Treatment of Carcinoma of the Thyroid with Radioiodine

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Carcinoma of the thyroid is not a common disease: Table I shows the mortality from malignant tumours of the thyroid in England and Wales to be between 300 and 400 persons per annum. A registration rate of between 1 and 2 cases per 100,000 population has been recorded in some cancer registries.

TABLE I.—*Malignant Tumours of Thyroid. Comparative Mortality Figures for England and Wales, 1959-61*

	Deaths: Annual Average over 3 Years		
	Males	Females	Total
From malignant tumours of thyroid ..	100*	277*	377*
" " " " lung ..	18,841	3,117	21,958
" " " " stomach ..	7,853	6,086	13,939
" " " " breast ..	69	9,018	9,087

* Proportion of deaths from malignant tumours of thyroid per 1,000 of all deaths due to malignant disease: males, 1.9; females, 6.0; total, 3.8.

It is probable that no more than 15-20% of the patients who do have tumours of the thyroid are likely to benefit from an attempt at treatment with radioactive iodine. Thirty per cent. of the patients with malignant tumours of the thyroid seen at the Royal Marsden Hospital in the period 1949-62 were given ^{131}I therapeutically, but some of these would not be so treated to-day, and some were brought to the hospital only because such treatment was available there. With small numbers of patients it is clear that few radiotherapy centres can gain sufficient experience to judge how best to manage this treatment or to assess its value and its complications. In addition, the long natural history of many tumours of the thyroid, and emphasis in reports on a few selected cases, restrict the value of some of the published work that is available. The natural history of this disease must be taken into account when judging results. If understanding is to grow it is important that larger series of patients treated with radioactive iodine for thyroid carcinoma be reported; only then will the results be seen in relation both to the prevalence of the disease and to what can be achieved with other treatments.

Radioactive iodine treatment is based on the fact that functioning thyroid tissue may concentrate iodine from the plasma, so that radioactive iodine administered systemically can selectively destroy such functioning thyroid tissue wherever it may be. Provided that a normal thyroid gland is not competing successfully for the material available, differentiated thyroid tumours may in favourable circumstances, even when disseminated throughout the body, destroy themselves by their ability to concentrate the radiation effect.

In the 14-year period 1949-62 59 patients were treated with radioactive iodine for thyroid carcinoma at the Royal Marsden

Hospital, which was the first British hospital to employ this method; the period therefore includes the earliest days of trial in this country. There was a good deal of variation at first in the selection of patients and in the treatment regime. The treatment was carried out in the Professorial Unit of the Radiotherapy Department, where a number of registrars helped in the development of the work, notably Dr. R. J. Walton, who was with us in 1949 when the first patients were treated (Walton, 1950; Smithers, 1951). This beginning was made possible by the pioneer work done by Professor W. V. Mayneord with radioactive isotopes in Great Britain; it was supported throughout by members of his staff in the Physics Department of the Royal Marsden Hospital, the first of whom involved in the work reported here were Miss H. E. A. Farran and Dr. W. K. Sinclair.

Physical Measurements and Dosimetry

For all the patients in this series various physical measurements were made so that full information might be available on the pattern of retention of the administered ^{131}I . The data sought can be summarized as follows:

1. The variation with time of the activity at sites of functioning thyroid tissue, and in the whole body.
2. The distribution of sites of functioning thyroid tissue in the body.
3. The variation with time of the activity in the blood.
4. The radiation dose to functioning thyroid tissue, to the blood, and to the whole body.

It was not always possible to obtain for each administration all the data required under items 1, 2, and 3, and even if these were available the calculation of the radiation dose delivered, as listed under item 4, was subject to many uncertainties.

