BNWL-SA- 5065
Conf-740715--10

# Carcinogenicity of Iodine-131 Relative to Age at Exposure



M. R. Sikov and D. D. Mahlum

Biology Department
Pacific Northwest Laboratories
Richland, Washington 99352

There have been a number of epidemiologic studies which suggest that the thyroid glands of children are more susceptible to the carcinogenic action of radiation than are the thyroids of adults. There have been a number of studies to evaluate the carcinogenicity of radioiodine in various animal species but the quantitative relationships between age and thyroid tumor development has not been defined. The present study was undertaken to establish these relationships in the rat.

The experiment was performed in five increments, separated by about 4-6 weeks. For each subset, adult rats of the CD strain were purchased from the Charles River Breeding Laboratories. As shown on the FIRST SLIDE some of these were retained for use as adults, while others were mated to provide rats for the younger age groups.



A solution of carrier-free $^{131}I$, in NaOH, was diluted to appropriate concentrations, with resulting pH values of 8 to 9, and used for exposure of the experimental animals. SLIDE 2 - The adults and weanlings were exposed by stomach tube, receiving 5 daily doses (Table 1). The mothers of the rats in the newborn and prenatal groups were exposed to the same doses as the experimental adults, so that the experimental animals received the $^{131}I$ through the milk or through a

---

For presentation at the 5th International Congress of Radiation Research, July 14-20, 1974, Seattle, Washington. Abstract cleared as BNWL-SA-4906A.

## DISCLAIMER

combination of cross-placental transfer and milk.

The highest dose used in the adults was expected to produce a moderate degree of morphologic and physiologic change in the thyroid glands, while the medium dose was selected to be below the threshold for subacutely demonstrable overt change. This dose was further reduced by a factor of 15 to obtain the low dose. The weanling animals received approximately the same doses, on a μCi/g body weight basis. It was anticipated that the youngest animals would be more susceptible to the carcinogenic action of radiation, so a lower range of doses to the thyroid gland was used. For convenience, at each age these doses were designated as "low", "medium", or "high".

There were approximately 50 rats of each sex in each age-dose group. We planned on a control group of approximately twice this size, i.e., 100 males and 100 females, distributed over the four age groups. In all cases, the control animals or their mothers received a comparable solution not containing the radioiodine.

These rats were followed until death or until thirty months of age, at which time they were sacrificed. Skip serial sections of the thyroid and pituitary glands were prepared by routine techniques and examined histologically. The animals which were sacrificed at 30 months of age received a tracer dose of iodine-125 twenty-four hours prior to sacrifice, and the incorporation in the thyroid gland was determined at sacrifice. At the completion of the exposure of the experimental animals in the carcinogenesis study, additional groups of animals of each age were exposed to the same doses and sacrificed at intervals. The thyroid glands were removed, weighed, and the activity of $^{131}I$ determined by gamma-counting. The radiation doses to the thyroids were calculated, correcting for non-absorbed beta particles.

SLIDE 3 shows the calculated radiation at the medium dose level.

The radiation doses were not completely proportional to the administered doses, and fell off at high radiation doses. At each administered dose level, the adults received somewhat more than twice as great a radiation dose to the thyroid as did weanlings. The prenatally exposed animals, which also received further $^{131}I$ in the milk, received a slightly lower dose than did the weanlings, and those exposed neonatally received an even smaller dose.

The effect of the administered dose of $^{131}I$ on the $^{125}I$ uptake of the thyroids of the rats which survived to 30 months of age is shown in SLIDE 4. In the adults, the medium dose, which gave 2000 rad, decreased uptake slightly, while the high dose or about 16.6 rad decreased uptake to 28% of control uptake. In the weanlings, thyroid function was unaffected by any dose other than the highest, about 5400 rads, which decreased uptake to about 44% of control levels. In those exposed prenatally, 3400 rad - the high dose - reduced uptake to about 70%. In the newborn animals, the medium dose decreased function slightly, but the high dose, which gave only 2200 rad, reduced uptake to only 57% of control values.

There was no sex difference in the development of thyroid tumors and the sexes were combined to calculate the incidences shown on the NEXT SLIDE (5). In the adults the low dose, which gave accumulative radiation dose of about 175 rad to the thyroid, produced 22% tumor incidence and there was a fall off in incidence among the rats of the medium and high dose groups which received about 2,000 and 17,000 rad, respectively. In the weanlings, 50 rad, which corresponds to the low dose, slightly increased tumor incidence, 700 rad produced a marked

increase to 40% while the high dose, which gave about 5500 rad, resulted in a lesser incidence. Although not strictly comparable, this would suggest that the weanling was more sensitive than was the adult.

