infancy. Not many cases make a complete recovery from a severe attack. Robb¹³ gives the proportion as 8.8 per cent., but a certain percentage more had only a slight change mentally and nervously. However, a large proportion of cases which have encephalitis lethargica are permanently and severely damaged.

Pathologically there may be no naked-eye lesions. In the acute stage microscopical lesions are diffuse, and tend to be in the basal nuclei, the cerebrum, and mid-brain, especially the latter. Occasionally they are in the cortex cerebri, pons, medulla, and posterior cornua of the cord. They are not in the anterior cornua. Later the typical cuffing appearance is seen round the perivascular lymphatic spaces. There is a similarity between the distemper and epidemic encephalitis. This is discussed by Pugh¹⁴ and in articles in the *Lancet*.¹⁵ In the distemper cases there was sleepiness, hiccup, and ocular palsies, and there were similar "cuff" lesions in the brain. This is an argument in favour of the encephalitis syndrome being caused by more than one virus, and might even support the idea that encephalitis lethargica is really a variety of influenza.

Treatment consists in alleviating distress, providing rest to the nervous tissues, and aiding the elimination of toxins. Lumbar puncture may relieve pressure, and various chemical drugs can be given intravenously. Belladonna and hyoscine may be useful in the later stages, and for sequelae, but they are not so important for the acute stages. For sequelae trypan-blue is the latest drug recommended.¹⁶ Vaccines have been tried,¹⁷ and the serum of convalescents is, as with other virus diseases, perhaps the most likely method of affording some immediate action on the disease and its acute stages. Up to the present, however, this does not appear to have been tried to any extent.

EXANTHEMATAL ENCEPHALITIS

This may follow an acute infectious disease, especially measles. Encephalitis of measles is often severe in effect at first, but tends to clear up and leave no bad effects.

One patient of mine, a child of 8 years, developed encephalitis after measles. She became unconscious, had a high temperature, and a cerebro-spinal fluid under pressure, but with only a very moderate cell increase. The optic disks were normal, and there were no signs of other disease. She remained "blind" and semiconscious for some seven or eight days, and then slowly improved and made a complete recovery.

Pathologically there are perivascular zones of demyelination in the brain and cord in fatal cases, and the lesion is very like that of vaccinia encephalitis.¹⁸ Measles does not seem to produce such severe after-effects as do the neurotropic virus diseases. It may not be a true inflammatory process, but rather a toxic condition. Acute toxic encephalitis may occur in diphtheria.¹⁹

REFERENCES

- ¹ Jorge, R.: *Lancet*, 1932, i, 215, 267.
- ² Brain, W. R.: *British Medical Journal*, 1931, i, 81.
- ³ Bergman, G.: *Hygeia*, September 15th, 1932, p. 673. Quoted in *British Medical Journal*, February 4th, 1933, *Epitome*, para. 73.
- ⁴ Rolleston, J. D.: *British Medical Journal*, 1930, i, 153.
- ⁵ Horder, T.: *Lancet*, 1929, i, 1301; *ibid.*, 1930, ii, 307.
- ⁶ Hekman, J.: *Bull. de l'Acad. de Méd.*, 1930, ciii, 539. Quoted in *British Medical Journal*, 1930, i, *Epitome*, para. 541.
- ⁷ Jitta, N. M. J.: *Bull. Office Internat. d'Hyg. Publ.*, October, 1931, p. 1804. Quoted in *British Medical Journal*, 1932, i, *Epitome*, para. 31.
- ⁸ Peremans, G.: *Le Scalpel*, November 17th, 1923. Quoted in *Lancet*, 1924, i, 143.
- ⁹ Bruno, J.: *Munch. med. Woch.*, September 9th, 1913, p. 1995.
- ¹⁰ Lovett, R. W., and Sheppard, P. A. E.: *Boston Med. and Surg. Journ.*, 1911, clxiv, 737.
- ¹¹ Cleland, J. B.: *Proc. Roy. Soc. Med.* (Section of Pathology), 1918-19, xii, Part III, 33.
- ¹² Macnamara, Jean, and Morgan, F. G.: *Lancet*, 1932, i, 469.
- ¹³ Robb, A. G.: *British Medical Journal*, 1927, i, 615.
- ¹⁴ Pugh, P. P.: *Lancet*, 1926, ii, 950.
- ¹⁵ *Lancet*, 1926, i, 29; 1927, i, 619; 1927, i, 766.
- ¹⁶ Laignel-Levastine and Sterne: *Bull. et Mém. Soc. Méd. des Hôp. de Paris*, May 23rd, 1932, xlviii, p. 689. Quoted in *Lancet*, 1932, i, 1319.
- ¹⁷ Marie and Poincloux: *Bull. de la Soc. de Therap.*, March 12th, 1924. Quoted in *Lancet*, 1924, i, 814.
- ¹⁸ Wohlwill, F.: *Lancet*, 1931, ii, 599.
- ¹⁹ Hall, A. G.: *Canadian Med. Assoc. Journ.*, May, 1932, p. 566. Quoted in *British Medical Journal*, 1932, ii, 47.