Several reports covering only certain parts of our work have already appeared. Kramer, Concannon, Evans, and Clark (1955) reported the treatment at the Royal Marsden Hospital of the first 12 patients and noted the value of scintillation scanning in detecting metastases previously unsuspected. The scanner incorporating an image storage tube was described by Mayneord, Evans, and Newbery (1955). A simplified clinical scanner was built here in 1956 (Hughes, Hodt, Newbery, and Sbresni, 1960) and was used for a number of years; the work was subsequently carried out with a more sensitive and versatile commercial instrument (TriD, Atomation Inc.). Dyche (née Clark) and Taylor (1961) detailed the work done over a period of two years in assessing the variation with time of radioactivity in the plasma of 15 patients after 32 treatment doses; their measurements extended over periods of up to 22 days. Dyche and Taylor showed how widely the blood radiation dose per 100 mc administered could vary between successive treatments and from patient to patient. They pointed out the value of tracer tests before a second or third treatment of the patient with functioning metastases showing significant uptake; in such patients doses exceeding 100 rads per 100 mc of ^{131}I administered may be delivered to the blood, and a preliminary tracer test may be useful in assessing the maximum activity that should be given in the next treat-

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ment. Other relevant publications from the Royal Marsden Hospital included a comparative study of the 15-minute continuous thyroid uptake test with other radioiodine tests (Howard, Field, and Dyche, 1960), and reference to the use of a whole-body low background counting system for measurement of residual activity in these patients some eight weeks after administration of the radioiodine (Trott, Parnell, and Cottrall, 1965).

For the past few years the equipment and procedures used in measurements following therapeutic administration of ^{131}I for the treatment of thyroid carcinoma have been as follows:

(a) Measurement of uptake in the gland or at other selected sites with a Geiger-Müller counter (Dyche and Taylor, 1961). The counter is fitted with a shield and collimator designed for measurements on sites in functioning tissue which vary widely in dimensions. Measurements are usually begun two to three days after giving the radioiodine and continued for three days, with the counter set at several different distances from the neck on each occasion. A suitable inverse square plot is used to determine the counting rate for a standard distance, at which the counter has been calibrated for a phantom. In this way the variation with time of the activity in the selected site is determined. These estimated values are plotted on semi-log. paper; over this period of measurement clearance is generally exponential with a single component, and the "effective half-life" is determined from the three values. Extrapolation to time of administration gives the "initial uptake" (see Figs. 2 and 3). A mobile counterpoised 1-in. (2.5-cm.) thick lead block is used as required to screen the counter from other known sites of uptake.

(b) Automatic scintillation scanning to investigate the distribution of activity in the neck and to detect metastases.

(c) The total activity remaining in the body, determined for as long as possible after giving the radioiodine. For many years this was carried out by assessing the activity in urine and faeces. More recently, after a change of policy regarding the collection of radioactive excreta, an external counting method has been used, the patient generally being allowed to excrete directly to a particular W.C. (Trott and Cottrall, 1965). The curve of residual activity versus time, plotted on semi-log. paper, can usually be analysed into two components, and extrapolation of the longer component to zero time gives the "initial uptake" (see Figs. 2 and 3).

(d) Blood samples taken at 2, 24, 48, and 72 hours, and the dose to the blood estimated by the method of Seidlin, Yalow, and Siegel (1952).

When practicable an attempt is also made to estimate the energy absorbed or dose in rads to the particular sites in which uptake has been detected. Such estimates may, of course, be of dubious significance because of the difficulty in estimating the volume of tissue in which the uptake has occurred, and because of uncertainty in the interpretation of calculations of dose to functioning thyroid tissue in view of the known heterogeneity of distribution (Sinclair, Abbatt, Farran, Harriss, and Lamerton, 1956). Nevertheless, it seems advisable to attempt some calculation of the dose, if only to stimulate interest in the problems of heterogeneity of distribution, so important in radioisotope dosimetry.

The Patients

The 59 patients with carcinoma of the thyroid in this series were first seen at varied stages of their disease. Some came without having had any treatment, some soon after a partial and some after a total thyroidectomy with or without block dissection of the nodes or external irradiation of the neck, and some after many years of repeated treatments. A few patients were suspected of having local residual disease, some had an obvious primary tumour or local recurrence, and some had widespread tumour dissemination. These diverse patients were selected from 196 with malignant tumours of the thyroid seen at the Royal Marsden Hospital during the period under review (Table II).

