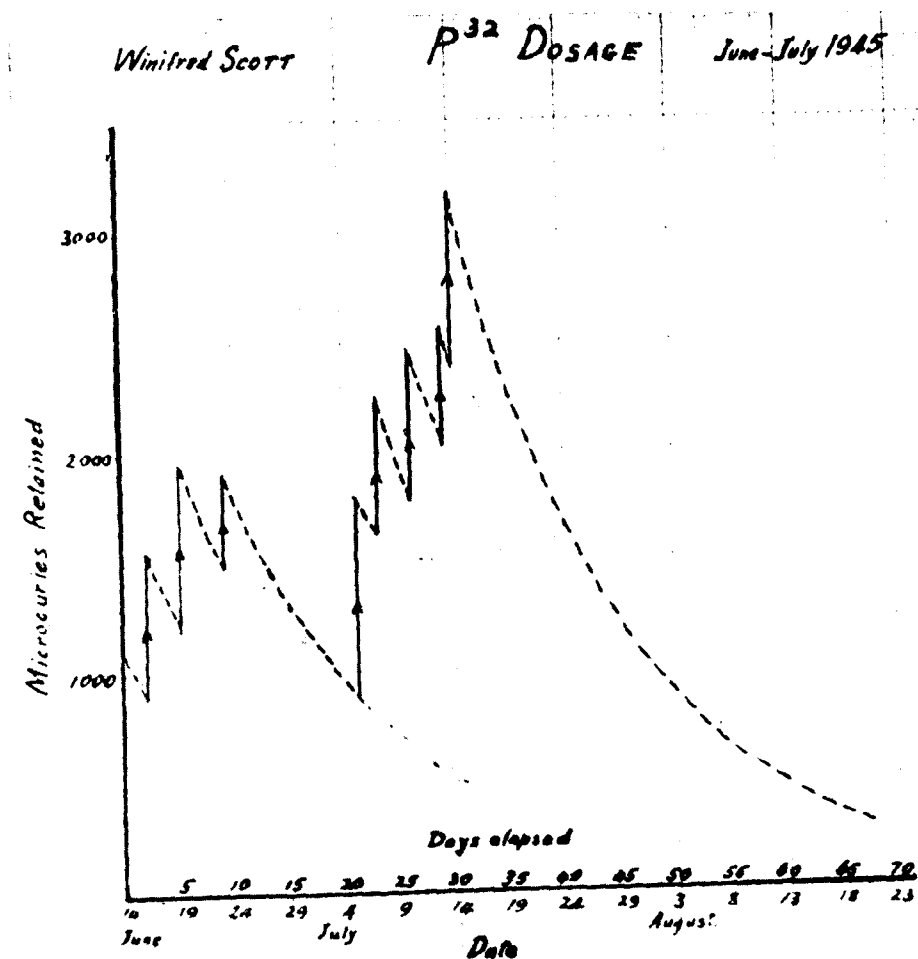


FIG. 5. Graph from typical treatment chart of patient suffering from chronic myeloid leukaemia. [Vide page 152.]

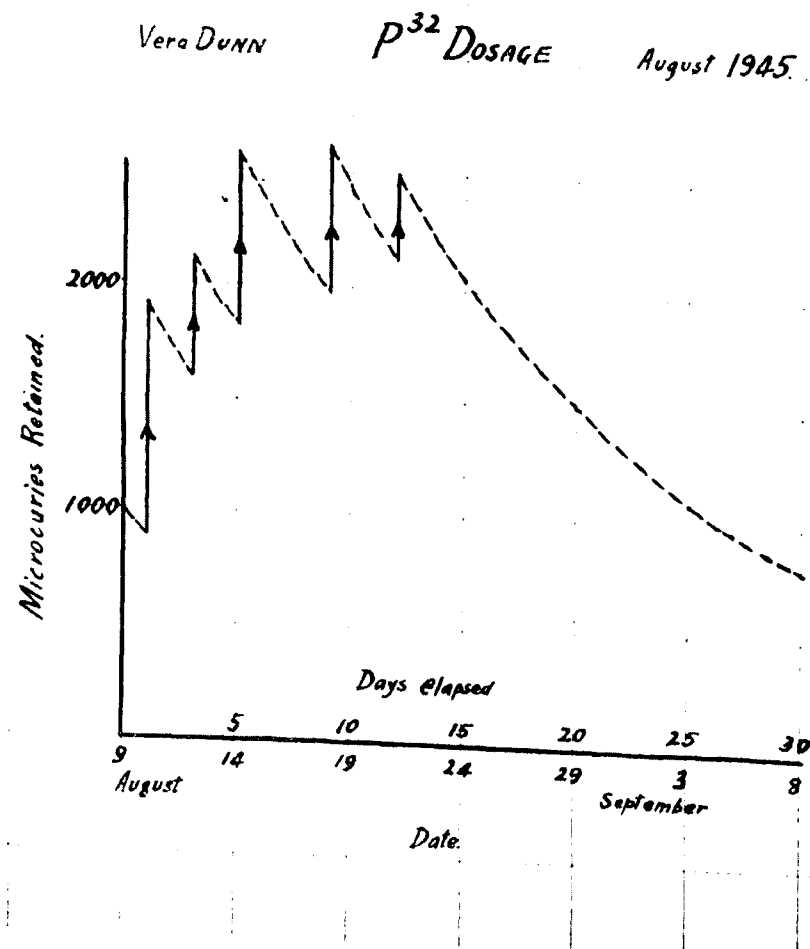
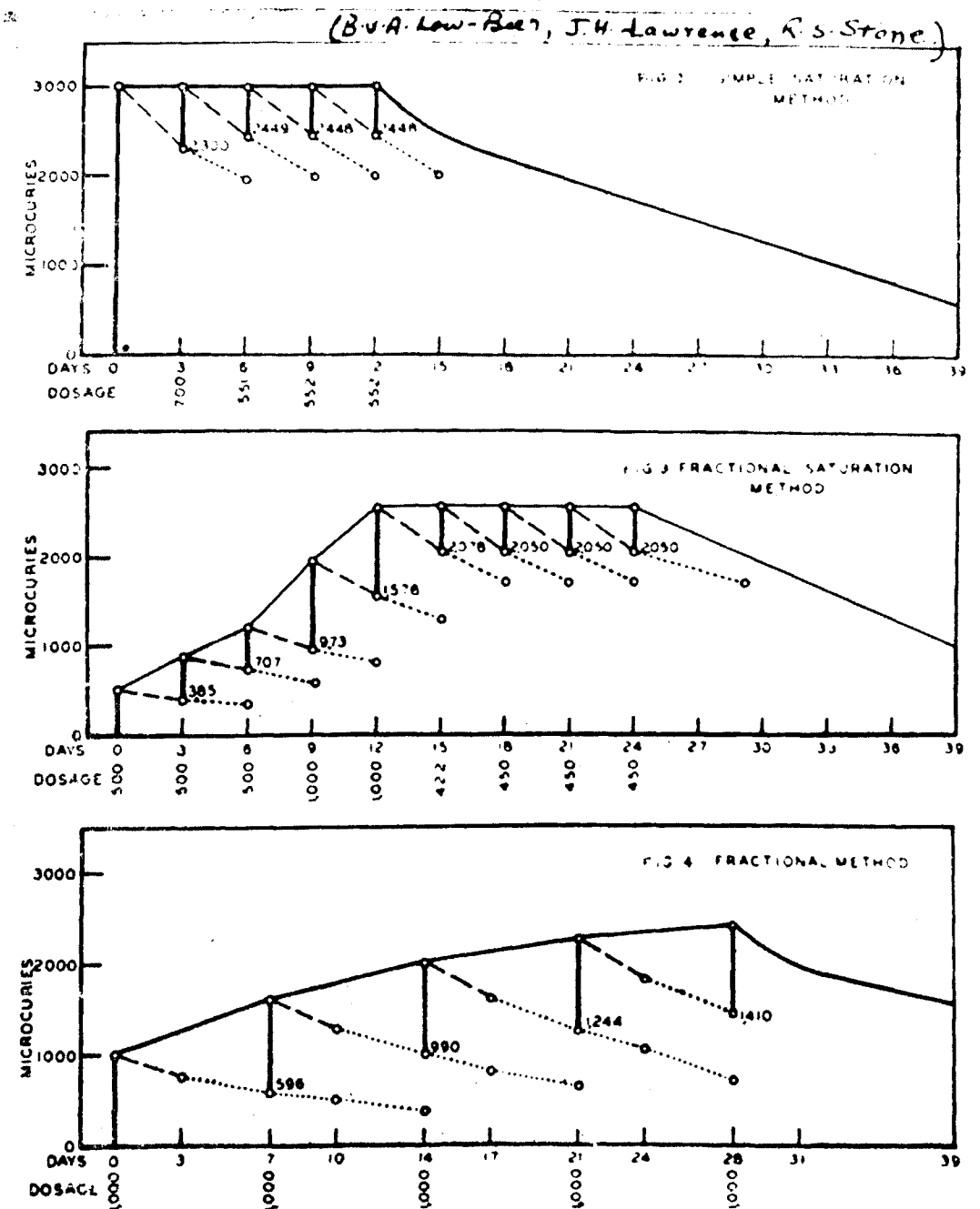
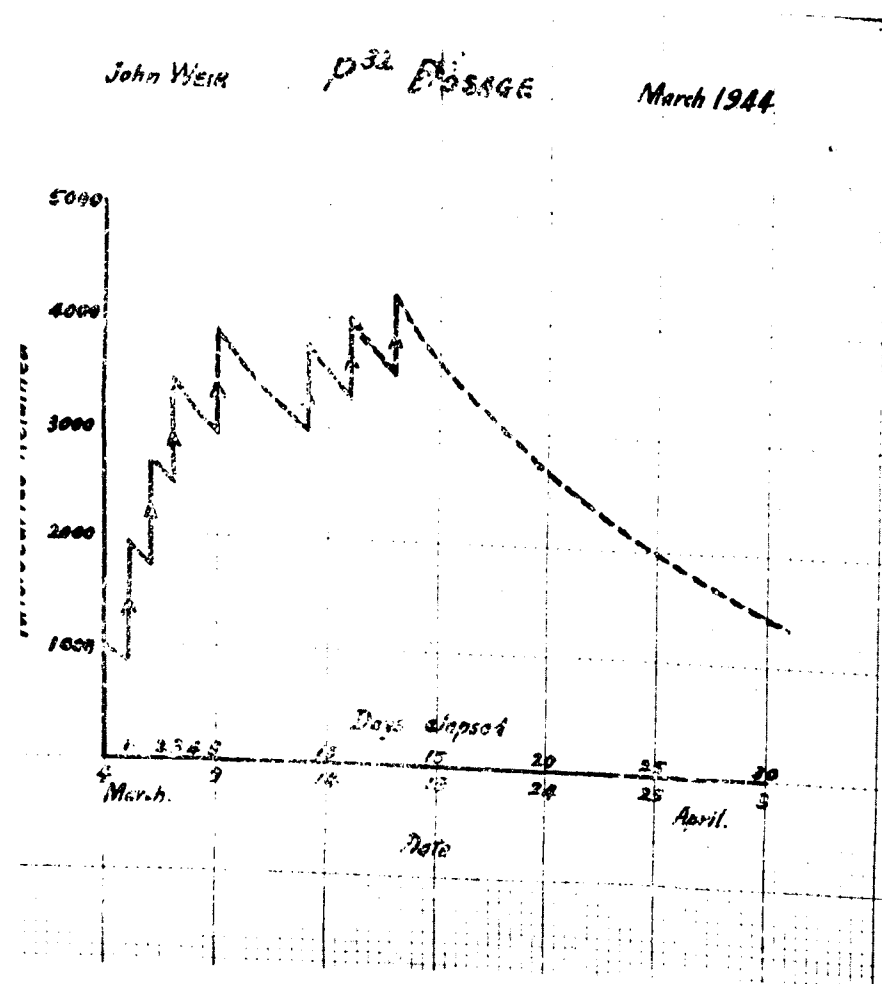


