

EFFECT OF IRRADIATION ON THYROID GROWTH
IN MOUSE FOETUSES AND GOITROGEN CHALLENGED
ADULT MICE

by

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Proliferating tissue displays greater sensitivity to ionizing radiation than cell populations in a more steady state of growth, a rule that probably applies with few exceptions. It is therefore important that special consideration should be paid to the unborn and the young when the probable consequences to a civilian population of reactor accidents and nuclear explosions are being assessed; this also applies when suitable measures for counteracting such hazards are under discussion. The international norms usually applied in the evaluation of radiation risks suggest that the radioiodines often determine the maximum permissible concentrations of airborne fission products, and hence the demands for tightness and tenacity of reactor containments as well as the extent and duration of restrictions on food consumption, evacuations, and the like.

It seems generally agreed today that roentgen irradiation of the thyroid gland in infancy increases the risk of thyroid carcinoma in later life (WARREN 1966, HEMPELMAN et coll. 1967, DOLPHIN 1968). CONARD et coll. (1966) noted a very high incidence of nodules among young people who were living on the Rongelap

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atoll at the time of the nuclear weapon test at Bikini in 1954 and who were then under 10 years of age. The high incidence of thyroid changes among the children 11 years after exposure, the only persisting evidence of injury, indicates that even after a short-term exposure to radioiodine in combination with non-lethal external doses, the growing thyroid may be a 'critical organ' in young people exposed to radioactive fallout. It is not possible, however, to make direct comparisons between the dose of ^{131}I , effect, and age, from these observations as the external gamma radiation had probably played a considerable part in producing the end-result.

A large number of animal investigations have disclosed that the growing thyroid gland is especially sensitive to radiation from ^{131}I accumulated in the gland, and not least in the carcinogenic effect of the irradiation. Growth was usually provoked in adult animals by increasing the TSH content of the blood; this was effected either by subtotal thyroidectomy (GOLDBERG et coll. 1964), by means of goitrogenic stimulation (DONIACH & LOGOTHEOPOULOS 1955, DONIACH 1963, LINDSAY & CHAIKOFF 1964), or by feeding with an iodine-deficient diet (AXELRAD & LEBLOND 1955). A connection between thyroid growth, radiation, and incidence of thyroid neoplasms probably also exists in adult man (DONIACH et coll. 1966).

The present investigation was concentrated on the effect of ^{131}I on the normal and propylthiouracil (PTU) stimulated growth of the thyroid in foetuses and young mice. These dose-effect relations were compared with the corresponding connections between dose and impairment of the goitrogenic response in adult mice. The radiation effect on the PTU stimulated glands in adult mice was investigated as a function of the time interval between ^{131}I injection and the commencement of the PTU treatment as well as a function of the iodine content of the food. In addition, the effect of ^{131}I was compared with that of irradiation with roentgen rays in adult mice.

^{131}I experiments

Animals and Materials

Both sexes of CBA mice were examined in the experiments with foetuses while only males were used in the investigation in adults. One mother (with her litter) was accommodated in each cage during the gestation and suckling periods. After weaning, and in the 'adult' series, 10 (or less) animals were housed in each cage. The animals were kept in thermostat-regulated rooms with controlled humidity in which the lights were automatically turned on at 6 a.m. and off at 6 p.m.

The ^{131}I solutions injected consisted of carrier-free Na^{131}I (from the Radiochemical Centre, Amersham, England and AB Atomenergi, Studsvik, Sweden)

dissolved in 0.9 % saline. Propylthiouracil (AB Pharmacia, Uppsala, Sweden) 0.1 % was administered to the animals in drinking water. The latter was made slightly alkaline (pH 8 to 8.5) in order to prevent precipitation of the PTU. The iodine content of the diet was determined by activation analysis at AB Atomenergi, Studsvik, Sweden.

Dose calculations

The determination of the dose to the thyroid gland was carried out in accordance with the formulas in an earlier paper (WALINDER 1971). The iodine concentration in the pellets was not constant during the course of the experiments and consequently the uptake and retention of ^{131}I in the thyroids varied somewhat from time to time. Consideration had also to be paid to the interdependence between the ^{131}I dose and the thyroid growth rate as well as to the fact that the hormonal secretion rate increased with the dose. The parameters necessary for dose calculations — uptake, retention, size of the thyroids, etc. — were accordingly not identical with those given in the earlier paper (WALINDER 1971). This underlines the importance of making dose calculations and not merely relying on the dose being proportional to the amount of radioactivity injected.