TABLE II.—Age, Sex, and Tumour Histology of Patients with Malignant Tumours of Thyroid Seen at Royal Marsden Hospital, 1949–62

Histology	Age-group (Years)									Age Un-known	Total
	0-	10-	20-	30-	40-	50-	60-	70-	80-		
Uncertain or unconfirmed*				1	2	8	6	6	4	5	32
Unspecified carcinoma ..			3	2	12	11	11	9	2		50
Anaplastic carcinoma ..		1		1	4	13	15	12	1		47
Differentiated adenocarcinoma ..	1	3	1	7	11	8	12	4	4		51
Other types, not carcinoma ..				2		3	5	5		1	16
Total ..	1	4	4	13	29	43	49	36	11	6	196
Males ..				1	7	15	18	8	3	3	55
Females ..	1	4	4	12	22	28	31	28	8	3	141

* Sections for this group of patients were either not available or not reviewed at the Royal Marsden Hospital.

The youngest patient was aged 13 and the oldest 83. There were 14 men and 45 women in the series.

Preparation for Treatment

As a preliminary in the preparation of the patient for treatment anything which would interfere with the uptake of radioiodine was first excluded—the taking of thyroid or anti-thyroid drugs, or any medicine or contrast media containing iodine. As a result, investigation with radioiodine was sometimes delayed for three to four weeks.

FIG. 1.—Papillary carcinoma of thyroid, firmly adherent to trachea, with bilateral lymph-node involvement. A, Clinical assessment. B, Scan.

For the first tracer study 100 μ c of radioiodine has generally been found sufficient to detect and measure uptake in the thyroid and to carry out a preliminary survey for possible metastases by scanning. When, as is usual, some normal thyroid tissue remains, this must be ablated, preferably by radioiodine (which is slower but more certain than surgery) before any final estimate of uptake in the tumour can be made. With anaplastic carcinomas the chance of uptake has been found to be so low that we regard thyroid ablation as no longer justifiable. The amount of radioiodine prescribed for ablation has varied considerably, but we now give 80 mc, which is usually sufficient and causes only occasional mild reactions, such as soreness of the throat or faint erythema of the skin.

After thyroid ablation six to eight weeks are allowed to pass before further studies are made, to leave time for the cessation of normal function. At this stage, if there has already been some evidence of tumour uptake, the course of radioiodine treatment is started. If there has been no evidence of uptake further tracer studies with 1 mc of radioiodine are carried out, and after neck-scanning (Fig. 1), trunk-scanning, and profile-counting a decision about treatment is made.

Treatment with Radioactive Iodine

The amount of radioiodine given has varied considerably, but 150 mc has been found to be a satisfactory first treatment and is often given for subsequent ones as well (Fig. 2); amounts ranging from 100 to 250 mc have been given at one time. The largest total amount of radioiodine administered to a patient in this series up to the end of 1962 was 655 mc over a period of nine months (Fig. 2). Higher total amounts have been given to patients since then, however: over 1,000 mc in two cases.

A large amount of ^{131}I occasionally produces nausea and sometimes a little parotid discomfort. The white-cell count tends to fall temporarily, usually by about 2,000 cells/c.mm. in a patient with a normal count of between 5,000 and 10,000 cells/c.mm. Menstruation is sometimes affected temporarily.

After the first treatment with radioiodine, excretion rates and uptake are again measured so that future treatment can be planned. A course of treatment in a patient with radioiodine uptake in metastases may take a year or more to complete. It needs to be pursued with caution, but also with determination. The timing of successive treatments is a matter which still needs much attention. Intervals of 6 to 12 weeks are usual with us, the shorter intervals for the larger

tumours. The number of treatments depends on the progress of the disease; in favourable cases treatment continues until there is no further uptake in tumour tissue (Fig. 3).

Between treatments patients are maintained on triiodothyronine (T3). It is important that they should not remain in a hypothyroid state, since a low serum thyroid-hormone level encourages the pituitary output of thyroid-stimulating hormone (T.S.H.) which may stimulate any active tumour remaining to further growth. T3 is used because of its rapid excretion and because it need be stopped for only one week before giving more radioiodine, whereas L-thyroxine or thyroid extract needs to be discontinued for about four weeks before treatment. On the grounds both of economy and of suitability L-thyroxine is substituted for T3 as soon as radioiodine treatment is completed. In patients with evidence of functioning metastases but with low radioiodine uptake 10 units of exogenous T.S.H. have been given intramuscularly on each of the four days immediately preceding the next therapy dose to supplement the endogenous T.S.H. output stimulated by normal thyroid ablation.

