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I^{131} Content in Ovarial and Other Tissues at Different Times After Oral Administration[1]

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One of the problems of hazard evaluation of I^{131} therapy when treating women before or during the child-bearing age is that of possible harm to the ovaries. Such sterility and genetic hazards have been discussed by Dr. Edith Quimby (1,2) and pertinent data in this connection may be found in references (3-16). There appears to be a general agreement that in the human, the Differential Absorption Ratio (DAR) (I^{131} content per gram relative to that of 1 ml of blood) for the ovary is not more than one. The dose to the ovary is then considered not to be higher than for internal organs in general. It has been found in mice and in other small animals that moderate-to-large doses of I^{131} did injure the ovary. (17,18,19,23) The results of these experiments do not apply directly to the problem in the human because, on a weight basis, the doses were much higher than those being considered here. Also, in the human, the beta irradiation of the ovary is more restricted to that from the blood flowing through the gland, and the gamma contribution from I^{131} in such organs as the liver and urinary bladder would be relatively lower than in a small animal.

In spite of the lack of evidence of concentration of radioiodine in the human ovary, some physicians and lay persons have from time to time urged us to obtain more information on the subject. We have, therefore, done a few such studies on young women undergoing pelvic surgical procedures which precluded further pregnancies.[3] Four cases involved necessary termination of early pregnancy so we were able to do additional studies as well.

Radioiodine (I^{131}) was given (from 3 to 72 hours) before surgery. At the time of the operation, the surgeon removed a small piece of tissue from the ovary, uterus, and rectus muscle. The activity of these tissues was compared with that of the blood taken at the same time. The results are shown in Table I. These show that although there was considerable individual variation, there was a rapid decrease in activity of the blood, and none of the tissues examined showed a concentration higher than that of the blood. There did not appear to

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Human Studies Project

be a change in DAR with time, so the results are in general agreement with present published findings. It indicates that measurements of blood activity from time to time would be a satisfactory indication of I^{131} concentration in ovary, myometrium or rectus muscle.

It is known (12,13) that the salivary glands and stomach mucosa may temporarily concentrate I^{131} over that of the blood. It should also be kept in mind that the ovaries and other organs may receive gamma irradiation from large blood vessels and adjacent vascular organs as well as from urine in the bladder. In the present investigation there were two controlled and one uncontrolled variables. Four of the cases involved pregnancies that had to be terminated (F22, F23, F25, F26). The DAR values in these instances did not appear to be different from the general trend. In some of the other cases, stable iodine in the form of Lugol's solution was given before administration of the I^{131} and again it did not appear to make a significant change in the DAR of the tissues under study (which did not include the thyroid). The uncontrollable factor was introduced by necessary variation in surgical procedures and several of the lower blood activities appeared to be related to larger blood loss and transfusion during the surgery.

It is generally recognized that during therapy there are two phases of blood radioactivity. The first is due to I^{131} in the inorganic phase and the second is related to the I^{131} released from the thyroid to the blood in the organic form. We studied two patients who were treated with I^{131} for hyperthyroidism by daily measurements of blood radioactivity. The results are shown in Table II. These data were in agreement with findings of others in indicating a relatively high concentration in the blood for a few hours during the first day with a rapid loss in time. This was followed by a slight increase in radioactivity during the following few days with a slow decrease due primarily to physical decay.

TABLE I

DAR (Differential Absorption Ratio)

Hrs Hrs	*Activity in Blood in mμc/g/mc given*	*Ovary*	*Uterus*	*Rectus Muscle*	*Patient Number*
3	150	0.93	0.93	0.4	1**
6	14	1.06	0.59	0.21	7**
14	10	0.34	0.48	0.05	10(*F23)
15	77	0.88	1.28	0.24	2**
15	7	0.06	0	0.04	12
16	13	0.25	0.25	——	13**
17	5	1.0	0.93	0.48	11(*F25)
20	3	0.6	0.9	0.05	6**
21	10	0.8	0.8	0.37	14**
24	50	0.6	0.24	0.23	3(*F22)
48	1	1.0	0	0.25	4*
72	0.6	0.8	0.4	0.33	5*

*Fetal I^{131} uptake obtained also

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The results shown in Table III are of interest in that it shows the tremendous DAR of the fetal thyroid. It also indicates that the DAR increases as the age of the fetus and development of the thyroid progresses. The DAR is also higher the longer the time after administration of the I^{131}, and this is related to the loss of I^{131} activity from the blood.