TREATMENT OF CARCINOMA OF THE BREAST BY RADIUM EMANATION

BY

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In writing on any form of radium treatment at the present time one is faced by the dilemma that either one's conclusions are premature or one's methods are out of date. It is, however, only by the accurate record of new technical methods and of their results that progress can be made, and even a small group of cases of the same class treated by the same methods and carefully watched is of definite value. From this point of view the small group of fifty-two cases of carcinoma of the breast here recorded is of interest, since all the cases were treated with very nearly the same technique, radon seeds, and over a period of three years up to one year ago, more recent cases having been excluded.

The technical advantages of seeds over needles are very obvious to those who have used the former. Yet in this country they have scarcely received the recognition which they deserve, while on the Continent they are almost ignored. It is asserted by those who have not used them that they cannot be introduced with accuracy, and that they act for too short a time to be effective. With proper apparatus, however, almost mathematical accuracy can be obtained, and the results here recorded are at least evidence of their effectiveness. It will, of course, be many years before sufficient evidence is accumulated to show whether irradiation or amputation gives the best results, and it is possible that both may be replaced by beam radiation with large quantities of radium or by some other form of treatment. At present, however, it would seem to be useful to place on record the results which have been obtained by a uniform and systematic technique.

The technique which I now adopt has been slightly modified from that which I described three years ago in an article on the use of radon seeds (*British Medical Journal*, August 23rd, 1930). Radon seeds are implanted into the tissues beneath the breast in such a manner that the whole of the breast and its lymphatic drainage is exposed to a uniform radiation sufficient to destroy any carcinoma cells whether in the tumour, in the breast, or in the lymphatics. The seeds are introduced by means of a special introducer described in the article mentioned, and consisting essentially of a long hollow needle and a rotating barrel, which holds the seeds. The seeds can be introduced to any depth and planted in long columns. Both the columns and the seeds in each column can be accurately spaced from one another; this is of vital importance, as otherwise some portion of the suspected tissues may escape irradiation. About 100 seeds may be introduced, each containing 0.5 to 1 millicurie, the precise amount varying with the dimensions of the breast, and the bulk of the seeds will lie in the fascia covering the pectoralis major. Through a single puncture it is quite possible, by displacing the skin, to insert four parallel rows of seeds in the fascia beneath the tumour. Through a second puncture another group can be inserted in the same situation, but in lines at right angles to the first,

thus forming a kind of grid of seeds beneath the tumour, and actually in the primary area of its lymphatic drainage. Where the tumour is very large a layer of seeds may be inserted into its substance, but no seeds should be inserted in the more superficial portions of the tumour, as these will only destroy the skin. Through a puncture in the axilla two rows of seeds are deposited beneath the pectoralis major about 1 to 2 cm. below the line of the axillary vessels, and through the same puncture two parallel rows are introduced along the axillary border of the pectoralis major. The whole arrangement aims at a uniform irradiation of the breast itself and of the lymphatic drainage; in fact, one should endeavour to perform a complete Halstead by means of radiation. The natural tendency to concentrate on the tumour should be avoided, and its disappearance should be used as an index of the adequacy of the radiation as a whole rather than as the immediate object.

A few days after the introduction of the seeds it will be noticed that the tumour has become softer, and at the end of a week the tumour will have lost the induration which is so characteristic of carcinoma. Small tumours may disappear completely in six weeks, and even large fungating masses may have disappeared and the surface have healed in three months. Secondary glands and recurrences disappear with greater ease than the original tumour, and in the majority of cases all traces of active carcinoma will have disappeared in three months. It must not be imagined that this indicates the cure of the patient, but it certainly represents a very substantial step in that direction. It is an open question whether the patient is any more secure after a complete amputation of the breast.

In advanced cases and in elderly patients there can be no possible question but that irradiation by means of seeds presents immense advantages. Although a general anaesthetic is required, the whole procedure takes less than fifteen minutes, and, as it is carried out through a few small punctures, the patient may go home the next day. In a younger patient with an early carcinoma the problem is more difficult, and I am fully aware of the grave responsibility involved in suggesting that under these conditions the breast should not be amputated. On the other hand, it is a very grave responsibility to advise amputation of the breast if an equally satisfactory result can be obtained by such a simple means as the introduction of radon seeds, and with no disfigurement. It has been my custom in such cases to advise a trial of radium, with the express condition that if, in three months, the result is not completely satisfactory, the breast must be removed.

