Cancer Hospital (Free); Dr. J. Patterson, pathologist to Charing Cross Hospital; and Dr. Rouillard, Waterloo Hospital, for samples of blood and for clinical diagnoses.

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TREATMENT OF CARCINOMA IN THE PHARYNX AND LARYNX BY IRRADIATION*

BY

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In this brief survey I would like to emphasize a few points. They are: (1) operation should be done where possible; (2) all patients undergoing irradiation treatment should be treated as in-patients; (3) radium has its particular uses, and so has x-ray treatment.

Apart from growths which are better treated by irradiation because of their histology or their position, I will say with all emphasis that where (with due consideration of anatomical and histological limitations) an operation can be adequately performed, that is the treatment of choice. Of course irradiation can be used as an aid to operation, but this I will discuss later. Speaking generally, the results of operation are more satisfactory than those of irradiation alone—partly no doubt because the cases for operation are carefully selected and are not so advanced.

The suitability of a growth for irradiation depends on its histological character and its situation. If the cells are young and undifferentiated and the growth is rapid and large it is better treated by irradiation, because such a growth is radiosensitive, and at the same time the results of operation alone are so unsatisfactory. On the other hand, if an epithelioma is of the more mature type with a good deal of fibrous tissue, or has been treated previously by irradiation or operation so that there is an increase in scar tissue, it has little radiation-sensitivity and is better operated on.

Now let us consider the subject with regard to the position of the carcinoma. We know that carcinomata arising in certain sites only slightly removed from others are especially sensitive to irradiation treatment and the results are good. The tonsil, if the growth has not become adherent to the more solid structures, is particularly suitable for interstitial irradiation. My cases were all rather advanced and all had glands, but, excluding one patient who is alive and well after seven and a half years, the average life is eleven and a half months for all.

Intrinsic carcinoma of the larynx, if it has not spread posteriorly to the arytenoids or anteriorly to the epiglottis, is particularly susceptible to irradiation—so also is epithelioma of the soft palate—and there is no resulting deformity or alteration of voice. Firm fixation of the growth and involvement of muscle and cartilaginous or

bony tissues are indications that irradiation alone will not be successful. Here are Coutard's figures for 1937.

Epithelioma of palato-tonsillar region . . .	66 cases—32% 5-year survival
" pharynx	226 " —11% " "
" larynx	126 " —24% " "

In comparing results five years is a useful period to take, but at this point I would like to mention that our President in 1934 had a case of carcinoma of the larynx which had recurred twenty-four years after operation. It was successfully treated by irradiation.

If there are glands present the results of irradiation are not so good. Glands are more resistant than the primary growth: five of my series of eighteen cases of extrinsic carcinoma of the larynx which have lost the primary growth still have glands that can be felt. Unfortunately nearly all the cases we see have glandular enlargement, except, of course, the intrinsic carcinomata.

Though metastases are associated with irradiation treatment, I am aware of no grounds for saying, nor has it been proved, that metastases are *encouraged* by irradiation. The survival period of the patient is increased by irradiation, which also is so often employed as a forlorn hope for extensive and inoperable cases. All it can do in such cases is to heal an ulcer, stop haemorrhage and pain, and otherwise ease local discomfort.

Comparative Results

In comparing results we must also remember that operation cases are of necessity hospitalized, whereas many of those treated by irradiation attend as out-patients and are ill clad, under-fed, have dirty mouths, and have to travel home after each treatment in all weathers. There is no doubt that very much better results would be obtained with irradiation if the patients could be taken into hospital. The statistics of private patients bear out the above facts.

Irradiation has its uses in combination with operation. It destroys the young and active cells of the growth and renders an adherent growth more movable. Coutard advises operation before the twenty-fifth day after irradiation—that is, before the reappearance of any new cells and any skin reaction. Hautant also advocates irradiation before operation. Although some believe they have had better results from their operations by using irradiation afterwards, Coutard is not much in favour of it: it is the scar tissue that limits the usefulness of the radiation in these cases.

Methods of Irradiation

With reference to the different modes of irradiation, I limit my treatment to the use of radium needles or radon seeds, and those requiring external irradiation I refer to Mr. Carter Brain or Mr. White Phillips. On the whole I think I get better results with radium needles than I do with radon seeds. The dosage of the latter I feel is initially uncertain, and radium needles give just as big a dose at the end of the week of insertion, when it is wanted most.

Care is required in the spacing of the needles if they are to be completely effective; also, the results are better if there is a previous wide external application of radiation. Interstitial irradiation with needles is more effective than external irradiation in the treatment of the older cell type of growth. Needles are indicated particularly in carcinoma of the tonsil, soft palate, and intrinsic carcinoma of the larynx, using the fenestration method. Harmer has had a 75 per cent. five-year survival result. One of my patients is alive and well after eight years.

* Read in the Section of Oto-Rhino-Laryngology at the Annual Meeting of the British Medical Association, Plymouth, 1938.