Both the low dose and controls had a similar incidence in the newborn group with a sharp rise to 33% at the medium dose or 280 rads, with a drop to control levels at 2200 rads. Even the low dose, which delivered 40 rads, markedly increased incidence in the prenatally exposed animals with no drop in incidence at higher doses.

A number of pituitary tumors were noted in both the control and the experimental animals, SLIDE 6. Although all types of pituitary tumors were combined for this tabulation, about 2/3 of the tumors have been diagnosed as chromophobe adenomas. In addition, a large number of animals, controls included, showed cystic enlargement of the pituitary with marked hemorrhage.

# AGES EXPOSED

| | |
|---|---|
| ADULT | ~ 4 months - 5 consecutive days |
| WEANLING | 21-25 days of age |
| NEWBORN | 0-4 days of gestation |
| PRENATAL | 17-21 days of gestation |

SLIDE 2

# $^{131}$I EXPOSURE LEVELS

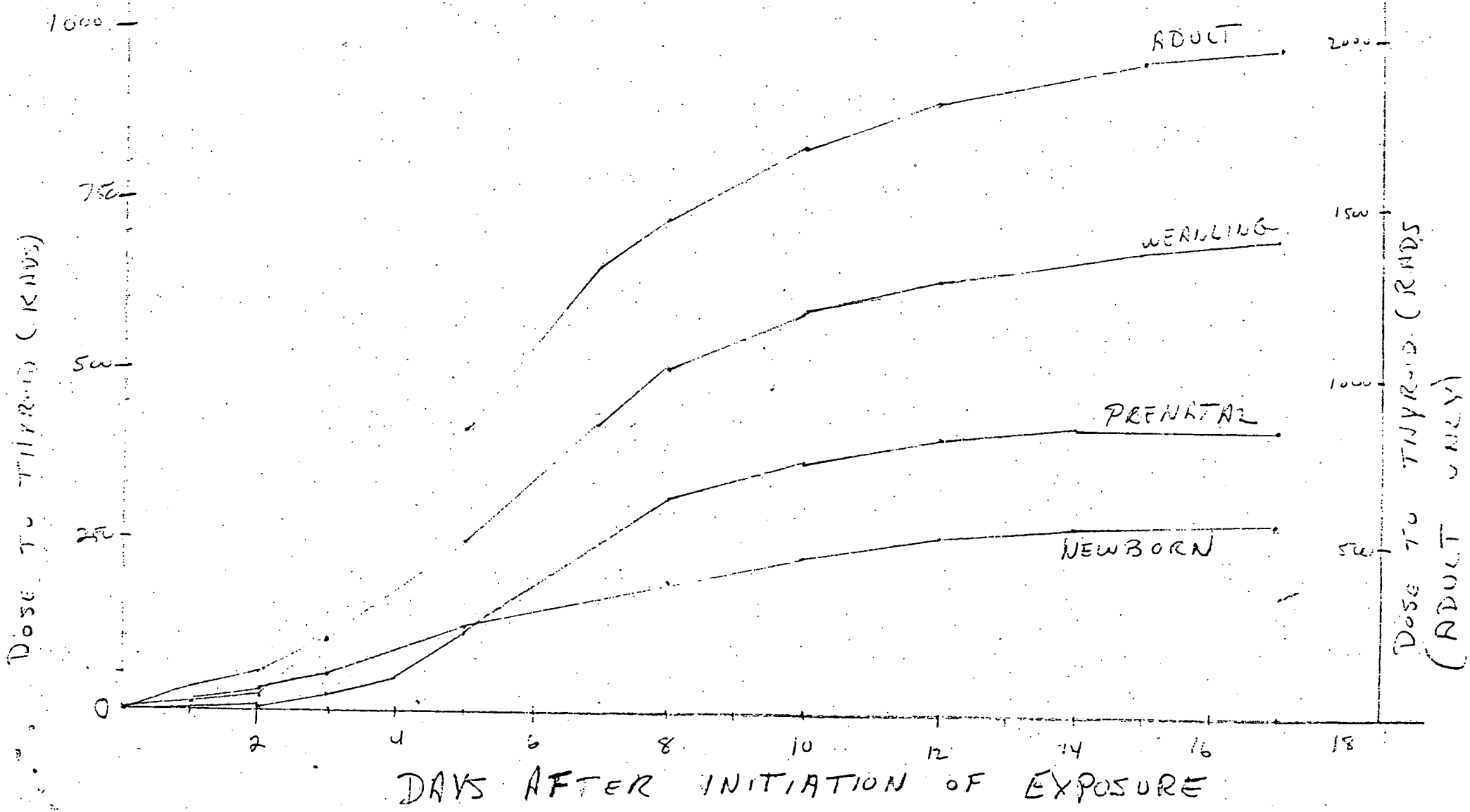
| Exposure Level | Adults & Mothers of Prenatals & Newborns | | Weanlings | |
|---|---|---|---|---|
| | µCi/day | Total µCi | µCi/day | Total µCi |
| Low | 0.2 | 1 | 0.05 | 0.25 |
| Medium | 3 | 15 | 0.75 | 3.75 |
| High | 30 | 150 | 7.5 | 37.5 |