Analysis of Patients Treated at the Royal Marsden Hospital

Of the 196 patients with malignant tumours of the thyroid seen at the Royal Marsden Hospital between January 1949 and December 1962 (Table II) 153 were new patients and 43 had been previously treated elsewhere. Fifty-nine were treated with radioactive iodine for thyroid carcinoma. These 59 patients have been divided into two groups: those who had local disease, detected or suspected, in the thyroid or lymph-nodes of the neck only, of whom there were 29; and those who already showed clear evidence of established distant metastases, of whom there were 30.

Patients with Disease Clinically Confined to the Neck at Time of Treatment with Radioiodine

In this group of 29 patients four were only suspected of having local residual tumour and may have been free of disease; removal, however, in each case had appeared to the surgeon to be inadequate, and, while no clinically detectable tumour remained post-operatively, the extensive involvement found or the limited scope or difficulty of the operation performed suggested that disease persisted. In all these four patients radioiodine tracer studies showed uptake in the neck—probably in remaining areas of normal thyroid tissue only—but one of the four had three radioiodine treatments, because persistent neck uptake suggested that residual tumour had indeed

FIG. 2

FIG. 3

FIG. 2.—G. F., woman aged 66; 025423. Recurrent thyroid carcinoma treated with ^{131}I . Chart of radioiodine treatment over one year. First treatment was given too soon after ablation. The uptake values given are those of "initial uptake" referred to in the text. FIG. 3.—D. W. H., man aged 62; 047024. Thyroid carcinoma treated with ^{131}I : Hemithyroidectomy: mass 7.5 by 4.5 cm., fixed to trachea, cut across. Papillary and acinar adenocarcinoma. Chart of radioiodine treatment for a man aged 62 with residual local disease following surgery. No recurrence 1965.

been present and had persisted after treatment had started. All four patients had differentiated adenocarcinomas and all had had partial thyroidectomies. The patient with persistent uptake had had infiltration of the carotid sheath and of the superior laryngeal nerve, with a retrosternal extension; she was a woman aged 66 who died after a cerebral haemorrhage without any sign of recurrence just over two years after radioiodine treatment. Another of these four patients was a woman of 64 who died from heart failure more than 10½ years after treatment without sign of recurrence; and two others, aged 50 and 18¹ when first treated, are alive and well at two and a half and three¹ years respectively. So far this appears satisfactory considering that all four patients were thought likely to develop recurrence; but the small number of cases and the short time since treatment do not permit any judgment of the value of the treatment which could be set against the disadvantage for these patients of having to take thyroxine for the rest of their lives. It seems worth while to continue such a therapeutic policy for similar cases for the time being, but a wide collective experience must be reviewed before a proper assessment can be made.

Of the 25 patients treated for known local disease six had persistent tumour present after operation, seven were inoperable at the time of their first visit to hospital, and 12 had recurrence after previous treatment.

Persistent Post-operative Local Disease.—The six patients with persistent local disease were two men, aged 62 and 68, and four women, aged 13, 57, 67, and 74. All had well-differentiated tumours, all had some demonstrable uptake of radioiodine, and all but one (the woman of 57) had two or three treatments. Two died with metastases at five years, one died at one and a half years, and three are alive and well three years after radioiodine treatment.

Tumour Inoperable at Time of First Attendance.—Of the seven patients with inoperable tumours who had not been treated previously, four had thyroid ablation and then showed no uptake. Of these four two died within one month and one at six months, and the fourth patient, who was subsequently treated with external irradiation to the neck, died six and a half years after treatment. Three of these seven patients did show uptake. One, a man of 66, had two treatments, and died with local recurrence over seven years later. The other two patients in this group are worthy of special mention.

No. 044143, a woman aged 69, was seen in February 1961 in an oxygen tent with her trachea almost completely obstructed by tumour; she also had a mass in the right lobe of the thyroid measuring 3 by 4 cm. She was said to have a thyroid adenoma removed nine years previously; no section of this, or any detailed report, could be obtained. She was in a critical condition and was given immediate treatment with radioiodine. She was dramatically relieved of her gasping stridor and was walking about the ward the next day. Scanning demonstrated uptake in both tumours. A small piece obtained for biopsy from the trachea was so well differentiated that it may have been normal ectopic thyroid tissue. Unfortunately no biopsy material was removed from the tumour in the right lobe of the thyroid. Both tracheal and thyroid masses regressed, she was put on thyroxine, and has remained well with no sign of recurrence for four years.

