Proceedings
of the
Society
for
Experimental Biology and Medicine

VOL. 85 MARCH, 1954 No. 3

SECTION MEETINGS

BALTIMORE, MD.	
Johns Hopkins Hospital	February 5, 1954
DISTRICT OF COLUMBIA	
George Washington University	February 4, 1954
IOWA	
State University of Iowa	February 23, 1954
PACIFIC COAST	
Univ. of California Medical Center	February 24, 1954
SOUTHERN	
Tulane University	January 21, 1954
Louisiana State University Medical School	January 28, 1954

Effects of Aureomycin and P^{32} on Growth of Young Rats.* (20887)

LEONARD ROSENTHALL† AND JAMES F. MARVIN. (Introduced by K. W. Stenstrom.)
From the Department of Radiology, University of Minnesota Hospitals, Minneapolis, Minn.

The following is a report of observations made in a preliminary investigation of the effect of aureomycin in combatting growth retardation induced by a single intraperitoneal injection of P^{32}.

Methods and materials. Forty male rats of a Holtzman-Rolfsmeyer strain were divided into 4 groups. Group A was fed a Purina fox-checkers diet. Group B was fed Purina fox-checkers ground up with aureomycin-HCl (Lederle) at 2 mg per gram of feed(1,2). Group C was given the same diet as Group B, but each animal was injected intraperitoneally with P^{32} at 2 μc/g body weight just before the diet was offered(3). Group D was maintained on Purina fox-checkers, but each animal was injected intraperitoneally with P^{32} at 2 μc/g of body weight. All animals were 26 days of age at time of treatment and were housed two per cage; the pairs being from the same group. Cages were of plastic construction, containing a thick layer of wood shavings which was changed frequently. Food and water were available *ad libitum*. The animals were weighed at various intervals and were serially roentgenographed to determine tibial length. For roentgenography the animals were anesthetized with ether, and then firmly secured with adhesive tape face down onto the film casette. Special precaution was taken to see that both knee and ankle were firmly against the casette. X-ray exposure factors were 38 KVP, 100 ma., 1/20 sec and 125 cm target-film distance. Tibial lengths were measured on the x-ray film with a pair of micrometer calipers.

Results. All animals were alive at the

* Supported in part by the Atomic Energy Commission.

† Now at McGill University, Montreal, Canada.

TABLE I. Effects of Aureomycin and Radioactive Phosphorus on Weight Gain of Rats.

A (normal) 9 animals			B (aureomycin) 11 animals			C (P^{32} + aureomycin) 10 animals			D (P^{32}) 10 animals		
Days post-treatment	Avg wt, g	% of wt at treatment	Days post-treatment	Avg wt, g	% of wt at treatment	Days post-treatment	Avg wt, g	% of wt at treatment	Days post-treatment	Avg wt, g	% of wt at treatment
0	45.1	100	0	46.8	100	0	43.1	100	0	43.9	100
7	84.7	188	7	93.9	200	7	72.6	168	7	70.5	160
14	131.3	291	14	143.5	306	14	114.4	265	14	104.4	238
21	176.5	391	21	190.7	407	21	158.2	367	21	145.8	332
27	205.8	456	28	238.2	509	28	182.8	424	28	158.7	361
36	238.6	529	—	—	—	36	226.2	526	36	183.1	417
42	255.3	566	42	290.0	616	42	255	591	42	202.1	460
49	278.5	617	49	303.4	648	49	275.8	640	49	225	513
67	329.5	730	68	353.2	754	65	327.8	760	67	281.2	640

TABLE II. Effects of Aureomycin and Radioactive Phosphorus on the Relationship between Weight Gain and Increase in Tibial Length.

