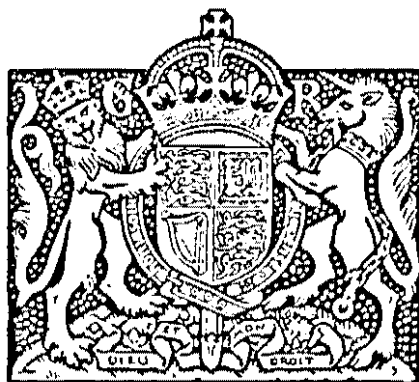


Privy Council
MEDICAL RESEARCH
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MEDICAL USES OF RADIUM
Summary of Reports from Research
Centres for 1934



LONDON
HIS MAJESTY'S STATIONERY OFFICE
1935

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PREFACE

This report continues the accounts given in the twelve which have preceded it*, of the research done with radium and radium emanation distributed by the Medical Research Council to selected centres in Great Britain and Ireland. On the clinical side, the report deals mainly with the treatment of various forms of cancer, but it contains also a brief section on the use of radium for some non-malignant conditions. In addition to describing work done during 1934, the report gives statistical data relating to the after-histories of patients treated in previous years. There is, further, a preliminary section dealing with purely experimental studies in the fundamental aspects of irradiation. The whole scheme of work is under the general supervision of the Radiology Committee, to whom the Council are indebted for the preparation of these reports. No account is included here of the research work in the treatment of cancer by "radium beam therapy" which the Council and other bodies are assisting under independent arrangements.

The original stock of radium entrusted to the Council by H.M. Government—and lent by the Council to various centres—is supplemented by further quantities provided by the British Empire Cancer Campaign and by the National Radium Commission. Support has also again been given by the Campaign to the Radon Centre maintained by the Council at the Middlesex Hospital for the supply of radium emanation. For the continued co-operation of these bodies the Council would here again express their thanks.

MEDICAL RESEARCH COUNCIL,
38 Old Queen Street,
Westminster, S.W.1.

1st October, 1935.

* Nos. 62, 90, 102, 112, 116, 126, 144, 150, 160, 174, 186 and 197 in this Series.

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INTRODUCTION

As was foreshadowed last year, the present report contains a fuller complement of experimental work than any previous one. The results of the experimental researches recorded here are of the most varied description, ranging from experimental findings in pure physics to facts relating to the reactions of the tissues under irradiation. Many readers will be prepared to find a more ready application of some of the purely physical findings to clinical problems than is possible in the case of the newly discovered biological reactions.

The research work which has been continued for several years at the Strangeways Laboratory, Cambridge, has systematically yielded new information year by year, tending to show that biological effects produced by radiation can be repeated over and over again with a measure of accuracy not always attained in purely physical fields, provided that the most rigorous attempt is made to limit the number of variables operating at one and the same time. Dr. Spear's main contribution in the present issue is one relating to a study upon intensity effects. The reaction of the tissue which he and his colleagues have been using is not a simple function of the dose of energy released in it. They find, in fact, that to get a well recognised effect there is an optimum intensity at which the release of energy may occur. That is to say, the effect is observed with a minimum absorption of energy, provided that the energy is absorbed by the tissue at a particular rate. It has long been known that tissues react differently according to the time intervals over which the physical doses are applied, according to the type of radiation that is

involved, and obviously according to the dose which is given, but this apparently new finding is one which must sooner or later be taken into account in clinical conditions, and although definite information cannot be said to be available regarding the optimum intensity of doses applicable to cancer patients, nevertheless it appears inevitable, provided such researches are encouraged, that the information must soon come to hand.

In other categories of biological work the studies of Dr. Muriel Robertson upon *Bodo caudatus* have shown that cell division in these organisms is affected by gamma rays in a manner which closely resembles some of the results obtained at Cambridge with tissue cultures. After an exposure to radiation a certain number of cells, the oldest and largest, are only a little affected, and go into division; but the division of those cells next in size is delayed, and their actual size increases. The cells appear to be able to adapt themselves to irradiation to some extent, as this initial check in the division of cells is greater than it is in subsequent generations, if the radiation is carried on continuously. Once an effective check has been produced, the increase in cells can be restrained by properly spaced interrupted exposures just as effectively as by continuous irradiation. There is no evidence of primary stimulation immediately following irradiation. The cells show a gradual return to the normal, and after an interval which is found to bear a relation to the length of irradiation, an acceleration of multiplication takes place, and a return to normal size. This acceleration eventually enables the exposed culture to catch up the normal. If irradiated cells which have approached normal again are re-conditioned and then exposed again to irradiation they apparently go through the same check in rate and rise in size as after the original exposure. Here again it is not possible to say wherein lies any immediate clinical application, but any new and outstanding facts about the possible modes of reaction to irradiation are welcome to the radiologist.

The problem of artificially varying the degree of radio-sensitivity of tissues is obviously one of great practical interest. Dr. Mottram, in investigating this matter, has endeavoured to ascertain whether those agents which are active in one direction or the other in animal cells, produce corresponding effects in vegetable cells. So far as the present experiments go the answer would appear to be in the affirmative.

The contribution from the Bland Sutton Institute of Pathology at the Middlesex Hospital appears to be of vital interest to those who, while attaching considerable importance to biopsies of cancer patients, hesitate to adopt them as a routine measure owing to the dangers of dissemination of the disease. This contribution shows that when a portion of tissue is removed by the method of electro-coagulation, good sections can be prepared from it for microscopical examination, and there is the clinical assurance that dissemination is almost certainly prevented.

The chief interest in the clinical division of the report for the past year lies in the comparative data afforded by the contributions from different centres. In last year's report reference was made to some outstanding differences in the results obtained in the treatment of cancer of the cervix uteri. As a result of these differences an enquiry was initiated by the Medical Research Council and a questionnaire was circulated to the centres concerned. It may be possible from the information which is now being collected to give reasons for the differences in question.

The following centres have again contributed the data collected in Table 1, showing the relative frequency of surgical and radiological treatment for malignant disease: Aberdeen Royal Infirmary, Cardiff Royal Infirmary, Irish Radium Centre, Marie Curie Hospital, Middlesex Hospital, Royal Free Hospital, St. Bartholomew's Hospital*, St. George's Hospital, St. Peter's Hospital, The Scottish Associations of the Medical Women's Federation and University College Hospital.

TABLE 1.—*Relative Frequency of Surgical and Radiological Treatment*

	Number Treated (1934).	Percentage of Total Number Treated.
By all methods	2,475	100·0
By surgery alone	612	24·7
By radium alone ‡	1,145	46·3
By X-rays alone	251	10·1
By surgery + radium	218	8·8
By surgery + X-rays	106	4·3
By radium + X-rays	118	4·8
By surgery + radium + X-rays	25	1·0

‡ Treatment by " radium alone " may involve surgery of access.

Adding the figures contributed by various centres for 1930, 1931, 1932, 1933 and 1934, a total of 10,430 cases of malignant disease has been treated, of which 2,887 have been treated by means of surgery alone, making 28 per cent., and 4,560 have been treated by means of radium alone, making 44 per cent.

The arrangement of the subject matter of this report follows the lines of previous years, references to Radium Centres being made alphabetically in the various sections. The report from University College Hospital has already been published, by John Bale, Sons & Danielsson, Ltd., under the title *Report on Radiotherapy for 1934*. The *Report of the Irish Radium Committee for the year 1934* has been published in the Scientific Proceedings of the Royal Dublin Society, Vol. 21 (N.S.), No. 25, July, 1935.

* The figures from this centre refer only to the Surgical Professorial Unit.

A. EXPERIMENTAL SECTION

At the IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY several pieces of experimental work have been undertaken.

Mr. J. V. HUGHES has, as mentioned in last year's report, been attempting to diffract β rays, and reports that this attempt has now been successful. In 1924, de Broglie suggested that every particle in motion should be accompanied by a train of waves, of which the wavelength should be proportional to the reciprocal of the momentum of the particle. This has been confirmed for electrons for energies up to 250 Kv., by Rupp, and up to 520 Kv. by Kosman and Alichanian. The latter, however, did not verify de Broglie's law connecting the wavelength and the momentum of the electrons, but merely verified that diffraction of electrons did occur at this potential. In the present investigation, electrons up to 1,000 Kv. energy were diffracted, and de Broglie's law verified up to this energy. These electrons were natural β rays from radon, the high energies being thus obtained without the necessity for high potential discharge tubes used by previous investigators.

In the apparatus used, the β rays from a radon source were focussed by means of a magnetic field, which also sorted out electrons of one velocity only. This of course was necessary as the wavelength and hence the diffraction effect to be expected varied with the velocity. After traversing the magnetic field, the electrons passed through a thin gold foil (which should diffract them in the same way as it would X-rays) and were received on a photographic plate to record them. (Details of this research published Phil. Mag. May 19, 1935, p. 129.)

Care was taken to focus only on prominent lines of the β ray spectrum. Three different β ray lines were used, corresponding to energies of 264; 520; and 1,037 Kv. respectively. The radii of the corresponding diffraction rings were measured, and compared with the values calculated from de Broglie's law, which was thus verified.

Thus β rays have been shown to have a wave nature as well as the more generally known particle nature; according to present theory, when they strike anything electrons (including of course β rays) act as particles, but when in free flight the wave nature predominates.

Dr. P. B. MOON and Mr. J. R. TILLMAN, working in Prof. G. P. Thomson's laboratory, have investigated the properties of slow neutrons. It is well known that when powdered beryllium is mixed with radon, neutrons are ejected as a result of the bombardment of the beryllium nuclei by α -particles. These neutrons have kinetic energies of several million electron-volts. Fermi and his co-workers in Rome have recently shown that neutrons can be absorbed into the nuclei of many elements with the formation of new radioactive isotopes of ordinary elements. They have further found that the amount of this induced radioactivity may, in many cases (for example, that of silver), be increased tens or hundreds of times by surrounding source and specimen with water, paraffin wax, or some other material rich in hydrogen; this they interpreted as evidence

that neutrons which have lost energy by collisions with protons are more effective than are the original very fast neutrons. They suggested that the neutrons might, after many collisions, come into thermal equilibrium with the hydrogenous material and thus constitute a neutron "gas".

Dr. Moon and Mr. Tillman have been searching in various ways for experimental evidence of neutrons of thermal energies, and finally succeeded in establishing their existence in the following manner:—A radon-beryllium source of neutrons was placed in a cavity within a large block of paraffin wax. A second cavity in the same block contained a hollow cylinder of wax whose temperature could be lowered to the boiling point of liquid oxygen. The radioactivity induced in a specimen of silver placed within this cylinder was some 20 per cent. more intense when the cylinder was cold than when it was at room temperature. Now it is inconceivable that the properties of the neutrons should be influenced by the thermal agitation in the medium through which they are passing unless their velocities are at least comparable with those appropriate to thermal energies. There must, therefore, be at least some approximation to the thermal equilibrium between neutrons and matter envisaged by Fermi and his collaborators.

Dr. Moon and Mr. Tillman have also investigated the absorption of slow neutrons by silver, copper and iodine, measuring the intensity of the transmitted flux of neutrons by the radioactivity induced in various elements (Ag, Cu, I, Rh). For a given absorbing element, the value of the absorption coefficient is found to depend upon the detector used; this indicates that the absorption of neutrons into the nuclei of these elements is selective with respect to the velocity of the impinging neutron, the favoured velocities varying from one element to another.

Dr. W. V. MAYNEORD, of the Cancer Hospital, reports that further experimental work has been carried out on the applicability of the röntgen to gamma ray therapy. The value previously found (of approximately 8.3 röntgens per milligramme hour, one centimetre from a point source filtered with 0.5 mm. platinum) has been confirmed by Dr. Mayneord as well as by certain other observers. Further work on the design of air-wall ionisation chambers for such measurements has been performed. In addition, by the condenser dosimeter method mentioned in a previous report, an attempt has been made to find the most appropriate distribution of radium on surface applicators. From mathematical investigation it appears that flat uniform fields of irradiation may in certain cases be obtained by distributing radium, according to certain rules already worked out, on flat surfaces parallel to those to be irradiated. As an example of such radiation fields the case of radium distribution around the rim of a circular applicator may be quoted. Such a ring of radioactive material will produce a uniform distribution in a plane parallel to the ring at a distance equal to 0.71 of its radius and of roughly the size

of the ring. For planes nearer the ring, the intensity at the edge is greater than the intensity at the centre. Conversely, if the distribution near a uniformly distributed disc is considered, for planes close to the disc, the intensity opposite the centre is approximately twice that near the edge (*Brit. J. Radiol.*, 1932, 5, 677). It is therefore possible by adding extra radium towards the edge of a uniformly loaded circular applicator to oppose these two effects, and obtain an approximately uniform distribution of radiation parallel to any circular applicator. Curves showing the amount of radium required on ring and disc respectively for various sizes of applicator and radium skin distances are reproduced here (Figs. I and II). Having obtained a uniform distribution, it is now easily possible to construct curves to read off the absolute amount of radium required on flat circular applicators of different sizes at different distances in order to produce a standard dosage-rate. The same end-result may evidently be obtained by use of radioactive surfaces uniformly distributed with radium, but of appropriate curvature. In general this implies making the radiating surface concave as seen from the irradiated surface. Experiments have been made to find the best curvature in such cases, and the experimental results shown to be in rough agreement with theory.

A series of measurements of absorption coefficients of gamma rays in various elements has been begun. The latter measurements have been made in conjunction with others using nearly monochromatic X-rays. The main object is to test certain theories of absorption of short wavelength electro-magnetic radiations in light elements, such as are the main constituents of animal tissues.

The investigations reported by Dr. F. G. SPEAR and carried out by a group at the STRANGWAYS LABORATORY, CAMBRIDGE, on the biological effects of radiation have followed two main lines: (1) observations on tissue cultures *in vitro*, and (2) experiments with chick embryos irradiated *in ovo* or explanted *in vitro*.

(1) *In vitro (Tissue Culture) Experiments*.—For somatic cells in culture there is a minimum threshold dose which it is necessary to give if an irradiation is to be effective. There is usually a latent period before the results of exposure reach their maximum. The magnitude of the threshold dose and the duration of the latent period vary according to (a) the type and condition of cell exposed to irradiation, and (b) the particular biological response selected as the criterion of effect. One of the first effects to be recognised is a diminution in cell division. After small doses of gamma or X-rays, diminution in cell division is followed by recovery, and normal mitosis reappears. In certain circumstances the diminution in mitosis is compensated by a subsequent increase above the control count, before the normal rate is finally re-established. After larger doses cell division may disappear almost entirely for a time and then reappear as strikingly abnormal mitotic figures, which, however, are not caused by irradiation only but may result from the action of other

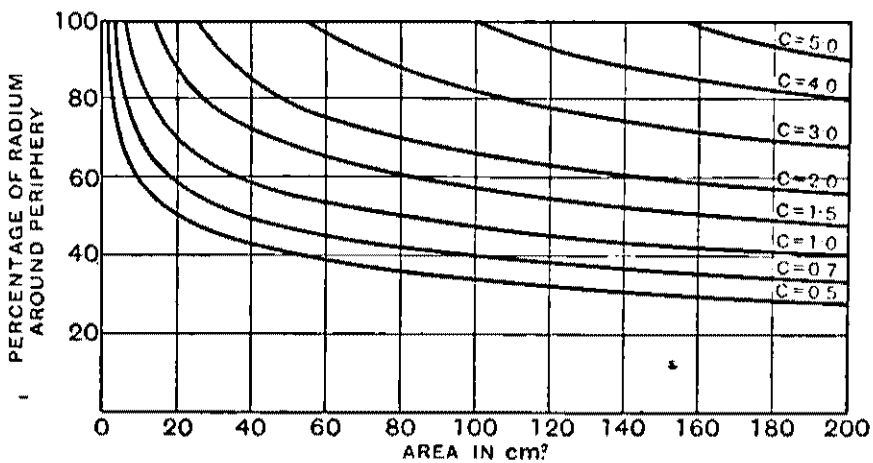


FIG. I.

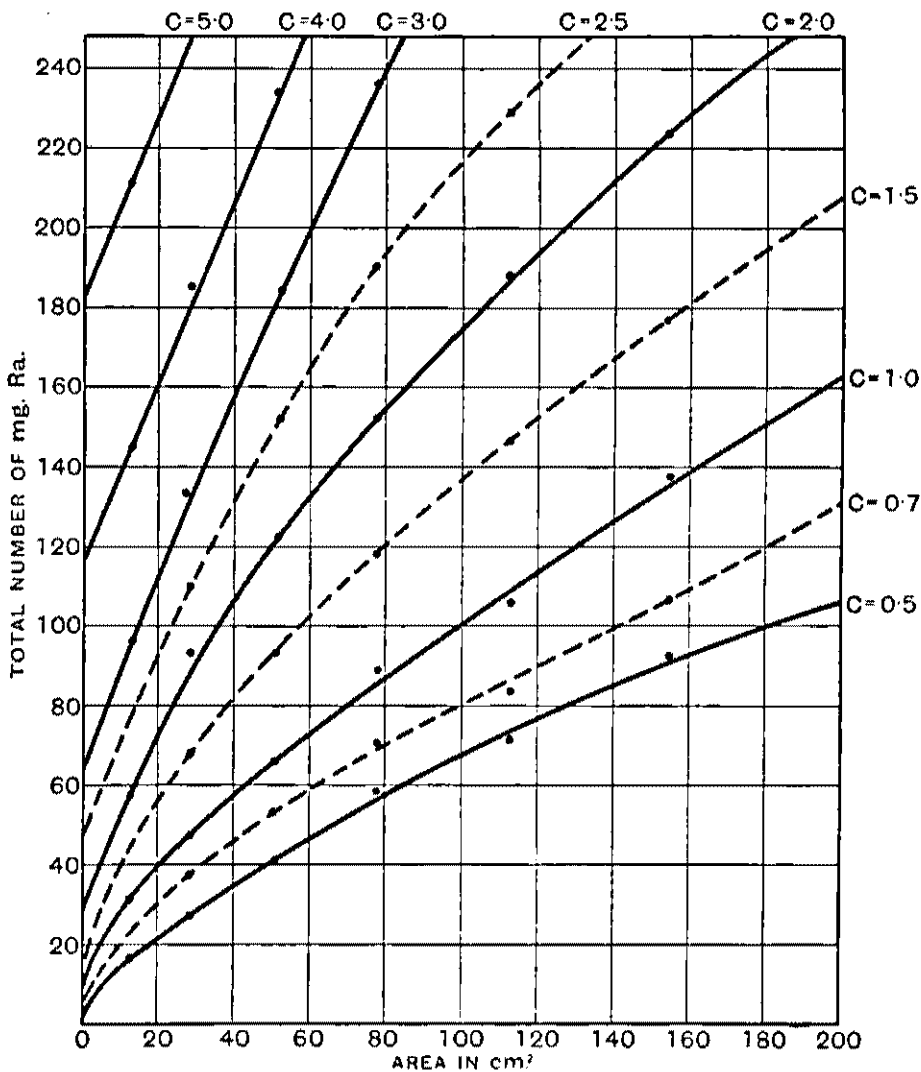


FIG. II.

injurious agents as well. Some of these abnormal cells break up and disappear, others complete the process of division, but probably die later without further division, since cells in mitosis invariably disappear from a culture which has received a heavy irradiation, some days before the cessation of outwandering. The greater the amount of cell division in a culture, the larger is the number of degenerating cells seen after exposure.