No. 030334, a woman aged 24 (Mill, Gowing, Reeves, and Smithers, 1959), presented with a rapidly growing, bleeding, obstructing carcinoma in a lingual thyroid. One treatment with radioiodine produced complete regression of the tumour. She remains alive and free from recurrence eight years later.

In neither of these two patients was a preliminary ablation needed; one had little and the other had no normal thyroid tissue; both had high degrees of concentration of iodine in their tumours; both were immediately relieved of distressing symptoms. They are unusual examples of the most satisfactory treatment which could be given to patients whose lives

were endangered by obstructive or bleeding tumours (even though one may have been non-malignant), since treatment for each consisted of no more than one small drink, which was followed by immediate relief and lasting regression.

Recurrent Tumours.—Of the 12 patients presenting with local recurrence five showed no uptake and seven some uptake in the tumour, usually of moderate degree and often in parts of the tumour only. Of the five patients with no uptake, four were dead within the year, but one—a woman of 52 with an 11-year history who had had surgery and external irradiation

TABLE III.—Patients With Thyroid Carcinoma Clinically Confined to the Neck at Time of Treatment with Radioiodine. Histology and Survival

Histology	No. of Patients	Survival
Uncertain or unconfirmed ..	6	{ 4 died within 1 year 2 alive at 3½ years Died within 3 months
Anaplastic carcinoma ..	2	
Differentiated adenocarcinoma:		
Unspecified ..	3	{ 2 died at 6½ and 6½* years 1 alive at 4 years Died within 5 years
Hürthle-cell ..	1	
Papillary ..	8	{ 7 died at 1½, 2*, within 5 years, over 5 years, at 6½, 7, and 10½* years 1 alive at 2½ years
Follicular ..	4	
Papillary and follicular ..	5	{ Alive at 3, 4, 4, and 8 years 2 died at 2 months and at 11 years 3 alive at 3 years
Total ..	29	

* From intercurrent disease.

TABLE IV.—Patients With Thyroid Carcinoma Clinically Confined to the Neck at Time of Treatment with Radioiodine. Uptake of Radioiodine and Survival

Survival after Radioiodine	No. of Patients	Inoperable, No Uptake	Recurrent, No Uptake	Suspected, Residuum Only	Persistent Local Disease, Some Uptake	Inoperable, With Uptake	Recurrent, With Uptake
Died in first few months ..	7	3	4	—	—	—	—
„ „ 5 years ..	4	—	—	1	2	—	1
Died at over 5 „ ..	7	1 (6½)	—	1 (10½*)	1 (5)	1 (7)	3 (6½, 6½, 11)
Alive at 2-5 „ ..	10	—	1	2	3	—	3
„ at over 5 „ ..	1	—	—	—	—	1 (8)	—
Total ..	29	4	5	4	6	3	7

Survival for over 5 years after radioiodine is shown by the figures in parentheses.
* From intercurrent disease.

Fig. 4.—Patients with thyroid carcinoma clinically confined to the neck when treated with 131I.

¹ This patient was married in 1964 and gave birth to a normal child at the beginning of 1965.

—is still alive three and a half years after ineffective administration of radioiodine. The seven patients with some uptake have all lived four years or more. Three are alive at four years; four are dead, having lived for periods of nearly 5, 6½, 6½, and 11 years: the first and fourth of these patients died with local recurrence present, the second with metastases in the axilla, and the third with an intercurrent carcinoma of the cervix uteri but no sign of recurrence of her thyroid tumour. All seven patients in this subgroup had long histories of from 6 to 34 years before radioiodine was used; there was some tumour regression in each case but no complete control.

Tables III and IV and Fig. 4 sum up our experience in this group of 29 patients with thyroid carcinoma clinically confined to the neck at the time of treatment with radioiodine: Table III shows survival against histology of the tumour, Table IV survival against tumour uptake of radioiodine, and Fig. 4 the fate of each of these 29 patients after their initial or ablative radioiodine treatment.