all Caps across
~~Title column~~

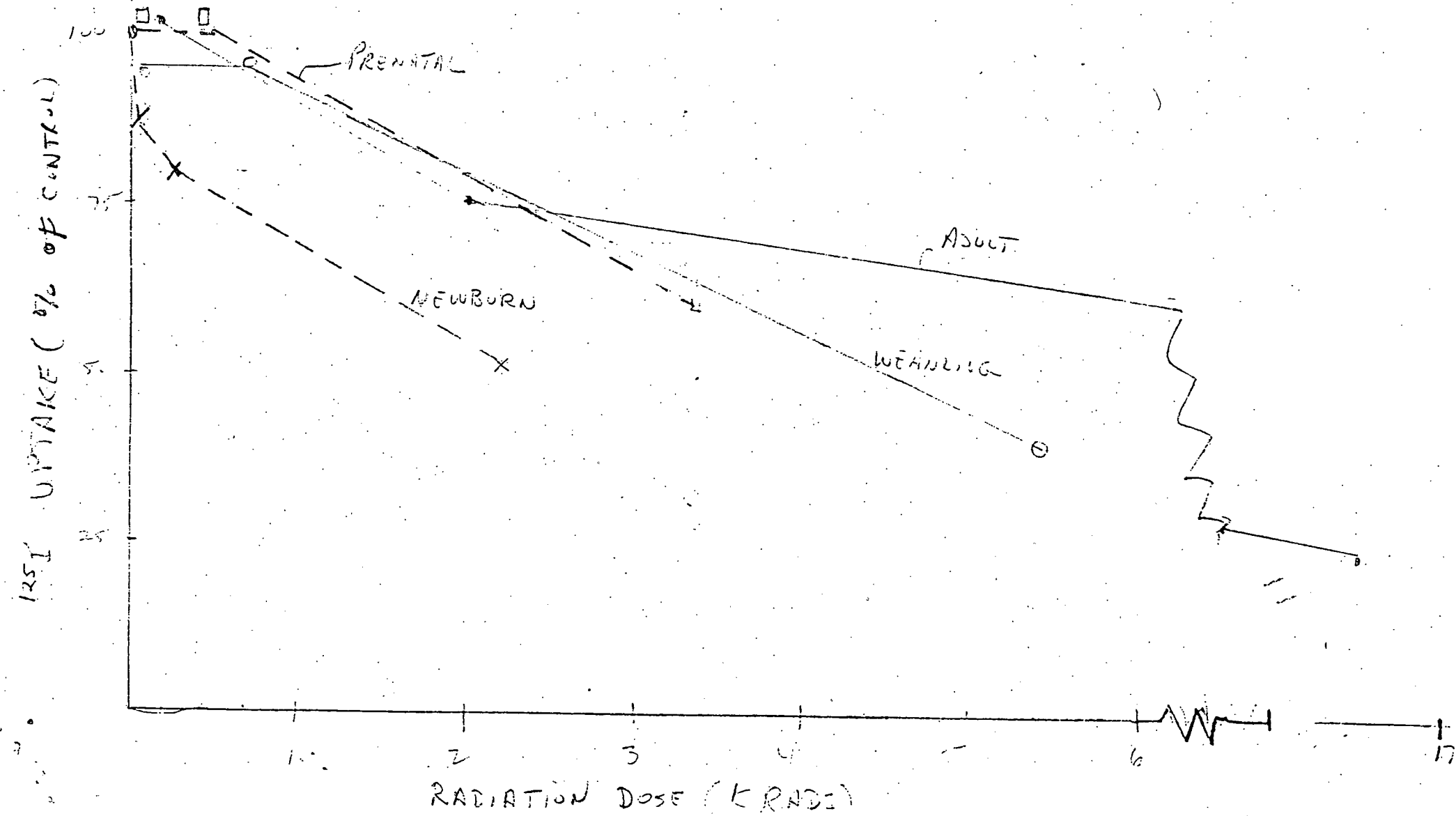
SLIDE 3

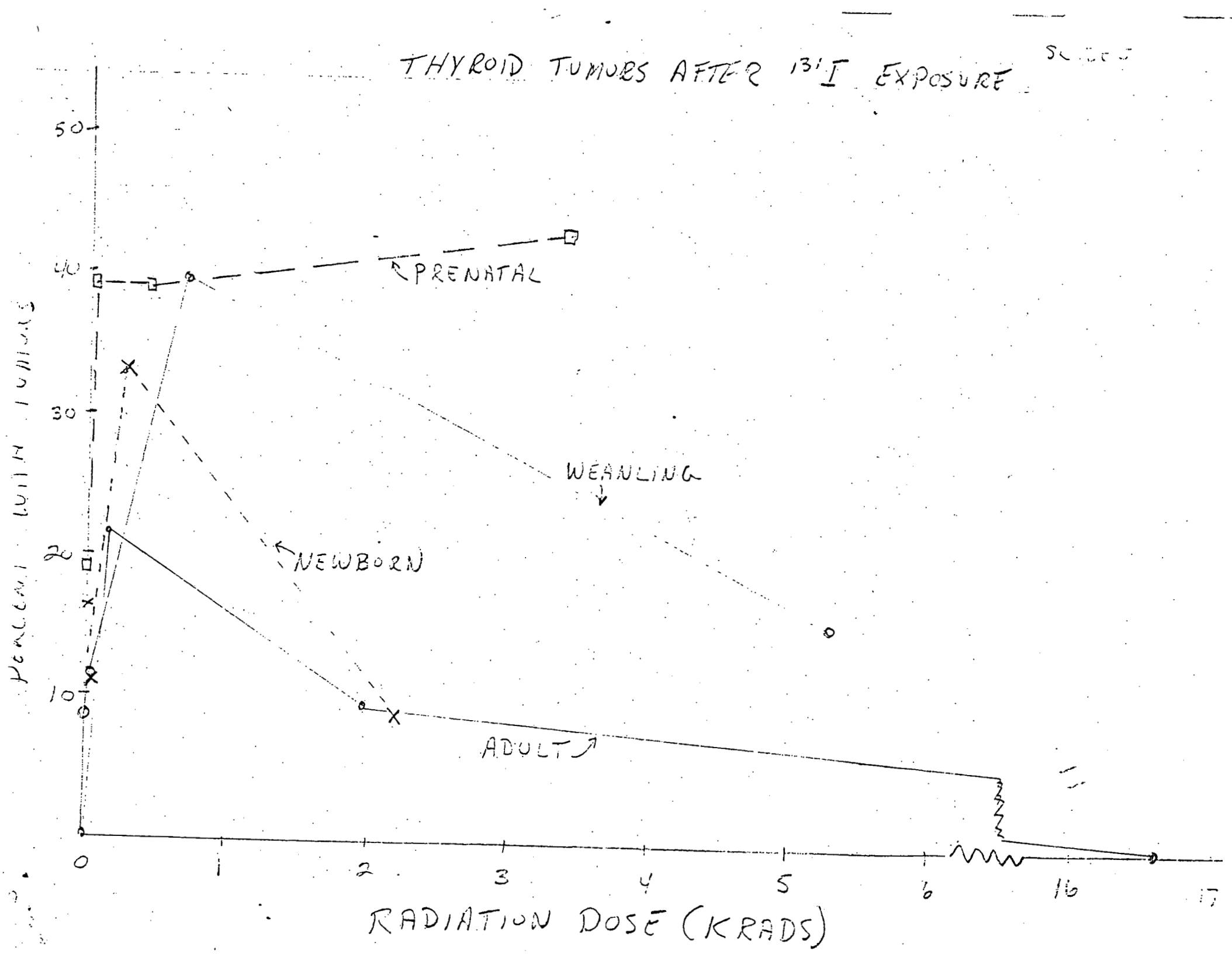
Source curves do NOT show pt.

# RADIATION DOSE TO THYROID AFTER $^{131}I$
(5 Daily Doses)



# $^{125}I$ UPTAKE 30 MONTHS AFTER $^{131}I$ EXPOSURE




THYROID TUMORS AFTER $^{131}I$ EXPOSURE
PERCENT WITH TUMORS
50
40
30
20
10
0
PRENATAL
WEANLING
NEWBORN
ADULT
0
1
2
3
4
5
6
16
17
RADIATION DOSE (KRADS)

SLIDE 6

# PITUITARY TUMORS