

The Effect of Complete Ablation of Thyroid Tissue by Radioactive Iodine on the Survival of Tumor-bearing Mice*

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Recent work in this laboratory with a radioactive iodine (I^{131}) derivative of Nile blue 2B (an oxazine dye) has demonstrated that this radioactive dye has a significant effect in prolonging the life of mice bearing transplanted tumors (12). It was found, in this study, that considerable radioactivity was present in the thyroid glands of animals to which this dye was administered. Presumably, in the living animal some of the organically bound iodine is split from the dye molecule, and the resulting iodide is concentrated in the thyroid gland. Thus, it is possible that some thyroid tissue might have been destroyed by the radioactive iodine and that this might have had some effect on the survival of the tumor-bearing mice. Accordingly, the present study was undertaken to evaluate the effect of ablation of thyroid tissue by radioactive iodine on the survival of tumor-bearing mice.

Previous studies on the effect of surgical removal of the thyroid gland on the growth of tumors have yielded variable results. It has been reported that surgical thyroidectomy has no effect on growth of tumors (1), causes regression of tumors (9, 13), causes resistance to induction of tumors (11), and accelerates growth of tumors (7, 8). Surgical thyroidectomy is frequently accompanied by unintentional removal of the parathyroid glands. (Operative mortality in the experimental animal is generally high.)

Gorbman (5) showed that complete destruction of thyroid tissue without concomitant complete destruction of parathyroid tissue could be achieved by the administration of radioactive iodine (I^{131}) to adult mice. Similar studies in the adult and newborn rat (3, 4) have shown that thyroidectomy without parathyroidectomy can be achieved with radioactive iodine.

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EXPERIMENTAL

Inbred mice of the C3H strain, each weighing approximately 25 gm., were used. The mice were allowed Purina Laboratory Chow and tap water *ad libitum*. Either of two fibrosarcomas (Nos. 13 and 14), which had been originally induced in mice of this strain with methylcholanthrene, was used. These tumors have been transplanted through many generations with a zero incidence of spontaneous regression. The tumors were implanted by subcutaneous injection into the right axillary region. Radioactive iodine (carrier-free I^{131} obtained from the Oak Ridge Laboratories of the Atomic Energy Commission) was administered by a single subcutaneous injection at a site distant from the tumor.

The experiments were divided into two groups. In the first group, radioactive iodine was administered after the tumors had grown to appreciable size. In the second group, radioactive iodine was administered either 34 days or 103 days prior to implantation of the tumor. In each case the number of days that elapsed between implantation of the tumor and death of the mouse was noted and recorded as survival time.

In one experiment the mice were housed individually in separate cages to eliminate any possible effect of external radiation from one mouse to another. In the other experiments each group of mice was housed in a single large cage.

The dosage of radioactive iodine was 250 μ c. per mouse, except in one experiment in which the dosage was 210 μ c. Gorbman (5) has reported that a dose of 200 μ c. is sufficient to destroy all thyroid tissue in the mouse.

RESULTS

Table 1 shows the survival times of mice which received 210 μ c. of radioactive iodine 8 days after implantation of a fibrosarcoma (tumor No. 13) and of control mice which bore the same tumor and were treated in identical fashion except that

they received no radioactive iodine. The average weight of the mice at the time of administration of radioactive iodine was 22 gm. Seventeen days later the average weight was 26 gm. for the treated mice and 28 gm. for the control mice. The mice

TABLE 1

210 MICROCURIES I^{131} ADMINISTERED 8 DAYS AFTER IMPLANTATION OF TUMOR (NO. 13)

DAYS SURVIVED	
Controls (No I^{131})	Treated
27	18
27	18
28	29
31	31
31	31
35	31
36	32
37	43
42	43
42	43
42	44
44	44
44	44
45	53
46	
AV. 37	AV. 36

were normally active until shortly before death, at which time all had very large tumors. The only suggestion of apparent difference between the treated and control mice was that the treated mice seemed to consume a little less food than the controls.