Measured by diminution in cell division, biological response to gamma radiation is a function of the time and of the intensity factors. Fractioning a given dose alters its effectiveness according to the time interval between the exposures: there is an optimum spacing for diminishing mitosis. Some effects of radiation remain latent and only become evident as a result of a second or of subsequent exposures.

There is also an optimum intensity of radiation at which the dose required to produce any given percentage fall in cell division is minimum. If normal and malignant tissues are cultivated under similar conditions, the same dose of gamma rays causes a greater fall in cell division in the cultures derived from malignant material than in those resulting from normal growth. No evidence of a direct stimulation has been observed.

If growth rate is taken as a measure of biological response a higher level of dosage is required to produce measurable effects and it is found that the latent period following exposure is long compared with that which obtains in the case of cell division. The effect on growth rate and on cell division, indeed, seem to a large extent to be independent of each other.

When the dose of radiation necessary to produce different biological responses in tissue cultures is tabulated, evidence of a definite sequence is obtained, which seems to indicate an increasing complexity of response as the dose is enlarged. For example, taking the effects of gamma radiation we find that 250 units of dose (Sievert-minutes) are required before any diminution at all is seen in cell division, but once this threshold is passed the effect on mitosis is sudden and well marked. Larger doses have an increased effect, but until the dose exceeds 460 units a compensatory increase in mitosis follows the initial diminution. Between 460 and 1,660 units of dose the existence of the compensatory increase depends on the intensity* at which the dose was given. It is seen with lower intensity and longer time of exposure, but not with the higher intensity. After a dose of 5,500 units no compensation is seen with either intensity. 84,000 units are required to produce a delayed lethal effect on cultures *in vitro* (within 3 weeks) or 140,000 units for a delayed lethal effect to occur within 2 weeks of exposure, while a dose in the neighbourhood of 700,000 units is required to produce death of the tissue as a whole. A similar kind of sequence is obtained with

* The intensities used were 184 and 469 Sievert units, now usually called intensity millicuries, Imc.

X-radiation, but the levels of dosage at which the different kinds of response become recognisable have not yet been precisely determined.

(2) *In vivo* (Chick Embryo) Experiments.—In the case of the whole chick embryo, radiation has both a direct action on the cells, from which they may recover, and an indirect action *via* the circulatory system (Dr. Hughes, Mr. Wilson and Dr. Glücksmann).

An attempt is now being made to assess the relative importance of direct and indirect effects of radiation by observations on the growing chick embryo irradiated *in ovo*. As compared with tissue cultures, which for experimental purposes can be regarded as infinitely small, the finite size of the chick embryos makes it desirable to provide as far as possible a distribution of radium giving a uniform intensity throughout the volume of the embryo. When such precautions are not taken, the usual effect of radiation is to produce gross abnormalities in the embryo or even monsters resulting from the uneven dosage to which the several parts of the chick are exposed. By irradiating the whole embryo *in ovo* and studying serial sections prepared at various periods after exposure, it is found that degeneration is most marked in those regions where cell division occurs; it is generally absent from areas where mitosis is not normally found. The blood-vessels are quite unaffected by relatively small doses and appear as perfectly normal structures. The degeneration is due to a direct action of radiation since it is "regional" in character. If blood-vessels are destroyed, the resulting degeneration is general. In many of the stained sections it is possible to see two areas of degeneration separated by a perfectly normal and uninjured blood-vessel.

In further experiments chick blastoderms were explanted whole and cultivated *in vitro* by a special technique. Under these conditions the eye of a 2-day chick exposed for 8 minutes to an intensity of 116 ± 4 per cent. Sievert units shows a complete absence of mitosis when examined 80 minutes after exposure. A similar specimen exposed to the same dose of radiation, but incubated for 120 minutes after the exposure, shows mitotic figures which are greatly in excess of the normal, and cell division is seen occurring over a wide area of the epithelium and not restricted to the free margin of the lumen as in the control specimen. Similar specimens examined 240 minutes after exposure were found to be practically normal. Thus, following an irradiation, there is found to be a fall in mitosis followed by a very rapid compensatory increase above the average and then a return to normal.

A quantitative measure of the effect of radiation upon the post-circulatory chick embryo was obtained by making actual counts of mitotic figures at five different levels of the irradiated chick, and comparing them with those obtained at similar levels in a control. These numerical results are plotted as a curve in Fig. IV. The similarity of form of this curve to that obtained with tissue cultures, irradiated with about half the dose used for the embryos (Fig. III)

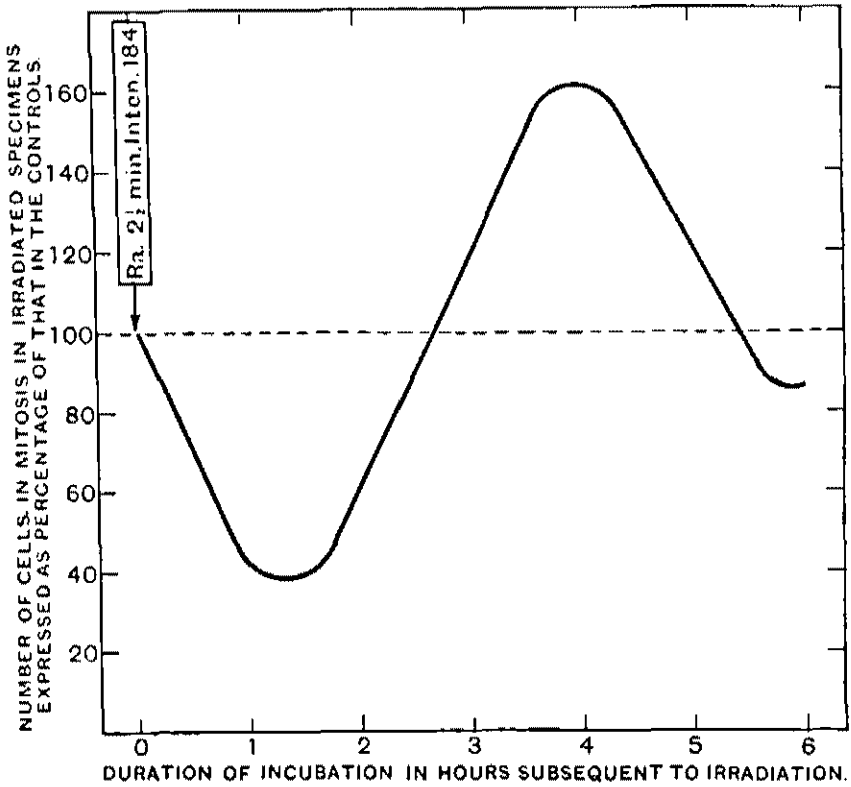


FIG. III.—Graph showing the variation in mitosis (all phases) in tissue cultures after exposure to gamma rays. $2\frac{1}{2}$ min. exposure to 184 Imc. Cultures examined over period of 6 hours following irradiation.

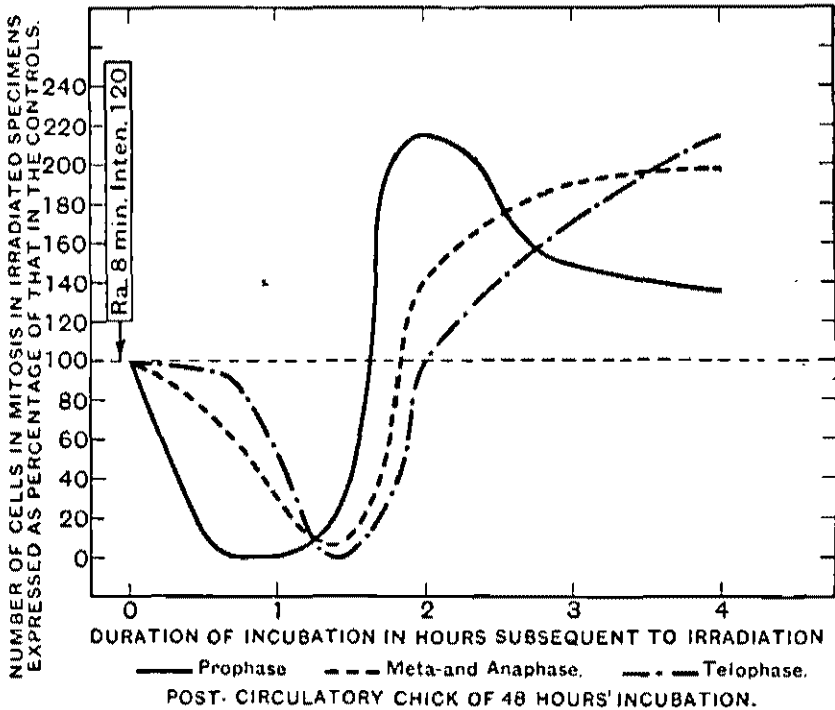


FIG. IV.—Graph showing the variation in mitosis (phases shown separately) in the post-circulatory chick after exposure to gamma rays. 8 min. exposure to 120 Imc. (approx.). Specimens examined over period of 4 hours following irradiation.

is very striking and shows that the effect of gamma rays on dividing cells in the growing embryo is similar to that observed among cells isolated *in vitro*. In the presence of an intact blood circulation however recovery is more rapid than in the case of cells (fibroblasts) cultivated *in vitro*. The steepness of the upward curve (Fig. IV, $1\frac{1}{2}$ hours after exposure) indicates that mitotic recovery from the effects of radiation was almost instantaneous. This is in striking contrast to the effect obtained when an embryo is exposed to the same dose of gamma rays before the circulation has been established. In this case mitosis remains practically at zero for about an hour and then only reappears very gradually. Fig. V shows graphically the results of such an experiment and indicates the remarkable difference in response to radiation of the pre-circulatory and post-circulatory chick.

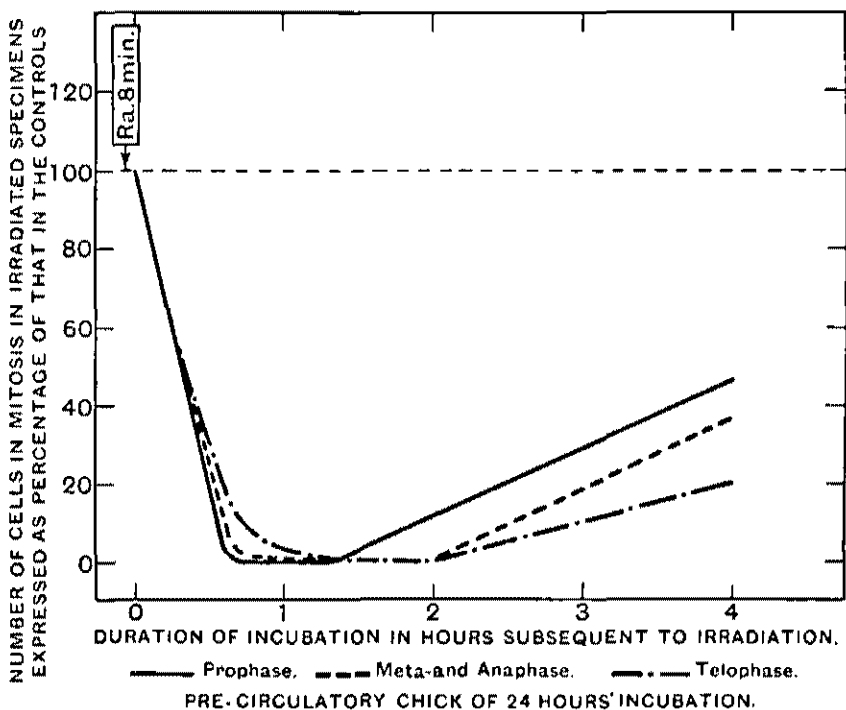


FIG. V.—Graph showing the variation in mitosis (phases shown separately) in the pre-circulatory chick after exposure to gamma rays. 8 min. exposure to 120 Imc. (approx.). Specimens examined over period of 4 hours following irradiation.

When the dose of gamma rays is raised considerably above the level which affects cell division in the epithelial cells, an effect upon the endothelial cells of the blood vessels is seen. Mitosis in them is first diminished, then it recovers, shows an excess, and finally returns to normal, as already described for fibroblasts in culture and epithelial cells *in vivo*.

Intermediate between the doses affecting mitosis in epithelial and endothelial cells, is that which has a direct effect upon the circulating

erythroblasts. This is the earliest effect which is seen on the circulatory system. The erythroblasts became bunched together as if some alteration had occurred in the surface protoplasm, causing them to adhere together. The aggregation of the erythroblasts is followed by the appearance among them of degenerative cells proportional in number to the normal occurrence of mitosis among the blood cells. Following the arrest of the circulation by the bunching together of the erythroblasts the vascular endothelium contracts upon the "rope" thus formed breaking it up into islands connected by a mere chord of cells. Experiments now in progress suggest that this biological response to gamma rays is—like that of mitosis *in vitro*—a function of the intensity of irradiation and that the optimum intensity has practically the same value in the two cases. After some hours mitosis may reappear in the erythroblasts but with the doses so far used ultimate survival of the chick has not occurred.

These experiments seem to throw some light on the vexed question of the relative importance of the direct and indirect (*i.e.*, circulatory) effects of irradiation. So long as the embryonic circulation is intact, its action favours recovery from the effects of the rays. Once involved, however, it enhances the degenerative effects of the rays by the generalised destruction which normally follows any interference with blood supply. It is interesting to note that the dose which has a delayed lethal effect on the embryo (*i.e.*, effectively prevents hatching) is only a little over half that which affects the blood vessels and destroys the circulation.

The variation in mitosis following irradiation *in vivo* thus closely resembles that following exposure of tissue cultures. It remains to be seen how many of the other changes caused in tissue cultures by radiation can be recognised under *in vivo* conditions, in both normal and malignant tissues. A promising field of investigation has been opened up to which both *in vitro* and *in vivo* experiments contribute essential parts. The two methods are complementary and either method may afford confirmatory evidence of results obtained by the other.

Dr. MURIEL ROBERTSON, of the LISTER INSTITUTE, reports that the work on *Bodo caudatus* has been continued, and that the results can be summarised as follows :—

There is upon exposure to gamma ray irradiation of a multiplying culture of the protozoon *Bodo caudatus* a primary carry over into division (with only a relatively slight lowering of the rate) of individuals whose state is such that they are not affected at this time by the irradiation. There then occurs a definite and increasing check in the production of new cells with a subsequent reappearance of division. Thereafter a continuation of multiplication takes place in the presence of the radium at a rate which is not far removed from that of the normal but which does not permit of any further

overtaking of the normal by the irradiated, and the discrepancy of about 40 per cent. in the total numbers remains constant from about the 11th hour to the end of the growth period of 22 hours. The period of the greatest check in multiplication varies somewhat with the part of the curve irradiated and the state of nutrition of the cells, but is found with exposures of between 4 and 8 hours.

The production of the first complete generation, that is the entry into division of all the cells extant at the moment of the inauguration of the irradiation, occupies a much longer time than the production of the second and subsequent generations in a continuous exposure. This implies a certain degree of recovery in the presence of the radium.

The behaviour of an irradiated culture during the period of the greatest check in multiplication was examined, and it was found that after the division of the relatively insensitive group consisting of the oldest and largest individuals at the time of the inauguration of the irradiation, the next size groups are delayed in entering into division and are forced to grow into a larger size than normal before they can accomplish this process. The larger size was maintained in longer exposures and appeared to be a condition of growth in the presence of radium. It is this process of temporary morphological and physiological adaptation that appears to permit of the resumption of the division rate and may be termed the "radium conditioning" of the cells.

The sensitive period in the life of the cell upon a first exposure is deduced from the age of the cells at the time of the beginning of the irradiation and their subsequent coming into division (and also from the redistribution of sizes in the material) after 4 to 5 hours' exposure. A clearly sensitive period was found to occupy the time between the end of the first two-fifths of the generation time and some period in the fourth fifth. Cultures showed a greater or less sensitiveness within certain limits during the evolution of the first generation of exposed cells, in accordance with the state of the cells at the inauguration of the irradiation and of their previous history.

While the sensitive period appears to be established upon the experimental evidence, the insensitive state of the oldest cells during the first one to two hours is less well documented and could be interpreted by the failure of the cells to be affected in the time. There is no evidence of primary stimulation of growth as a result of irradiation.

A further study has been made of the behaviour of cultures of *Bodo caudatus* upon release from irradiation and of the effect upon the growth of interrupted or repeated irradiations. The particular aspects dealt with are:—

- (1) The behaviour in regard to multiplication and size of the cells of a culture irradiated for known periods and subsequently released from the plaque, or briefly the reactions of cultures released from irradiation.

- (2) The effect of re-irradiating a released culture. This constitutes also a study of interrupted or multiple irradiations, the observations being carried out within the four to four and half normal generations of cells produced during the growth period of 22 hours.

The results can be summarised very briefly as follows :—

An effective irradiation for the present purpose was considered to be one of 5 or more hours' duration, producing a discrepancy in the *total number* of cells upon the irradiated plate of not less than about 25 per cent. of the normal, while the maximum values lay between 35 and 40 per cent. in the cases available for study.

A culture released from the plaque after a time under normal conditions shows a compensatory acceleration in multiplication. The time at which this sets in is found to bear a relation to the length and effectiveness of the irradiation. The complete overtaking of the normal by the released culture is shown to occur, if sufficient time is allowed, and during this process a compensatory increase in new cells on an all-over calculation during the time of as much as 100 : 151 to 100 : 184 as between normal and released plates was recorded.