FIG. 6. Graph from typical treatment chart of patient suffering from chronic lymphatic leukaemia. [Vide page 152.]



Figs. 2-4. Methods of administration of radiophosphorus

FIG. 7. Methods of administration of P^{32} .



3. Graph from treatment chart of patient suffering from generalised lymphosarcoma.
[Vide page 153.]

(a) *Simple saturation method*:—This consists of one large initial dose which is followed by smaller doses at intervals of three days to bring the level up again to the original figure.

(b) *Fractional saturation method*:—This is similar to the first method with the exception that the peak radiation level is attained gradually over a period of ten to twelve days.

(c) *Fractional method*:—This is a less intense course, comprising doses of approximately 1,000 microcuries given at longer intervals (often seven days). (Fig. 7, vide picture).

To adhere to any of these methods would necessitate a continuous and unfailing supply of radioactive material. In Brisbane, a rapid fractional saturation method was developed from considerations of expediency and economy of P³². In general the total retained activity was built up to 2,500 or 3,000 microcuries and kept at this level for a period of ten to fifteen days. (Fig. 8, vide picture). No immediate radiation reactions were experienced.

Results of treatment.—In polycythæmia vera claims have been made for long remissions and workers with experience hold that the results are better than those obtained with deep X-ray therapy. The treatment of this condition requires large quantities of P³² and has the one drawback that dosage is not as

readily controllable as in X-ray therapy.

In the chronic forms of myeloid and lymphatic leukaemia some excellent remissions have been obtained and these have endured somewhat longer than remissions after X-radiation.

The results in suitable types of lymphosarcoma give an impression of parallelism with those of X-ray therapy. Cases with large glandular masses are unsuitable for P³² alone.

One feels that continuity of supplies would result in many improvements in technique with consequent benefits reflected in the results. Furthermore, it is possible that organic compounds containing phosphorus may be selectively absorbed in greater ratio than the inorganic preparations commonly used at the present time.

Possibilities as a superficial Beta-rayer.—Low-Beer⁽⁷⁾—gives an interesting account of the experimental use of P³² for application to the skin. The method adopted was to allow discs of blotting paper to absorb known amounts of P³² in solution. After drying, the discs were applied direct to the skin and the reactions produced were carefully observed and tabulated. In this manner it was found that erythema with dry desquamation was produced by an exposure

of 1,900 microcurie hours per sq. cm. giving an estimated equivalent "r" dosage of 7,200r on the surface. Biopsy studies revealed appreciable radiation effects to a depth of 5 mm. in tissue treated.

Under the conditions employed by Low-Beer, 48% of the radiation was absorbed in the first millimetre of tissue. This gives a depth dosage comparable to that of a radium plate and it is obvious that the method should be restricted to the treatment of very superficial lesions having a maximum depth less than two millimetres.

Possibilities in therapy of materials other than P^{32} .—These may be arbitrarily subdivided into:—

(a) A group with possibilities as new Beta-ray sources.

(b) A group in which the Gamma-ray activity is of primary importance.

(c) A group the usefulness of which depends on the property of selective absorption.

A. A suitable Beta-ray source should comply with the following criteria:—

(1) Half-life period preferably greater than 30 days to facilitate transportation and to render less frequent the necessary changes in exposure times.

(2) Ready availability, i.e., it should be a fission product of ura-

nium, or easily produced in good quantity by the pile.

(3) Freedom from strong Gamma-ray production.

(4) Freedom from gaseous radioactive products.

We are informed⁽¹¹⁾ that there are in fact two fission products in the above category—

Radio-Strontium (Sr^{89}) half life 55 days.

Radio-Yttrium (Y^{91}) " 57 "

Each of these materials lends itself to incorporation in sheets of plastic material which could be readily moulded to fit a lesion of irregular shape or curved contour. The problem of protection of staff would be simplified in the absence of any penetrating Gamma-rays, and the construction of holding devices would be simplified as no radioactive emanation is produced.

B. Of the radioactive materials emitting Gamma-rays radio-cobalt (Co^{60}) promises to become, at least in some measure, a substitute for radium. It has a half-life period of 5.3 years and conveniently produces almost monochromatic Gamma-rays of greater energy than those emitted by the decay products of radium. In addition, the Beta-rays given are of a soft type easily removed by filtration, and there are no gaseous radioactive products. For convenience in use, lengths of cobalt wire of calibre, say 0.25 mm. could be activated to any desired intensity

in the pile. Lengths of this wire would be mounted in needles constructed of stainless steel or other convenient metal of medium atomic weight in order to keep as low as possible the factor of characteristic Beta-radiation from the outer wall of the container⁽⁹⁾. Sievert and Benner found that substances with atomic numbers between 26 and 50 emitted weaker Beta-rays than lighter or heavier substances. Should a non-rigid mouldable sheath be required it would be easy to house the narrow wire in gold or lead capillary tubing.

Other Gamma-ray emitting substances are radiotantalum (Ta^{182}) of half life 97 days and radio-antimony (Sb^{124}) which has a half life of 60 days.¹² Stable tantalum has already been used surgically owing to the fact that it is well tolerated by the tissues.

Present day telerradium therapy (radium "bomb") treatment carries the disadvantages of high capital outlay, low output and resulting prolongation of treatment times even when a relatively short radium-skin distance is employed. All these drawbacks would be eliminated if unseparated fission products or radio-cobalt could be obtained at a moderate price.

Radio-gold (Au^{198}) has a half life period of 2.7 days which compares with 3.8 for radon. This isotope

would lend itself to the permanent seed implant but would entail much difficulty in transportation owing to the rapid decay. It would still require some form of screenage for interstitial use and would appear to offer no material advantage over radon seeds prepared with gold capillary tubing.

C. At least seven different radioactive isotopes of iodine have been prepared but most of these are substances of very short half-life. The two which appear to offer the best prospects in medicine are I^{130} and I^{131} and these have been prepared by deuteron bombardment of metallic tellurium. More recently it has been announced that these isotopes are obtainable as fission products from the pile.

Experimental work has shown that iodine is taken up rapidly by the thyroid gland and in greater measure by the non-iodised gland. Both the normal and hyperplastic gland absorb a greater proportion of a small, than a large dose of iodine. The selective uptake by normal thyroid tissue is such that it contains up to 200 times the concentration of any other tissue. It has, further, been shown that this avidity for iodine is greater in diffuse hyperplasia and in non-iodised cases.