For determination of the activity in the thyroid, the glands were removed, hydrolyzed in 1 ml conc. NaOH and measured for activity in a well-type crystal connected to a two-channel scaler (Picker, Twinscaler II). The difficulties in carrying out *in vivo* measurements of ^{131}I in the thyroid glands of mice necessitated the uptake and retention being determined by *in vitro* assays in thyroid glands excised from mice in a special 'retention group' kept parallelly with the experimental groups. The animals were killed with chloroform.

The doses in Tables 1 to 4 are means to the centres of the glands (\bar{D}_{max}). The dose in the thyroid decreases towards the periphery of the gland so that at the edge of the thyroid it is approximately $0.4 \cdot D_{\text{max}}$ in adults and $0.5 \cdot D_{\text{max}}$ in foetuses and juveniles.

Experimental procedures

The experiments with ^{131}I were divided into four groups.

Foetuses. The foetuses were given ^{131}I by intravenous injections to the mothers on the 18th day of gestation. The mothers were maintained on an iodine-deficient diet ($0.3 \mu\text{g}$ iodine per g pellet) from the first day of pregnancy; from the 19th day of pregnancy and onwards the food was iodine-enriched (standard diet: ca. $27 \mu\text{g}$ I per g pellet).

Experiment 1. Different amounts of ^{131}I given to foetuses. The experiment was carried out at three different times and the results are presented in three tables (1A, 1B, 1C). The animals in section 1A were killed at the age of 75 days and those in the two other sections at 60 days.

Experiment 2. This experiment was identical with experiment 1 with the exception of further thyroid growth stimulation provoked by PTU in the drinking water for one month immediately after the weaning. As this experiment was conducted at the same time as experiments 1A and 1B, the results are presented in a similar way in Tables 2A and 2B.

Adult mice. The adult mice were 75 to 87 days old at the start of the experiments. They were fed on pellets with a low iodine content for 14 days, after which they were given ^{131}I by intraperitoneal injections. Two experiments (3 and 4) were carried out to examine the significance of the time interval between irradiation and the start of the goitrogen challenge and the iodine content in the diet.

Experiment 3. Different amounts of ^{131}I to adult mice. As in experiment 1 this was divided into three series (3A, 3B, and 3C). The animals had been fed with an iodine-deficient diet ($0.3 \mu\text{g I per g pellet}$) for 14 days before the ^{131}I injection following which the diet was changed to iodine enriched pellets (ca. $27 \mu\text{g I per g pellet}$). Fourteen days later, PTU was administered in the drinking water until later the animals were killed. An additional control group of animals that received the iodine deficient diet was maintained during the entire course of the experiment.

Experiment 4. Different amounts of ^{131}I to adult animals. The animals were maintained on a diet fairly low in iodine ($0.75 \mu\text{g I per g pellet}$) during the entire course of the experiment. PTU was given in the drinking water for 30 days from the day after the ^{131}I injection.

Results

Experiment 1. Effects of ^{131}I on foetal and juvenile thyroid glands. Significant effects on the thyroid growth in the foetus and young mouse could be observed with ^{131}I doses of 3 700 rad and higher to the centre of the thyroid glands (Table 1).

It should be stressed that the doses given in the tables refer to those delivered to interfollicular areas in the central part of the glands (\bar{D}_{max}). The dose to the epithelium surrounding the sparsely scattered follicles in the foetal thyroid is higher than the calculated value of \bar{D}_{max} (WALINDER 1971).

Experiment 2. Effects of ^{131}I on PTU challenged foetal and juvenile thyroid glands. A significant effect on the normal thyroid growth in the foetus and young

Table 1

Body and thyroid weights ($\pm SE$) in 2-month-old mice given different amounts of ^{131}I by intravenous injection of the mothers on the 18th day of gestation. *P*-values obtained by Student's *t*-test denote the significance of the growth impairment in the irradiated thyroid glands in relation to the thyroid weights of the controls. The three tables (A, B, C) present the results from three different experimental series running at different times.