No irradiation considered to be effective could be cancelled by five hours' growth upon release or by the production of up to 1.5 generations of cells since the end of the exposure. It was found that 1.7 to 3.0 generations were required to be produced and between 8 and 11 hours of time had to elapse after the end of the irradiation to bring the numbers upon the exposed plate to within 10 per cent. of the normal controls.

The behaviour of the released cells in regard to their size was also followed ; they showed a gradual return to the normal, and the complementary nature of this phenomenon with its physiological implications was considered to be of particular interest as affording evidence from a different point of view that the growth in the presence of the radium demands a high response in physiological activity and produces, as already recorded, a cell of enhanced size and with stored energy above that required for ordinary conditions. So that the inevitable result of removal from the plaque is the re-adaptation to the less exacting conditions of ordinary culture by the obvious method of accelerated multiplication and return to normal size.

As regards re-irradiation it was shown that the second exposures after periods of 4 to 5 hours' growth under normal conditions were always effective in some degree. The cells having approached the normal again had to be reconditioned if they were exposed for a second time and apparently went through the check in rate and rise in size just as in a first irradiation. In so far as they had not returned to normal during the release period the power to evince the rise in rate of increase which was then imminent, was held in check by the re-exposure, the multiplication was kept at the uncompensated level

or further depressed and the discrepancy in the mass of cells as compared with the control was maintained or further increased. The discrepancies in the production of new cells during second irradiations where the first one had not been longer than six hours and where the released period had been of about 5 hours' duration, compared well with the average effect of similar first exposures but never exhibited the maxima obtainable in the most effective examples of first irradiations.

Throughout the whole of these experiments an elaborate system of controls was maintained.

As a matter of practical efficiency in holding down the total number of cells, once an effective irradiation had been administered remissions of rather more than a full generation time or of 5 to 6 hours between re-irradiations may be used without significant loss of total effect.

A report from Dr. J. C. MOTTRAM, of the MOUNT VERNON HOSPITAL and THE RADIUM INSTITUTE, states that Crabtree and Cramer have shown, using animal tumours and the tissues of rats, that the radio-sensitivity of cells is greatly altered by treatments known to be specially effective in having an action on cellular respiration. Their results suggest that radiation may have a special action on the respiratory system, which appears to be especially sensitive in its non-functioning oxidized phase. Dr. Mottram has repeated some of their experiments, using the growing roots of beans (*Brit. J. Radiol.* 1935, 8, 32) and has confirmed their results as regards increased sensitivity associated with the exposure to cold and to hydrocyanic acid, and decreased sensitivity under nitrogen anaerobiosis.

Side by side with these experiments, observation has been made upon the mitotic activity of the cells of the bean roots, and it was found that the observed variations in sensitivity were unrelated to the mitotic activity; for instance, exposure to hydrocyanic acid and to nitrogen anaerobiosis both reduce the number of dividing cells almost to extinction, yet they sensitise the roots in opposite ways; and whereas cold leaves the number of dividing cells unaltered, yet such cooled beans are more sensitive than normal beans.

These results suggest that the varying sensitivity of tumours to radiation is probably not directly related to mitotic activity, but rather to the metabolic and perhaps the respiratory activity of the cells. In view of the small percentage of cells undergoing mitosis during treatment with radiation, it is difficult to see how mitosis *per se* can be taken advantage of in therapy.

During the year a short paper (*Brit. J. exp. Path.*, 1934, 15, 71) has been published, having to do with the mutation hypothesis for cancer. This postulates that the cancer cell differs from the normal cell in its content of genes. The most likely cause of such abnormality is undoubtedly some disturbance during mitosis, leading to unequal distribution of genes to the daughter cells. This can be assumed to occur under experimental conditions if visible disturbances in the

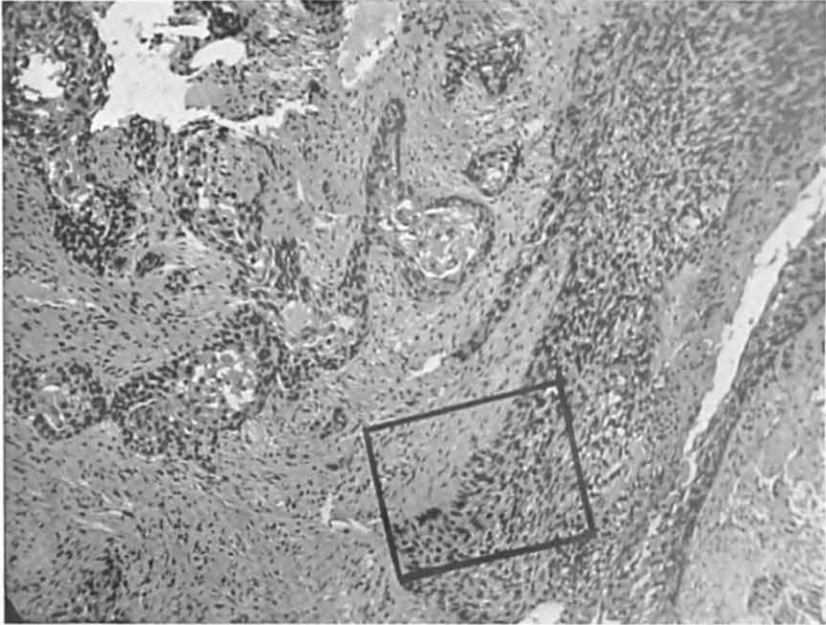
distribution of chromosomes, or parts of chromosomes, are observed. Growing bean roots were therefore subjected to a number of agents known to produce cancer, gamma radiation, heat, solutions of tar and of gentian violet. In all cases fragmentation of chromosomes and irregular migration were observed. It is, however, well known that other conditions not known to produce cancer have the same effect, *e.g.*, exposure to acids, anaesthetics, high concentration of carbon dioxide, high osmotic pressure, fertilisation with foreign sperm. This does not of course rule out the mutation hypothesis. It may be that, for instance, tar can penetrate the horny layers of the skin and act on the living basal layers, whilst other agents fail in this respect.

Professor D. P. D. WILKIE reports that at the SURGICAL RESEARCH DEPARTMENT, EDINBURGH UNIVERSITY, experiments have been continued during the past year on the effect of radiation (by radium) on normal tissues in the rabbit. The tissues investigated were—skin, stomach, intestine, bone, lung, kidney, ovary and testicle. In the case of internal organs and deep-seated tissues the element of trauma had to be considered and control experiments, using unloaded needles, were carried out. This precaution proved to be very necessary because after the exposure of several varieties of normal tissues, such as small intestine, stomach and kidney, to weak sources of radium, *e.g.*, 1 mg. Ra., for as long as a week, there was practically no consistent difference in the microscopical appearances between these irradiated tissues and those which had been implanted with unloaded needles. The ovary and testicle, however, are in a class by themselves and both show pronounced degenerative changes of the germinal tissues with some proliferation of the interstitial elements after exposure to small doses of radium.

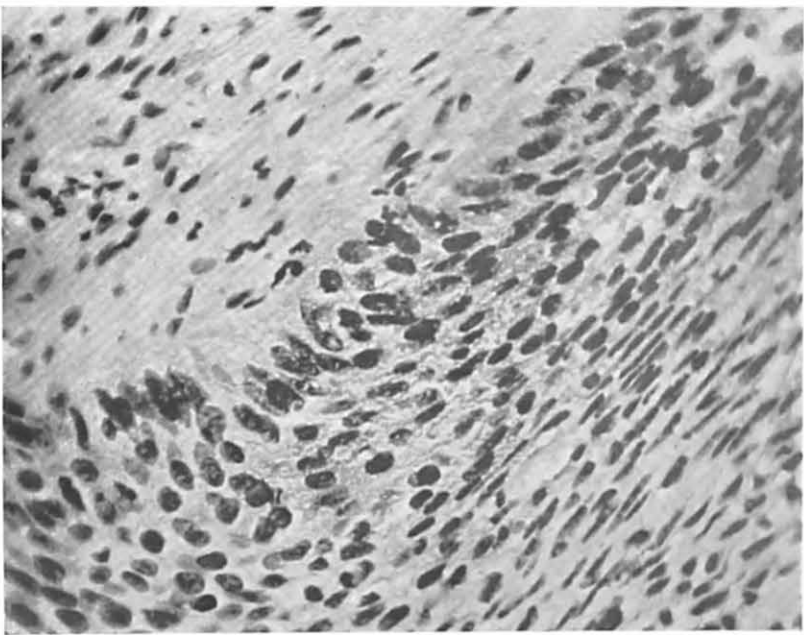
In the BLAND SUTTON INSTITUTE OF PATHOLOGY at the MIDDLESEX HOSPITAL most of the pathological work in connection with the use of radium has consisted of routine confirmatory diagnosis of the presence of growth, and of the analysis of the type of growth present. In some of the cases the portion of tissue for section has been removed after electro-coagulation of the area, and it is of interest that such material gives reasonably good histological preparations. It is obvious that the advantages of this procedure are numerous, but two are of special importance: (1) any possible risk of dissemination of the growth by the biopsy is minimised; (2) it is more likely that an adequate piece of tissue will be removed. The micro-photographs in Figs. VI and VII show the type of histological picture obtainable. They show tissues sectioned after electro-coagulation in: Fig. VI carcinoma of the skin; Fig. VII carcinoma of the cervix.

In addition to this routine diagnosis and classification, further material has been obtained from tumours at varying times after irradiation; examination of this has confirmed the views previously expressed as to the mode of action of radium, namely, that there is a

BIOPSY AFTER ELECTROCOAGULATION



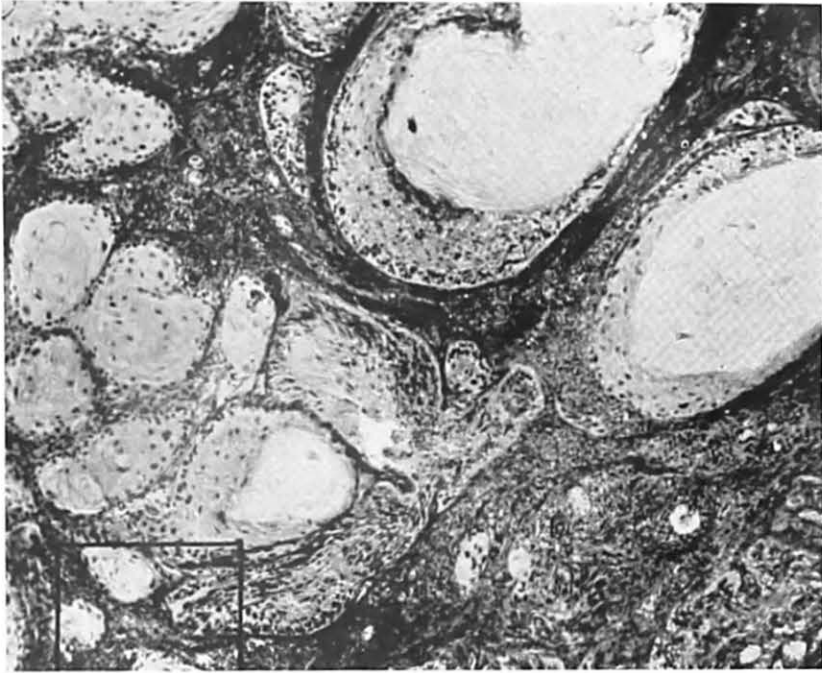
A. Microphotograph of carcinoma of the skin ($\times 70$).



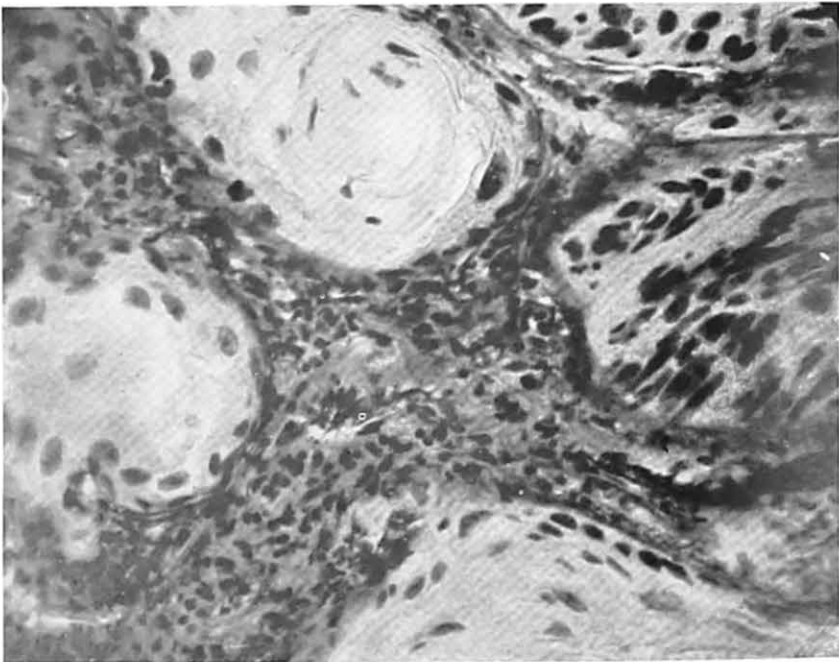
B. Microphotograph of carcinoma of the skin, enlargement of ruled area of A. ($\times 350$).

FIG. VI.

BIOPSY AFTER ELECTROCOAGULATION



A. Microphotograph of carcinoma of the cervix ($\times 80$).



B. Microphotograph of carcinoma of the cervix, enlargement of ruled area of A. ($\times 350$).

direct action on tumour cells and that the main action is not on the vascular supply of the tumour, a contention that has been upheld by some workers. It would appear that both these reactions may occur and that the predominance of one or the other depends on the intensity of the irradiation ; thus, with large doses over short periods histological examination shows a considerable degree of vascular change with thrombosis, whereas with small doses over longer periods the main effect is directly on the cells, and vascular changes are slight or absent. In all cases it is probable that the main action is directly on the cell, but that with a high intensity of irradiation vascular changes are superimposed.

B. CANCER OF THE BREAST TECHNIQUE

In 1932 and 1933 ABERDEEN ROYAL INFIRMARY reported a series of 13 patients with carcinoma mammae from whom the breast had been removed after Radium treatment (Medical Uses of Radium : Summary of Reports from Research Centres for 1932, p. 8, seven cases ; ditto for 1933, six cases). In every case the breast was sectioned and microscopically examined. Table 2 gives the subsequent history and shows that of the 13 patients, 8 were alive and well in 1934 on the anniversary of their first radium treatment. Of these 8, 4 are free from malignant disease as judged by repeated clinical and radiological examination. In the other 4 patients, although there is certainly no active malignant disease, it is possible that fibrotic indurations in irradiated fields may contain quiescent neoplastic cells, and for the time being these patients may be regarded as doubtfully free from malignant disease. Five of the 13 patients are dead. One, who before treatment was suffering from advanced cancer of the breast (Stage III), died of intercurrent disease, but for the eight months preceding death had been free from signs of malignant disease. The other 4 patients died with malignant disease present, each having a recurrence within a treated area, either at the site of the original primary growth or in one or more groups of the related lymph nodes. Three of these 4 patients had distant metastases as well.

Throughout 1934 no case referred for radium treatment proved suitable for a combination of radium and surgery, either on account of extensive local disease or on account of age or general condition.

At BIRMINGHAM GENERAL HOSPITAL the standard method of treatment of carcinoma of the breast has been a full interstitial irradiation along the lines of Keynes' technique. Particular care is taken to irradiate the tumour mass very thoroughly and the positions, strength, and number of needles are so arranged as to give an equal dosage throughout the tumour mass. The position of the needles is subsequently verified by radiographs. In two or three months' time after the above treatment the breast is again irradiated by a sectional surface applicator or deep X-rays, to the limit of skin tolerance. Many extremely advanced cases of fungating growths

apply for treatment and here the breast and growth is removed locally by diathermy or scalpel and at the same time the axilla and neck fully irradiated by needling. After a period this is followed by irradiation by a sectional surface applicator or by deep X-rays.

It is found extremely difficult to refuse treatment and the figures for 1934 include cases which, if judged by surgical and not humanitarian standards, would undoubtedly have been best left untreated. The problem of the very advanced case is rendered more difficult by the fact that occasionally an apparently hopeless case yields quite a fair result.

The following is reported as an interesting case :—

Patient, aged 43 (married) :

Admitted in June, 1934, with an advanced carcinoma of the right breast. There was a firm growth attached to the skin, involving the nipple and the upper and outer quadrant. Nodules could be felt beneath the skin over it ; the nipple was retracted and the breast as a whole presented a peau d'orange appearance. The lump was noticed twelve months previously. No enlarged glands were palpated in the axilla. The growth was judged inoperable owing to the extensive involvement of the skin and fixity. Radium treatment was given on 28th June, 1934, on the lines of Keynes' technique, a total of 22,000 mg. hours being given. The dose received at the centre of the tumour was 5,500 r. units. As is often the case with irradiation of this type the axilla was probably inadequately irradiated. Following the insertion there was a *pyocyanus* infection of the wound.

The patient was sent to the Deep X-ray Department in October, 1934. The local result proved very good, but it was suggested that some radiation be given to the axilla. Only a small dose was given (1,200 r. units) and as the patient then complained of some pain and the breast still felt rather firm, she was sent to see the surgeon again, who found that though some thickening could be felt in the breast the condition appeared to be quite operable. It was thought that some carcinoma was still present, and radical amputation was performed in January, 1935. The pathological report was as follows :—

- (1) The skin is thin and atrophic and there is some oedema of the cutis ;
- (2) In one part there is a slender sinus, epithelialised towards the surface. At some distance from this there is plasma cell and lymphocyte infiltration ;
- (3) Scattered areas of scirrhous carcinoma are seen in the axillary fat, though no glands can be found. No tumour is seen in the breast tissue itself, which is atrophic and fibrous, but there are occasional swollen necrotic cells which might be its remains.

At the MARIE CURIE HOSPITAL the treatment of primary and recurrent carcinoma of the breast has been carried on according to the principles discussed in earlier reports. In primary cases, with few exceptions a radical operation has been performed whenever possible. Inoperable and recurrent carcinomata have been treated by interstitial or surface radium. During 1934 X-ray therapy has also been used.