Hertz and Roberts⁽¹⁾ at the Massachusetts General Hospital recently published results of treatment

of 29 cases of hyperthyroidism claiming 70% three to five year cures. A mixture of I^{130} and I^{131} was used and the dose administered orally varied from 0.7 to 28 millieuries, gauged by clinical estimation of the size of the gland.

Two other workers, Chapman and Evans, gave larger dosage but where this exceeded 0.8 me per estimated gram of thyroid tissue myxœdema resulted. As success in treatment appears to depend on a clinical estimation of the weight of the gland it behoves all concerned to develop some measure of skill in determining the size of the thyroid gland in the living subject.

In general, it has been found that cancerous lesions of the thyroid fail to concentrate the isotope and it would appear that radio-iodine is of very little use in the treatment of malignant disease.

In a few recorded cases, metastases containing colloid have exhibited a degree of selective uptake, but this is by no means a consistent finding.

Another substance which is selectively absorbed is radio-strontium Sr^{89} , of half life period 55 days. It is deposited in bone and it has been suggested that it might prove useful in the treatment of various malignant tumours of bone. The problem is still under investigation but it would appear likely that the vulnerability of bone marrow will

constitute a limitation to its employment in adequate cancericidal dosage. (Fig. 9, vide picture).

Conclusions.—A great future is predicted for radioactive isotopes both in therapy and in the field of medical research. The high cost of radium is sometimes factor in the use of unduly economical treatment measures which are not in the best interest of the patient. The availability of moderately priced fission products in small adjustable packs might justify the hope that radium plates will not, in future, be applied to thick, unsuitable lesions. In place of small radium sources, radio-cobalt should offer mechanically stronger and better screened needles which would have a greater relative active length than is possible with radium needles constructed of platinum. Gamma-ray beam therapy in its own narrow field, should be possible as never before. Weighty problems of protection will demand the attention of that important member of the radio-therapeutic team—the hospital physicist. Selectively absorbed materials have a limited sphere of usefulness in our present state of knowledge but it is possible that the field may be broadened by scientific experimentation and utilisation of products in other chemical forms.

In conclusion, it is suggested that we endeavour to view these new

TABLE I
ISOTOPES FOR USE AS RADIOACTIVE TRACERS
PRODUCED BY MEANS OF THE PILE

Isotopes	Reaction	Type of radiation	Half life	Energy of radiation in MeV	
				particles	rays
H^3	$H^2 + n$	β^-	~ 10 years	0.014	
Li^8	$Li^7 + n$	β^-	~ 80 years	0.014	
C^{14}	$N^{14} + n \rightarrow C^{14} + p$	β^-	$\sim 20,000$ years	0.14	
Na^{24}	$Na^{23} + n$	β^-	14.8 hours	1.1	2.85
P^{32}	$P^{31} + n$	β^-	14.3 days	1.71	
S^{35}	$S^{34} + n$	β^-	87 days	0.167	
Cl^{36}	$Cl^{35} + n$	β^- , γ , K	$\sim 10^5$ years†		
Ca^{45}	$Ca^{44} + n$	β^-	159 days	0.9	0.7
Sc^{46}	$Sc^{45} + n$	β^- , γ , K	85 days	0.26	1.25
Cr^{51}	$Cr^{50} + n$	K, ϵ , γ	26.5 days	0.36	0.51
Ti^{46}	$Ti^{45} + n$	β^-	72 days	0.26	1.0
Fe^{59}	$Fe^{58} + n$	β^-	45 days	0.46	1.90
Co^{60}	$Co^{59} + n$	β^-	5.3 years	0.31	1.33
Cu^{64}	$Cu^{63} + n$	β^- , γ , K	12.8 hours	0.58	0.66
Zn^{65}	$Zn^{64} + n$	K, ϵ , γ	240 days	0.4	0.45
As^{75}	$As^{74} + n$	β^- , γ , K, ϵ	26.8 hours	1.1	1.00
Br^{80}	$Br^{79} + n$	β^-	54 hours	0.465	0.547
Rb^{87}	$Rb^{86} + n$	β^-	19.5 days	1.60	0.787
Sr^{89}	$Sr^{88} + n$	β^-	55 days	1.5	1.50
Zr^{95}	$Zr^{94} + n$	β^- , γ	65 days	0.4	0.75
Mo^{99}	$Zr^{95} \rightarrow Mo^{99}$	β^-	67 hours	1.5	0.4
Ag^{108m}	$Ag^{108} + n$	K, ϵ , γ	225 days		0.650
Sb^{125}	$Sb^{124} + n$	β^- , γ	60 days	2.45	0.925
Pb^{210}	$Pb^{209} + n$	β^- , γ	8.0 days	0.74	1.51
Cs^{137}	$Cs^{136} + n$	β^- , γ	1.7 years	0.6	1.82
Cs^{134}	$Cs^{133} + n$	β^-	~ 33 years	0.9	0.4
Ba^{140}	$U^{235} + n$	β^-	12.7 days	1.2	
La^{140}	$Ba^{140} \rightarrow La^{140}$	β^-	40 hours	1.41	2.04
Ta^{182}	$Ta^{181} + n$	β^- , γ	97 days	1.0	1.6
W^{187}	$W^{186} + n$	β^- , γ	77 days	0.65	
Au^{198}	$Au^{197} + n$	β^- , γ	2.7 days	0.8	2.5
Hg^{201}	$Hg^{200} + n$	β^- , γ	51.5 days	0.46	0.44
Tl^{204}	$Tl^{203} + n$	β^-	3.5 years	0.87	0.28
$Br^{82} (RbE)$	$Br^{81} + n$	β^-	5.0 days	1.17	0.30

‡ The growth of H^3 in a heavy water pile is a natural by-product.

† A proportion of this γ radiation consists of two softer γ rays in cascade.

‡ The data for Cl^{36} are very vague except for a definite neutron absorption cross-section believed to be due to the reaction stated.

§ Cl^{36} is a metastable state of half-life 33 days of the stable isotope Cl^{35} . It comes into transient equilibrium with Zr^{95} .

Note: Fast Neutron Irradiation within Reacting Core of Pile.

The following isotopes are amongst those that can be produced in all probability in small amounts:

Cu^{64} , Fe^{59} , Fe^{55} , As^{75} , Y^{90} .

β^- = negative beta-particles

γ = gamma rays

K = K-electron capture

β^+ = positive beta-particles (positrons)

α = alpha-particles

ϵ = internal conversion electrons

Fig. 9. List (taken from article by J. S. Mitchell) of isotopes for use as radioactive tracers.

[Vide page 156.]

developments with a clear perspective and in a spirit of true scientific inquiry. Their advent will undoubtedly entail much extra study for those who intend to make use of the newer radioactive products. Radiotherapists, however, are aware that there is no branch of medicine more subject to innovation and

technical change than our particular speciality. It is to be hoped that, when radio isotopes become available, their use will be solely in the hands of radiotherapists, who would be wise to employ these dangerous, but nevertheless life-saving, weapons in close collaboration with a radiation physicist.

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Radio-therapy in Certain Mediastinal Tumours*

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MEDIASTINAL tumours are not commonly encountered. They form a small proportion of all tumours at any Tumour Clinic. In our country where patients often seek scientific treatment for their troubles in a rather advanced stage of disease, this disease is no exception. When patients report they are in a fairly advanced stage and are very often beyond surgical help. This is very unfortunate indeed, especially when of late Thoracic Surgery has made rapid strides. Naturally therefore a large percentage of malignant disease occurring in the mediastinum finds its way to the Radiotherapeutic department.

Mediastinal tumours may be benign or malignant and the latter may again be primary or metastatic. The whole group of tumours occurring in the mediastinum may be grouped as follows:—

From lymphatic tissue.—Hodgkin's disease. Lympho sarcoma. Leukaemic tumours.

From thyroid gland.—Substernal and aberrant thyroid (simple or malignant).

From thymus.—Simple hyperplasia. Thymic cyst. Thymic tumour (carcinoma & sarcoma).

From connective tissue.—Lipoma. Fibroma. Xanthoma. Chondroma. Chondro-sarcoma. Sarcoma.

From connective tissue.—Ganglioma. Neuro-fibroma. Neuroblastoma.

From Pleura.—Endothelioma.

From Embryonic elements.—Dermoids. Teratoma. Rare cysts.

Radiology plays an important role in the diagnosis of mediastinal tumours but it is not always possible to say whether a particular tumour is benign or malignant. Benign tumours occur at a younger age, are slow in their growth and produce only mild symptoms. They are not radiosensitive.

It is often said that a benign tumour has a definite clear cut outline and a malignant tumour an irregular fuzzy border thereby suggesting its invasive property. This is a popular but an erroneous belief. A malignant tumour may show a clear cut outline, for a pretty long time and a benign one may show an irregular outline sometimes. Placed as the malignant tumour is between the two mediastinal pleura, a line of defence to the malignant process is offered by the pleura and like any other endothelial structure it resists invasion for a

pretty long time; and as during this period it is only pressed upon the outline of the tumour is well defined and clear cut. On the other hand the border of a benign or malignant tumour may be irregular due to any associated inflammatory state that may be present; e.g. in a case of tuberculous adenitis, the periadenitis leads to a pneumonitis of the surrounding lung and this gives fuzzy outline to the tumour.