Inj. ^{131}I (μCi)	\bar{D}_{max} (rad)	Males				Females			
		No. of animals	Body weight (g)	Thyroid weight (mg)	p	No. of animals	Body weight (g)	Thyroid weight (mg)	p
A									
—	—	14	25.2 \pm 0.4	3.00 \pm 0.12		13	20.3 \pm 0.3	2.70 \pm 0.11	
1.0	1 900	17	25.0 \pm 0.4	3.05 \pm 0.12		19	20.7 \pm 0.3	2.50 \pm 0.14	—
B									
—	—	46	23.1 \pm 0.2	2.80 \pm 0.7		52	18.8 \pm 0.2	2.42 \pm 0.05	
2.0	4 900	48	22.6 \pm 0.2	2.14 \pm 0.07	<0.001	48	18.1 \pm 0.2	1.99 \pm 0.98	<0.001
3.0	6 700	26	22.9 \pm 0.4	1.71 \pm 0.10	<0.001	17	17.5 \pm 0.5	1.64 \pm 0.08	<0.001
5.0	11 000	23	22.4 \pm 0.4	1.64 \pm 0.13	<0.001	36	17.8 \pm 0.2	1.27 \pm 0.07	<0.001
C									
—	—	12	22.3 \pm 0.3	2.40 \pm 0.10		10	18.8 \pm 0.4	2.37 \pm 0.15	
2.5	3 700	20	23.2 \pm 0.4	1.97 \pm 0.08	<0.01	20	19.9 \pm 0.3	1.93 \pm 0.06	<0.01

Table 2

Radiation effect on the increased thyroid growth obtained by treating young mice with PTU from the time of weaning until they were killed at 50 days.

Inj. ^{131}I (μCi)	\bar{D}_{max} (rad)	Males			Females		
		No. of animals	Thyroid weight (mg)	p	No. of animals	Thyroid weight (mg)	p
A							
—	—	13	6.6 \pm 0.2		13	6.3 \pm 0.3	
0.5	1 000	10	7.0 \pm 0.5		10	6.0 \pm 0.3	
1.0	1 900	16	5.7 \pm 0.2	<0.01	19	5.3 \pm 0.2	<0.01
B							
—	—	10	6.7 \pm 0.4		10	6.5 \pm 0.3	
2.0	4 900	17	4.8 \pm 0.2	<0.001	11	4.0 \pm 0.3	<0.001

mouse could not be observed with ^{131}I doses of the order of 2 000 rad (Table 1A). Nevertheless some action on the gland cells obviously occurs at doses of this magnitude as is evident from the fact that the PTU stimulated extra growth between the ages of 20 to 50 days was impaired (Table 2A).

Table 3

Body and thyroid weights ($\pm SE$) in adult male mice with PTU started 14 days after injection of varying amounts of ^{131}I . As in the preceding tables, p denotes the significance of the growth impairment in the PTU challenged thyroid glands after different doses of ^{131}I . The three tables (A, B, C) collect the results from three different experimental series running at different times.

Age of animals (days)	Inj. ^{131}I (μCi)	\bar{D}_{max} (rad)	Duration of PTU treatment (days)	No. of animals	Body weight (g)	Thyroid weight (mg)	p
A							
140	—	—	—	19	32.3 ± 0.5	3.95 ± 0.10	
140	—	—	30	20	28.7 ± 0.4	6.59 ± 0.17	
140	0.60	1 900	30	20	29.1 ± 0.2	6.56 ± 0.16	—
140	1.5	4 700	30	20	29.3 ± 0.6	5.90 ± 0.20	<0.02
B							
119	—	—	14	20	27.3 ± 0.7	5.77 ± 0.27	
119	3.0	9 000	14	20	27.3 ± 0.6	4.89 ± 0.11	<0.01
130	—	—	—	20	31.3 ± 0.4	3.64 ± 0.21	
130	—	—	25	20	29.1 ± 0.4	7.41 ± 0.32	
130	3.0	9 000	25	20	28.1 ± 0.4	5.51 ± 0.15	<0.001
130	4.5	14 000	—	10	30.1 ± 0.5	4.00 ± 0.17	
C							
133	—	—	30	30	26.6 ± 0.3	7.11 ± 0.21	
133	1.5	4 700	30	36	25.8 ± 0.3	7.04 ± 0.13	—
133	2.1	6 600	30	10	30.6 ± 0.4	5.93 ± 0.23	<0.01

Table 4

Body and thyroid weights ($\pm SE$) in adult male mice with PTU treatment started 24 hours after injection of 1.5 and 2.1 μCi ^{131}I . The animals were maintained on iodine-deficient pellets during the entire course of the experiment. P denotes the significance of the growth impairment.