One small point in technique should be remembered. Immediately after the insertion of radium the whole of the breast and the surrounding region should be covered with an ointment consisting of equal parts of castor oil and zinc ointment, and this should be removed and replaced daily. If this is done from the outset there will be little or no skin reaction, and the patient will be saved from the discomfort of the ulceration which would otherwise occur.

CASES TREATED

The cases were divided into three groups—early, advanced, and inoperable. In the early cases a small local tumour was present, not adherent to either the skin or the fascia, and with no discoverable enlargement of the glands. In the advanced group the tumour was attached either to the skin or the fascia, and in most instances there were secondary deposits in the glands. The inoperable cases showed, for the most part, large ulcerating masses of carcinoma fixed to the chest wall with secondary deposits in the glands.

In the early group there were twelve cases; of these, four died from generalization over an average period of three and

a half years, and eight remained alive and well after an average period of two and a half years. Of the four who died one failed to respond at all, and an amputation was performed four months later. In another a local excision followed by radium was satisfactory until the full term of a pregnancy eighteen months later, when a local recurrence appeared which was treated satisfactorily for the time being; two years later, however, the patient died of generalization. Of the successful cases three had small recurrences, which were again treated by radium, but they all remain well and free from any further recurrence after more than three years.

Of the twenty-nine advanced but operable cases seven died from generalization after an average of eighteen months, two died from other causes at fifteen months with no recurrence, and twenty are alive and well at periods up to four years. Of the cases which remain well, an amputation was performed in three: one for a local recurrence after eighteen months, one for a suspected recurrence which, however, was not present on pathological examination, and one because after four months there was no reaction whatever. In three other cases small recurrences were again treated with radium with success after periods of twelve, eighteen, and twenty months respectively.

Of the eleven inoperable cases only one remains alive and well after three years. This, however, is scarcely surprising, considering that the average age of the remaining ten was 70, and that four died of old age and six of generalization (one at 86). In every case the tumour was enormously reduced in size, and in most cases complete healing was secured. The patient who remains alive and well was a woman of 50 who had a recurrence after a complete Halstead performed twelve years before. The recurrence formed a large mass fixed to the costal cartilages and to the skin, but it disappeared entirely with radium, and has not recurred. Some of these cases were very advanced, one having a huge fungating tumour of four years' standing, with a large mass of secondary glands in the axilla and a few above the clavicle. Complete healing with disappearance of all the glands was obtained in four months, but the patient died of dissemination nineteen months after treatment, five and a half years after the onset of the disease.

Fifty-two Cases of Carcinoma of the Breast treated with Radon Seeds

	Well	Average Period	Died of Generalization	Average Period	Died of Other Causes	Total
Early... ..	8	2½ years	4	3½ years	—	12
Advanced ...	20	2½ "	7	1½ "	2	29
Inoperable...	1	3 "	6	1 year	4	11

In recording these cases my object is to present the facts as they have emerged, and not to make any claim either for or against radium as contrasted with operation. Of the three groups the early cases are definitely disappointing, because, although 66 per cent. remained free after an average of two and a half years, this is far too short a period on which to base any opinion. This short period is due to the fact that it was only after a considerable experience of advanced cases that I ventured to treat those in which the disease was still early. My feeling at the moment is that such treatment is justifiable provided the patients are kept under close observation. In almost every instance all trace of carcinoma will disappear, but any recurrence would, I feel, be better treated by complete amputation than by a repetition of the radium. It is not, however, always possible to obtain consent.

The advanced cases show a much more satisfactory result, 70 per cent. remaining alive and well after an average of two and a quarter years. Moreover, among these only six have required any further treatment. In some of these cases very large tumours were present; in one the breast was distended by a tumour which had been growing steadily for over a year, but even in this

case the tumour disappeared completely, leaving an almost normal breast. These results compare very favourably with those obtained by amputation.

In the inoperable cases, where no alternative method of treatment was possible, the results quite exceeded expectation; large fungating masses disappeared, and ulcerating surfaces healed over. As most of the patients were 70 years of age or more, this was really all that one could ask, and in the majority of cases the patient was saved from a distressing condition. It is remarkable, however, that even at the age of 86, extensive generalization can occur. It would, of course, have been impossible if the ulcer had not been treated, since the patient would have died of exhaustion.

It will be seen, then, that in inoperable cases radium can give a relief which cannot be otherwise obtained. In advanced cases the evidence seems to show that radium can give results at least as good as those obtained by amputation, at the cost of far less inconvenience and with no disfigurement. In early cases it may certainly be used with a considerable prospect of success, on condition that the case is most closely watched, and with the stipulation that in the event of a recurrence a complete amputation shall immediately be performed. Most surgeons will agree that the wider their experience of carcinoma the less inclined they feel to dogmatize either as to the treatment to adopt or the result which may be expected. Sometimes they are surprised by a brilliant result in an apparently hopeless case, and have some compensation for the many disappointments they are bound to meet. The use of radon seeds in the treatment of carcinoma of the breast furnishes them with a method which is applicable to almost every case. There is no case so advanced that local relief is impossible, while in the earliest cases I am convinced, from my own experience, that the surgeon is fully justified in offering this alternative to amputation, and that he need have no fears of prejudicing the interests of his patients. We are all only too familiar with patients who refuse to ask for help until the condition is so far advanced that it can no longer be concealed, and I feel that if the possibilities of radium were more widely known patients would be inclined to seek advice at a much earlier date, to their own inestimable advantage.