In addition certain other causes also play a part in producing an irregular outline. (1) The tumour may cause compression of the adjacent lung tissue; (2) a tumour mass in the hilar region may press on the vessels, leading to venous congestion in the lung fields. Both these factors contribute to the irregular outline of the tumour.

Many workers have emphasised the fact that the benign tumours are potentially malignant and should be removed. These tumours are not a Radiotherapeutic problem and are a fertile field for the manoeuvres of the Thoracic Surgeon.

The common primary malignant tumours in this region are the Hodgkin's disease, the Lympho-sarcoma, the Bronchogenic tumours, and tumours of Thymus and the Thyroid. The secondary tumours are mostly metastatic carcinoma and less commonly sarcoma.

The Bronchogenic tumours are included in this list as the hilar type of tumour with its associated glandular enlargement gives a radiological picture not unlike that of any other mediastinal tumour.

A distinction between the various types of tumours is not always easy. A very thorough radiological examination which includes Fluoroscopy, Stereoscopy, Tomography, Bronchography, Kymography etc. often give us a clue as to the probable nature of the tumour. Endoscopy and histological examination of the tissue from the primary or its peripheral manifestations, hæmatological and serological examinations etc. often aid the diagnosis. But in spite of all these it is sometimes not possible to conclude as to the nature of the tumour. A course of test irradiation may help. This test has been elaborated by Reynolds and Leucutia and Evans and Witwer among others. Because of the varying response of these tumours to irradiation it is possible to differentiate them to some extent. The maximum amount of irradiation that can safely be tolerated by the normal structures of the chest is administered over a mediastinal tumour. After this, check up X-rays are made at intervals of 2, 6, 12 weeks and so forth, following irradiation and the rate of regression is expressed in percentage of the size of the original tumour. According to this, mediastinal

*Paper read before the Third All-India Radiological Conference at Calcutta, 1948.

tumours may be grouped under 4 headings.

Group I.—Consists of all tumours that resolve in 2 to 3 weeks after the cessation of the treatment. These include Lymphosarcoma, Lymphatic leukaemia and Lymphosarcoma of the thymus.

Group II.—Consists of those tumours where one gets 50% or more regression within 6 weeks and complete disappearance after a second series of irradiation. Among these may be classified Hodgkin's disease, Reticulum cell sarcoma, and Endothelioma.

Group III.—Here the rate of regression is slow. After two weeks there is hardly any change. After 6 weeks regression amounts to 20 to 25%, and after 3 months there is an increase in the size. In this group such tumours as Fibro-sarcoma, Thymic carcinoma, Thyroid carcinoma and Malignant teratoma can be included.

Group IV.—Here no changes occur during the observed period. The benign neoplasms come under this heading but however a fibroma may regress here as it happens in the case of an uterine fibroma.

Lenk differentiates bronchogenic tumours from other mediastinal tumours as follows. A tumour in the mediastinum unless prevented by external factors grows equally in all directions; hence in most cases the

widest diameter of the roentgen shadow will correspond to the site of origin of the tumour. In primary pulmonary tumours it will lie in the pulmonary field and merge with the mediastinal shadow at a more or less acute angle. In the primary mediastinal process the widest diameter will be parallel to the mediastinal shadow and forms an obtuse angle with it.

It is stated by some authors that Lymphosarcoma is the commonest of all malignant mediastinal tumours, while others say that Hodgkin's disease is the commonest. In our series of 61 cases of mediastinal tumours treated at the Barnard Institute of Radiology, Madras, during a period of 4½ years, the incidence of Lymphosarcoma and Hodgkin's disease is about the same. The various conclusions drawn from this series are embodied in the following table.

Mediastinal Tumours (Total 61).

AGE IN YEARS.

1-10	..	2	
11-20	..	16	26.2%
21-30	..	12	20.0 "
31-40	..	14	21.3 "
41-50	..	8	
51-60	..	9	

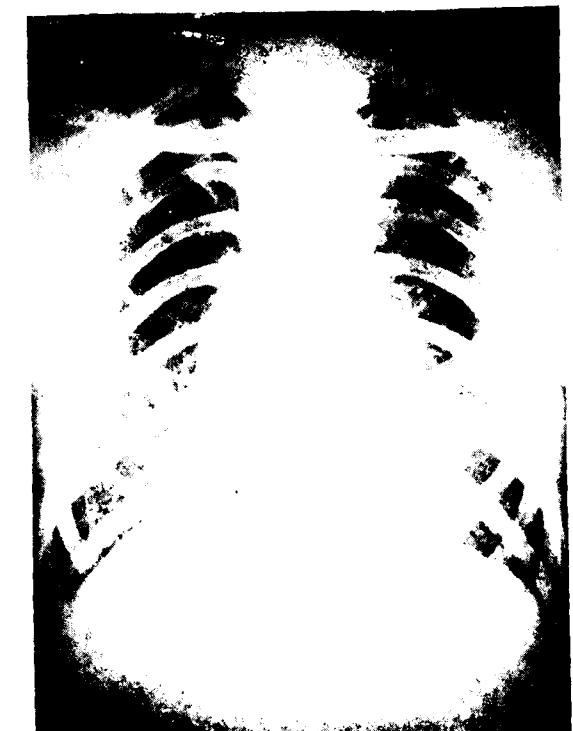
Total .. 61

Minimum age	..	5 years.
Maximum age	..	55 "

Second decade shows maximum incidence.



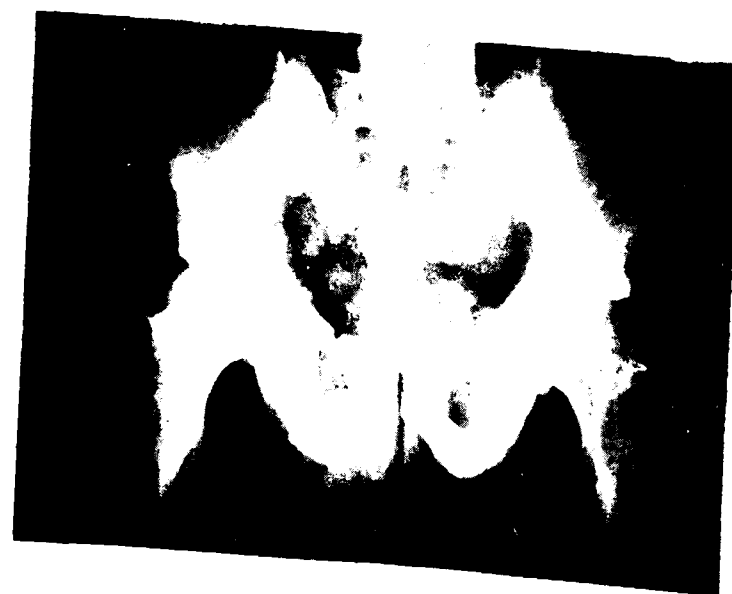
CASE I.—1. Before X-Ray Therapy.
(Vide page 161.)



CASE I.—2. Condition about 2½ years after X-Ray Therapy.
(Vide page 161.)



CASE I.—3. Osteolytic deposit in the region of left Acetabulum.
[Vide page 161.]



CASE I.—4. Consolidation of the lesion in the region of left Acetabulum after X-Ray Therapy.

[Vide page 161.]

Next comes third and fourth decades with practically the same percentage of incidence.

SEX :

Males	..	48	..	79%
Females	..	13	..	21%

This works out males : females :: 3.75 : 1.

SYMPTOMS :

Pain	19	..	36.8%
Cough	15	..	26.0%
Nerve palsies	7	..	12.3%
Irregular fever	7	..	12.3%
Hæmoptysis	5	..	8.8%
Loss of weight	5	..	8.8%
Dyspnœa	2	..	3.5%
Dysphagia	1	..	1.7%

The most common symptom is pain. The next is cough. Nerve palsies were present in 12.3%. Dyspnœa and dysphagia were not common symptoms in our series. Irregular fever was noticed in 12.3%; Hæmoptysis in 8.8%.

Primary tumours	..	54
Secondary tumours	..	7

Histological findings were available only in 13 primary cases *i.e.* in 21.3% of the total, Hodgkin's six cases, lymphosarcoma six cases and Thymo-sarcoma one case.

Treatment of the primary malignant tumours is radiotherapeutic in the Reticulo-endothelial group and surgical in the Thyroid and Bronchogenic tumours etc. But a great number from among the latter group come for Radiotherapy as by the time the patient reaches the surgeon the condition is no longer in an operable stage, or the patient refuses operation.

The reticulo-endothelial tumours are radiosensitive and sometimes melt away quickly. But permanent cure of these is exceptional; irradiation makes patient's life comfortable, and this comfortable period sometimes extends over a number of years as in Hodgkin's disease.

The bronchogenic tumours are mainly a surgical problem. Radio-therapy is mostly of palliative value. But sometimes especially in the Oat-cell type of tumours the response is encouraging and there results considerable symptomatic improvement due to regression of the primary, the secondary and associated atelectasis.