Twenty-four cases of primary carcinoma of the breast and 20 recurrent after radical operation have been treated during the year. Sixteen of the primary cases had very advanced growths. Fourteen primary carcinomata and 14 recurrent after operation were treated by radium alone. Five primary and 5 recurrent cases were given X-ray therapy alone and 5 primary cases and one recurrent were treated by radium and X-rays. The cases of carcinoma of the breast

TABLE 2.—An Analysis of 13 cases of Carcinoma of the Breast Treated by Radium followed by Amputation at the Aberdeen Royal Infirmary (Cases 1-7, Report for 1932 ; Cases 8-13, for 1933)

No.	Name.	Stage.	Date of Radium.	Date of Mastectomy.	Histology.		Alive.	General Condition.	Dead.	Local Condition at Site of Primary.	Related Lymph Areas.	Distant Metastases.
					Breast.	Nodes.						
1	Mrs. B. S.	1	Feb., 1932, radical needling.	Jan., 1933, local removal of breast.	No tumour cells found.	—	—	—	June, 1934.	Local deposit (? blood stream dissemination).	+ S.C. + ax.	Spinal pulmonary.
2	Mrs. M. L.	1	Apr., 1931, radical needling.	May, 1931, radical operation.	Degenerated tumour cells found.	No Histol. report.	Apr., 1934.	Good	—	No disease	No disease.	None.
3	Mrs. J. L.	1	Mar., 1931, radical needling ; May, 1931, surface radium.	Sept., 1931, local removal of breast.	No tumour cells found.	—	Mar., 1934.	Good	—	No disease	?? S.C. (doubtful).	None.
4	Miss L. F.	1	May, 1931, radical needling.	Oct., 1931, local removal of breast.	No tumour cells found.	—	May, 1934.	Good	—	No disease	No disease.	None.
5	Mrs. A. M.	2	July, 1931, radical needling.	Nov., 1931, radical operation.	No tumour cells found.	Degenerated tumour cells (axilla).	—	—	Aug., 1932.	Local recurrence.	+ S.C.	—
6	Mrs. C. T.	2	Dec., 1931, radical needling.	Dec., 1931, radical operation.	Tumour cells extremely degenerated.	No Histol. report.	Dec., 1934.	Good	—	No disease	No disease.	None.
7	Mrs. I. F...	1	Mar., 1931, radical needling.	Apr., 1931, local removal of breast.	Degenerated tumour cells.	—	Mar., 1934.	Good	—	No disease	No disease.	None.
8	Miss M. C.	3	Sept., 1932, radical needling ; Feb., 1933, surface radium.	Nov., 1933, local removal.	No tumour cells found.	—	—	—	Oct., 1934, strept. empyema.	No malignant disease.	No disease.	None.

TABLE 2.—An Analysis of 13 cases of Carcinoma of the Breast Treated by Radium followed by Amputation at the Aberdeen Royal Infirmary (Cases 1-7, Report for 1932 ; Cases 8-13, for 1933) (cont.)

No.	Name.	Stage.	Date of Radium.	Date of Mastectomy.	Histology.		Alive.	General Condition.	Dead.	Local Condition at Site of Primary.	Related Lymph Areas.	Distant Meta-stases.
					Breast.	Nodes.						
9	Mrs. M. G.	1	Aug., 1932, radical needling.	Aug., 1933, local removal.	Degenerated tumour cells.	—	—	—	Oct., 1933.	Local recurrence.	No disease.	Spinal meta-stases.
10	Mrs. M. D.	2	July, 1933, radical needling ; Oct., 1933, surface radium.	Dec., 1933, local removal.	Degenerated tumour cells.	—	July, 1934.	Good	—	? Residual disease (doubtful).	No disease.	None.
11	Mrs. J. C...	2	May, 1933, radical needling ; Aug., 1933, surface radium.	Dec., 1933, radical amputation.	No tumour cells found.	Not found in specimen.	May, 1934.	Fair	—	No disease	No disease.	? Spinal meta-stases developing.
12	Mrs. J. P...	2	Aug., 1932, radical needling ; Nov., 1932, surface radium.	Feb., 1933, radical operation.	Viable tumour cells.	Tumour cells found.	—	—	Jan., 1934.	No disease	+ Ax.	Pulmonary meta-stases.
13	Mrs. C. F.	2	Oct., 1932, radical needling.	Aug., 1933, radical operation.	Tumour cells found.	No Histol. report.	Oct., 1934.	Fairly good.	—	No disease	± S.C.	None.

Stage I = Breast tumour : nodes not palpable.
 Stage II = " " nodes palpable.
 Stage III = " " fixed and ulcerated ; nodes palpable.

+ = Malignant deposits present.
 S.C. = Supraclavicular lymph nodes.
 Ax. = Axillary lymph nodes.

treated by X-rays were post-operative recurrences, post-radium recurrences, supraclavicular glands in cases where the breast and axilla had been treated by interstitial radium, and a few primary breast carcinomata. The primary breast cases treated so far varied quite considerably in their response to treatment and it is apparent that there must be no fixed routine and that each case must be considered individually. It is found that if a pronounced erythema is avoided and no damage produced in the connective tissue, daily treatment may be continued until a very large dose has been given. The general condition of the patient is carefully noted and frequent blood counts done. The principles of X-ray treatment followed have been those elaborated by Dr. Coutard.

At the MIDDLESEX HOSPITAL the same general technique as before has been employed in treatment of carcinoma of the breast. Radical operation is performed by some surgeons and radium tubes inserted as a prophylactic measure into the intercostal spaces. In some cases interstitial irradiation on the general lines of the Keynes' technique has been carried out. An increasing number of patients are sent for X-ray therapy as a preliminary to either radical operation or interstitial irradiation. It has not been possible with only one gramme in the form of teleradium at the disposal of this centre to treat cases of carcinoma of the breast by this means, as the unit is fully occupied in the treatment of lesions situated in the mouth and throat.

At the ROYAL FREE HOSPITAL the techniques described in previous reports for the treatment of primary carcinoma of the breast have been employed with certain modifications during the year under review. In early cases a radical amputation has been performed, in some cases continued with radium treatment to the regions of possible invasion beyond the scope of surgical operation. More advanced cases have received interstitial supplemented by surface radium treatment.

During the year 4 cases were treated by radical surgery, 1 of these received interstitial and 3 received surface radium treatment post-operatively. Nine cases were treated with radium only; in all cases the primary growth was fixed to the pectoral muscles or the skin or to both and glands were clinically evident.

In a report by Mr. Geoffrey Keynes, from ST. BARTHOLOMEW'S HOSPITAL, it is stated that during the last three years the procedure in the treatment of cancer of the breast has been varied by performing an excision of the tumour with diathermy when it is small, or a local removal of the breast when the growth is larger. The routine treatment with radium is then carried out 14 to 21 days later. It is probable that the local excision reduces the incidence of local recurrence in the breast by removing the gross part of the disease. During 1934, 5 new patients were treated in this way, and 4 were treated by the older method with radium alone. All the patients treated in 1934 are free from any signs of disease. Two patients previously treated by radium, 1 in 1931 and the other in 1933, were given deep X-ray therapy for recurrences.

The Surgical Unit of this hospital has for a number of years carried out an investigation into the comparative results of treatment of carcinoma of the breast by (a) surgical operation, (b) interstitial radium. The results have been carefully traced by means of the Follow-up Department and recorded graphically. The conclusions arrived at so far have been set out in the Presidential Address delivered before the Surgical Section of the Royal Society of Medicine. The results obtained show that the five-year survival rate of the two methods of treatment is not materially different, being in each case 40 per cent. It became evident therefore, that if improvement was to be reached, a new line of approach should be tried. After careful consideration it was decided that the next attempt should be to combine interstitial radium with surgery; that after interstitial radiation the breast and glands should be excised. The patients thus treated are to be followed up, and their five-year survival rate ascertained and compared with that obtained by operation and radium respectively.

Opportunity will be taken to make an intensive histological study of the breast and glands after removal. The procedure adopted in these investigations was outlined in last year's report, and 39 cases have now been studied in detail in this manner. It is intended, however, to study a series of 50 cases before coming to any conclusion, and it is hoped that the work will be completed by September, 1935.

STATISTICAL DATA
TABLE 3.—*Cancer of the Breast*

	Year.	No. of Cases Treated.	Primary.		Recurrent.	
			Living.	Dead.	Living.	Dead.
Aberdeen, Royal Infirmary.	1930	13	1	8	0	4
	1931	41	11	15	1	14
	1932	39	7	24	1	7
	1933	30	10	14	2	4
	1934	38	23	5	6	4
Birmingham, General Hospital.	1930	43	12	31	—	—
	1931	45	16	29	—	—
	1932	47	21	26	—	—
	1933	41	21	20	—	—
Cardiff, Royal Infirmary	1930	14	1	13	—	—
	1931	25	8	17	—	—
	1932	29	9	20	—	—
	1933	26	14	12	—	—
Marie Curie Hospital ..	1926	4	0	1	*1	2
	1927	1	0	0	1	0
	1928	5	0	1	0	4
	1929	13	1	5	1	6
	1930	23	6	8	1	8
	1931	32	9	8	5	10
	1932	44	6	13	6	19
	1933	32	12	6	3	11
	1934	44	23	1	16	4

* One patient untraced and counted as dead in 1933, now traced as living.

STATISTICAL DATA (cont.)
TABLE 3.—*Cancer of the Breast* (cont.)

	Year.	No. of Cases Treated.	Primary.		Recurrent.	
			Living.	Dead.	Living.	Dead.
Middlesex Hospital ..	1925	46	4	21	1	20
	1926	36	3	18	0	15
	1927	37	6	18	1	12
	1928	45	9	26	0	10
	1929	54	7	30	0	17
	1930	53	10	30	4	9
	1931	54	15	33	1	5
	1932	62	30	25	3	4
	1933	53	35	8	4	6
	1934	48	43	1	3	1
Royal Free Hospital ..	1928	5	0	2	0	3
	1929	42	4	23	0	15
	1930	33	8	15	2	8
	1931	22	6	8	3	5
	1932	34	11	8	8	7
	1933	24	10	4	9	1
	1934	29	12	1	15	1
St. Bartholomew's Hospital.	1925	6	0	6	—	—
	1926	6	0	6	—	—
	1927	13	6	7	—	—
	1928	40	10	30	—	—
	1929	53	20	33	—	—
	1930	36	13	23	—	—
	1931	31	20	11	—	—
	1932	23	13	10	—	—
	1933	26	18	8	—	—
University College Hospital.	1925	2	0	1	0	1
	1926	1	0	1	—	—
	1927	2	—	—	0	2
	1928	3	0	1	0	2
	1929	9	0	3	0	6
	1930	20	0	4	3	13
	1931	9	2	2	3	2
	1932	12	2	5	2	3
	1933	21	8	3	6	4
	1934	20	1	0	17	2

Table 4 shows results collected from Table 3.

TABLE 4.—*Cancer of the Breast*

Year.	No. of Cases Treated.	Primary.		Recurrent.	
		Living.	Dead.	Living.	Dead.
1925 ..	54	4	28	1	21
1926 ..	47	3	26	1	17
1927 ..	53	12	25	2	14
1928 ..	98	19	60	0	19
1929 ..	171	32	94	1	44
1930 ..	235	51	132	10	42
1931 ..	259	87	123	13	36
1932 ..	290	99	131	20	40
1933 ..	253	128	75	24	26

C. CANCER OF THE UTERUS

(1) **Cervix Uteri**

TECHNIQUE

At the ABERDEEN ROYAL INFIRMARY, 36 patients received radium treatment for cancer of the cervix uteri in 1934, the Heymann technique or a modification thereof being employed. Six of these patients are expected to complete the three-stage treatment in 1935 and at present must be classified as undergoing treatment. Of the remaining 30 patients, 21 received a three-stage Heymann treatment, 8 received a two-stage Heymann treatment, and 1 received a one-stage Heymann treatment. Thus, 9 patients must be regarded as incompletely treated, the reason being that 3 patients refused further treatment; 3 died before the third treatment was given; and in 3 instances the treatment had to be abandoned for the following reasons:—(a) a vesico-vaginal fistula; (b) a recto-vaginal fistula; (c) a metastatic deposit in the os calcis.

The 36 patients who began radium treatment, and received either the whole or part of it in 1934, were graded in terms of extent of disease (international classification) at the time of the first treatment.

Stage I	16 patients
Stage II	5 "
Stage III	13 "
Stage IV	2 "

In 1934, 10 patients completed the three-stage Heymann treatment begun in 1933. Another 2 patients who were undergoing treatment at the end of 1933, and who should have received the third treatment early in 1934, were too ill to receive it and are therefore to be relegated to the group of incompletely treated 1933 patients.

Histology.—A biopsy was made in each case at the time of the first radium treatment. Squamous epithelioma was found in 34 cases and adeno-carcinoma in two. It was in a patient with a adeno-carcinoma of the cervix that a metastatic deposit in the os calcis occurred, causing further treatment to be abandoned.

Post-radiation fistulae. 1934 Patients.—Of 21 patients who received a full three-stage Heymann treatment in 1934 none has so far developed a fistula. 2 patients developed a fistula after the second-stage of treatment, 1 (aged 27), Stage IV, a vesico-vaginal fistula, the other, Stage I, a recto-vaginal fistula, and further treatment was abandoned.

1933 Patients.—Of the patients who completed their radium treatment in 1933, none is known to have developed a fistula in 1934. Of the 10 patients who completed in 1934 the course of treatment begun in 1933, 1 patient (Stage II) developed both vesico- and recto-vaginal fistulae. The dosage in this case was 3,300 mg. hrs. *in utero*, 4,950 mg. hrs. *in vagina*, spread over three treatments. The dosage in the two 1934 cases was considerably less.

Intra-abdominal irradiation.—A patient treated in April, 1932, by the Heymann technique remained well and free from signs of malignant disease until July, 1934, when she complained of pain in the distribution of the left obturator nerve. A laparotomy was performed and a hard mass of obturator lymph nodes, 8 cm. in diameter, found on the left side adherent to the pelvic wall. The mass and neighbouring lymph nodes were irradiated with fully-screened element. The radium (24 mg.) was removed seven days later. The patient remains under observation.

The MARIE CURIE HOSPITAL reports that it is now the tenth year since the Marie Curie Clinic was established and the sixth year since the work was centralised at the Marie Curie Hospital. During this time 960 cases of carcinoma of the cervix have been treated. All cases seen by members of the surgical staff have been treated by radium. An analysis of the results obtained shows that although there has been a general improvement during the ten years, it has not been steadily progressive, the falling off in the percentage of five-year cures in some years being due to the differences in the initial material. It appears that the technique used is obtaining fairly consistent results.

During the past few years there has been a definite though moderate increase in the number of early cases applying for treatment, but there is no diminution in the number of very advanced cases, and during the past year a larger number of cases (five) were refused treatment on account of distant metastases. It is hoped that the various forms of propaganda now being carried on will induce many more patients to seek earlier consultation or that some more effective form of propaganda may be devised.

X-ray therapy is now given in some cases of carcinoma of the cervix uteri, the principles of treatment followed being those elaborated by Dr. Coutard. The cases treated were all in late stages of the disease (stages III and IV). In most instances X-ray therapy has followed the radium treatment, but it is intended, in the future, to give pre-radium treatment to a greater number of cases especially advanced stage III cases. Fragments taken by small punch from the surface of the growth at intervals during treatment are being studied for the changes produced in the cervical growth by the external irradiation.

At the MIDDLESEX HOSPITAL the number of cases of carcinoma of the cervix uteri referred for radio-therapeutic treatment has remained about constant during the last five years. The large proportion of cases in stages III and IV (81·5 per cent.) is due to the fact that radical hysterectomy is the routine treatment for all patients who are found to be operable and suitable for operation. The radium technique, as developed and carried out at the Radium Institute, Paris, is the routine treatment at this hospital. X-ray therapy to the parametria is given as a preliminary to or after the completion of local radium treatment.

MEDICAL USES OF RADIUM

STATISTICAL DATA

TABLE 5.—Cancer of the Cervix Uteri

	Year.	Interval since Irradiation.	No. of Cases Treated.	Stage.							
				I.		II.		III.		IV.	
				L.	D.	L.	D.	L.	D.	L.	D.
Aberdeen, Royal Infirmary	1930	4	14	3	2	1	5	1	2	—	—
	1931	3	25	4	10	1	10	—	—	—	—
	1932	2	30	8	5	5	4	1	7	—	—
	1933	1	37	9	3	5	9	2	5	2	2
	1934	—	36	16	0	5	0	9	4	0	2
Birmingham, General Hospital ..	1930	4	16	4	5	0	2	0	3	0	2
	1931	3	48	12	3	1	12	2	11	1	6
	1932	2	38	9	2	3	6	3	10	1	4
	1933	1	33	6	1	6	6	7	3	1	3
Cardiff, Royal Infirmary	1922	12	6	—	—	0	1	0	5	—	—
	1923	11	19	—	—	0	3	0	16	—	—
	1924	10	17	1	1	0	3	0	11	0	1
	1925	9	28	1	0	0	4	1	22	—	—
	1926	8	27	—	—	—	—	0	27	—	—
	1927	7	18	—	—	0	2	2	14	—	—
	1928	6	32	2	0	0	10	0	20	—	—
	1929	5	39	1	1	2	5	4	23	0	3
	1930	4	52	6	2	4	17	2	18	0	3
	1931	3	24	—	—	2	1	3	12	0	6
	1932	2	33	3	0	2	1	7	15	0	5
	1933	1	48	2	0	5	2	13	20	2	4
	1934	—	48	2	0	7	2	23	7	6	1
Dublin, Richmond, Sir P. Dun's, Dr. Steevens' and Coombe Hospitals.	1930	4	11	1	2	1	4	0	3	—	—
	1931	3	19	2	3	1	5	0	8	—	—
	1932	2	13	1	3	0	3	0	6	—	—
	1933	1	7	1	0	1	2	0	3	—	—
	1934	—	18	3	1	5	1	4	4	—	—
Marie Curie Hospital	1925	9	14	0	0	2	1	2	6	0	3
	1926	8	59	2	0	2	5	9	33	0	8
	1927	7	57	1	0	5	4	9	19	0	19
	1928	6	85	5	2	10	8	15	31	2	12
	1929	5	109	4	0	11	5	19	50	2	18
	1930	4	136	5	1	23	9	31	50	4	13
	1931	3	126	7	2	15	5	27	48	2	20
	1932	2	113	7	0	29	5	24	35	2	11
	1933	1	106	5	0	25	6	31	22	4	13
	1934	—	107	8	0	29	2	44	9	7	8
	Middlesex Hospital	1925	9	25	0	1	0	4	1	10	0
1926		8	9	0	0	0	1	0	6	0	2
1927		7	19	1	1	0	3	2	5	0	7
1928		6	45	2	1	1	11	2	20	0	8
1929		5	37	1	4	1	7	2	18	0	4
1930		4	20	1	1	0	3	0	7	1	7
1931		3	24	1	2	0	2	5	6	0	8
1932		2	29	7	1	2	2	3	9	0	5
1933		1	23	0	1	0	1	6	5	5	5
1934		—	27	3	0	2	1	8	1	9	3
Royal Free Hospital	1929	5	3	—	—	1	1	0	1	—	—
	1930	4	8	1	0	4	0	0	3	—	—
	1931	3	3	2	0	0	1	—	—	—	—
	1932	2	11	—	—	2	3	1	5	—	—
	1933	1	10	4	0	4	0	0	1	0	1
1934	—	19	5	0	10	0	4	0	—	—	
St. Bartholomew's Hospital	1921	13	18	—	—	1	6	0	8	0	3
	1922	12	20	—	—	0	7	0	10	0	3
	1923	11	17	1	1	0	5	0	8	0	2
	1924	10	35	1	3	0	11	1	12	1	6
	1925	9	33	2	2	0	5	0	12	0	12
	1926	8	38	3	3	2	5	4	11	2	8
	1927	7	31	1	2	1	4	4	9	1	9
	1928	6	45	5	7	3	5	6	9	3	7
	1929	5	21	2	3	1	5	5	5	—	—
	1930	4	21	3	5	6	2	2	2	1	0
	1931	3	14	1	2	2	4	2	3	—	—
	1932	2	11	4	2	3	2	—	—	—	—
	1933	1	10	4	0	1	1	0	4	—	—

STATISTICAL DATA (cont.)