THE INTRADERMAL TUBERCULIN TEST IN NON-TUBERCULOUS ADULTS

BY

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AND

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The investigation here described had for its object the study of the variations in "tuberculin sensitivity" manifested by adults free from clinically recognizable tuberculosis and the comparison of the findings in non-tuberculous with those in clinically tuberculous groups.

One of us (S. L. C.) had already published, with his colleague Dr. S. B. H. Walker, the results of preliminary studies on this subject, and he makes some further use of the material then collected for the purpose of the present inquiry. The other (A. C. E.), as pathologist to the Denbighshire Mental Hospital, was in a position to carry out tuberculin tests on a considerable number of patients suffering from mental symptoms only, but otherwise in average bodily health.

The tests were arranged so as to correspond as closely as possible with those previously carried out in Cardiff. One of us (S. L. C.) prepared the dilutions of tuberculin on standard lines and supplied them as required so that

they should be used fresh. The other (A. C. E.), having worked for some time in the tuberculosis laboratory at Cardiff, was in a position to carry out the tests and read the results on lines similar to those applied in the previous series.

The tuberculin used was selected for us as of standard strength by Dr. R. A. O'Brien, director of the Wellcome Physiological Research Laboratories. Its description is as follows: "P.T. No. B 1648. B. W. and Co." Dilutions in tenths were prepared with 0.5 per cent. carbolic in normal saline solution, ranging from 1 in 10 to 1 in 100,000.

Previous observations having satisfied us that all persons giving a definite positive reaction to any given dilution tend to react still more markedly to the next in order of strength, we decided to start the tests on each individual with the highest dilution and to excuse all positive "reactors" from further tests, applying successively stronger dilutions to the "negatives" only. In this way we gradually narrowed down the "negatives" to those failing to react to a dilution of 1 in 10.

"Control" tests with "glycerin broth" were omitted, previous observations having satisfied us that these are always negative until strong concentrations are reached. The non-specific reactions which tend to occur with very strong concentrations of "glycerin broth" have been shown by D'Arcy Hart to be confined to those persons who also react to tuberculin; so the possibility of non-specific reactions need not be taken into account.

Intradermal tuberculin tests on these lines were applied to three successive series of persons under treatment in the mental hospital: a first male group of 304, a second male group of 141, and a female group of 150 persons. In the tables which follow the two male series have been combined into one group of 445 persons for comparison with the female group.

The following table shows, by sexes, the percentages of persons reacting to the various dilutions of tuberculin used.

TABLE I.—*Tuberculin-sensitivity Variations in Terms of "End-point" of Reactivity in Healthy Persons*

	Dilutions					
	1 in 100,000	1 in 10,000	1 in 1,000	1 in 100	1 in 10	Negative to 1 in 10
Males (445): Positive per cent.	14.1	45.8	88.3	96.6	99.1	0.9
Females (150): Positive per cent.	21.3	58.0	88.0	93.3	97.3	2.7

The female group, while including a larger number of negatives than the male, showed a decidedly higher percentage of "positive" reactors with the higher dilutions. It will be noted, too, that while 85.9 per cent. of the males and 78.7 per cent. of the females were "negative" to a dilution of 1 in 100,000, only 11.7 per cent. of males and 12 per cent. of females were negative to 1 in 1,000. This point is stressed as a reminder of the fact that, while "positive" is an absolute term, the expression "tuberculin negative" is relative only, and depends on the technique employed and the dilution of tuberculin used. The von Pirquet scarification method, for instance, when carried out with undiluted old tuberculin, has been shown to be not quite so stringent a test as the intradermal inoculation of a 1 in 1,000 dilution of the same tuberculin. "Negatives" to the von Pirquet test, therefore, may be taken to include at least 10 per cent. of persons who would prove to be "positive" if tested intradermally with 1 in 100 and 1 in 10.

For comparison with the above the results of intradermal tuberculin tests in 100 persons, forty-five males and fifty-five females, suffering from active pulmonary tuberculosis are set forth in Table 1A.

It was not thought safe to give intradermally of 1 in 100 and 1 in 10 to actively tuberculous persons, so a final concentration of 1 in 500 was used instead. Here again the females included a larger percentage of "negatives" than the males, but, in the higher dilutions, the findings