Among Thymic tumours, the Thymo-sarcoma responds better to radiation than Thymo-carcinoma. In Chondro-sarcoma and Fibro-sarcoma the response to radiation is little.

In Reticulo-endothelial tumours a tumour dose of 3000r—4000r in 3—4 weeks is delivered and wide areas are treated. In Bronchogenic tumours a tumour dose of 6000r in about 5 weeks is aimed at and small fields are used.

In illustration of the response of these tumours to irradiation, a few case reports are furnished.

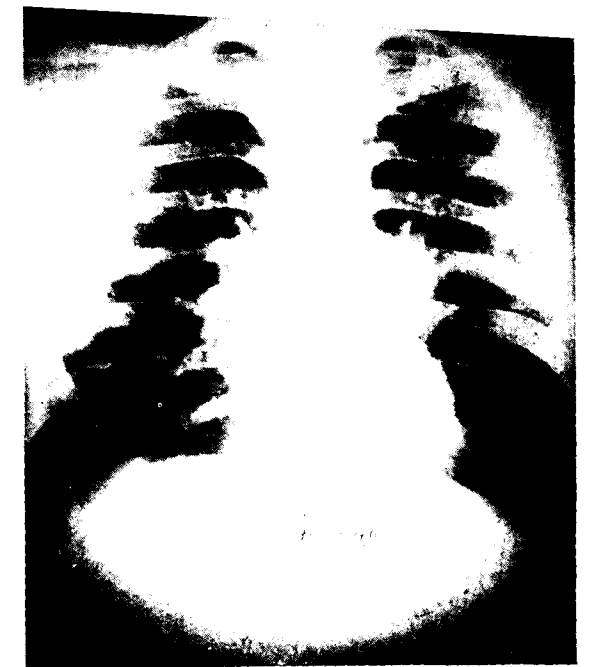
Case I.—Hodgkin's disease.—R. B., male, aged 35 years reported on 10-12-1945 with a mediastinal

lymphadenoma with involvement of glands on both sides of the neck. Face swollen, eyes injected, and vessels in the neck engorged. The mediastinal shadow was grossly enlarged to both sides. History dated back to about 3 months. The patient is a University library attender and had been carrying on his normal duties until the time he reported sick. He was given a course of deep X-ray therapy with an anterior and a posterior field over the mediastinum and a total dose of 5000r (air dose) was given over a period of five weeks. The glands in the neck completely regressed without any treatment to this region. The œdema of the face and difficulty in breathing disappeared and X-ray of chest showed regression of the mediastinal tumour. Patient reported four months later with pain over the right frontal bone and an X-ray examination revealed an osteolytic secondary deposit on the right side of the frontal bone. X-ray therapy for this was instituted and an air dose of 3000r was given in a period of about 3 weeks. The swelling of the frontal bone subsided completely. There was no pain and examination later revealed reossification of this osteolytic lesion. The patient again reported on 6-9-46 i.e. 3 months later with enlarged glands on the right side of the neck. The mass was about $3\frac{1}{2}$ inches by 2 inches;

this in turn was treated with X-ray therapy resulting in complete regression. A month later he again came in with a swelling over the lower third of the right thigh. The swelling was hard, warm and was 5x3 inches. The skiagrams revealed some alteration in the architecture of the trabeculae of the femur associated with slight periosteal reaction. X-ray therapy was instituted for this and this resulted in relief of the symptoms. During this time he developed Herpes Zoster in the region of the 3rd dorsal segment on the left side. This was also treated by X-radiation with relief of symptoms. The patient was discharged on 9-12-46 greatly improved with no pain in the legs and no pain due to the Herpes. Patient again reported early in 1947, with involvement of the abdominal glands. There was a large, hard fixed mass occupying the left hypochondrium extending on to the epigastrium. X-ray therapy was instituted for this. During this period the patient complained of pain in the left ischium and ilium and the skiagram showed irregular destruction of these bones. This was also treated with X-radiation. At the end of the treatment the abdominal mass greatly regressed and was hardly palpable. There was no pain in the hip; later skiagrams showed complete consolidation of the diseased region. The patient has been well ever since and is



CASE II.—1. Before X-Ray Therapy.



CASE II.—2. After X-Ray Therapy.

CASE II.—3. Multiple deposits in lungs.
[Vide page 163.]



CASE IV.—1. Before X-Ray Therapy.

CASE IV.—2. 1½ Years after X-Ray Therapy.
[Vide page 164.]CASE V. Bronchogenic Carcinoma.
[Vide page 164]

attending to his routine duties. This case illustrates very fully the usefulness of radiation therapy even in such apparently advanced conditions; the patient in this case has been kept going comparatively comfortably and has been attending to his duties for over a period of two years without recurrence.

Case II.—R. K., a medical student, aged 24 years; history of fever on and off of about 2 to 3 days duration for the previous 3 months. No symptoms to complain of with reference to respiratory system, but complained of intense itching all over the body. X-ray examination of the chest revealed enlarged mediastinal glands and the condition was diagnosed clinically as one of Hodgkin's disease. He reported for treatment on 21-8-'46 and treatment was completed on 10-10-'46 with an air dose of 6000r delivered by two fields, antero-posterior and postero-anterior. Radiographic examination revealed complete regression of the tumour. Patient reported 9 months later with intense pruritus; a few glands in both the hila and also bronchial glands near the left cardiac border were enlarged. These were treated with X-radiation and complete regression of the glands resulted. The patient reported again 4 months later with glands in the left cervical and supraclavicular region. The X-ray of the chest showed that the mediastinum was

clear but the left hilar glands still showed certain amount of enlargement but were definitely smaller. The supraclavicular glands were treated with X-radiation with complete regression. The patient again came four months after with multiple secondary metastases in both lungs. It was decided that no further X-ray treatment was to be given and the patient died of large hæmatemesis about the beginning of November 1948. This patient lived only for 2 years from the time of commencement of the treatment.

Case III.—P., aged about 52 years; reported at the Institute in 1940 for a large superior mediastinal tumour. (Unfortunately these skiagrams are not available now). He had a complete course of X-ray therapy to the superior mediastinum. A total dose of 6000r air dose was given using two fields. The patient had no trouble for over 8 years but reported recently with slight dyspnoea and cough. Skiagrams revealed a large mediastinal tumour but now mostly in the inferior mediastinum, extending on to the right side; there was slight enlargement of the superior mediastinum. The patient was given another course of treatment with very good regression of the tumour at the time of discharge, and is alive and well uptodate.

We have recently come across another similar case where the supe-

rior mediastinum was treated about $1\frac{1}{2}$ years back with complete regression of the shadow but where a similar recurrence occurred in the inferior mediastinum. These two cases illustrate that in the treatment of these conditions sufficiently wide areas should be irradiated; the fields used should cover the entire mediastinum although there may not be any apparent involvement of the whole of the mediastinum at the time of treatment.

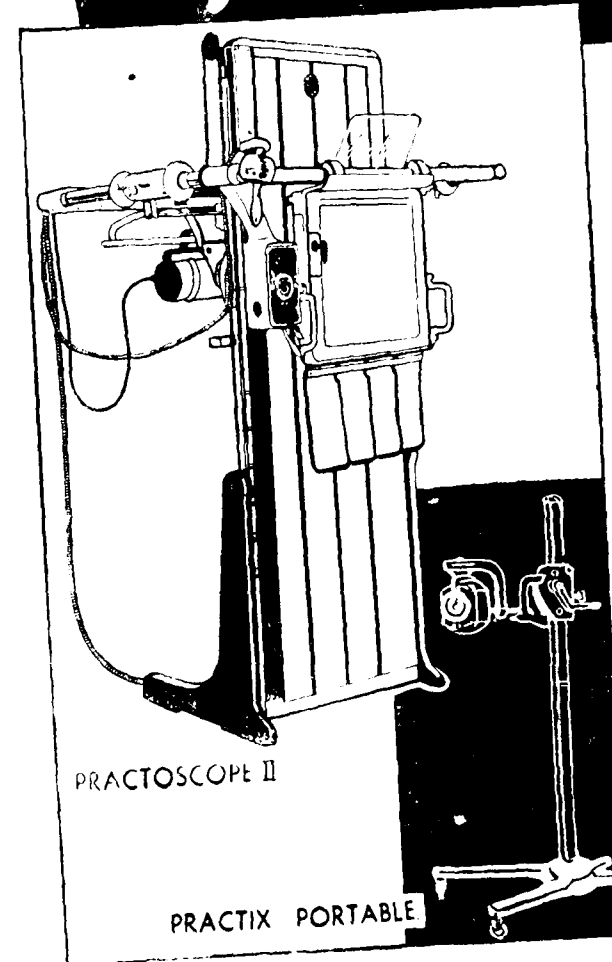
Case IV.—R., a student, aged 20 years, reported with typhoid like fever for over 50 days, the general condition being extremely poor. The mediastinal glands were enlarged as also a few cervical glands. Biopsy of one of these revealed it to be Hodgkin's disease. The patient was treated only for the mediastinum with complete regression of the mediastinal shadow; at the same time the cervical glands regressed without any treatment. This observation has been made by other workers and our experience confirms this—that very often there is a regression of the secondary glands along with the regression of the primary.