TABLE 5.—*Cancer of the Cervix Uteri* (cont.)

	Year.	Interval since Irradiation.	No. of Cases Treated.	Stage.							
				I.		II.		III.		IV.	
				L.	D.	L.	D.	L.	D.	L.	D.
Scottish Associations of the Medical Women's Federation.	1931	3	16	0	1	1	1	2	7	0	4
	1932	2	20	—	—	0	1	5	6	0	8
	1933	1	15	—	—	2	0	4	3	1	5
	1934	—	11	—	—	2	0	5	0	2	2
University College Hospital	1921	13	23	1	3	1	6	0	12	—	—
	1922	12	11	1	3	1	2	0	3	0	1
	1923	11	26	1	3	0	6	0	10	0	6
	1924	10	21	1	1	1	9	1	5	0	3
	1925	9	24	3	3	2	7	0	5	0	4
	1926	8	12	—	—	0	4	0	3	0	5
	1927	7	21	1	1	2	5	1	6	0	5
	1928	6	33	2	5	4	10	1	8	1	2
	1929	5	25	6	1	4	7	2	1	1	3
	1930	4	17	3	1	1	4	1	7	—	—
	1931	3	21	0	1	4	10	0	3	0	3
	1932	2	14	2	2	0	2	1	5	0	2
	1933	1	23	5	1	4	4	1	5	2	1

Table 6 shows the results collected from Table 5.

TABLE 6.—*Cancer of the Cervix Uteri*

Year.	Interval since Irradiation.	No. of Cases Treated.	Stage.							
			I.		II.		III.		IV.	
			L.	D.	L.	D.	L.	D.	L.	D.
1921.. ..	13	41	1	3	2	12	0	20	0	3
1922.. ..	12	37	1	3	1	10	0	18	0	4
1923.. ..	11	62	2	4	0	14	0	34	0	8
1924.. ..	10	73	3	5	1	23	2	28	1	10
1925.. ..	9	124	6	6	4	21	4	55	0	28
1926.. ..	8	145	5	3	4	15	13	80	2	23
1927.. ..	7	146	4	4	8	18	18	53	1	40
1928.. ..	6	240	16	15	18	44	24	88	6	29
1929.. ..	5	234	14	9	20	30	32	98	3	28
1930.. ..	4	295	27	19	40	46	37	95	6	25
1931.. ..	3	320	29	24	27	51	41	98	3	47
1932.. ..	2	312	41	15	46	29	45	98	3	35
1933.. ..	1	312	36	6	53	31	64	71	17	34

(2) *Corpus Uteri*

TECHNIQUE

At the ABERDEEN ROYAL INFIRMARY 6 patients with cancer of the corpus uteri were treated by radium during the year. Of these, 3 had very advanced primary growths and 3 had moderately advanced primary growths. In 4 patients radium only was employed, a modification of the Heymann technique being used. In 2 patients

irradiation of the cavity of the uterus was followed by pan-hysterectomy. Four of the 6 patients died before the end of the year. In each of the 6 cases the histology was that of an adenocarcinoma of the corpus uteri.

The history of one case re-treated in 1934 is as follows :—

Mrs. E. M. D., aet 47

February, 1933.—The patient received cavity irradiation for an adenocarcinoma of the body of the uterus. The tumour was palpable one finger's breadth below the umbilicus.

October, 1933.—*Per abdomen*.—Upper level of the body of the uterus found at a distance of two fingers' breadth above the pubis.

March, 1934.—*Per abdomen*.—The tumour palpable just below the level of the umbilicus. *Per vaginam*.—Occlusion of vaginal vault and canal of cervix consequent on previous irradiation.

10th March, 1934.—*Laparotomy performed* and 25 seeds (1·5 mc. Radon each) (0·3 mm. Pt screenage) implanted into an inoperable tumour of the body of the uterus (16 cm. vertical axis by 10 cm. broad).

May, 1934.—*Per abdomen*.—Tumour no longer palpable. *Per rectum*.—A residual thickening palpable in the pouch of Douglas.

December, 1934.—Symptoms appear indicating pressure on the bladder. *Per rectum*.—A lump palpable in the pouch of Douglas.

15th December, 1934.—*Abdomen reopened* and 30 seeds (1·5 mc. Radon) (0·3 mm. Pt) implanted (after reflecting the peritoneum) into a mass, 10 cm. diameter, occupying the pouch of Douglas.

Uneventful recovery and disappearance of symptoms.

March, 1935.—*Per rectum*.—An indefinite thickening palpable in the pouch of Douglas. Patient very well.

The MARIE CURIE HOSPITAL reports that in the ten years since the Marie Curie Clinic was started, 93 cases of carcinoma of the corpus uteri have been treated by radium. These cases have, when possible, been treated by hysterectomy, and only 40 per cent. have had radium treatment. With few exceptions the irradiated cases were inoperable, or operation was contra-indicated on general grounds.

The SCOTTISH ASSOCIATIONS OF THE MEDICAL WOMEN'S FEDERATION report that three new cases of cancer of the corpus uteri, all inoperable, have been treated during 1934, and the special technique of the Marie Curie Hospital which consists in the introduction of small cylinders of radium to the uterine fornices has been tried; tubes containing 10 mg. of radium in thick rubber tubing were used, and the low filtration of 0·5 mm. of platinum has not led to any untoward reaction. Of these cases two are symptom-free, the third, an advanced case, had a further slight haemorrhage 8 months after treatment and was found in spite of heavy dosage to have a small recurrence in the fundus which was given two further treatments.

One case of primary cancer of the uterine body treated in 1933 by pan-hysterectomy following radium to the interior of the uterus is alive and free from symptoms, but a case of recurrence following hysterectomy 5 years earlier died of spinal metastases without local symptoms. Of the two cases treated in 1931 one is alive and symptom-free, the other died 3 years after treatment probably with metastases

in the liver, although the actual cause of death is said to have been a cardiac lesion which had made her an invalid for years.

Table 7 shows the results of treatment of cancer of the corpus uteri at various centres since 1925.

STATISTICAL DATA
TABLE 7.—*Cancer of the Corpus Uteri*

	1925.		1926.		1927.		1928.		1929.		1930.		1931.		1932.		1933.		1934.	
	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.
Birmingham, General Hospital.	-	-	-	-	-	-	-	-	-	-	1	3	3	0	1	2	1	0	-	-
Cardiff, Royal Infirmary ..	0	5	0	2	0	2	0	2	0	6	1	3	1	3	4	0	2	2	3	1
Marie Curie Hospital ..	1	1	0	1	2	2	1	4	4	5	3	8	9	7	10	8	14	1	10	2
Middlesex Hospital ..	0	2	0	1	0	1	1	1	0	3	0	1	1	2	1	2	1	0	3	0
Royal Free Hospital ..	-	-	-	-	-	-	-	-	-	-	1	0	1	0	2	2	2	0	-	-
University College Hospital	0	2	1	0	1	0	0	1	-	-	0	1	-	-	2	1	-	-	-	

Table 8 shows results collected from Table 7.

TABLE 8.—*Cancer of the Corpus Uteri*

Year.	No. of Cases Treated.	Living.	Dead.
1925	11	1	10
1926	5	1	4
1927	8	3	5
1928	10	2	8
1929	18	4	14
1930	22	6	16
1931	27	15	12
1932	35	20	15
1933	23	20	3

D. CANCER OF THE MOUTH, NASOPHARYNX, LARYNX AND OESOPHAGUS

TECHNIQUE

The ABERDEEN ROYAL INFIRMARY reports that in the treatment of primary carcinoma of the *lower lip* the method of choice is interstitial irradiation. If an ulcerated epithelioma is heavily infected a preliminary surface irradiation by a mould is given until the ulcer becomes cleaner and then it is needled. Twenty-three patients with primary carcinoma of the lower lip were treated in 1934. In 19 patients there was complete disappearance of the primary growth followed by a healing of the lip so complete that a few months after treatment it was difficult to detect the site of the lesion.

Comment is made upon the subject of the lymph nodes in epithelioma of the lip. Concerning the 23 cases of lip epitheliomata treated in 1934, it is stated that:—

In 20 cases the lymph nodes were *not* palpable at the time of the radium treatment of the lip and have not become palpable subsequent to healing of the lip.

In 2 cases the lymph nodes *were* palpable at the time of radium treatment of the lower lip, but disappeared without treatment with the healing of the lip. They did not possess malignant characteristics.

In 1 case the lymph nodes were not palpable originally but became palpable subsequent to healing of the lip. They possessed malignant characteristics and treatment was indicated.

At BIRMINGHAM GENERAL HOSPITAL the cases of carcinoma of the buccal cavity have been treated either by interstitial irradiation or by surface irradiation from intrabuccal dental appliances built for each case. Great care has been taken to ensure uniformity of dosage throughout the tumour as far as possible and by adequate protection to reduce damage to normal tissue to a minimum.

The importance of maintaining the normal tissues as far as possible undamaged becomes increasingly obvious with experience, since it is upon the reaction of these that successful treatment so largely depends. The treatment of the *gland fields* wherever possible has been a block dissection followed by a careful irradiation to the limits of tolerance by surface applicators. This treatment does not give good results and recurrence is frequent, moreover these recurrences are very resistant to both radium and X-rays. The depth to which an adequate irradiation is given in the case of a surface applicator in the neck depends on its dosage, distance from the skin, etc., but in numerous cases quite heavy dosages at considerable depths must have been given because laryngeal symptoms due to the irradiation have been produced. It would seem that a more focal method of irradiation such as that provided by the radium bomb might be productive of improved results.

In the *larynx* a fresh technique has been adopted with the Harmer's window operation, and larger numbers of needles have been inserted, from nine to twelve of 1 mg. each, and left *in situ* for eight days. This has been followed by deep X-ray therapy through the port-hole in the larynx, and the early results are noticeably better than those previously attained, although it is still too soon to speak very definitely.

The radium results in the *tongue* and *tonsil* continue to be satisfactory and further experience has shown the great value of dividing the ascending ramus in cases of trismus due to adhesions after operative insertion of radium. In one case a man, aged 52, had a growth in the right upper alveolus, which was excised by diathermy and surgery. It recurred in the deeper part of the cheek involving the masseter muscle. This resulted in a severe trismus, and despite all efforts he was unable to open his teeth at all. A simple division of the ascending ramus was undertaken from the outside. He is now able to open his mouth without pain or difficulty and swallow his food. This is considered a better method than excising the head of the mandible when adhesions result from fibrosis of the muscle attached to the ascending ramus.

STATISTICAL DATA

TABLE 9.—*Cancer of the Mouth, Nasopharynx, Larynx and Oesophagus*

	Year.	No. of Cases Treated.	Tongue.		Floor of Mouth.		Palate, Tonsil and Fauces.		Lip.		Cheek.		Larynx.		Pharynx, Nasopharynx and Pharyngeal Wall.		Oesophagus.		
			L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	
			Aberdeen, Royal Infirmary	1930	26	0	6	2	1	1	6	2	3	0	5	—	—	—	—
	1931	37	0	10	0	4	1	1	8	10	0	2	—	—	1	0	—	—	—
	1932	50	1	8	2	0	4	6	18	5	0	2	—	—	1	1	0	2	—
	1933	57	2	4	5	3	4	5	21	3	1	0	—	—	1	6	0	2	—
	1934	56	7	1	2	7	2	0	24	0	4	3	—	—	2	2	2	0	—
Birmingham, General Hospital	1926	14	0	6	1	4	0	1	—	—	0	2	—	—	—	—	—	—	—
	1927	16	1	10	0	2	—	—	0	1	1	1	—	—	—	—	—	—	—
	1928	25	3	10	1	5	2	2	—	—	2	0	—	—	—	—	—	—	—
	1929	27	3	10	1	0	1	1	2	2	3	4	—	—	—	—	—	—	—
	1930	104	10	26	2	8	3	10	3	5	2	1	0	14	0	2	0	18	—
	1931	124	11	23	4	11	5	8	11	12	2	1	0	4	0	5	0	27	—
	1932	92	15	11	4	10	2	12	4	3	3	0	1	3	0	8	2	14	—
	1933	83	9	15	4	3	15	5	12	0	4	2	1	3	1	2	1	6	—
Cardiff, Royal Infirmary	1930	48	0	15	2	6	0	1	1	7	1	4	0	3	1	5	0	2	—
	1931	55	6	11	1	2	—	—	4	8	0	2	0	3	0	15	0	3	—
	1932	61	7	15	3	1	1	3	15	2	0	2	0	4	0	6	0	2	—
	1933	83	9	12	1	0	3	3	18	9	5	4	2	3	1	9	0	4	—
Dublin, Richmond, Sir P. Dun's, Dr. Stevens' and Coombe Hospitals.	1931	48	4	16	1	6	2	4	5	6	1	3	—	—	—	—	—	—	—
	1932	57	2	18	1	5	3	10	7	8	1	2	—	—	—	—	—	—	—
	1933	51	6	12	2	5	3	9	7	5	2	0	—	—	—	—	—	—	—
	1934	51	10	11	4	0	4	4	12	5	1	0	—	—	—	—	—	—	—

STATISTICAL DATA (cont.)

TABLE 9.—Cancer of the Mouth, Nasopharynx, Larynx and Oesophagus (cont.)

	Year.	No. of Cases Treated.	Tongue.		Floor of Mouth.		Palate, Tonsil and Fauces.		Lip.		Check.		Larynx.		Pharynx, Nasopharynx and Pharyngeal Wall.		Oesophagus.	
			L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.
			Middlesex Hospital.	1925	38	1	7	0	2	0	5	1	2	0	3	0	5	0
	1926	48	0	8	0	7	0	6	1	2	0	2	0	7	0	4	0	11
	1927	60	2	17	1	4	0	8	3	3	0	2	0	7	0	1	0	12
	1928	83	0	29	0	6	1	10	5	3	1	5	0	9	0	0	0	14
	1929	104	4	23	2	16	1	4	7	9	0	2	0	7	0	3	0	26
	1930	90	3	23	3	3	0	7	6	8	2	4	1	13	0	2	0	15
	1931	88	3	17	3	11	2	10	9	2	1	2	3	6	0	1	1	17
	1932	87	11	16	4	3	2	11	8	3	2	1	0	9	0	1	1	15
	1933	82	7	14	9	2	3	8	11	1	3	2	4	5	0	3	1	9
	1934	102	15	8	11	3	9	2	18	0	4	1	9	2	1	1	11	7
University College Hospital (Column marked * includes malignant lymphatic tumours.)	1925	4	0	1	—	—	0	1	—	—	—	—	—	—	*0	2	—	—
	1926	1	—	—	—	—	0	1	—	—	—	—	—	—	—	—	—	—
	1927	1	0	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	1928	13	0	5	0	1	0	4	—	—	—	—	—	—	0	3	—	—
	1929	23	3	5	0	1	3	3	0	2	—	—	—	—	—	—	—	—
	1930	38	0	12	1	2	1	3	2	8	—	—	—	—	1	5	—	—
	1931	22	1	6	3	1	1	1	4	1	—	—	—	—	0	4	—	—
	1932	26	4	4	2	2	1	3	1	2	—	—	—	—	1	6	—	—
	1933	37	1	7	2	2	2	3	5	0	—	—	—	—	1	14	—	—

At the MIDDLESEX HOSPITAL cases of malignant disease in these sites have been treated by means of the one gramme unit* in association with either interstitial radium, intra-buccal surface applications of radium on dental applicators or diathermy coagulation. The number of cases, however has been so great that it has been impossible to treat them all by this method and it has been necessary to treat some cases by means of moulded surface applicators instead of by the telerradium unit.

The question of the management of the teeth in patients being treated by radium for lesions in the *mouth* and *pharynx* is one to which considerable attention has been given during the last year. The present practice is to scale and clean the mouth thoroughly, removing those teeth which are obviously infected and at a distance from the neoplasm, but to abstain from wholesale extractions of teeth situated in close proximity to active ulceration where there may be the possibility of implantation growth. The whole question is receiving very detailed consideration in conjunction with the dental department.

Table 10 shows results collected from Table 9.

