sociated with a fall in concentration of clotting factors. Moderate disturbances in coagulation with surgery and transfusion during hypothermia were in most regards similar to those observed during surgery and transfusion at normal body temperature. The one significant difference was a decrease in prothrombin consumption.

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Received September 5, 1957. P.S.E.B.M., 1958, v97.

Potentiating Effects of Prenatal X-Irradiation on Dental Caries in the Rat.* (23690)

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It is well established that x-irradiation during the prenatal period will result in abnormalities or death of the young depending on the time of gestation and the dosage of x-irradiation administered. The pertinent literature in this field has been extensively reviewed by Russell(1). These studies, however, have dealt primarily with the effects of x-irradiation on the young as judged by their morphological appearance or viability at the time of parturition or the period immediately following. Comparatively few studies have been conducted to determine the effects of x-irradiation during prenatal life on the subsequent post-weaning response of the young. Growth retardation, brain damage and damage of the retina, cord and ganglia, sterility, skin defects and cataracts, and impaired maze learning performance(1-3) have been observed in the surviving young of mother rats administered sublethal doses of x-irradiation during various periods of pregnancy. In the present communication data are presented on the effects of x-irradiation during the formative period of tooth development (18th, 14th or 10th day of pregnancy) on susceptibility to dental caries in the rat.

Procedure. Forty female rats of the Long-Evans strain which had been raised from weaning on a natural food stock ration† were selected at 3 to 4 months of age and an average body weight of 188 g. Animals were divided at random into 4 equal groups of 10 rats each and were mated to males of proven fertility. Pregnancy was dated by the finding of sperm in the vaginal smear.‡ Animals in Group I served as non-irradiated controls; those in Groups II, III and IV received a single exposure of 150 r x-irradiation on the 18th, 14th or 10th day of pregnancy respec-

* This investigation was supported in part by Medical Research Contract No. DA-49-007-MD-768 with the Surgeon General's Office, Department of Army, Washington, D. C.

† Rockland Rat Diet, Arcady Farms Milling Co., Chicago, Ill.

TABLE I. Effects of a Single Dose of 150 r X-irradiation during Various Periods of Prenatal Life on the Reproductive and Lactation Performance of Rats.

	Non-irrad.	Irradiated on following day of pregnancy: 18th day	14th day	10th day
No. of rats bred	10	10	10	10
No. of litters cast	9	9	10	10
Avg litter size*†	7.8 ± 1.1	7.7 ± .7	9.3 ± .5	7.6 ± .9
% young born dead	1.8	0	0	0
Avg birth wt of young, g*	6.1 ± .3	5.6 ± .2	5.5 ± .2	5.4 ± .2
% mortality of young during lactation period	7.0	9.8	9.6	39.5
% incidence of microphthalmia and anophthalmia in young	0	0	0	40.0
Avg weaning wt of young, g*	45.0 ± 1.4	40.3 ± 1.6	34.9 ± 2.7	44.4 ± 1.6

* Including stand. error of mean. † Including young born dead.

tively. The radiation factors were as follows: GE Model Maximar 250; 250 kv; 15 ma; 0.5 mm Cu and 1 mm Al filters plus a Cu parabolic filter;§ HVL, 2.15 mm Cu; target distance to top of box, 78 cm; and dose rate, 17.92 r per minute (measured in air). The animals to be irradiated were placed in a wooden box divided into 14 compartments 7 cm wide, 16 cm long and 10 cm deep. The partitions and top were made of ⅛" cellulose acetate sheeting; and the top, one side and bottom of each compartment were perforated with holes for purposes of ventilation. The container was rotated slowly on an electrically-driven turntable to insure equivalent irradiation Throughout pregnancy and lactation rats were continued on the same natural food ration on which they had been raised since weaning.† Food and water were provided *ad libitum*. No significant difference was observed between any of the groups in respect to the number of litters cast, the average number of young born or the average weight of the young at birth. The mortality of the young during the lactation period was greater for the offspring of Group IV (rats irradiated on the tenth day of pregnancy) than for those of other groups. The average weight of surviving young of Group IV, however, when weaned at 21 days of age, did not differ significantly from the weaning weight of the young of other groups.‖ In agreement with earlier findings(1,4), 40% of the young of Group IV exhibited anophthalmia or microphthalmia in contrast to a 0% incidence of these deformities among the offspring of the other groups. Findings are summarized in Table I.