Case V.—Mr. A. R., aged 66. This patient had extra-laryngeal carcinoma with secondary glands in the neck. The primary was in the left pyriform fossa. He reported for this condition $2\frac{1}{2}$ years ago and was treated with radical irradiation.

Complete regression of the primary and secondary glands resulted. He had no trouble for well over this period of about $2\frac{1}{2}$ years at the end of which he noticed a streak of blood in his expectoration after a fit of cough. He promptly reported for examination. There was nothing abnormal in the throat or larynx, the old lesion having completely healed. This naturally led to further investigation and a fluoroscopic examination of the chest revealed atelectasis of the right lower lobe. A bronchogenic carcinoma was suspected. Bronchoscopy revealed a flake like growth about 1 cm. long, readily bleeding during the examination. A biopsy was done and the histological examination revealed it to be epidermoid carcinoma. It may be of interest to mention here that the histological report on the primary tumour of the larynx was adenocarcinoma. This case reveals a multicentric origin of different types of carcinoma in the same person and also the radiological appearances of a typical case of fairly advanced bronchogenic carcinoma. He was irradiated for this condition, but succumbed to the disease about a year later.

Summary.—The classification of various types of mediastinal tumours is given. The radiological diagnosis and therapeutic test for diagnosis are dealt with. A few typical case histories are given.

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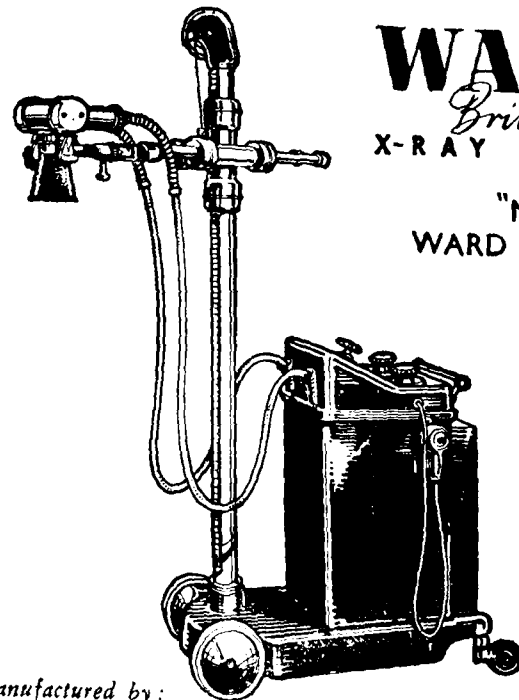
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Case Report

DR. A. N. K. MENON, M.B., B.S., D.M.R.,
STANLEY MEDICAL COLLEGE, MADRAS.

1. Calcification in Uterine Fibroid

ONE of the commonest Neoplasm in the uterus is Fibromyoma which under normal conditions is not radiopaque, being of the same density as the surrounding tissues. If calcification occurs, the fibroid becomes radiopaque. There are two varieties of calcified fibroids: (1) Those in which homogenous calcification occurs throughout the fibroid. (2) Those in which calcification occurs in patches throughout the tumour or on the surface. Calcification occurs mostly after menopause and does not usually give rise to symptoms.

Case report.—25-6-'47. Patient, S. M., female, aged 70 years. Referred by the Superintendent, Rajah Sir Ramaswamy Mudaliar Lying in Hospital, for radiography of the pelvis, with the following clinical notes.

Attained menopause about 20 years back. Complaint:—Pain in the abdomen and irregular bleeding per vaginum.

P. V. Report by the Assistant Superintendent, R. S. R. M. Hospital: Cervix soft and atrophied, uterus enlarged, hard and slightly movable. Fornices free. No blood on examining fingers. Cancer—Body of the uterus?

A radiograph of the pelvis was taken on 25-6-'47, which showed the existence of a calcified fibroid. The radiographic report is as follows:—

A dense circular opacity with a whorled appearance inside it is visualised in the pelvis in the region of the uterus—suggestive of calcified fibroid. This was confirmed by subsequent operation.

2. Intravenous Pyelography in a Case of Ectopia Vesicae

ECTOPIA Vesicae is a rare congenital malformation where there is a total absence of the anterior and lower wall of the bladder and of the lower portion of the anterior abdominal wall. There is gap in the symphysis pubis which is practically not developed, the pubic bones ending on either side of the inguinal region. This is due to a gross lack

of development of the whole of the lower part of the abdomen. The posterior wall of the bladder with its mucous membrane is pushed forwards by the abdominal contents behind it. This projects in the middle line below the navel as a reddish round swelling. The swelling moves in and out with respiration. At the lower part of this tumour there may

be seen the openings of the ureters through which urine is ejected at intervals.

Miss D., aged 20 years, a patient under Dr. C. Raghavachari, M.S., F.R.C.S., was sent to the X-ray Department of the Stanley Hospital for intravenous pyelography. She was a case of Ectopia Vesicæ in which the anterior abdominal wall was formed by the trigone of the bladder. The ureteric openings were seen with urine spurting out of each opening alternately.

P. V. Examination report by the Assistant Superintendent, R. S. R. M. Hospital.

Body of the uterus very small. Vagina and vulva not developed. An intravenous pyelography was done and radiographs of the urinary system taken after 7 minutes, 15 minutes, 30 minutes and an hour after the injection of Pylectan. Both kidneys have excreted the dye in seven minutes. There is a dilatation of both ureters, much more pronounced

on the left side where the lower end is greatly dilated and is bulbous in shape. Excretion by the right kidney is comparatively less and the calyces are not clearly defined.

This patient with an Ectopia Vesicæ lived a fairly useful and comfortable life for about twenty years with the excretory powers of the kidney not much impaired. She came to the Hospital for an operation as she was desirous of getting married. She was operated on by Dr. Ragavachary under spinal anæsthesia. The abdomen was opened by a right paramedian incision, the ureters dissected out and implanted into the sigmoid Colon. Ureteral catheter was passed into the ureter and drawn out through the anus, and the abdominal wall closed in layers. A week after the operation, an ascending infection of the kidneys developed and in spite of the best medical aid the patient expired. Radiographs of the urinary system and clinical photo are given below.

3. A Case of Ectromelus Monopus

A NEW born dead infant was sent from the Raja Sir Ramaswamy Mudaliar Hospital to the X-ray department of the Stanley Hospital. On 23-9-'47, for radiograph of the whole infant. Lateral and antero-posterior radio-graphs were taken which on examination revealed the following abnormalities. Right

lower extremity was absent (not developed). On the left side only the left femur was developed. No external genitals were present nor was there any anus. It is a very rare case of congenital mal-development known as Ectromelus Monopus. The delivery was natural with a thigh presentation but with the child born



CASE 1. Calcified fibroid.
[Vide page 167.]



Case 2. Clinical picture.



CASE 2. Intravenous Pyelogram.
[Vide page 167.]



Case 3. Clinical picture.



CASE 3. A. P. View.

[Wide page 168.]



CASE 3. Lat. View.

[Wide page 168.]

dead. Mother is a third para, both the two previous deliveries being natural with the children normal and alive.

My thanks are due to Superintendents of Government Stanley and Raja Sir Ramaswamy Mudaliar Hospitals respectively for giving me permission to publish these case reports.

Abstracts From Current Literature

Abstracts from the Symposium on Cancer of the Breast

Reported in the 'British Journal of Radiology,' December, 1948.

Article 1.—Johans Clemmson, Denmark Department of Statistics, Copenhagen.

He lays stress on the fact that clinical research is of as great a value in the etiology of human cancer as the laboratory experiments are in the case of animal tumours. His clinical study of the cancer statistics in Denmark have brought out the importance of the oestrogens, heredity and possible trauma in the etiology of human breast cancers.

Article 2.—Pre-cancerous Condition of the Breast by E. K. Dawson, Research Laboratories, Royal College of Physicians, Edinburgh.

He emphasises the instability of breast physiology at the time of the climatic and classes the age period between 40 and 50, the danger period for women in breast cancer. It is at this period that the benign-malignant ratio of the tumours of the breast is reversed. In this article Dawson elaborates again on her classic analysis of the types of epithelial hyperplasia that occur in the breast in the involution phase. The two types of epithelial hyperplasia are (1) adenosis and (2) epitheliosis. Adenosis is merely a lobular hyperplasia consisting of an increase in the lobules of the breast while maintaining its essential physiological pattern. Epitheliosis is on the other hand an intraductal proliferation of epithelial cells which Muir has called the "Intraduct cancer". According to Dawson this intraductal proliferation is not in itself a malignant disease. The proliferating cells within the ducts in the vast majority of the cases degenerate and are absorbed.

In many cases degeneration is followed by cyst formation and these are the blue-domed cysts of Blood-good.

Sometimes the epithelial cells undergo fatty degeneration and a fatty cholesterol cyst is formed instead of the usual serous one. These fatty cysts are absorbed slowly.

Dawson considers that neither adenosis nor the Blood-good cysts are pre-cancerous. She finds that cancer development in the breast is associated only, if not demonstrably always, with the presence of fatty material in mammary ducts.

Article 3.—Sir Stanford Cade, Surgeon, Westminster Hospital.