Age of animals (days)	Inj. ^{131}I (μCi)	\bar{D}_{max} (rad)	Duration of PTU treatment (days)	No. of animals	Body weight (g)	Thyroid weight (mg)	p
119	—	—	30	20	26.6 ± 0.4	8.84 ± 0.31	
119	1.5	3 600	30	20	27.3 ± 0.4	7.78 ± 0.23	<0.01
119	2.1	5 000	30	20	26.0 ± 0.4	5.80 ± 0.22	<0.001

A tracer dose of ^{131}I was injected intraperitoneally one day before the litters were killed. The 24-hour uptake gave consistently the same concentration of radioactivity in the thyroid gland, irrespective of the size of the earlier ^{131}I doses, in other words, the uptakes were proportional to the thyroid weight: $U_{24} = 1.00 \pm 0.05$ % of the injected amount of radioactivity per mg of thyroid tissue.

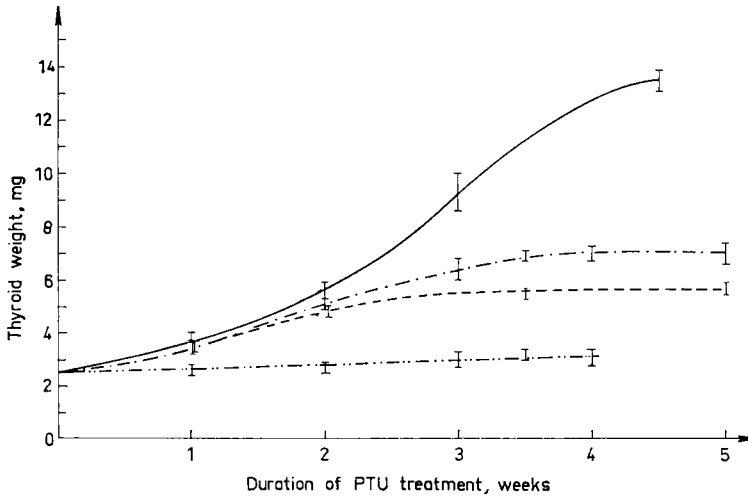


Fig. 1. The increase in thyroid weight in mice (90 days of age at the start of the experiment) as a function of the duration of the PTU treatment. The treatment procedures were: 1. PTU + iodine-deficient diet (—), 2. PTU alone (----), 3. 1.5 μCi ^{131}I ($\bar{D}_{\text{max}} = 4\ 000$ rad) one day prior to the start of the PTU regimen (-.-.-.-), and 4. unchallenged controls (-.-.-.-.-). The vertical lines through the mean values denote \pm SE.

Experiment 3. Effects of ^{131}I on PTU stimulated adult thyroids. Table 3 (A, B, C) indicates that the dose of ^{131}I necessary to produce significant impairment of goitrogen stimulated thyroid growth was of the order of 6 600 rad at the centre of the gland and around 2 600 rad at the periphery. The range of error in the tables is the standard error of the mean; the dose values are correct to two places. Mice injected with 4.5 μCi ^{131}I , which corresponded to an average dose at the centre of the thyroid of 14 000 rad, had no histologically verifiable effects in the unchallenged thyroid 39 days after the injection (Table 3B).

Experiment 4. Effects of ^{131}I on PTU stimulated, adult thyroids. An additional experiment was carried out to investigate the significance of the time interval between the ^{131}I injection and the start of PTU treatment. In this experiment the PTU treatment was started 24 hours after the ^{131}I injection but the mice were maintained during the entire course of the experiment on the same diet as that given before the PTU start; this diet contained 0.75 μg iodine per g pellet. The animals were injected with 1.5 μCi and 2.1 μCi , producing a total dose to the central parts of the glands of 3 600 and 5 000 rad, respectively. The results are presented in Table 4.

The increase in the thyroid weight is presented in Fig. 1 as a function of the duration of PTU treatment in unchallenged animals, as well as in animals given

PTU alone and in combination with injection of $1.5 \mu\text{Ci } ^{131}\text{I}$ ($\bar{D}_{\text{max}} = 4\,000$ rad). The upper curve in Fig. 1 represents the thyroid growth after PTU stimulation in mice maintained during the entire course of the experiment on an iodine-deficient diet containing $0.33 \mu\text{g}$ iodine per g pellet.