TABLE 10.—*Cancer of the Mouth, Nasopharynx, Larynx, and Oesophagus*

Year.	No. of Cases Treated.	Tongue.		Floor of Mouth.		Palate Tonsil and Fauces.		Lip.		Cheek.		Larynx.		Pharynx, Nasopharynx and Pharyngeal Wall.		Oesophagus.	
		L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.
		1925	42	1	8	0	2	0	6	1	2	0	3	0	5	0	5
1926	63	0	14	1	11	0	8	1	2	0	4	0	7	0	4	0	11
1927	77	3	28	1	6	0	8	3	4	1	3	0	7	0	1	0	12
1928	121	3	44	1	12	3	16	5	3	3	5	0	9	0	3	0	14
1929	154	10	38	3	17	5	8	9	13	3	6	0	7	1	8	0	26
1930	306	13	82	10	20	5	27	14	31	5	14	1	30	2	17	0	35
1931	374	25	83	12	35	11	24	41	39	4	10	3	13	1	25	1	47
1932	373	40	72	16	21	13	45	53	23	6	7	1	16	2	22	3	33
1933	393	34	64	23	15	30	33	74	18	15	8	7	11	4	34	2	21

E. CANCER OF THE RECTUM

TECHNIQUE

ST. BARTHOLOMEW'S HOSPITAL gives the following report upon one case of carcinoma of the rectum, which contains details of a new technique :

Case No. 92. J.C., male, age 48. Admitted 9th October, 1934, with ten months' history of constipation followed by diarrhoea and blood-stained stools, and rapid loss of weight.

P.R. ulcerated growth 2 inches from anal margin on posterior wall extending half-way round. Firmly fixed and extending upwards for 2½ inches.

15th October, 1934.—Colostomy. Liver free. No glands felt.

* A statistical report on the work carried out with the one gramme unit has been submitted to the Radium Commission and will be incorporated in a publication from this Body later in the year.

20th October, 1934.—Irradiation. Peri-rectal radium $5 \times 3 \times 240 = 3,600$ mg. hrs., needles. Intra-rectal radium $6 \times 3 \times 168 = 3,024$ mg. hrs., needles.

25th January, 1935.—Growth much reduced in size. Recommended for course of deep X-ray treatment.

The technique adopted in this case differed from any of the techniques previously employed. The growth was attacked by surface irradiation from within by needles passed through the perineum. No needles were introduced into the substance of the growth.

The following are the details of the method employed:—

Eleven 3 mg. needles, 6 cm. long (active length 4.8 cm.) with 0.8 mm. platinum filtration were employed. Five of these were passed through the perineum behind the anus through a special trocar which allows the silk thread to pass in with the needles. These needles were passed with one finger in the rectum and made to lie close up to the outer surface of the growth at about 1 cm. interval. After this a long rectal tube was passed down through the lower colostomy opening, and brought out through the anus. A piece of corrugated rubber sheeting was cut to the size of the growth, and the remaining six needles were threaded in a vertical plane (1 cm. from each other) in and out through the rubber tissue. The centre of this rubber rectal plaque was then stitched to the rectal tube. The rubber plaque was then folded round the tube, drawn back into the rectum until the needles were opposite to, and covered the growth. The unfolded rubber sheet was then kept in contact with the growth by gauze packing placed in front of it. The intra-rectal plaque was left in for ten days, and the needles removed from the perineum at the end of seven days.

It is hoped by this method to get an efficient direct attack on low growths which are limited to the posterior half of the rectum. Hitherto this has been carried out at St. Bartholomew's either by surgical exposure and the so-called posterior barrage, or by intra-rectal radon combined with peri-rectal radium (passed through a trocar through the perineal skin as above). The object of the method described above is (1) to employ a constant irradiation, with a minimum of beta rays, using radium (heavily filtered), as distinct from radon, both from behind and in front, and (2) to avoid penetration of the substance of the growth.

It is intended to repeat this method in suitable cases and to follow the treatment with deep X-rays.

STATISTICAL DATA

TABLE 11.—*Cancer of the Rectum*

	1925		1926		1927		1928		1929		1930		1931		1932		1933		1934.	
	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.
Birmingham, General Hospital.	-	-	-	-	-	-	-	-	-	-	2	11	3	5	1	3	2	1	-	-
Cardiff, Royal Infirmary ..	-	-	-	-	-	-	-	-	-	-	0	9	4	6	2	6	4	3	-	-
Marie Curie Hospital ..	-	-	-	-	-	-	1	3	0	2	1	10	2	2	3	4	2	3	7	1
Middlesex Hospital ..	0	4	0	1	1	3	0	13	4	18	3	3	0	2	2	2	2	3	4	1
Royal Free Hospital ..	-	-	-	-	-	-	-	-	0	8	-	-	0	2	-	-	1	1	-	-
St. Bartholomew's Hospital	0	4	1	5	0	7	3	10	2	26	3	11	1	11	0	4	1	2	1	0

Table 12 shows results collected from Table 11.

TABLE 12.—*Cancer of the Rectum*

<i>Year.</i>	<i>No. of Cases Treated.</i>	<i>Living.</i>	<i>Dead.</i>
1925	8	0	8
1926	7	1	6
1927	11	1	10
1928	30	4	26
1929	60	6	54
1930	53	9	44
1931	38	10	28
1932	27	8	19
1933	25	12	13

F. SARCOMA

At UNIVERSITY COLLEGE HOSPITAL several cases of sarcoma have been treated with X-rays, mention of which is made here because of the close parallelism they offer to what has been previously reported in this series concerning patients treated by means of radium.

Two new cases of primary sarcoma of the bone were treated during the year. Both cases were diagnosed on clinical and radiological evidence only. The technique of treatment was similar to that described in previous reports from this centre. One patient discharged himself too soon for the response to irradiation to be seen. The second patient, who had a sarcoma of the clavicle, has shown a most satisfactory response. The tumour has subsided, the skin over it, which was of a cyanotic hue, is now normal in colour, and the radiogram shows a deposit of calcium throughout the tumour area. A fracture of the clavicle had occurred. This has united.

Two cases of recurrent sarcoma of bone were also treated. In the first of these an amputation through the middle of the thigh was performed in 1927 for sarcoma of the tibia. The patient had remained well until a recurrence appeared in the neck of the femur in September, 1934. There were also metastases in the chest and a large pleural effusion. The treatment has been without effect. In the second case of recurrent sarcoma amputation through the middle of the thigh was performed in April, 1934, and a recurrence occurred in the stump at the end of October, 1934. The case is too recent to see the effect of irradiation.

Two patients with primary sarcoma of the femur who had received treatment in 1933 had further courses of treatment. One is in good health eighteen months after the beginning of treatment and the radiogram shows that the tumour area has been completely ossified. One case reported as an osteo-chondroma of the pelvis in 1933 was found to be an osteo-chondro-sarcoma at autopsy.

Table 13 shows the results of treatment of sarcoma at the Birmingham General Hospital and Middlesex Hospital since 1925.

TABLE 13.—*Sarcoma*

		1925.		1926.		1927.		1928.		1929.		1930.		1931.		1932.		1933.		1934.	
		L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.	L.	D.
Birmingham, Hospital.	General	-	-	-	-	0	1	1	2	0	2	1	11	7	5	4	7	3	4	-	-
Middlesex Hospital	..	4	10	2	12	1	8	3	12	4	18	2	5	7	5	4	9	6	3	12	3

G. TELERADIUM THERAPY

In August, 1932, the King Edward's Hospital Fund for London, acting with the Radium Commission, put at the service of three London hospitals—the Cancer Hospital, University College Hospital, and the Middlesex Hospital—one gramme radium units, so that their utility in the treatment of malignant disease might be investigated. The first reports from these Centres were published in the Annual Report of the Radium Commission last year, but as two of these Centres are also associated with the research scheme of the Council, a brief mention is made of this work in their annual reports, from which the following information is taken :—

The report from the MIDDLESEX HOSPITAL states that the telerradium unit has continued to prove its usefulness to the radium department, and has been in constant use both day and night. One hundred and nineteen patients have been treated by this means during the year. Quite apart from the curative value, which cannot be assessed until after a period of years has elapsed, it is a method of therapy which is more convenient and associated with less danger to the staff than is the case when large moulded applicators are used.

From the UNIVERSITY COLLEGE HOSPITAL report it appears that during the first *two* years of its use 109 patients were treated with the one gramme unit. The construction of the unit is unchanged from that described in the hospital's report for 1932, radium-skin distance 5.5 cm., diameter of circular port of entry 5 cm., filtration equivalent 1 mm. Pt. The arrangement of the ports of entry has become to a certain extent standardised where the number of cases submitted for treatment has permitted of this. In the case of the neck and of the groin the ports are arranged to cover an area larger than that included in a gland dissection of the same area. In the case of primary lesions situated in the mouth, pharynx and larynx the ports have been worked out after reference to frozen sections to give the minimum tissue depth.

The latter factor is of particular importance with the existing unit, the percentage of the skin dose reaching increasing depths of tissue falling off rapidly in the deeper layers. The values at 2, 5, and 10 cm. are respectively 50, 23 and 8.5 per cent. The maximum dosage it has been found practicable to give to a single area over a period of three to four weeks is 18 gramme hours, this producing a fairly severe "radio-epidermite." To get a total tumour dose comparable to the

skin dose of a single port it is obviously necessary to select the maximum number of ports at the minimum distance, at least five at 5 cm., say.

This is also in general conformity with the immediate clinical effects. Rapid regression of the irradiated lesion is common when the latter does not lie more than 2 cm. from the skin, or where the site of the lesion is such that four or five equidistant ports of entry can be found for it, as in the case of the anterior part of the floor of the mouth. In the case of a lesion less favourably situated, the limit of skin tolerance through the available ports has not infrequently been reached before the lethal tumour dose. The solution of this difficulty appears to lie in the direction of increased radium-skin distance with the corresponding increase of radium element and possibly increased filtration.

H. NON-MALIGNANT CONDITIONS

The MARIE CURIE HOSPITAL reports that 833 cases of non-malignant uterine haemorrhage have now been treated, and of these 549 have been followed up from one to six years. The cases fall into three categories:—(1) haemorrhage of the menopause, (2) haemorrhage of the childbearing age (20–40) and (3) haemorrhage of adolescence.

Dosage and technique.—After the tentative treatment of a few cases the radium dosage was standardised for each group of cases and the majority of all groups have since been given the typical dose. A few have had repeat doses and in groups 1 and 2 in a few cases when malignancy has been suspected a larger initial dose has been given. The dose is not varied on account of the extent of the haemorrhage.

50 mg. E. (or 30 mg. E. in a small uterus) screened by 1 mm. platinum and 1.5 mm. rubber is inserted into the cavity of the corpus uteri, the empty cuff of the rubber tube, which has been cut to correspond with the entire length of the uterine cavity, occupies the cervical canal. With this method of application it is hoped to avoid the cervical stenosis which sometimes leads to later complications. A diagnostic curettage is always done at the same time. When the haemorrhage is associated with myomata a slightly larger dose is sometimes given, but even in such cases the majority (74 per cent.) have had the standardised dose.

The standard dose in each group is as follows:—

Menopausal haemorrhage	1,100–1,200 m.e.h.
20–40 years	600–700 m.e.h.
Under 20 years	300 m.e.h.

The results obtained in the 549 cases are as follows:—

Group.	Total No.	Well.	Improved.	No Result.
1	399	384	15	0
2	138	117	7	14
3	12	11	1	0

With regard to the results, the aim in group 1 is to produce an artificial menopause and in groups 2 and 3 to restore the normal functions. As the small dosage used is successful in a large percentage of all groups it does not seem advisable to increase the standard dose, but to give a repeat dose in cases which have not responded.

In a number of the younger patients there was irregular haemorrhage for two or three months, followed by amenorrhoea before the periods became normal. In a few cases, all having doses under 750 m.e.h., the amenorrhoea has persisted during the three or four years they have been under observation. In the adolescent cases improvement developed slowly and in some, although the haemorrhage has been cured, the periods are irregular.

Myomata.—There were 87 cases of myomatous uteri amongst the haemorrhage cases, 74 in group 1, and 13 in group 2. With two or three exceptions all were small tumours. The radium dosage in 86 per cent. of the myomatous cases was from 1,100–1,400 m.e.h. A few had 1,500–2,000 m.e.h., and a few others 500–800 m.e.h. In four cases hysterectomy was performed later.

NOTE.—A preliminary report on 141 cases of non-malignant uterine haemorrhage treated by radium at the Marie Curie Hospital was published in 1933 by Dr. Phyllis Epps. (*J. Obstet. Gynaec.*, 1933, 40, 835.)

APPENDIX

List of Research Centres and Local Committees

The centres taking part in the scheme covered by the foregoing Report are the institutions named below. Nine of these have continued to hold fractions of the stock of radium salt entrusted by H.M. Government to the Medical Research Council for the purposes of research into its medical uses. The list includes two additional centres, one of which has shared in a further quantity of radium provided by the British Empire Cancer Campaign for the extension of the scheme.

Most of these centres and a few others have also been able to draw upon a source of radium emanation ("radon") at the Middlesex Hospital: the salt required for this has been set aside from the Council's stock, accommodation for the work being provided by the courtesy of the Governors of the Hospital and expenses partly by the British Empire Cancer Campaign.

The work of the different clinical centres is being done under the direction of the local research committees named in the following list. For the co-operation of these the Council again take the opportunity of making grateful acknowledgment.

The Middlesex Hospital, London :

G. Gordon-Taylor, O.B.E., M.S., B.Sc., F.R.C.S. ; E. L. Pearce Gould, M.D., Ch.M., F.R.C.S. ; R. V. Hudson, F.R.C.S. ; E. W. Riches, M.C., M.S., F.R.C.S. ; Victor Bonney, M.D., M.S., B.Sc., F.R.C.S. ; C. P. Wilson, F.R.C.S. ; C. E. Lakin, M.D., F.R.C.P., F.R.C.S. ; J. H. Douglas Webster, M.D., F.R.C.P. ; H. E. A. Boldero, M.A., F.R.C.P. ; A. E. Webb-Johnson, C.B.E., D.S.O., M.B., F.R.C.S. ; B. W. Windeyer, M.B., F.R.C.S.E. ; Professor James McIntosh, M.D. ; Professor E. C. Dodds, M.V.O., M.D., Ph.D. ; and Professor Sidney Russ, C.B.E., D.Sc.

University College Hospital, London :

Gwynne Williams, M.S., F.R.C.S. ; W. J. Pearson, D.S.O., M.C., M.D., F.R.C.P. ; A. M. H. Gray, C.B.E., M.D., F.R.C.P. ; Professor C. C. Choyce, C.M.G., C.B.E., M.D., F.R.C.S. ; E. K. Martin, M.S., F.R.C.S. ; J. Taylor, O.B.E., M.S., F.R.C.S. ; R. W. A. Salmond, O.B.E., M.D., Ch.M., D.M.R.E. ; Professor F. J. Browne, M.D., D.Sc., F.R.C.S.E., F.C.O.G. ; H. A. Kisch, M.B., F.R.C.S. ; J. W. McNee, D.S.O., M.D., D.Sc., F.R.C.P. ; C. W. Flemming, M.Ch., F.R.C.S. ; N. L. White, M.D., F.R.C.S., M.C.O.G. ; P. M. D'Arcy Hart, M.D., M.R.C.P. ; and Professor E. N. da C. Andrade, D.Sc., Ph.D.

St. Bartholomew's Hospital, London :

The Rt. Hon. Lord Horder of Ashford, K.C.V.O., M.D., F.R.C.P. ; Sir Charles Gordon-Watson, K.B.E., C.M.G., F.R.C.S. ; M. Donaldson, M.B., B.Chir., F.R.C.S. ; W. D. Harmer, M.Chir., F.R.C.S. ; R. G. Canti, M.D. ; N. S. Finzi, M.B., D.M.R.E. ; Professor Hopwood, D.Sc. ; Professor Hadfield, M.D., F.R.C.P. ; A. E. Gow, M.D., F.R.C.P. ; Geoffrey Keynes, M.D., F.R.C.S. ; W. M. Levitt, M.D., M.R.C.P., D.M.R.E. ; J. Paterson Ross, M.S., F.R.C.S. ; R. M. Vick, O.B.E., M.Chir., F.R.C.S. ; R. Phillips, M.S., F.R.C.S. ; F. d'Abreu, Ch.M., F.R.C.S. ; Bernard Stewart, M.D.

St. Peter's Hospital, London :

J. Swift Joly, M.D., F.R.C.S. ; A. Clifford Morson, F.R.C.S. ; F. J. F. Barrington, M.S., F.R.C.S. ; R. Ogier Ward, M.Ch., F.R.C.S. ; J. Alban Andrews, Ch.B., F.R.C.S. ; and John Sandrey, M.B., Ch.M., F.R.C.S.

Marie Curie Hospital, London :

Miss M. M. Chadburn, C.B.E., M.D., B.S. ; Lady Barrett, C.H., C.B.E., M.D., M.S. ; Lady Briscoe, M.B., B.S. ; Miss F. Huxley, M.D., B.Sc., F.C.O.G. ; Miss E. Hurdon, M.D., C.M. (Tor.) ; Professor Dame Louise McIlroy, D.B.E., M.D., D.Sc. ; Miss L. Martindale, C.B.E., J.P., M.D., B.Sc. ; and Miss M. Rawlins, M.B., B.S.

Royal Free Hospital, London :

C. A. Joll, M.S., F.R.C.S. ; L. E. C. Norbury, O.B.E., M.B., F.R.C.S. ; Miss Dearnley, M.D. ; Professor Amy Fleming, M.D., D.Sc. ; C. E. Shattock, M.S., F.R.C.S. ; Miss E. C. Lewis, M.S., F.R.C.S. ; H. Haldin Davis, M.D., F.R.C.P., F.R.C.S. ; C. B. Heald, C.B.E., M.D., M.R.C.P. ; and Mrs. H. M. Hill.

St. George's Hospital, London :

C. H. S. Frankau, C.B.E., D.S.O., F.R.C.S. ; D. W. Roy, F.R.C.S. ; and L. Colledge, F.R.C.S.

The General Hospital, Birmingham :

Sir Gilbert Barling, Bt., C.B., C.B.E., M.B., F.R.C.S. ; Seymour Barling, C.M.G., M.S., F.R.C.S. ; W. Stirk Adams, F.R.C.S. ; Ernest Bulmer, M.D., M.R.C.P. ; E. Ashley Cooper, D.Sc., A.R.C.S. (Lond.) ; A. B. Danby, F.R.C.S. ; H. P. Gilding, M.A., M.D. ; H. H. Sampson, M.C., F.R.C.S. ; H. B. Keene, D.Sc. ; Stuart McDonald, M.A., M.B. ; J. B. Leather, M.A., M.B., B.Ch., F.R.C.S.E. ; G. Percival Mills, M.B., F.R.C.S. ; F. S. Phillips, B.Sc. ; C. A. Raison, M.B., Ch.B., F.R.C.S. ; B. T. Rose, B.Sc., M.Ch., F.R.C.S. ; R. P. Scott Mason, M.C., F.R.C.S. ; F. A. R. Stammers, B.Sc., M.B., Ch.B., F.R.C.S. ; C. G. Teall, M.B., Ch.B. ; A. P. Thomson, M.C., M.D., F.R.C.P. ; Professor H. Beckwith Whitehouse, M.S., F.R.C.S. ; D. L. Woodhouse, D.Sc. ; and E. Musgrave Woodman, M.S., F.R.C.S.