The 3 interesting features in Cade's article are No. 1—the effect of treatment on the average expectation of life in women having cancer of the breast of 55 years of age.

Normal expectation of life is 18.87 years.

In untreated carcinomas of the breast it is 3.8 years.

With treatment under average conditions, expectation of life is 5.78 years.

With treatment under best conditions, expectation of life is 12.93 years.

This is important because it shows the vast difference in results that may be obtained when treatment is conducted under average conditions and by a trained team.

II. The effect of the stage of the disease on the 5 year survival rate.

Stage 1—Anything between 64 and 87%.

Stage 2—Average 30%.

The difference which axillary lymph node involvement, however slight or skin involvement, makes in the prognosis is dramatic.

III. The effect of pre-and post-operative irradiation in cancer of the breast. It was found that with post-operative irradiation alone the number of local recurrences were greatly reduced. But the cases continued to die in the same way from distant metastases.

Therefore pre-operative irradiation was also added. The dramatic change that pre-operative irradiation made in the prognosis is shown by the following figures.

In stage I—with post operative irradiation alone the 5 year survival rate was only 53%. With pre-operative irradiation the 5 year survival rate was 73% (after Dr. Stoll).

Elis Berren, Radium Hemmet, Stockholm.

In cancer breast with fixed axillary lymph nodes—post-operative irradiation alone gave a 5 year survival of 9.7% while with pre-and post-operative irradiation the 5 year survival was 32%.

Cade does not believe that local mastectomy has any place in the treatment of malignant disease of the breast except as a palliative measure.

Article 4.—*The Value of Simple Mastectomy and Radiotherapy in the Treatment of Cancer of the Breast by Prof. McWhirter, F.R.C.S., Royal Infirmary, Edin.*

This is the most intriguing and the most thought provoking article of the entire series. McWhirter has made a virtual declaration that radical mastectomy as such in the treatment of malignant disease of the breast has no place at any stage. His fundamental declaration that the effectiveness of a method of treatment for a particular disease should not be judged by the percentage of success obtained in the cases to which it has been applied, but also by the percentage of cases to which it could not be applied is very sound.

He suggests the following as the ideal method of assessment:

(a) When the value of any method is being assessed, no case should be deducted

from the total. Cases failing to complete treatment and cases where the method of treatment could not be applied are just as much failures as cases fully treated and failing to be cured.

(b) The limitations of any method of staging—clinical, histological, or a combination of the two—must be recognised and while results may be presented by stages, the figure of greatest value is a survival rate of all the stages taken together. These figures should always be stated.

(c) If the number of untraced cases is high, the maximum and the minimum value of the survival rate should be stated.

(d) While deaths from intercurrent diseases may be deducted the death rate from these cases should not exceed that of the corresponding age group of the population as a whole.

While admitting that the 10 year survival rate is preferable it is submitted that the 5 year survival rate is adequate enough. The above basis of assessment would preclude the improvement of results by means of better selection.

Factors which suggested the use of simple mastectomy and Radio therapy.—(1) It was found that if the breast alone was involved there was no need to submit a patient to an axillary dissection. If the axillary lymph nodes were involved it was found the result of axillary dissection was not far superior to proper irradiation as far as local recurrences were concerned. But on the other hand the axillary dissection, in cutting through the tumour laden tissues, was a powerful factor in dissemination of the disease to a distant site. This is proved by the large number of cases that died from distant metastases after radical mastectomy though locally they were free from disease.

(2) With this method of treatment a larger proportion of cases can be submitted to treatment.

(3) After simple mastectomy the healing of the wound is quicker.

(4) Radio therapy can be applied earlier.

(5) The tissues tolerate the radio therapy better.

(6) Chronic oedema of the arm does not follow this method of treatment.

Definition of operable cases:—The primary tumour which may be of any size may show any degree of skin involvement upto and including ulceration but there must be no isolated skin nodules or other manifestations of invasion of the cutaneous lymphatics. The extent of skin involvement must not be so great as to necessitate skin grafting when radical mastectomy is performed, and the tumour must not be fixed to the pectoral muscles. The axillary glands of the same side may be enlarged but they must not be fixed. The supra clavicular glands must not be enlarged and there must be no clinical or radiographic evidence of distant metastases.

Statistics:—Classification of stages is according to Paterson of Manchester, in all cases.

TABLE I.
All primary cases referred in the period.

	Stage I	Stage II	Stage III	Stage IV	Total
Number	405	344	182	43	1334
Per cent	30	26	14	3	100

TABLE II.
1941-46.

	Operable cases	Advanced cases without distant metastases	Advanced cases with distant metastases	Total
Number	749	387	198	1334
Per cent	56	29	15	100

(a) *Survival rate of all operable cases in the period 1941-45—total cases 757.* McWhirter technique—5 year survival—62.1 per cent; radical mastectomy followed by radio therapy 50.1 per cent.

(b) *Survival rate of all advanced cases without distant metastases for the period from 41-45.* In these cases radical mastectomy was out of question. This group includes all cases where the primary tumour was fixed to the pectoral muscle or to the underlying ribs and all cases where there were fixed axillary glands or glands present in the supra clavicular region. 5 years survival rate according to McWhirter technique—21 per cent.

(c) *Survival rate of all cases referred in the period 41-45—total cases 1345.* 5 years survival rate 43.7 per cent. Original technique of radical mastectomy followed by radio therapy had only 32.4 per cent.

(d) *Survival rate of all cases without clinical or radiographic evidence of distant metastases in the period 41-45* total cases 1146. 5 year survival rate—50.5 per cent i.e. half the number of such patients who had no evidence of distant metastases were alive at the end of 5 years.

Principles in the application of McWhirter technique.—The method of treatment is the combination of the two procedures which must be co-ordinated if the best results are to be obtained. The following points are of importance in the surgical aspect of this question.

(a) Pre-operative preparation of iodine is contra indicated as it lowers skin tolerance to radio therapy.

(b) The undermining of the skin flaps should be as limited as possible so that the tissue spaces outside the area to be irradiated will not be contaminated by malignant cells liberated during operation.

(c) Excessive skin should not be removed. Tension on the skin flaps may be associated with failure of the wound to heal and delay in the application of radio therapy. Tightly stretched skin flaps tolerate radiation badly. Skin grafting does not overcome the difficulty, as skin grafts do not tolerate X-ray treatment well.

(d) When the primary tumour is mobile on the pectoral fascia, the fascia should not be removed as this promotes fibrosis of the pectoral muscle. If the tumour is firmly fixed to the pectoral fascia, the muscle should be removed with the breast.

(e) If there are no palpable axillary glands no dissection should be performed. But superficial glands of the sub pectoral group and the axillary fascia may be removed. Any further dissection of the axilla will defeat the whole purpose of the treatment and method advocated.

(f) If the patient is very stout it is better to carry out radical mastectomy because in such patients it is difficult to deli-

ver an adequate depth dose of X-rays to the axilla.

(g) Supra clavicular glands should never be removed because these glands are easily and effectively dealt with by radio therapy.

(h) Adhesives should not be applied to the skin after the operation because this lowers the tolerance of the skin to radiation.

The following points are of importance in the post operative treatment of radio therapy.

(i) One full course of X-ray treatment should be given.

The practice of repeated courses at intervals of 3 to 6 months has no place in the treatment of any form of malignant disease where a cure is to be attempted.

(ii) X-ray treatment should be commenced as soon as possible after the operation.

(iii) Four fields are used and every field treated every day. The axilla is irradiated by two opposed fields and the anterior field includes the supra clavicular region. The chest wall must be treated by tangential or glancing fields so as to avoid lung fibrosis.

(iv) X-ray set used should not be of a lower voltage than 250 k.v. The half value layer of the beam is 3.7 mm. copper.

Article 5.—*Surgical Aspect of Carcinoma of the Breast by Ledlie—Royal Cancer Hospital, London.*

The Stage 1 can be treated by radical mastectomy, Stage 2 by pre-operative and post-operative irradiation with radical mastectomy. The radical mastectomy is performed 2 to 6 months after the pre-operative irradiation. Stage 3 and Stage 4 are treated with roentgen therapy alone or in combination with the local mastectomy. Roentgen therapy alone has been employed in mastitis carcinomatosis.

5 years survival rate of patients subject to radical mastectomy and pre-operative and post-operative irradiation—Stage 1—73%, Stage 2—67%, Stage 3—50%, Stage 4—Nil. Total 5 year survival rate 63%. Of those cases subjected to radio therapy alone 79% were dead at the end of three years of distant metastases. Of the remaining 21%

the disease had recurred in all of them by the 7th year. In this connection there is one note of interest by Ledlie. He says that no breast removed after roentgen therapy showed complete sterilization of malignant cells. This is in contra distinction to the claims of Gordon Richard of the Ontario Institute of Radio Therapy, Toronto General Hospital that 25% of his cases coming to operation after a course of X-ray therapy were negative for cancer.