Discussion

Marked impairment of the normal growth of the thyroid gland in foetal and juvenile mice was evident after a maximum ^{131}I -dose of 3 700 rad to its central parts. This impairment of thyroid growth led to considerable histologic tissue changes (WALINDER 1972).

No histologically verifiable effects were present in the thyroid tissue of adult mice after 14 000 rad to the central part of the gland 39 days after the injection of ^{131}I . It is possible, however, to produce a sensitivity to radiation of the adult thyroid gland similar to that observed in young animals by provoking growth of the gland with goitrogens. Experimental results, not now reported, moreover indicate that mice following a dosage of 5 400 rad ^{131}I have thyroid weights at 1.5 years of age that are only half as great as those observed in unirradiated controls at the same age (WALINDER, unpublished).

These observations and the fact that the function (uptake of ^{131}I) of surviving cells appears to be unaffected by the doses used in the present investigation, call for no further explanation of the difference in radiosensitivity of the normal adult and foetal mouse thyroid than the higher cell division rate of the latter. This conclusion is corroborated by the observation made by a number of investigators that the growth impairment in a goitrogen challenged thyroid gland irradiated with ^{131}I is due to disturbance of the reproductive integrity of the epithelial cells. The increase in size of the cells does not seem to be affected to any great degree (AL-HINDAWI & WILSON 1965, DOBYNS *et coll.* 1967, DONIACH & LOGOTHEOPOULOS 1955, GREIG *et coll.* 1965, MALOOF *et coll.* 1952).

Roentgen experiments

As mentioned in the introductory section, fairly general agreement appears to exist today that roentgen irradiation of the cervical region in children increases the risk that malignancy will develop in the thyroid gland in later life. The thyroids of these subjects seem in this respect to be more sensitive to radiation than those of adults (UNSCEAR 1964, DOLPHIN 1968). Although available data strongly indicate a correlation between roentgen irradiation over the neck region in infancy and later development of thyroid carcinoma, there is a paucity of information concerning the corresponding effects of ^{131}I (*cf.* DOLPHIN 1968).

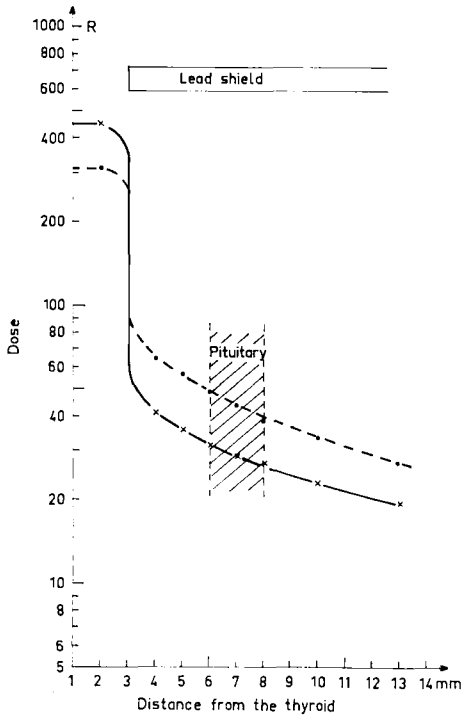


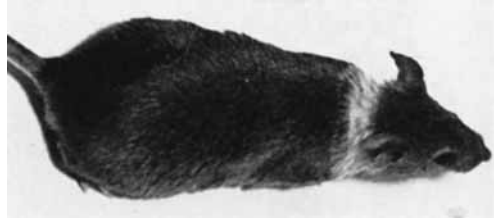
Fig. 2. Roentgen dose to the neck and shielded parts of an adult mouse body. The shaded area indicates the position of the pituitary gland in relation to the edge of the aperture of the lead shield. The aperture was centered over the thyroid.

Certain significant effects (thyroid growth inhibition and induction of adenomas) are however produced by roentgen irradiation of the thyroid in animals and human subjects at lower dose levels than those required to give rise to corresponding changes with ^{131}I (DONIACH 1963, UNSCEAR 1964). An important question that arises in this connection is why radiation with roentgen rays is so much more effective than radiation from ^{131}I to the thyroid. This problem was therefore investigated in a number of roentgen experiments in mice. Such experiments can obviously not be carried out in mouse foetuses, so that the investigation was necessarily limited to a comparison of the inhibitory effect produced by the two types of radiation on goitrogen stimulated thyroid growth in adult mice.