The Royal Infirmary, Cardiff :

Emeritus Professor Sir Ewen J. Maclean, M.D., F.R.C.P. ; J. W. Tudor Thomas, M.D., M.S., F.R.C.S. ; Professor G. I. Strachan, M.D., F.R.C.P., F.R.C.S. ; Professor A. W. Sheen, C.B.E., M.S., F.R.C.S. ; H. A. Scholberg, M.B. ; Cyril Lewis, M.D., C.M. ; Professor J. B. Duguid, M.D. ; Owen L. Rhys, M.D. ; R. D. Owen, F.R.C.S.E. ; J. H. Shaxby, D.Sc., F.Inst.P. ; Professor R. T. Dunbar, M.A., Ph.D. ; R. Armstrong, M.B. ; J. B. Haycraft, F.R.C.S. ; R. G. Maliphant, M.D., F.R.C.S. ; and V. T. Powell, M.R.C.S., L.R.C.P.

The Royal Infirmary, Aberdeen :

Professor J. R. Learmouth, M.B., Ch.M., F.R.C.S.E. ; M. Connon, M.D. ; Professor Robert G. McKerron, M.D. ; D. P. Levack, M.B. ; A. Mitchell, M.B., Ch.M. ; and H. Ross Souper, M.D.

The Irish Radium Committee, Dublin :

Sir Edward Coey Bigger, M.D. ; Sir John Purser Griffith, M.Inst.C.E. ; J. M. O'Connor, M.D. ; R. J. Rowlette, M.D. ; Professor A. F. Dixon, Sc.D. ; Surgeon Denis Kennedy ; Oliver Chance, M.D. ; Surgeon C. J. Macauley ; Oswald Murphy, M.D. ; T. Gillman Moorehead, M.D. ; C. L. McDonagh, M.D. ; Professor H. J. Seymour, B.A., B.Sc. ; and Professor Felix Hackett, Ph.D.

(The salt allocated to the last-named centre has been used as a source of emanation for distribution in Ireland.)

In addition, fractions of radium salt have been lent for research by Dr. J. C. Mottram, Mount Vernon Hospital, Northwood, Dr. W. V. Mayneord, Cancer Hospital, London, Dr. Joan M. Ross, Royal Free Hospital, London, Dr. J. Ralston Paterson, Holt Radium Institute, Manchester, and by Sir Leonard Hill at the St. John Clinic and Institute of Physical Medicine, London.

A quantity of radium lent to the Council by the National Radium Commission has been allocated to Professor D. P. D. Wilkie's Department at Edinburgh, the Royal Free Hospital, London and the Strangeways Research Laboratory, Cambridge. A fraction of it has also been lent for experimental work by Dr. Muriel Robertson at the Lister Institute, London, and by Mr. J. J. M. Shaw at the Royal Infirmary, Edinburgh.

Privy Council

MEDICAL RESEARCH COUNCIL

(Formerly Medical Research Committee, National Health Insurance.)

LIST OF PUBLICATIONS

(The prices given are net : those in brackets include postage.)

October, 1935.

The following publications relating to the work of the Medical Research Council can be purchased directly from **H.M. Stationery Office**, at the following addresses : Adastral House, Kingsway, London, W.C.2 ; 120 George Street, Edinburgh 2 ; York Street, Manchester 1 ; 1 St. Andrew's Crescent, Cardiff ; 80 Chichester Street, Belfast ; or through any bookseller.*

In addition, numerous memoirs upon work aided by the Medical Research Council have appeared in Scientific Journals : particulars of these may be seen in the Annual Reports.

ANNUAL REPORTS

Medical Research Committee, Nos. 1-5, 1914-15 to 1918-19.

Medical Research Council, 1919-20 to 1931-32.

(Price of each report from 1920-1 to 1925-6, † 3s. 6d. (3s. 8d.) ; from 1926-7 to 1928-9, 3s. (3s. 2d.) ; 1929-30 and 1930-31, 2s. 6d. (2s. 8d.) ; 1931-32, 2s. (2s. 2d.) ; 1932-33, 2s. 6d. (2s. 9d.) ; 1933-34, 3s. (3s. 2½d.)

SPECIAL REPORTS, &c.

Alcohol :

No. 31. Alcohol : its Absorption into and Disappearance from the Blood under different conditions. By E. Mellanby. [1919.] *Out of print.*

No. 34. The Influence of Alcohol on Manual Work and Neuro-muscular Co-ordination. By H. M. Vernon. [1919.] *Out of print.*

No. 56. The effects of Alcohol and some other Drugs during Normal and Fatigued Conditions. By W. McDougall and May Smith. [1920.] 1s. (1s. 1d.).

No. 168. Alcohol and Inheritance : An Experimental Study. By F. M. Durham and H. M. Woods. [1932.] 1s. 3d. (1s. 4½d.).

(Book). Alcohol : its Action on the Human Organism. Second Edition. [1924.] 1s. paper covers, 1s. 6d. cloth bound.

Anaerobic Bacteria : see WOUND INFECTIONS.

Animals, Diseases of :

No. 121. Borna Disease and Enzootic Encephalo-Myelitis of Sheep and Cattle. By S. Nicolau and I. A. Galloway. [1928.] 5s. (5s. 2½d.).

See also TUBERCULOSIS (Nos. 94, 122, 149, 184, and 189).

Bacteriology (MISCELLANEOUS) :

No. 35. The Reaction of Culture Media, by S. R. Douglas, J. W. H. Eyre, P. P. Laidlaw, and C. G. L. Wolf. Second Edition, revised by P. P. Laidlaw. [1927.] 6d. (7d.).

No. 49. On the Destruction of Bacteria in Milk by Electricity. By J. M. Beattie and F. C. Lewis. [1920.] *Out of print.*

No. 51. The Laboratory Diagnosis of Acute Intestinal Infections, including the Principles and Practice of the Agglutination Tests. By the Committee upon Pathological Methods. [1920.] 4s. 6d. (4s. 8d.).

* For overseas agencies see p. xii. † 1923-4 out of print.

No. 64. Catalogue of the National Collection of Type Cultures. Third Edition. [1931.] 2s. (2s. 1d.).

No. 169. The Haemolytic Streptococci: Their Grouping by Agglutination. By F. W. Andrewes and Ethel M. Christie. [1932.] 1s. 3d. (1s. 4½d.).

No. 203. The Pathogenic Aerobic Organisms of the Actinomyces Group. By Dagny Erikson. [1935.]

See also SURGERY (No. 138) and IMMUNITY.

A SYSTEM OF BACTERIOLOGY IN RELATION TO MEDICINE. (*See last page.*)

Blood Physiology :

No. 72. The Acid-base Equilibrium of the Blood. By the Haemoglobin Committee. [1923.] 2s. (2s. 1d.).

Blood Vessels, Diseases of :

No. 193. Dissecting Aneurysms. By T. Shennan. [1934.] 2s. 6d. (2s. 8½d.).
See also SHOCK, SURGICAL.

Borna Disease : *see* ANIMALS, DISEASES OF.

Brain Surgery : *see* SURGERY.

Bright's Disease : *see* NEPHRITIS.

Burns :

No. 141. The Tannic Acid Treatment of Burns. By W. C. Wilson. [1929.] 1s. (1s. 1d.).

Cancer :

No. 99. An Investigation into the Statistics of Cancer in Different Trades and Professions. By Matthew Young and W. T. Russell. [1926.] 1s. 6d. (1s. 7d.).

See also RADIUM.

Catgut : *see* SURGERY (No. 138).

Cerebro-spinal Fever :

No. 2. Report of the Special Advisory Committee upon Bacteriological Studies of Cerebro-spinal Fever during the Epidemic of 1915. [1916.]

Out of print.

No. 3. Bacteriological Studies in the Pathology and Preventive Control of Cerebro-spinal Fever among the Forces during 1915 and 1916. By M. H. Gordon, Martin Flack, P. W. Bassett-Smith, T. G. M. Hine, and W. J. Tulloch. [1917.]

Out of print.

No. 17. (I.) A Report upon the Seasonal Outbreak of Cerebro-spinal Fever in the Navy at Portsmouth, 1916-17. By Paul Fildes and S. L. Baker. (II.) The Treatment of Cerebro-spinal Meningitis by Antimeningococcus Serum at the Royal Naval Hospital, Haslar, 1915-16-17. By G. P. Adshhead. [1918.] 2s. 6d. (2s. 8½d.).

No. 50. Cerebro-spinal Fever. Studies in the Bacteriology, Preventive Control, and Specific Treatment of Cerebro-spinal Fever among the Military Forces, 1915-19. By M. H. Gordon and others. [1920.] 4s. (4s. 3d.).

No. 124. The Meningococcus. By E. G. D. Murray. [1929.] 3s. 6d. (3s. 8½d.).

Chemotherapy : *see* STREPTOCOCCAL INFECTIONS.

Child Life (ANTENATAL AND POSTNATAL INVESTIGATIONS) :

No. 10. The Mortalities of Birth, Infancy, and Childhood. By A. K. Chalmers, W. A. Brend, L. Findlay, and J. Brownlee. [1917.] *Out of print.*

No. 74. The Relation between Home Conditions and the Intelligence of School Children. By L. Isserlis. [1923.] 1s. (1s. 1d.).

No. 81. The Effect of Maternal Social Conditions and Nutrition upon Birth-weight and Birth-length. By M. Bruce Murray. [1924.] 1s. (1s. 1d.).

No. 82. Maternal Syphilis as a cause of Death of the Foetus and of the New-born Child. By J. N. Cruickshank. [1924.] 1s. 6d. (1s. 7½d.).

- No. 86. The Estimation of Foetal Age, the Weight and Length of Normal Foetuses, and the Weights of Foetal Organs. By J. N. Cruickshank, M. J. Miller, and F. J. Browne. [1924.] 2s. 6d. (2s. 7½d.).
- No. 101. Poverty, Nutrition, and Growth: Studies of Child Life in Cities and Rural Districts of Scotland. By D. Noël Paton, Leonard Findlay, and others. [1926.] 10s. (10s. 4½d.).
- No. 109. A Clinical and Pathological Study of 1,673 Cases of Dead-Births and Neo-natal Deaths. Compiled by E. L. Holland and J. E. Lane-Claypon. [1926.] 3s. 6d. (3s. 7½d.).
- No. 114. Social Conditions and Acute Rheumatism. [1927.] 2s. 6d. (2s. 8d.).
- No. 117. The Toxaemias of Pregnancy: A Clinical and Biochemical Study. By J. N. Cruickshank, J. Hewitt, and K. L. Couper. [1927.] 4s. (4s. 2d.).
- No. 118. The Cause of Foetal Death in 144 Cases. By A. C. Palmer. [1928.] 3s. (3s. 2d.).
- No. 145. The Causes of Neo-natal Death. By J. N. Cruickshank. [1930.] 1s. 6d. (1s. 7½d.).
- No. 157. Nutritional Anaemia in Infancy: The Influence of Iron Deficiency on Infant Health. By H. M. M. Mackay, L. Goodfellow, and A. Bradford Hill. [1931.] 2s. (2s. 2d.).
- No. 162. Intelligence and Disease. By Shepherd Dawson assisted by J. C. M. Conn. [1931.] 1s. (1s. 1½d.).
- No. 190. A Study of Growth and Development: Observations in Successive Years on the Same Children. By R. M. Fleming. With a Statistical Analysis by W. J. Martin. [1933.] 1s. 6d.

See also NUTRITION; RICKETS.

Dental Disease:

- No. 70. The Structure of Teeth in relation to Dental Disease. By J. Howard Mummery. [1922.] 2s. (2s. 1d.).
- No. 97. The Incidence of Dental Disease in Children. By the Committee for the Investigation of Dental Disease. [1925.] 1s. 6d. (1s. 7½d.).
- No. 140. Diet and the Teeth: An Experimental Study. Part I. Dental Structure in Dogs. By May Mellanby. [1929.] 17s. 6d. (18s.).
- No. 153. Diet and the Teeth: An Experimental Study. Part II. A.—Diet and Dental Disease. B.—Diet and Dental Structure in Mammals other than the Dog. By May Mellanby. [1930.] 2s. 6d. (2s. 8½d.).
- No. 159. The Influence of Diet on Caries in Children's Teeth (Interim Report). By the Dental Committee. [1931.] 6d. (7d.).
- No. 171. Facial Growth in Children, with Special Reference to Dentition. Part I, by Corisande Smyth. Part II, by Matthew Young. [1932.] 1s. 6d. (1s. 8d.).
- No. 191. Diet and the Teeth: an Experimental Study. Part III. The Effect of Diet on Dental Structure and Disease in Man. By May Mellanby. [1934.] 5s. (5s. 4d.).

Diphtheria:

- No. 115. The Prevention of Diphtheria. By J. Graham Forbes. [1927.] 2s. (2s. 1½d.).
- (Book). Diphtheria: its Bacteriology, Pathology, and Immunology. By the Bacteriological Committee. [1923.] 12s. 6d. (13s. 3d.).
- See also EPIDEMIOLOGY (Nos. 75, 137 and 195).

Dust: see VENTILATION, ETC.

Dysentery:

Reports upon Investigations in the United Kingdom of Dysentery Cases received from the Eastern Mediterranean:—

- No. 4. I.—Amoebic Dysentery and the Protozoological Investigation of Cases and Carriers. By Clifford Dobell. [1917.] *Out of print.*

- No. 5. II.—Report upon 878 Cases of Bacillary Enteritis. By L. Rajchman and G. T. Western. [1917.] *Out of print.*
- No. 6. III.—Report upon recovered Cases of Intestinal Disease in the Royal Naval Hospital, Haslar, 1915–16. By Paul Fildes and others.
- IV.—Report upon combined Clinical and Bacteriological Studies of Dysentery Cases from the Mediterranean. By S. R. Douglas and L. Colebrook. [1917.] 4s. 6d. (4s. 7½d.).
- No. 7. V.—Report upon 2,360 Enteritis "Convalescents" received at Liverpool from various Expeditionary Forces. By E. Glynn and others. [1918.] 6s. (6s. 2d.).

- No. 15. A Study of 1,300 Convalescent Cases of Dysentery from Home Hospitals: with special reference to the Incidence and Treatment of Amœbic Dysentery Carriers. By Clifford Dobell, H. S. Gettings, Margaret W. Jepps, and J. B. Stephens. [1918.] 1s. 3d. (1s. 4d.).
- No. 29. A Contribution to the Study of Chronicity in Dysentery Carriers. By W. Fletcher and Doris L. Mackinnon. [1919.] 9d. (10d.).
- No. 30. An Investigation of the Flexner-Y Group of Dysentery Bacilli. By H. S. Gettings. [1919.] 1s. (1s. 1d.).
- No. 40. Studies of Bacillary Dysentery occurring in the British Forces in Macedonia. By L. S. Dudgeon and others. [1919.] 3s. (3s. 1½d.).
- No. 42. A Study of the Serological Races of the Flexner Group of Dysentery Bacilli. By F. W. Andrewes and A. C. Inman. [1919.] 2s. (2s. 1½d.).

See also FOOD POISONING.

Encephalitis :

- No. 108. The Sheffield Outbreak of Epidemic Encephalitis in 1924. [1926.] 1s. 9d. (1s. 10½d.).

Enteric Infections :

- No. 9. A Report upon the Use of Atropine as a Diagnostic Agent in Typhoid Infections. By H. F. Marris. [1917.] 1s. (1s. 1d.).
- No. 48. A Report on the probable Proportion of Enteric Infections among Undiagnosed Febrile Cases invalided from the Western Front since October, 1916. By W. W. C. Topley, S. G. Platts, and C. C. Imrie. [1920.] 3s. (3s. 1½d.).
- No. 179. Chronic Enteric Carriers and their Treatment. By C. H. Browning with others. [1933.] 1s. 6d. (1s. 7½d.).

See also BACTERIOLOGY ; FOOD POISONING.

Epidemiology :

- No. 75. The Schick Test, Diphtheria and Scarlet Fever. By S. F. Dudley. [1923.] 1s. (1s. 1½d.).
- No. 111. The Spread of Droplet Infection in Semi-isolated Communities. By S. F. Dudley. [1926.] 1s. 6d. (1s. 7½d.).
- No. 120. An Inquiry into the Relationship between Housing Conditions and the Incidence and Fatality of Measles. By J. L. Halliday. [1928.] 1s. (1s. 1d.).
- No. 137. Scarlet Fever, Diphtheria, and Enteric Fever, 1895–1914: A Clinical-Statistical Study. By E. W. Goodall, M. Greenwood, and W. T. Russell. [1929.] 2s. (2s. 1½d.).
- No. 180. Epidemiological Study of Scarlet Fever in England and Wales since 1900. By Hilda M. Woods. [1933.] 1s. 3d. (1s. 4½d.).
- No. 192. Housing Conditions and Respiratory Disease. Morbidity in a Poor-class Quarter and in a Rehousing Area in Glasgow. By C. M. Smith. [1934.] 9d. (10d.).
- No. 195. Active Immunization against Diphtheria: its effect on the Distribution of Antitoxic Immunity and Case and Carrier Infection. By S. F. Dudley, P. M. May, and J. A. O'Flynn. [1934.] 3s. (3s. 2½d.).

See also SMALL-POX ; TUBERCULOSIS ; ETC.

Flying, Medical Problems of :

Reports of the Air Medical Investigation Committee :—

No. 28. The Sense of Balance and Stability in the Air. By Henry Head. [1919.] 9d. (10d.). (Included in No. 53.)

No. 37. The Effects of Diminished Tension of Oxygen, with especial reference to the Activity of the Adrenal Glands. By C. H. Kellaway. The Ear in relation to certain Disabilities in Flying. By S. Scott. [1919.] 1s. (1s. 1d.).

No. 53. The Medical Problems of Flying (including reports on oxygen want, selection of candidates for flying, sense of balance, and flying strain). [1920.] 6s. (6s. 4d.).

No. 84. The Application of the Air Force Physical Efficiency Tests to Men and Women. By L. D. Cripps. [1924.] 1s. 6d. (1s. 7½d.).