Twelve male and 12 female rats (consisting of at least 1 male and 1 female from each litter) were selected at weaning from the young of each of the above groups. Animals were placed in metal cages with raised screen bottoms (3 animals per cage) and were fed *ad libitum* a cariogenic skim milk-containing ration similar to diet 635 of McClure and Folk (5). This ration consisted of roller process skim milk powder, 35%; glucose, 18%; corn starch, 45%; and dehydrated liver, 2%. To

‡ The start of pregnancy was timed from the time that sperm were actually observed in the vaginal smear. Inasmuch as mating may have occurred at any time from 5 P.M. of the previous day to 8 A.M. of the day that sperm were found, fertilization may actually have occurred as much as 15 hours before the time that sperm were observed. The first day of pregnancy covered the first 24 hours following finding of sperm. It is estimated that actual time of x-irradiation was approximately 17½, 13½ and 9½ days post fertilization.

§ A non-uniform filter which produces a flat isodose surface of X-ray intensity constructed by the method of Greenfield and Hand(9). We are indebted to Dr. M. Greenfield and Miss Katherine Hand of the Atomic Energy Project, University of California at Los Angeles, for construction of the parabolic filter. The center of filter was 1.7 mm Cu, the edge, 0.5 mm Cu thick.

‖ The normality in weaning weight of this group may be deceptive since such a high proportion died and the survivors thus had a better chance for weight gain than did young of other groups.

TABLE II. Effects of Prenatal X-irradiation on Incidence and Severity of Dental Caries in Rats Subsequently Fed a Cariogenic Skim Milk-Containing Ration.

Exp. group	Non-irrad.	Offspring of rats irradiated on following day of pregnancy: 18th day	14th day	10th day
No. of rats	24	24	24	24
Initial wt, g	41.2	41.4	41.4	41.2
Final wt, g*	281.2	234.5	216.4	238.2
Carious incidence (%)				
Carious rats	58.3	45.8	62.5	70.8
Occlusal carious rats†	29.2	20.8	58.3	54.2
Surface " "	58.3	37.5	62.5	58.3
Caries distribution and severity (No./rat)				
Occlusal carious areas	.6	.3	1.9	3.3
Lingual " "	.0	.0	.0	1.5
Buccal " "	1.3	.5	2.2	4.0
Score/rat‡	1.8	.8	9.3	23.1
Score/carious rat‡	3.1	1.8	15.4	32.0

* After 90 days feeding, animals were sacrificed and evaluated for caries.

† Data were based on No. of rats with occlusal caries irrespective of whether or not surface caries were also present.

‡ The caries lesions were recorded and scored as follows: occlusal, lingual and buccal surfaces were each divided into 3 areas in the case of the 1st molar and 2 areas in the case of the 2nd and 3rd molars and each carious defect was scored one, 2 or 3, according to the extent of the carious destruction. The maximum possible caries score for a 1st molar tooth was therefore 3 × 3 × 3 or 27, whereas the maximum possible caries score for a 2nd or 3rd molar was 3 × 2 × 3 or 18. The maximum possible caries score/rat based on evaluations of the lower teeth only (2 each of the 1st, 2nd and 3rd molars; incisors were not included) was therefore 126. "Score/rat" was determined by dividing the total caries score by the No. of animals in the group. "Score/carious rat" was obtained by dividing the total caries score by the No. of carious rats.

each kg of the above were added 5000 U.S.P. units of Vit. A, 500 U.S.P. units of Vit. D_2 and 100 mg alpha-tocopherol acetate. The vitamins were added in place of an equal amount of corn starch. Previous findings by McClure and co-workers(5,6) indicate that rats fed a ration similar to the above (diet 635) develop a high incidence of surface type caries similar in a number of respects to the type of dental caries found in man(7,8). In addition 12 male and 12 female rats similar to the above were selected at weaning from the young of each group and were continued on the same ration that had been fed during pregnancy and lactation.[†] After 90 days of *ad libitum* feeding, all rats were sacrificed; the heads were autoclaved, cleaned of adhering soft tissues; and the lower teeth were evaluated for caries according to the procedure of McClure and Folk(5).