Patients with Distant Metastases Present at Time of Treatment with Radioiodine

There were 30 patients who had demonstrable distant metastases at the time of their first treatment with radioiodine.

Patients with No Uptake of ¹³¹I in Tumour.—Thirteen patients (11 women, 2 men) did not show uptake of ¹³¹I in any tumour tissue. The youngest was aged 42 and the oldest 73, the average age being 59. No histological report was available for five patients; one of these lived for three years, another lived for six months, and the others all died within four months. Five patients had anaplastic growths; one survived for three months, the other four for shorter periods. Three patients had differentiated or partly differentiated tumours, and two of these died within three months, while the third lived for over a year and a half. Nine of these 13 patients had primary tumour present in the thyroid or local recurrence as well as distant metastases at the time of treatment with ¹³¹I. Nine patients had metastases in the lungs, two had pleural effusions, and one had extension into the mediastinum. In the case of one man metastases in bone were evident before carcinoma of the thyroid was suspected; the diagnosis was not confirmed histologically, as no post-mortem examination was performed. Five other patients had metastases in bone in addition to their chest metastases. Some patients died with widespread metastases in several organs. The average survival in this group was six and a half months from the date of the ablation dose of ¹³¹I.

Patients with Limited Uptake of ¹³¹I in Tumour.—Eight patients showed some uptake, usually in one or two metastases only. One patient with an anaplastic tumour showed uptake in one vertebral metastasis only; she died within two months. Two patients with bone metastases and disease present in the thyroid died after eight and nine months respectively. The youngest patient in this subgroup, a woman of 35 who had a papillary tumour with anaplastic elements, died with miliary lung metastases after five days. One man aged 70 had an invasive squamous-cell carcinoma of the thyroid and died in three weeks. A patient with multiple metastases in the liver and lungs died within four months. Of two patients, each with some tumour still present after partial regression, one died with recurrent pleural effusion at just under three years, and the other is alive at over three and a half years with metastases in lungs and bones. Seven of the eight patients in this subgroup had an untreated primary tumour or local recurrence as well as distant metastases at the time of treatment with ¹³¹I. Five patients had lung or pleural metastases. Three patients had bony metastases without ante-mortem evidence of spread to the lungs, but with no post-mortem examination.

Patients with Good Uptake of ¹³¹I in Tumour.—Nine patients showed good uptake in some or all metastatic sites.

Only three of these had tumour at the primary site. There was no histological confirmation for one patient; the other eight all had differentiated tumours. Four of these nine patients are now dead, their metastases eventually uncontrolled; one of them had a carcinoma of the body of the uterus which was successfully treated before she died after 19 months with metastases in both lungs and bone; two others also had metastases in lung and bone, and one died with bony and cerebral metastases. Five are alive and clinically free of disease: in four the lungs are now radiologically clear of tumour; in the fifth the uptaking metastases in the liver (seen at laparotomy for appendicectomy in May 1955) have presumably regressed. At present these patients are living after treatment with ¹³¹I at 4, 4, 9, 10, and over 15½ years. The

TABLE V.—*Patients With Thyroid Carcinoma Having Distant Metastases at Time of Treatment with Radioiodine. Histology and Survival*

Histology	No. of Patients	Survival
Uncertain or unconfirmed ..	8	6 died within 9 months 2 died at 2 and 3 years
Anaplastic carcinoma ..	8	7 died within 4 months 1 alive with metastases at 3½ years
Differentiated adenocarcinoma: Unspecified ..	7	4 died at 3 and 9 months and 2½ and 5 years 3 alive and well at 9, 10, and 15½ years
Papillary ..	5	4 died, 2 within 3 months, 1 at 1½ years, and 1 within 3 years 1 alive at 4 years
Follicular ..	1	Alive at 4 years
Papillary and follicular ..	1	Died at 1½ years
	30	

TABLE VI.—*Patients With Thyroid Carcinoma Having Distant Metastases at Time of Treatment with Radioiodine. Uptake of Radioiodine and Survival*

Survival after Radioiodine	No. of Patients	Uptake of Radioiodine in Metastases		
		Good	Some	None
Died within 6 months ..	14	—	4	10
" at 6 months–1 year ..	3	—	2	1
" 1–2 years ..	3	2	—	1
" 2–5 " ..	4	2	1	1
" 5–10 " ..	3	2	1	—
" over 5 years ..	3	3	—	—
		(9, 10, 15½)		
Total ..	30	9	8	13

Survival for over 5 years after radioiodine is shown by the figures in parentheses.