Food Poisoning :

No. 24. A Report on the Investigation of an Epidemic caused by *Bacillus aertrycke*. By H. Marrian Perry and H. L. Tidy. [1919.] 9d. (10d.).

No. 91. An Investigation of the Salmonella Group, with Special Reference to Food Poisoning. By W. G. Savage and P. Bruce White. [1925.] 3s. 6d. (3s. 8d.).

No. 92. Food Poisoning: a Study of 100 Recent Outbreaks. By W. G. Savage and P. Bruce White. [1925.] 2s. 6d. (2s. 8d.).

No. 103. Further Studies of the Salmonella Group. By P. Bruce White. [1926.] 5s. (5s. 2½d.).

Goitre :

No. 154. Iodine Supply and the Incidence of Endemic Goitre. By J. B. Orr. [1931.] 4d. (5d.). See also NUTRITION (Nos. 123, 201).

Haemoglobin : see BLOOD.

Hearing :

No. 166. Reports of the Committee upon the Physiology of Hearing. I.—The Localization of Sounds in the Median Plane. By J. H. Shaxby and F. H. Gage. II.—Some Factors in Auditory Localization. By H. E. O. James and Marion E. Massey. [1932.] 1s. (1s. 1½d.).

Heart :

No. 8. Report upon Soldiers returned as Cases of "Disordered Action of the Heart" (D.A.H.), or Valvular Disease of the Heart. By Sir Thomas Lewis. [1917.] 1s. (1s. 1d.).

No. 147. The Electrocardiogram. By W. H. Craib. [1930.] 1s. 3d. (1s. 4½d.).

Heredity : see IMMUNITY (No. 196).

Immunity :

No. 194. The Chemistry of Antigens and Antibodies. By J. R. Marrack. [1934.] 2s. 6d. (2s. 8d.).

No. 196. The Inheritance of Resistance to Infection in Animal Species. A Review of the Published Experimental Data. By A. Bradford Hill. [1934.] 1s. 3d. (1s. 4½d.).

See also EPIDEMIOLOGY.

Industrial Health :

The Annual Reports of the Industrial Health (formerly Fatigue) Research Board, and special reports on particular subjects, are published for the Council in separate series. The subjects dealt with include accident causation, rest pauses, spells of work, movement study, vocational selection, and problems of particular industries. A list can be supplied on application to the Secretary of the Board, 38, Old Queen Street, Westminster, S.W.1.

Influenza :

- No. 36. Studies of Influenza in Hospitals of the British Armies in France, 1918. [1919.] 3s. 6d. (3s. 8d.).
- No. 63. Studies in the Aetiology of Epidemic Influenza. By J. McIntosh. [1922.] 2s. 6d. (2s. 7d.).

Jaundice :

- No. 113. Spirochaetal Jaundice. By G. Buchanan. [1927.] 4s. (4s. 2d.).

Light Treatment :

- No. 131. Irradiation and Health. Two Experimental Studies. By Dora Colebrook. [1929.] *Out of print.*

Malaria : see QUININE.**Maternal Mortality : see CHILD LIFE and STREPTOCOCCAL INFECTIONS.****Measles : see EPIDEMIOLOGY (No. 120).****Milk : see TUBERCULOSIS, No. 189.****Miners' Dietsaries : see NUTRITION.****Miners' Diseases, etc. :**

- No. 89. Report on Miners' "Beat Knee," "Beat Hand," and "Beat Elbow." By E. L. Collis and T. L. Llewellyn. [1924.] 1s. 6d. (1s. 7d.).
See also JAUNDICE (No. 113).

Miners' Nystagmus : see VISION.**Nephritis :**

- No. 43. Albuminuria and War Nephritis among British Troops in France. By H. MacLean. [1919.] 2s. 6d. (2s. 8d.).
- No. 142. A Classification of Bright's Disease. By Dorothy S. Russell. [1929.] 8s. 6d. (8s. 10d.).
- No. 178. A Study of Nephritis and Allied Lesions. By J. Gray. [1933.] 2s. 6d. (2s. 8½d.).

Nerve Injuries :

Reports of the Committee upon Injuries of the Nervous System :—

- No. 54. The Diagnosis and Treatment of Peripheral Nerve Injuries. [1920.] 2s. (2s. 1½d.).
- No. 88. Injuries of the Spinal Cord and Cauda Equina. [1924.] 1s. 6d. (1s. 7½d.).

Nutrition :

- No. 13. An Enquiry into the Composition of Dietsaries, with special reference to the Dietsaries of Munition Workers. By Viscount Dunluce and Major Greenwood. [1918.] *Out of print.*
- No. 87. Report on the Nutrition of Miners and their Families. By the Committee upon Quantitative Problems in Human Nutrition. [1924.] 1s. 3d. (1s. 4d.).
- No. 105. Diets for Boys during the School Age. By H. C. Corry Mann. [1926.] 2s. 6d. (2s. 7½d.).
- No. 123. Iodine in Nutrition : a Review of Existing Information. By J. B. Orr and I. Leitch. [1929.] *See also GOITRE (No. 154).*
Out of print.
- No. 135. The Carbohydrate Content of Foods. By R. A. McCance and R. D. Lawrence. [1929.] *Out of print.*
- No. 146. The Antiscorvy Vitamin in Apples. By Mary F. Bracewell, E. Hoyle, and S. S. Zilva. [1930.] 9d. (10d.).
- No. 151. A Study in Nutrition. An Inquiry into the Diet of 154 Families of St. Andrews. By E. P. Cathcart and A. M. T. Murray, assisted by M. Shanks. *Out of print.*
- No. 155. Studies of Nutrition : The Physique and Health of Two African Tribes. By J. B. Orr and J. L. Gilks. [1931.] 2s. (2s. 2d.).

- No. 158. The Quantitative Estimation of Vitamin D by Radiography. By R. B. Bourdillon, H. M. Bruce, C. Fischmann, and T. A. Webster. [1931.] 1s. (1s. 1½d.).
- No. 165. Studies in Nutrition. An Inquiry into the Diet of Families in Cardiff and Reading. By E. P. Cathcart and A. M. T. Murray, assisted by M. Shanks. [1932.] 6d. (7d.).
- No. 167. Vitamins: A Survey of Present Knowledge. By a Committee appointed jointly by the Lister Institute and Medical Research Council [1932.] 6s. 6d. (7s. 0½d.).
- No. 175. Vitamin Content of Australian, New Zealand, and English Butters. By M. E. F. Crawford, E. O. V. Perry, and S. S. Zilva. [1932.] 1s. (1s. 1d.).
- No. 187. The Chemistry of Flesh Foods and their Losses on Cooking. By R. A. McCance and H. L. Shipp. [1933.] 2s. 6d. (2s. 8½d.).
- No. 201. The Determination of Iodine in Biological Substances. By C. O. Harvey. [1935.] 1s. (1s. 1½d.).
- See also CHILD LIFE; RICKETS; DENTAL DISEASE.

Pituitary Extract: see STANDARDS.

Pneumonia:

- No. 79. Bacteriological and Clinical Observations on Pneumonia and Empyemata, with special reference to the Pneumococcus and to Serum Treatment. By E. E. Glynn and Lettice Digby. [1923.] 5s. (5s. 3d.).

Pneumothorax, Artificial: see TUBERCULOSIS.

Print, Legibility of: see VISION.

Protozoan Infections:

- No. 59. A Report on the Occurrence of Intestinal Protozoa in the inhabitants of Britain. By Clifford Dobell. [1921.] 2s. (2s. 1½d.).

Psychology:

- No. 170. Studies in the Psychology of Delinquency. By G. W. Pailthorpe. [1932.] 2s. (2s. 2d.).

Quinine:

- No. 96. Clinical Comparisons of Quinine and Quinidine. By the Committee upon Cinchona Derivatives and Malaria. [1925.] 1s. (1s. 1d.).

Radium:

- No. 62. Medical Uses of Radium: Studies of the Effects of Gamma Rays from a large Quantity of Radium. By various authors. [1922.] 5s. (5s. 3d.).
- No. 90. Medical Uses of Radium: Summary of Reports from Research Centres for 1923. [1924.] 1s. (1s. 1d.).
- No. 102. Ditto for 1924. [1926.] 1s. 6d. (1s. 7d.).
- No. 112. Ditto for 1925. [1926.] 1s. 3d. (1s. 4d.).
- No. 116. Ditto for 1926. [1927.] 1s. (1s. 1½d.).
- No. 126. Ditto for 1927. [1928.] 1s. (1s. 1½d.).
- No. 144. Ditto for 1928. [1929.] 1s. (1s. 1d.).
- No. 150. Ditto for 1929. [1930.] 9d. (10d.).
- No. 160. Ditto for 1930. [1931.] 1s. (1s. 1d.).
- No. 174. Ditto for 1931. [1932.] 1s. 3d. (1s. 4½d.).
- No. 186. Ditto for 1932. [1933.] 1s. (1s. 1d.).
- No. 197. Ditto for 1933. [1934.] 9d. (10d.).
- No. 204. Ditto for 1934. [1935.]

Respiration:

- No. 193. Test for Respiratory Efficiency. By A. Moncrieff. [1934.] 1s. (1s. 1½d.).

Rheumatism: see CHILD LIFE (No. 114).

Rickets:

- No. 20. A Study of Social and Economic Factors in the Causation of Rickets, with an Introductory Historical Survey. By L. Findlay and Margaret Ferguson. [1918.] *Out of print.*
- No. 61. Experimental Rickets. By E. Mellanby. [1921.] 4s. (4s. 2d.).

- No. 68. Rickets: the Relative Importance of Environment and Diet as Factors in Causation. By H. Corry Mann. [1922.] 2s. 6d. (2s. 7½d.).
- No. 71. The Actiology and Pathology of Rickets from an experimental point of view. By V. Korenchevsky. [1922.] 4s. (4s. 3d.).
- No. 77. Studies of Rickets in Vienna, 1919-22. [1923.] 7s. 6d. (7s. 10½d.).
- No. 93. Experimental Rickets: The Effect of Cereals and their Interaction with other factors of Diet and Environment in producing Rickets. By E. Mellanby. [1925.] 3s. 6d. (3s. 8d.).

Salvarsan: *see* VENEREAL DISEASES; STREPTOCOCCAL INFECTIONS; STANDARDS, BIOLOGICAL (No. 128).

Scarlet Fever: *see* EPIDEMIOLOGY (Nos. 137, 180).

Scurvy: *see* NUTRITION (No. 146).

Shock, Surgical:

Reports of the Committee on Surgical Shock and Allied Conditions:—

- No. 25. Wound-Shock and Haemorrhage. [1919.] 4s. (4s. 5½d.).
- No. 26. Traumatic Toxaemia as a Factor in Shock. [1919.] 1s. (1s. 1d.).
- No. 27. Blood Volume Changes in Wound-Shock and Primary Haemorrhage. By N. M. Keith. [1919.] 9d. (10d.).

Small-pox:

- No. 98. Studies of the Viruses of Vaccinia and Variola. By M. H. Gordon. [1925.] 3s. 6d. (3s. 8½d.).
- No. 106. Small-pox and Climate in India. Forecasting of Epidemics. By Sir Leonard Rogers. [1926.] 2s. (2s. 1½d.).
- No. 143. Diagnostic Value of the "Vaccinia Variola" Flocculation Test. By W. L. Burgess, James Craigie, and W. J. Tulloch. [1929.] 1s. 3d. (1s. 4d.).
- No. 156. Further Investigations on the Variola-Vaccinia Flocculation Reaction. By James Craigie and W. J. Tulloch. [1931.] 3s. (3s. 2½d.).

Spectroscopy:

- No. 177. Apparatus for the Rapid Study of Ultra-Violet Absorption Spectra. By J. St. L. Philpot and E. H. J. Schuster. [1933.] 1s. 3d. (1s. 4½d.).

Spinal Deformities: *see* SURGERY (No. 161).

Standards, Biological:

- No. 69. I.—Pituitary Extracts. By J. H. Burn and H. H. Dale. [1922.] 1s. 6d. (1s. 7d.).
- No. 128. II.—Toxicity Tests for Novarsenobenzene (Neosalvarsan). By F. M. Durham, J. H. Gaddum, and J. E. Marchal. [1929.] 1s. 9d. (1s. 10d.).
- No. 183. III.—Methods of Biological Assay depending on a Quantal Response. By J. H. Gaddum. [1933.] 1s. (1s. 1d.).
- See also* VENEREAL DISEASES (No. 44) and NUTRITION (No. 158).

Statistics (MISCELLANEOUS).

- No. 16. A Report on the Causes of Wastage of Labour in Munition Factories. By Major Greenwood. [1918.] 1s. 6d. (1s. 7d.).
- No. 60. The Use of Death-rates as a Measure of Hygienic Conditions. By John Brownlee. [1922.] 3s. (3s. 1½d.).
- No. 95. Internal Migration and its Effects upon the Death-rates: with Special Reference to the County of Essex. By A. B. Hill. [1925.] 3s. 6d. (3s. 8d.).

Streptococcal Infections:

- No. 119. A Study of some Organic Arsenical Compounds with a view to their use in certain Streptococcal Infections. By L. Colebrook. [1928.] 1s. 3d. (1s. 4d.).

Surgery :

- No. 125. A Study of Intracranial Surgery. By H. Cairns. [1929.] *Out of print.*
- No. 138. The Preparation of Catgut for Surgical Use. By W. Bulloch, L. H. Lampitt, and J. H. Bushill. [1929.] 4s. (4s. 3d.).
- No. 161. The Intervertebral Discs. Observations on their Normal and Morbid Anatomy in relation to certain Spinal Deformities. By O. A. Beadle. [1931.] 2s. (2s. 2d.).
- See also* BURNS ; SHOCK, SURGICAL.

T.N.T. Poisoning :

- No. 11. The Causation and Prevention of Tri-nitro-toluene (T.N.T.) Poisoning. By Benjamin Moore. [1917.] 1s. (1s. 1½d.).
- No. 58. T.N.T. Poisoning and the Fate of T.N.T. in the Animal Body. By W. J. O'Donovan and others. [1921.] 3s. (3s. 1½d.).

Tuberculosis :

- No. 1. First Report of the Special Investigation Committee upon the Incidence of Phthisis in relation to Occupations.—The Boot and Shoe Trade. [1915.] 3d. (3½d.).
- No. 18. An Investigation into the Epidemiology of Phthisis Pulmonalis in Great Britain and Ireland. Parts I and II. By John Brownlee. [1918.] *Out of print.*
- No. 22. An Inquiry into the Prevalence and Aetiology of Tuberculosis among Industrial Workers, with special reference to Female Munition Workers. By Major Greenwood and A. E. Tebb. [1919.] 1s. 6d. (1s. 7d.).
- No. 33. Pulmonary Tuberculosis : Mortality after Sanatorium Treatment. By Noel D. Bardswell and J. H. R. Thompson. [1919.] 2s. (2s. 2d.).
- No. 46. An Investigation into the Epidemiology of Phthisis in Great Britain and Ireland : Part III. By John Brownlee. [1920.] 2s. 6d. (2s. 7½d.).
- No. 67. Report on Artificial Pneumothorax. By L. S. T. Burrell and A. S. MacNalty. [1922.] 2s. 6d. (2s. 8d.).
- No. 76. Tuberculosis in Insured Persons accepted for Treatment by the City of Bradford Health Committee. By H. Vallow. [1923.] 6d. (7d.).
- No. 83. Tuberculosis of the Larynx. By Sir St. Clair Thomson. [1924.] 2s. 6d. (2s. 8d.).
- No. 85. An Inquiry into the After-Histories of Patients treated at the Brompton Hospital Sanatorium at Frimley during the years 1905–14. By Sir P. H.-S. Hartley, R. C. Wingfield, and J. H. R. Thompson. [1924.] 1s. 6d. (1s. 7d.).
- No. 94. Tuberculin Tests in Cattle, with special reference to the Intradermal Test. By the Tuberculin Committee. [1925.] 3s. (3s. 3d.).
- No. 122. The Intradermal Tuberculin Test in Cattle : Collected Results of Experience. By J. B. Buxton and A. S. MacNalty. [1928.] 1s. 6d. (1s. 7½d.).
- No. 149. Tuberculosis in Man and Lower Animals. By H. H. Scott. [1930.] *Out of print.*
- No. 152. Studies of Protection against Tuberculosis : Results with B. C. G. Vaccine in Monkeys. By A. Stanley Griffith. [1931.] 9d. (10½d.).
- No. 164. The Value of Tuberculin Tests in Man with special reference to the Intracutaneous Test. By P. D'Arcy Hart. [1932.] 2s. (2s. 6d.).
- No. 172. Tuberculosis Disease in Children : Its Pathology and Bacteriology. By J. W. S. Blacklock. [1932.] 3s. (3s. 6d.).
- No. 182. Tuberculous Bacillæmia, A Review. By G. S. Wilson. [1933.] 2s. 6d. (2s. 8d.).

- No. 184. The Eradication of Bovine Tuberculosis. By L. Jordan. [1933.] 2s. (2s. 2d.).
- No. 189. Tuberculous Infection in Milk. A Report by the Department of Health for Scotland. [1933.] 9d. (10d.).

Venereal Diseases :

- No. 14. The Wassermann Test. By the Committee upon Pathological Methods. [1918.] *Out of print* : see No. 129.
- No. 19. The Laboratory Diagnosis of Gonococcal Infections. Methods for the Detection of *Spironema pallidum*. By the Bacteriological Committee. *New Edition*. [1923.] 1s. 6d. (1s. 7½d.).
- No. 21. The Diagnostic Value of the Wassermann Test. By the Committee upon Pathological Methods. [1918.] *Out of print*.
- No. 23. An Analysis of the Results of Wassermann Reactions in 1,435 Cases of Syphilis or Suspected Syphilis. By Paul Fildes and R. J. G. Parnell. [1919.] 2s. (2s. 1d.).
- No. 41. (I.) An Investigation into the Ultimate Results of the Treatment of Syphilis with Arsenical Compounds. By Paul Fildes and R. J. G. Parnell. (II.) A Clinical Study of the Toxic Reactions which follow the Intravenous Administration of "914". By R. J. G. Parnell and Paul Fildes. [1919.] 2s. (2s. 1d.).
- No. 44. Reports of the Special Committee upon the Manufacture, Biological Testing, and Clinical Administration of Salvarsan and of its Substitutes. I. [1919.] 1s. (1s. 1d.).
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