In one instance (F27), I^{131} labeled triiodothyroine (liothyronine) was given by mouth and 16 hours later a 17-week-old fetus was removed. The percentage activity in the thyroid was 0.0014 and the percentage per gram was 0.02. The mμc/g/mc was 160 and the DAR was 8.5. The apparent uptake of the T3 by the fetal thyroid was low as compared with the usual uptake of I^{131}. The uptake of I^{131} as NaI in a fetal thyroid of about the same age was from 5 to 10 times that of the uptake of I^{131} as triiodothyroine in this case. A part of this thyroid was incubated with I^{131} as NaI for 30 minutes and it took up 0.27 per cent of the I^{131} available in the medium. On the other hand, as compared to its own blood, the DAR of the fetal thyroid was 60 and, as compared to the 110 of the amniotic fluid. As compared with the fetal liver, the DAR of the thyroid was 24.[1] In the mother's blood, all of the I^{131} was TCA precipitable and 84 per cent was non-enchangeable (ioresin). In the amniotic fluid, 94 per cent was TCA precipitable, but only 6 per cent was non-exchangeable.

One more case would be of interest in this connection.[2] This was a patient with marked hydramnoiois. A plasma volume determination was made using

[1]Following up this finding, we have incubated mouse thyroids in I^{131} labeled triiodothyroine several times and the uptake percentage was as high, if not higher, than with I^{131} as NaI. It was not bound very tightly, however, and although the activity did not wash out rapidly in saline, it did all come out in preserving fluids and we were unable to get autographs.

[2]We are indebted to Dr. H.J.B. Manderson of the Dept. of Obstetrics and Gynecology for collaboration in this particular study.

TABLE II

I^{131} IN BLOOD OF PATIENTS RECEIVING THERAPY FOR HYPERTHYROIDISM (MμC/ML/MC GIVEN)

Time, days:	0.16	1	2	3	4	5	6	7	8	9
Patient 8	——	1.6	3.2	3.2	2.5	3.4	3.4	——	——	——
Patient 9	79.5	1.35	0.98	1.12	0.7	0.9	1.2	0.9	0.76	0.46

TABLE III

I^{131} IN THYROID OF FETUS

Patient No.	*Hrs*	*% in gland*	*% per gram*	*mμc/g/mc*	*DAR*
10(F23)	16	0.003	0.08	800	74.5
3(F22)	24	1.4	5.4	54,000	1,080.0
11(F25)	17	1.1	4.95	49,500	19,000.0
(F26)	24	0.6	3.0	30,000	22,000.0

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radioiodinated albumin. The mixing time was found to be very long and the plasma volume was very large. The patient was in such difficulty that some amniotic fluid had to be removed. Within a few hours labor started and twins were delivered prematurely. They expired immediately and as soon as the post-mortem examination was finished we were given one of the thyroids for study. Although the amniotic fluid did not contain a significant amount of I^{131}, the fetal thyroid did contain a measurable amount (about 0.017% of the amount given to the mother). This would be about 0.06 per cent per gram or 600 mμc/g/mc given. The DAR of this fetal thyroid, as compared to mother's blood, was 0.7. The usual uptake (of glands of this size) is about 1 per cent and ion-exchange studies of the RISA used indicated that about 2 per cent of the I^{131} was exchangeable. Therefore, the uptake in the fetal thyroid could represent uptake of the fraction of the dose that was in the nonprotein form. The I^{131} washed out of the thyroid in the preserving fluid. A portion of the gland was incubated with NaI and the incorporated activity did not wash out in the preserving fluid. In fetal thyroids of this age when NaI^{131} was given to the mother, the activity of the gland was not reduced by the preserving fluids. One then must consider that a loose binding like that which occurred with the T3 might have taken place with a certain fraction of the iodinated serum albumin compound or its breakdown products. Related references of interest in this connection are listed below (20-29).

SUMMARY AND CONCLUSIONS

In addition to confirming the findings of others that the human ovary does not concentrate I^{131} when given as NaI, the great concentration in the fetal thyroid over that of the blood DAR has been demonstrated. The DAR of the fetal thyroid increases from about 75 to as much as 22,000 as the fetus develops from the third to the sixth month of gestation. It has also been demonstrated in one instance that I^{131} as T3 crossed the placenta and was concentrated loosely in the fetal thyroid with a DAR of about 8.5.

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