COMMENTARY.—I think close analysis of this very interesting symposium is necessary to evaluate the conflicting claims made by the various schools of thought for their particular type of treatment. Cade and Ledlie stand by the old time honoured methods of treatment of cancer of the breast except that they have accepted that pre-and post-operative irradiation have a very distinct value in securing a larger measure of cure. The emphasis has now shifted from post operative irradiation to pre-operative. It is uniformly agreed by all others that though post-operative irradiation is effective in preventing local recurrence it had no effect on distant metastases, from which most of these cases died. As Ledlie has put it in his own inimitable way it is "just locking the stable door after the horse has been lost." Beyond this there is no new thought in their line of treatment. The most intriguing article of the series is that of McWhirter of Edinburgh. His statements though conveying a great truth are not quite reasonable. In these McWhirter states that the assessment of the treatment with radical mastectomy should not lie merely in its applicability to a group of selected cases but also in its failure in the rest of the group which formed the large majority. It is admitted that radical mastectomy is limited in its scope of application, but to pass judgment on its results just because it cannot be applied to advanced cases is I think quite beyond the limits of reasonableness. The fact that it can produce 87% of 5 year cures in certain stages of the cancer of the breast show that it is the method par excellence for that group. Other methods may be of greater value in a different group. The treatment of cancer cannot be standardised in its applicability to a mass. It should be essentially individualised to the stage of the pathology

of the disease in each particular case. The line of treatment will have to vary according to the individual pathology. And particularly now with pre-operative radiotherapy added to it, it is definitely superior to simple mastectomy followed up by radiation. It is accepted in the experience of all cancer therapists that Roentgen therapy fails in a very large proportion of the cases when it is applied to secondaries in lymph nodes. Even the Radium Hemmet, the greatest protagonists of radio therapy, have accepted their failure to clear lymph node metastases by radio therapy alone. What applies to lymph node metastases in the neck naturally must apply to lymph node metastases in the axilla, especially in view of the fact that epitheliomas of the oral cavity are more susceptible to irradiation than the glandular cancers that arise in the breast. Again it has been repeatedly pointed out that clinically palpable lymph nodes do not mean histologically malignant lymph nodes, and where such lymph nodes cannot be subjected to microscopy as in McWhirter's technique, staging and grading of cases are bound to be fallacious.

It must again be remembered that the secondaries in lymph nodes may have a different grade from the primary.

The results of his treatment in operable cases are definitely inferior to those of Cade and Ledlie. In advanced cases without distant metastases the results are about the same as those of the other surgeons and is definitely preferable, because it involves much less trauma and much less risk in its treatment.

Therefore as far as treatment of cancer of the breast is concerned certain definite rules can be laid down.

(a) Stage 1 cancer breast—radical mastectomy with pre-and post-operative therapy.

(b) Stage 2 cancer of the breast—radical mastectomy with pre-and post operative irradiation unless there is involvement of the cutaneous lymphatics, in which case

irradiation should be depended upon mainly with simple mastectomy later if feasible.

(c) Stage 3 roentgen therapy alone.

(d) Stage 4 nothing is possible.

In this discussion except for a passing reference by Ledlie no one has paid much attention to the effect of hormonal therapy in the cancer of the breast. Experience has shown that hormonal therapy which by itself has been an abject failure so far, has in certain circumstances proved a valuable adjunct to other methods of treatment.

In the inflammatory cancer of the breast occurring in young women and in the medullary carcinomas of the breast bilateral ovariectomy has been definitely found to subdue the progress of the malignant process, aiding radio-therapy to definitely circumscribe and localise the tumour and render the patient fit for radical mastectomy.

It is therefore suggested that in all cancers of the breast occurring in women before the onset of menopause artificial menopause should be created either by surgery or by roentgen therapy as this controls the malignant process. This is especially applicable to women who have already had children.

Another interesting article in the series is Dawson's pre-cancerous condition of the breast. Here it is shown that cystic mastitis may be a pre-cancerous condition only when it is associated with a fatty degeneration of the intra-ductal epithelial cell. Otherwise it is never a pre-cancerous condition.

A third factor of interest in the series is what may be called a preventive measure. It has been found that menopause is the most dangerous period as far as the incidence of cancer breast is concerned, and therefore it is suggested that prolonged menopause should be immediately terminated by roentgen sterilisation.

And finally the indisputable proof that the average expectation of life in the hands of a team of specialists is 12.93 years whereas under average condition it is only 5.78 years, is a very strong argument for centralisation of cancer therapy.

S. KRISHNAMOORTHY.

BOOK REVIEW

THE JOURNAL OF THE FACULTY OF RADIOLOGISTS—Volume I, No. 1, 1949.

It gives us great pleasure to receive the first number of the *Journal of the Faculty of Radiologists*, London. The Faculty of Radiologists came into existence by the amalgamation of the British Association of Radiologists and the Society of Radiotherapists in 1939. The main object of this body is to encourage the study and improve the practice of Radiology. It protects the interests of radiologists and holds several scientific meetings. It conducts the examination for the Fellowship of the Faculty of the Radiologists (F.F.R.), the highest radiological qualification in Great Britain. It is recognised by the Government as the body representing Medical Radiology.

Since the inception of the Faculty we have been from time to time reading the scientific discussions of this body in the *British Journal of Radiology* and have often felt that such an important body as this should have a journal of its own, so that all its activities and proceedings may be more fully reported therein. This has at last come to be, and we extend to this new Journal of the Faculty of Radiologists, a hearty welcome to the field of the Radiological Journalism.

It is a quarterly and the subscription for non-members is £2 sh2 a year. Dr. Peter Kerley is the Editor, Dr. F. C. Golding and Dr. Frank Ellis are the Associate Editors. John Wright & Sons Ltd., Bristol are the Publishers. "The journal proposes to bring before its readers authoritative articles on current advances and problems." It "desires to establish a closer link between

the members of the Faculty and between them and radiological colleagues both at home and abroad." The standard of the contents of this journal are in keeping with the status of the important body of which it is the official organ. If the articles in this issue are to be considered as a forecast of what the journal wishes to lay a standard, it augurs well and will be hailed as a first class Radiological journal.

The subjects dealt with in this number are both diagnostic and therapeutic. Pathology finds its due place. The articles read at a symposium on Cerebral tumours held at the 1948 Annual Meeting of the Faculty are published; these include the role of Angiography in the diagnosis of cerebral tumours, the pathology of the cerebral tumours, and their treatment with Surgery and Radiotherapy respectively. There are two articles on Coal Workers' Pneumoconiosis; the first deals with a comparison of the radiological and pathological changes in this disease, and the second with the classification of the radiographic appearances. Other articles in the journal include Radiotherapy of Leukemia. There are two interesting articles on the "Doctor-Patient relationship in the treatment of cancer."

There are no abstracts; evidently the editors do not intend to have them. The print is clear and bold and the quality of reproduction of the radiographs and photographs is good. The format of the journal is impressive.

We heartily welcome this journal and wish the members of its organisation every success.

S.V.

ANNOUNCEMENT

FOURTH INDIAN CONGRESS OF RADIOLOGY, NEW DELHI, 1950.

(From 21st Jan. to 23rd January 1950).

Venue—Lady Hardinge Medical College Compound.

PROVISIONAL PROGRAMME

20-1-1950 - Friday

5 p.m. Central Council Meeting—Lady Hardinge Medical College.
(Dr. BAL'S OFFICE).

21-1-1950—Saturday

9-30 a.m. Registration of Delegates: Lady Hardinge Medical College Main Building.
11 a.m. Inauguration of the Conference by Hon'ble Minister Raj Kumari Amrit Kaur—Place: Lady Hardinge Medical College Convocation Hall.
1-00 p.m. Group Photograph.
1-30 p.m. Lunch.
3-00 p.m. Annual General Body Meeting of the Indian Radiological Association at Convocation Hall of Lady Hardinge Medical College.
5-00 p.m. Tea.

If any business of Annual General Body Meeting is left over, it will be continued after tea.

22-1-1950 - Sunday

10 a.m. to 1 p.m. Scientific Session.
1 p.m. Lunch.
2-15 p.m. to 4 p.m. Scientific Session.
4-15 p.m. Tea Party at Government House.
8-00 p.m. Dinner.

23-1-1950 - Monday

10 a.m. Scientific Session.
1 p.m. Lunch.
2 p.m. onwards. Sight seeing trips Red Fort and Qutub Minar.

N.B.—Accommodation for the delegates is being arranged in the hotels and the Constitution House, New Delhi from the 20th to 23rd Jan. '50. Members desirous of reserving their accommodation may kindly write to Dr. G. S. SRIN, Radiologist, Irwin Hospital, New Delhi. Delegates who wish to stay in New Delhi for the Inauguration Ceremony of the New Constitution of the Indian Republic on the 26th Jan. '50 will kindly make their own arrangements. It is not possible to obtain tickets to attend the Inauguration Ceremony on the 26th January. Delegates who wish to attend the ceremony may try to secure the tickets from the members of the Constituent Assembly of their area.

Detailed programme will be posted to members by Dr. N. G. GADEKAR, Secretary and Treasurer—Fourth Indian Congress of Radiology.

Radiologist, Irwin Hospital, New Delhi

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Printed by Dr. U. KRISHNA RAU, Proprietor of the "Antiseptic" at the Antiseptic Press, Madras, and Published for the
Indian Radiological Association by Dr. K. M. Rai, Editor-in-chief, "Lakeside" 110, Mount Road, Teynampet, O. Madras.