A (normal) 9 animals				B (aureomycin) 11 animals				C (P^{32} + aureomycin) 10 animals				D (P^{32}) 10 animals			
Days post-treatment	Gain in wt (W), g	Gain in tibial length (L), mm	W/L	Days post-treatment	Gain in wt (W), g	Gain in tibial length (L), mm	W/L	Days post-treatment	Gain in wt (W), g	Gain in tibial length (L), mm	W/L	Days post-treatment	Gain in wt (W), g	Gain in tibial length (L), mm	W/L
7	39.6	3.0	13.2	7	47.1	2.85	15.9	7	29.5	2	14.7	7	26.6	2	13.3
14	86.2	6.1	14.1	14	96.7	5.9	16.3	14	71.3	4.5	15.8	14	60.5	4.2	14.5
27	160.7	10.5	15.2	21	143.9	8.57	16.8	25	129.9	8.0	16.2	26	110.0	7.69	14.3
34	186.6	12.3	15.1	28	191.4	10.8	17.7	32	162.3	10.29	15.8	33	130.8	9.51	13.8
47	229.0	14.4	15.9	68	306.4	15.88	19.2	45	229.2	12.92	17.8	46	174.2	11.75	14.8
67	284.4	16.5	17.2	—	—	—	—	65	284.1	15.1	18.6	67	237.3	14.17	16.7

Avg tibial length at time of treatment: Groups A, C, and D—23.2 mm; Group B—24.3 mm.

termination of the experiment. No toxic effects such as diarrhea were noted. The animals of Group B which received no radiation but were maintained on an aureomycin supplemented regimen exhibited a stimulation in growth. At 42 days post-treatment, the difference in weight between Group B and the control Group A (Table I) was statistically significant ($P = 0.002$). At 65 days post-treatment, the significance was questionable ($P = 0.28$). This suggests that aureomycin will stimulate initial gain in weight, but does not alter significantly the ultimtae weight of the animal. It is noteworthy that the ratio of weight gain to tibial length increase for Group B (Table II) was significantly higher than for the control Group A for each value of tibial length. Aureomycin appears, (at this dosage) to favor soft tissue formation rather than a uniform increase in growth.

The animals of Group D (which received one dose of P^{32} but no aureomycin) exhibited a generalized growth retardation, evident both in weight gain and in tibial length compared to the control Group A. The ratio of weight gain to tibial length increase for Group D was not significantly altered from that for Group A for any value of tibial length. This indicates that, although P^{32} tends to accumulate in the metaphysis adjacent to the epiphyseal cartilage plate, no overall selective inhibition of bone growth occurs (with the dose of P^{32} administered).

The animals of Group C (which received the same amount of P^{32} but were maintained on the aureomycin supplement) showed complete weight recovery by about 42 days post-treatment. The ratio of weight gain to tibial length increase remained higher than the control Group A for all values of tibial length. Whether aureomycin mediates its effects through direct involvement in metabolic processes or indirectly through alteration of intestinal flora remain a topic for further investigation.

Summary. 1. One group of rats (D), maintained on a Purina fox-checkers diet, *ad libitum,* injected with 2 μc/g P^{32} at age 26 days, exhibited weight gain retardation of about 20% compared to a control group (A). 2. Another group of rats (C), injected with 2 μc/g P^{32} at age 26 days, but fed ground fox-checkers supplemented with 2 mg aureomycin per gram of feed showed no persistent retardation of weight gain, and ultimately attained normal weight. 3. A fourth group of rats (B), fed fox-checkers supplemented with the same quantity of aureomycin, showed initial increase of weight gain; final weight did not differ significantly from the controls. 4. The ratio of weight gain to tibial length increase was the same for rats which received P^{32} (Group D) and the controls (Group A). P^{32} (2 μc/g given at 26 days) did not selectively inhibit bone growth. 5. Addition of aureomycin to the diet resulted in an increased ratio of weight gain to tibial length increase compared to the control group (A). Aureomycin (at 2 mg per g of feed) appeared to favor soft-tissue formation rather than a stimulation in general growth.

1. Furth, F. W., Coulter, M. P., and Howland, J. W., *Am. J. Path.,* 1952, v28, 185.

2. Coulter, M. P., Furth, F. W., and Howland, J W., *ibid.,* 1952, v28, 875.

3. Koletsky, S., and Christie, J. H., *ibid.,* 1951, v27, 175.

Received July 20, 1953. P.S.E.B.M., 1954, v85.