Results. Findings indicate that x-irradiation during certain periods of prenatal development significantly increased the severity of dental caries in rats subsequently fed a cariogenic skim milk-containing ration (Table II). The effects of x-irradiation were most marked on the offspring of rats irradiated on the 10th day of pregnancy. 70.8% of the rats in the latter group developed caries when fed the skim milk-containing ration with an average severity score of 32.0 per carious rat in contrast to a 58.3% incidence of caries and an average severity score of 3.1 per carious rat for the offspring of non-irradiated rats fed a similar diet.[¶]

It would appear from these findings that x-irradiation enhanced the severity of the carious lesion but had little if any effect on its incidence. The offspring of rats irradiated on the 14th day of pregnancy also exhibited a significant increase in severity of caries when fed the skim milk-containing ration (average severity score, 15.4 per carious rat). In contrast to the above results, no increase in the severity of dental caries occurred in rats whose mothers were irradiated on the 18th day of pregnancy. Whereas x-irradiation during certain periods of prenatal development significantly increased the severity of dental caries in rats fed a cariogenic skim milk-containing ration, it had no such effect on rats maintained on the stock ration.[†] The incidence of caries in rats fed the latter diet did not exceed 10% in any of the groups, with such lesions as did occur being minimal in severity.

Summary. X-irradiation during certain periods of prenatal development significantly increased the severity of dental caries in rats subsequently fed a cariogenic skim milk-containing ration. The offspring of rats admin-

[¶] Distribution of caries lesion and increase in caries severity occurred with relative uniformity in all mandibular molars.

istered a single dose of 150 r x-irradiation on the 10th or 14th day of pregnancy showed a significant increase in severity of caries over that of the offspring of non-irradiated rats. Severity of caries was not increased in the offspring of rats administered a similar dose of x-irradiation on the 18th day of pregnancy.

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Received September 5, 1957. P.S.E.B.M., 1958, v97.

Creatine-Phosphate Utilization by Muscle Extracts of Rabbits on Vit. E-Deficient Diets.* (23691)

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The main pathway for creatine metabolism is presumed to be reaction I which is linked to glycolysis by reaction II. The overall reaction III was studied by following stabilization of phosphate from creatine-phosphate.

$$\text{C-P} + \text{ADP} \rightleftharpoons \text{ATP} + \text{Creatine} \quad \text{(I)}$$

$$\text{ATP} + \text{HMP} \rightarrow \text{ADP} + \text{HDP} \quad \text{(II)}$$

$$\text{C-P} + \text{HMP} \rightarrow \text{Creatine} + \text{HDP} \quad \text{(III)}$$

Since phosphate of creatine-phosphate also may be transferred to HMP with production of creatinine as measured by the Jaffe reaction(1), creatinine production was determined. It was necessary to ascertain that the effects observed in utilization of creatine-phosphate by muscle from Vit. E-deficient animals were specific for the system by which C-P is used. To observe whether generalized and similar changes occurred in other metabolic pathways in muscle, activity of another soluble enzyme, phosphoglucomutase, and rate of glycolysis by muscle strips were also investigated.

Materials and methods. Animals and diets. New Zealand male rabbits weighing 500-600 g were used. One group of 26 animals was fed Mason and Harris diet(2), and to half of them a supplement of cod liver oil (4 ml/week) was given while the other half received 75 mg of α-tocopheryl acetate (Distillation Products Industries)/week. A second group of 60 rabbits received the diet shown in Table I. Creatinuria (Cr/Cn values varied from 1 to about 5) occurred after 18 days on Mason-Harris diet in animals not receiving tocopherol. Neither of these diets produced a severe dystrophy, but instead a relatively mild effect on muscle in terms of weakness and wasting, similar to that reported with diets R-14 and R-20, by Hove and Copeland(3). The animals on Diet II survived for 100 days or more and, although they became weak,

* This investigation was supported by research grants from N. I. Arthritis and Metabolic Diseases, N.I.H.

† The following abbreviations will be used: C-P creatine-phosphate, ADP adenosine diphosphate, ATP adenosine triphosphate, HMP hexosemonophosphate, HDP hexosediphosphate, G-1-P glucose-1-phosphate, G-6-P glucose-6-phosphate, F-6-P fructose-6-phosphate, TCA trichloracetic acid, Cn creatinine, Cr creatine, PGM phosphoglucomutase, G-1-6-P glucose-1-6-diphosphate.