Table 2 shows the survival times of mice which received 250 μ c. of radioactive iodine either 12 days after or 34 or 103 days prior to implantation of a fibrosarcoma (tumor No. 14). The average body weight at the time of administration of radioactive iodine was 24 gm. for the control mice and 25 gm. for the mice which received radioactive iodine 12 days after implantation of tumors. Twenty-one days later the average weights were 27 gm. for both of these groups. Again, there was no noticeable difference between the control and treated mice except that in the group which received radioactive iodine 103 days prior to tumor implantation there was moderate loss of hair pigment on the ventral aspect of the body, especially around the area of tumor implantation.

There was no noticeable difference in the rate of growth of the tumors, and in all mice the tumors were very large at the time of death. In two groups, rough measurements of the tumor size of control and treated mice at 21 days and 28 days after implantation of tumors, showed that the average tumor volume was approximately the same for both control and treated mice.

Gorbman had shown (5) by serial section of the neck region that doses of radioactive iodine of the order of magnitude used in these experiments produced complete destruction of thyroid tissue in the mouse. In the present study the neck region of a mouse treated with radioactive iodine was serially sectioned. Microscopical examination of these sections showed only remnants of disrupted thyroid follicles and no thyroid tissue which appeared capable of function was seen. Other contiguous tissues were normal. In a number of other treated mice, sections of the thyroid region likewise showed no thyroid tissue capable of function. The thyroid glands of the control mice were grossly and microscopically normal.

TABLE 2

250 MICROCURIES I^{131} ADMINISTERED BEFORE OR AFTER IMPLANTATION OF TUMOR (NO. 14)

Controls (No I^{131})	DAYS SURVIVED		
	I^{131} 12 days after implan- tation of tumor	I^{131} 34 days prior to im- plantation of tumor	I^{131} 103 days prior to im- plantation of tumor
25	29	30	31
26	32	32	34
33	39	32	36
35	39	33	37
39	43	34	38
39	46	34	40
39	47	35	40
40	47	35	41
40	48	36	41
43	53	37	43
44	53	37	44
47	53	37	46
48	53	39	47
49	53	39	48
50	AV. 45	39	49
AV. 40		40	50
		40	AV. 42
		41	
		41	
		41	
		42	
		43	
		AV. 37	

DISCUSSION

It is apparent from the data of Tables 1 and 2 that there is no significant difference (P is greater than 0.05 for all groups) in survival time between the control animals and those whose thyroid glands were ablated either before or after implantation of the tumor. The results demonstrate reasonably well that, under the conditions of these experiments, ablation of thyroid tissue by injections of radioactive iodine has no appreciable effect on the growth of transplanted fibrosarcomas or on the survival of the host animal.

Drabkin (2) suggests that thyroid activity may be mediated via cytochrome c , and he has shown that there is a reduction in cytochrome c in all tis-

sues of the hypothyroid animal. Meyer, McTiernan, and Aub (10) found that alteration of thyroid activity (by administration of thyroxine) had no effect on either aerobic or anaerobic glycolysis of tumor tissue.

Neoplastic tissue is known (6) to be quite low in cytochrome c, and it might be expected that alterations in thyroid function would have less effect on tumor metabolism than on other tissues of the animal. Furthermore, tumor tissue has a greater ability for satisfying its metabolic requirements by glycolytic processes than does normal tissue. As a result of all this, little or no stress on the functioning of the tumor might be expected from the depression of oxidative processes such as results from thyroid ablation.

SUMMARY

1. Ablation of thyroid tissue in mice bearing transplanted fibrosarcomas has been carried out by administration of radioactive iodine (I^{131}). This ablation was done both prior to and after implantation of the tumors.

2. The average rate of growth of the tumors and the average period of survival of the mice in which thyroid tissue had been ablated were not significantly different from those of untreated tumor-bearing mice.

3. It is concluded that thyroid ablation has no significant effect on tumor growth.

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