Irradiation procedure and dose calculations

The irradiation factors were: 260 kV, 10 mA; filter: 4 mm Al (inherent) + 0.85 mm Cu; HVL: 2 mm Cu; focus — thyroid distance: 23 cm, giving a dose

Fig. 3. A roentgen irradiated mouse one month after exposure. The unprotected skin under the aperture of the lead shield was badly damaged and the hair had lost its colour. A sharp demarcation between this injured area and the shielded skin was evident.



rate to the gland of 300 rad/min. The mice were covered with 4 mm lead with an aperture over the neck region (including the thyroid gland) of 20 mm \times 7 mm. The animals were anaesthetized with Mebumal and placed with the back upwards towards the roentgen tube. The trunk and head could thus be screened off from the radiation. Special care was taken to avoid irradiation of the hypophysis; this was achieved by keeping the animal's head bent forward during the irradiation and by careful positioning of the aperture of the lead protector.

The dose measurements were performed with films (Cine Positive 5302) placed above and below the neck of dead animals in the afore-mentioned position under the aperture of the lead protector. The relation between dose and film blackening was obtained by calibration of the film against a well-calibrated thimble chamber coupled to a dosimeter (Philips Universal dosimeter 37470). The calibration was carried out under the aperture of the lead as well as below the lead itself. In order to maintain the linear relation between dose and film blackening two exposures of different durations were necessary to evaluate the doses under the aperture and under the shielded parts of the film. The dose in the hypophysis amounted to about 10 per cent of that to the thyroid (Fig. 2). A ring of white hair around the animals' necks was generally produced not long after the irradiation (Fig. 3). The control mice were treated in exactly the same way as the experimental animals but were protected completely by lead.

Two experimental series were set up, the first consisting of six groups of animals treated according to the following scheme. All animals were maintained for 14 days before irradiation on an iodine-deficient diet. One day after irradiation this was changed to a diet with a high concentration of iodine.

Group 1: 1 500 rad in a single dose. After 14 days, PTU was given in the drinking water (0.1 %) for 28 days.

Group 2: 1 500 rad in a single dose. After 24 hours, PTU was administered as in group 1.

Group 3: 1 500 rad in three doses of 500 rad, 14 days, 7 days, and 1 day before a PTU challenge as in groups 1 and 2.

Group 4: 1 500 rad without PTU challenge.

Group 5: Unirradiated controls.

Table 5

Body and thyroid weights in male mice irradiated with roentgen rays and challenged with PTU. The time interval between the exposure to radiation and the PTU treatment was 14 days. P denotes the significance of the growth impairment. The animals in this table were 1.5 to 2 months older than those in the other experiments.

Group	Age of animals (days)	Duration of PTU treatment (days)	No. of animals	Body weight (g)	Thyroid weight (mg)	p
1	193	28	20		7.00±0.39	<0.01
2	193	28	30	28.0±0.3	6.37±0.24	<0.001
3	193	28	40	28.9±0.3	7.28±0.15	<0.01
4	193	—	10		5.2±0.3	<0.001
5	193	—	20	35.3±0.5	5.0±0.3	<0.001
6	193	28	19		8.36±0.29	

Table 6

Body and thyroid weights in male mice irradiated with roentgen rays and challenged with PTU. The time interval between the injection of radioiodine and the start of PTU treatment was 24 hours.

Group	Age of animals (days)	Duration of PTU treatment (days)	No. of animals	Body weight (g)	Thyroid weight (g)	p
1	149	29	27	29.3±0.4	7.66±0.22	—
2	149	29	31	28.4±0.3	6.64±0.23	<0.01
3	149	29	20	29.8±0.6	7.75±0.24	

Group 6: Unirradiated controls that had access to PTU water for the same length of time as the other animals.

All the mice were males. The housing and management of the mice was the same as in the ^{131}I experiments.

An additional experimental series consisted of three groups of animals, two of which were irradiated in the same way as in groups 1 and 2 in the preceding experiment, but with 1 000 rad, and a control group that received PTU in the water as in group 6 in the preceding experimental series.

Results

Experiment 1. One day before the animals were killed, $0.1 \mu\text{Ci } ^{131}\text{I}$ was given to the mice in groups 4 and 5. The 24-hour uptakes were (percentage of injected amount $^{131}\text{I} \pm$ standard error of the mean): 2.89 ± 0.15 per cent and 2.83 ± 0.20 per cent, respectively. The mean thyroid weight in group 2 was significantly lower than that in group 3 ($p < 0.01$).