Extrinsic carcinoma of the larynx and other growths involving the pharynx are unsuitable for interstitial irradiation. Of eighteen cases that I have had treated by external irradiation all had glands, and in five the growth has disappeared comparatively quickly, but the glands are still palpable after two years. I have had poor success with post-cricoid carcinoma, my few patients all dying within six months.

X-ray and radium beam treatment are outside my province, but it is generally accepted that deep x rays are more satisfactory than the beam method, as they can be applied at a greater distance from the skin and for shorter time-doses than with the present small amounts of radium available for beam treatment. It must be remembered that irradiation renders a growth more resistant to its rays on a second occasion, and at the same time the normal tissues are also more sensitive; therefore a full carcinomacidal dose should be given at the first treatment.

As I have said, x rays are the best treatment for rapidly growing carcinomata, and they are the only treatment for extensive growths and serious gland involvements. Coutard gets good results with external irradiation of intrinsic carcinoma of the larynx, but I think the fenestration method is superior. The technique of treatment by irradiation is always being improved, with better results, and I expect still better results with an improvement in the facilities and in the condition of the patients.

HELIUM IN ANAESTHESIA

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Helium, like nitrogen, is a physiologically inert gas. But it is very much lighter. An artificial atmosphere of normal oxygen content (21 per cent.), but with 79 per cent. of helium replacing the normal nitrogen, is only one-third as heavy as ordinary air. It should require only one-third the amount of force to move it (force = mass $\times$ acceleration) and it should pass through narrow apertures twice as easily (the rate of diffusion of gases is inversely proportional to the square root of their densities).

Helium-oxygen mixtures have been suggested for deep-sea divers and caisson workers because of their rapid diffusibility (and low coefficient of solubility), which allows of quicker passage from the blood to the alveoli and consequently quicker decompression. Sayers and Yant (1926) found that small animals subjected to pressures of 10 atmospheres for one to five hours could be decompressed from helium-oxygen in one-third to one-quarter the time required for nitrogen-oxygen.

Lemmer and Rovenstine (1935) proposed putting this low solubility to practical use in anaesthesia. Their experiments on different gases (with the object of preventing post-operative atelectasis) showed that its actual absorption from the alveoli into the blood was the slowest of nine different gases tested. But it has another potential

use in anaesthesia—its facility in passing through narrow apertures. Barach and Eckman (1935) proved experimentally that 25 to 50 per cent. less pressure was required to move helium-oxygen mixtures. Eversole (1937), using the mixture clinically in seventy-two patients with respiratory obstruction, claimed nearly 90 per cent. of successful results. It has also been used in the treatment of bronchial asthma and in respiratory paralysis due to spinal anaesthesia.

The British Oxygen Company very generously presented one of us (W. S. S.) with a ten-cubic-foot cylinder of helium, which until recently was unobtainable except in the United States. The company can now supply it. This was tried in half a dozen cases during cyclopropane anaesthesia, but as the patients had no respiratory obstruction and were already breathing with the remarkable calmness and quiet typical of cyclopropane it had no apparent effect.

Personal Experiments

As no patients with respiratory difficulties were available personal experiments were carried out with artificial obstructions.

A Foregger-Waters soda-lime canister and rebreathing bag were used. The face-piece was replaced by an intratracheal adapter, to which was fitted a rubber mouth-piece which carried a screw clamp. This clamp was tightened until considerable constriction was caused. Actually a Magill tube of 5 mm. internal diameter was compressed until the lumen was about $\frac{1}{2}$ mm. wide and 8 mm. long. The subject then breathed in and out of the bag through the soda lime and through the constriction. A quarter of a litre of oxygen per minute was allowed to enter the bag through a flowmeter, while the expired carbon dioxide was of course removed by the soda lime.

In one series of experiments air only was used, in the other a helium-oxygen mixture of approximately similar percentage. In every case the subject breathed through the constriction until dyspnoea became intolerable. The times were taken by stop-watch.

In each experiment with helium the bag was emptied and refilled after the first half-dozen breaths in order to get rid of some of the residual nitrogen from the lungs. By refilling the bag several times it might be possible to improve upon our figures.

As we were using ourselves as subjects we disregarded Home Office regulations about killing the experimental animals at the close of the session. This led us into a trap which invalidated our first series of results. We tried to obtain many readings in one evening, and very soon found that the fatigue caused by semi-strangulation produced increasingly rapid intolerance to a repetition of the process.

The times given below were all taken after allowing a sufficient interval for complete recovery. The constriction caused by the screw clamp remained constant throughout.

Times Taken in Breathing to Exhaustion Point.

No. 1 subject, W. S. S. Aged 43, heavy smoker.

Nitrogen-oxygen (Ordinary Air, Regenerated)	Helium-oxygen, Regenerated
3 min. 15 sec.	6 min. 43 sec.
4 min. 13 sec.	7 min. 34 sec.
4 min. 47 sec.	7 min. 35 sec.
3 min. 50 sec.	8 min. 10 sec.
3 min. 59 sec.	7 min. 35 sec.
4 min. 30 sec.	7 min. 26 sec.
Average 4 min. 5 sec.	Average 7 min. 30 sec.