• Modifying Radionuclide Effects

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This project involves a study of the relationship of physiological and environmental factors to the metabolism and effects of radionuclides. We have studied placental transfer and suckling as pathways of americium entry into the newborn or juvenile rat. Rats were injected intravenously with 5 μCi of ^{241}Am while nulliparous (30 days prior to mating), pregnant (day 19 of gestation), or lactating (1 day after parturition), and subsequent litters were killed to determine ^{241}Am retention. A deficit in reproductive performance was observed in the group injected before mating, as evidenced by reduced number and weight of offspring.

In past studies, we have observed, in female rats injected intravenously with monomeric ^{239}Pu, that the incidence of mammary tumors was higher and the latency period shorter than those in control animals. To determine if these tumors were a direct result of ^{239}Pu deposition in the gland, the relationship between tumor incidence and plutonium deposition was investigated. It soon became clear that the amount of plutonium deposited in the mammary gland and uterus could be influenced by pregnancy and lactation. Data reported previously (Annual Reports, 1979, 1980) demonstrated that the relative amounts of plutonium reaching the offspring via the placenta and by nursing was a function of the temporal relationship between plutonium administration and pregnancy.

We have observed, in other experiments, that americium is deposited in the liver and other soft tissues of the nonpregnant rat and that only a small percentage is retained by bone, whereas plutonium is deposited to a greater extent in bone, where its retention is prolonged. Because of these differences, it seems likely that americium may also behave differently from plutonium under physiological stresses, such as pregnancy and lactation. Therefore, the objective of this study is to determine the effect of pregnancy and lactation on the transfer of ^{241}Am to the offspring of the rat. The experiment was designed so that female rats were dosed while nulliparous (30 days prior to mating), pregnant (day 19 of gestation), or lactating (1 day after parturtion); the subsequent transfer of ^{241}Am to the offspring was then measured as a function of their age.

Three-month-old, pregnant, Sprague-Dawley rats were divided into two groups of 23 each and intravenously dosed with 5 µCi of ^{241}Am on day 19 of gestation (pregnant) or 1 day postpartum (lactating). An additional 30 females were similarly dosed 30 days prior to conception (nulliparous). Females, and their progeny, from the pregnant and lactating groups were killed at 1, 4, 9, 14, or 21 days after injection. The nulliparous group, which were not bred until 30 days after injection, were killed when their progeny were -2, 1, 6, 11, or 18 days of age. Samples of liver, kidney, femur, spleen, mammary gland, and uterus were analyzed for ^{241}Am by gamma counting. Tissues with low concentrations of ^{241}Am (blood, nidation sites, milk, and fetuses) were ashed for analysis by liquid scintillating counting.

Approximately one-half of the ^{241}Am was found in the liver of the pregnant and lactating groups 1 day after injection. Retention by the liver appeared to be slightly greater in the lactating group than in the pregnant group at all times measured, but preliminary analyses (t-test) do not show statistical differences. The half-time of americium in the liver was approximately 22 days in both groups, nearly twice as great as previously observed in nonpregnant rats. Differences between the two groups are not apparent for other tissues measured to date.

An unexpected result of this experiment was a deficit in reproductive performance in the group injected while nulliparous. The weight of the offspring of the nulliparous and pregnant groups, at various ages, is shown in Table 1. Litter weights appeared less in the nulliparous group at all ages, although statistical evaluation (t-test) revealed that differences were significant only at -2, 11, and 18 days of age.

Approximately 40% (12 of 30) of the nulliparous group had small litters ($P < 0.01$), averaging only 2.6 fetuses per litter (Ta-

TABLE 1. The Weight of Offspring of Rats Injected With ^{241}Am When Nulliparous (30 Days Prior to Mating) or Pregnant (19 Days of Gestation).

Age of Offspring, days	Weight of Offspring, g[a]						P
	Nulliparous Group			Pregnant Group			
−2	2.93	0.11	(5)[b]	3.93	0.17	(5)	<0.01
1	6.64	0.21	(5)	6.83	0.18	(3)	NS
6	11.4	0.6	(5)	12.8	0.4	(5)	NS
11	20.3	1.0	(5)	24.0	0.5	(5)	<0.02
18	37.6	0.2	(5)	43.7	1.3	(5)	<0.05

[a] Mean ± SE
[b] The number of litters is shown in parentheses.

TABLE 2. Reproductive Performance of Rats Producing Either Normal or Small Litters After Being Injected With ^{241}Am While Nulliparous.[a]

Size of Litter	Total No. of Litters	No. Fetuses per Litter	No. Nidation Sites	No. Corpora Lutea
Normal	18	>8	10.6 ± 0.4	13.6 ± 0.8
Small[b]	12	2.6 ± 0.6	3.5 ± 0.6	10.8 ± 1.1
P		<0.01	<0.01	NS

[a] Mean ± SE
[b] Litters having five or less pups were arbitrarily classified as small litters.

ble 2). They were therefore arbitrarily divided into two subgroups based on litter size; i.e., normal or a reduced number (five or less per litter). A marked reduction ($P < 0.01$) in the number of nidation sites was also observed, but the number of corpora lutea were only slightly fewer than in the normal subgroup. These results imply that a significant number of preimplantation deaths occurred in a large fraction of the nulliparous group. No evidence of a similar effect was found in the pregnant or lactating groups.

Preliminary estimates indicated that the dose to the ovary, the reproductive organ having the greatest americium concentration, was approximately 1.5 rad per day. Further studies will be required to verify these findings and to accurately determine the dose received by reproductive organs.