FIG. 5.—Patients with thyroid carcinoma having distant metastases when treated with ¹³¹I.

longest survivor, a young woman alive and well in the sixteenth year, with two sons aged 8 and 5, has been reported several times before (Walton, 1950; Smithers, 1951; Kramer, Concannon, Evans, and Clark, 1955; Smithers, 1959a, 1959b); she was the first patient in this country to be successfully treated with radioactive iodine for disseminated thyroid carcinoma.

Table V shows survival for the whole group of 30 patients with distant metastases against the histology of the tumour; Table VI shows survival against uptake of radioiodine; and Fig. 5 shows the fate of each of these patients after their initial or ablative treatment with ^{131}I .

Summary

Thyroid carcinoma is not a common disease, and only a small proportion of cases benefit from radioiodine therapy. The variations in natural history and response to treatment make assessment difficult. Fifty-nine patients are reported who were treated with radioactive iodine for thyroid carcinoma.

A description is given of the physical measurements carried out to determine the pattern of retention of the administered radioiodine, and hence the radiation dose to the whole body, to the blood, and to functioning thyroid tissue. Preparation for treatment and rationale of the treatment dosage and schedule are discussed.

These 59 patients are analysed in two groups. The first comprises those in whom the disease was clinically confined to the neck, with persistent post-operative disease, with inoperable tumours, or with recurrent tumours. The second group comprises those with distant metastases, with no uptake,

with limited uptake, or with good uptake of radioiodine in the tumour. Patients with anaplastic tumours, whether localized or generalized, all did badly. Good uptake of ^{131}I in a differentiated tumour may lead to regression and long survival, even in cases where wide dissemination has occurred.

A plea is made for the reporting in detail of similar series of patients with carcinoma of the thyroid treated with ^{131}I , so that experience can be accumulated and the value of this treatment assessed.

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Metabolic Changes after Aorto-iliac Occlusion

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The value of surgery for aorto-iliac disease is well established, but there remain a number of problems awaiting solution. Systemic hypotension following release of aortic clamps is often encountered (Brooks and Feldman, 1962; John and Peacock, 1963; Burton *et al.*, 1964), and although its cause has been attributed to the development of metabolic acidosis this relationship is uncertain. The metabolic consequences of circulatory exclusion of the lower limbs is poorly documented and forms the subject of this report.

Patients and Methods

Six adult white patients, four men and two women, have been studied. Two were suffering from aneurysms and the remainder had occlusive disease. The patients were pre-medicated with Omnopon 0.3 mg./kg. and atropine sulphate 0.015 mg./kg. One hour later anaesthesia was induced with intravenous sodium thiopentone 5 mg./kg. and relaxation obtained with tubocurarine chloride 0.5 mg./kg. Endotracheal

anaesthesia was maintained with nitrous oxide and oxygen by intermittent positive pressure by means of a non-return circuit and a Pulmoflator.

The proportion of oxygen used in the inspired gases varied from 25% to 33%. The minute-volume was adjusted to maintain PCO_2 within the range 35–40 mm. Hg and was from 8 to 10 litres/minute. Additional curare was given as required. At the end of the operation any residual curarization was reversed with neostigmine, preceded by atropine, to minimize its muscarinic effects. In all the cases spontaneous respiration was re-established without difficulty.

The patients were conscious on return to the recovery ward, and were nursed in a semi-sitting position on a half-wedge, with the foot of the bed elevated. All the patients were given intranasal oxygen during the immediate post-operative period.

All six patients were treated by the insertion of bifurcation aorto-iliac grafts of woven Teflon, and in each case the lower anastomoses were made with the common iliac arteries. During the period from onset of the operation to release of the aortic clamp warmed blood was slowly infused; this is routine policy in the vascular unit of the department of surgery and serves to produce a temporary increase in blood volume.

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