Experiment 2. The effects of 1 000 rad roentgen irradiation on the PTU stimulated thyroïdal growth are presented in Table 6. The goitrogenic challenge was significantly impaired by 1 000 rad roentgen irradiation, when administered 24 hours before the start of the PTU treatment. If the time interval between the radiation exposure and the start of PTU treatment was increased to 14 days, the dose necessary for impairment of the goitrogenic challenge had to be increased to 1 500 rad (cf. Table 5).

Comparative aspects of roentgen and ^{131}I irradiation

The roentgen experiments established that a dose delivered 24 hours before the PTU treatment produced a more marked effect than if the same dose was delivered 14 days before the start of the PTU stimulation or if the dose was fractionated over a period of 14 days prior to the PTU challenge. This indicates that some recovery had taken place during the 14 days following the exposure; it also confirms the results of the ^{131}I experiments in which similar effects were obtained by reducing the time interval between the injection of the radioiodine and the PTU challenge from 14 days to 24 hours.

Significant impairment of thyroid growth after 28 to 30 days' treatment with PTU started 14 days after the roentgen exposure or the injection of ^{131}I , necessitated a roentgen dose of 1 500 rad or an integrated ^{131}I dose of about 6 600 rad to the centre of the gland (the peripheral dose is then 2 600 rad according to WALINDER 1971). The corresponding dose values after reducing the time interval between exposure (injection) and the start of the PTU treatment to one day were 1 000 rad and about 1 600 to 4 000 rad (peripheral — central dose), respectively. The 14 days' recovery thus implied a dose reduction factor of about 1.5, irrespective of the type of irradiation.

The continuous (but decreasing) dose from ^{131}I necessary to produce a significant impairment of thyroid growth after PTU stimulation proved to be twice to four times higher than that required after three to five minutes of roentgen irradiation. Fractionation of the roentgen dose as described did not imply a change of the radiation response as compared to that observed after a single exposure with the same dose 14 days prior to the growth stimulation. The inhibitory effect of irradiation on thyroid growth produced by goitrogen in mice is thus obviously dependent on dose rate. The skin changes observed in roentgen irradiated mice (Fig. 3) demonstrated that roentgen doses of this magnitude produce considerable extrathyroidal damage. Such an injury is, however, probably of less importance in explaining the higher efficiency of roentgen as compared with ^{131}I irradiation than the difference in the dose rates (WALINDER et coll. 1972).

SUMMARY

The radiosensitivity of the goitrogen challenged thyroid gland was investigated in foetal and adult mice both after irradiation with ^{131}I accumulated in the gland and after roentgen radiation. The similar effect in the normally growing thyroid in the foetuses and young mice and the goitrogen stimulated adult animals suggested that the rate of thyroidal growth rather than the age of the mouse was the decisive factor in determining the degree of the reaction. Roentgen irradiation proved to be twice to four times more 'effective' than radiation with ^{131}I .

ZUSAMMENFASSUNG

Die Strahlenempfindlichkeit der kropferzeugend behandelten Thyreoidea von fetalen und erwachsenen Mäusen wurde sowohl nach Bestrahlung durch ^{131}I angereichert in der Thyreoidea, als auch nach Röntgenbestrahlung untersucht. Die Ähnlichkeit der Wirkung bei der normal wachsenden Thyreoidea der fetalen und jungen Maus und derjenigen beim erwachsenen, kropferzeugend behandelten Tier deutet darauf hin, dass eher die Geschwindigkeit des Wachstums als das Alter der Maus der entscheidende Faktor ist, der die Grösse der Reaktion bestimmt. Röntgenbestrahlung erwies sich zwei- bis viermal 'effektiver' als Bestrahlung mit ^{131}I .

RÉSUMÉ

La radiosensibilité de la glande thyroïde stimulée par un goitrogène a été étudiée sur des foetus de souris et sur des souris adultes après irradiation par ^{131}I fixé dans la glande et par irradiation par rayons de Roentgen. La similitude de l'effet sur la thyroïde en croissance normale des foetus et des jeunes souris et sur la thyroïde des animaux adultes stimulée par un goitrogène fait penser que le facteur décisif qui détermine l'intensité de la réaction est plutôt le taux de croissance que l'âge des souris. L'irradiation par rayons de Roentgen a prouvé d'être deux à quatre fois plus 'effective' que l'irradiation par ^{131}I .

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