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Aureomycin and Blood Coagulation

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Moldavsky, Hasselbrook, and Cateno (*5*) were the first to report that the blood of patients receiving injections of penicillin clotted much more quickly than normally. These observations were corroborated and extended experimentally in animals and human beings by Macht (*1*) both after parenteral injections and when administered by stomach. Macht further determined the relative thromboplastic efficiency of the four principal penicillins G, X, F, and K; and also found that streptomycin shortened the coagulation time of whole blood. The clinical bearings of these findings in regard to possible thromboembolic accidents have been also discussed by him (*2*). Recently, the antibiotic aureomycin, discovered by B. M. Duggar, has been introduced into medical practice. It was therefore deemed worth while to study its influence, if any, on blood coagulation.

TABLE 1

EFFECT OF AUREOMYCIN ON BLOOD COAGULATION TIME IN RABBITS

Rabbit	Wt in kg	Normal coag. time in min	Aureomycin in mg	Coag. time in min*	Coag. time in min†
A	3	11	15	9	7
B	2.8	11	10	9	7
C	3.4	10	100	5	1.5
D	2.5	11	65	3	3

* Tested about 1 hr after administration of drug.
† Tested in about 1½–3 hr after administration of drug.

Experiments with aureomycin were made on rabbits and cats, and clinical tests were made on patients who had not received any previous medication. In all of the experiments, the drug was administered by stomach. The clotting time of whole blood was measured by the Lee and White method before administration of aureomycin, and at various intervals afterward.

Table 1 shows the results of 4 rabbit experiments, in which various doses of aureomycin were given to the animals. It will be seen that in each case coagulation time was markedly shortened. Blood in all these was secured by cardiac puncture.

Table 2 gives results of an experiment on a cat and illustrates strikingly that no change occurred in coagulation time of blood taken repeatedly from the carotid artery before giving aureomycin. It shows also the progressive diminution in clotting time after administration of this drug.

TABLE 2

EFFECT OF AUREOMYCIN ON BLOOD COAGULATION TIME OF A CAT*

When tested		Coagulation time in min
10.10 A.M.		10.5
10.20 "		11.5
10.30 "		11.5
10.35 "	200 mg Aureomycin	
11.20 "		8
11.30 "		6
11.40 "		4
11.50 "		4

* Wt—4 kg.

Table 3 presents the findings obtained in 14 patients before and after administration of aureomycin. The patients were given one or two capsules of aureomycin of 250 mg each, the usual clinical dosage. It will be seen that in every case some shortening in coagulation time was produced. Control experiments on human subjects who did not receive aureomycin did not reveal such changes after repeated blood examinations.

TABLE 3

EFFECT OF AUREOMYCIN ON BLOOD COAGULATION TIME OF HUMANS

Patient	Dose in capsules*		Coagulation time in min before dose	Interval hr and min	Coagulation time in min after dose
Mr. D.W.	1	8	1	30	5
Mrs. S.	1	10.5	1		7.5
Mrs. G.	1	9	2		7
Mrs. K.	2	10.5	1	20	3.5
	(1 hr apart)				
Mr. Z.	"	10	1	20	7
Mrs. P.	2	14.5	1	45	8.5
	(together)				
Mrs. I.R.	"	12	1	30	9
Mr. C.	1	8.5	1		7
Mrs. B.	1	11	2	30	7.5
Mrs. M.	1	11	2	30	7
Mrs. D.	1	12	2	30	8
Mrs. B.R.	2	9	3	30	6
	(1 hr apart)				
Mrs. Z.K.	"	9	3	30	6
Mr. J.	"	9	3	30	6.5

* Each capsule contains 250 mg aureomycin.

Tests made on both human subjects and lower animals revealed no difference in prothrombin time, thus indicating that the diminution in clotting time is due to other factors involved in blood coagulation. Repeated tests of blood sera before and after administration of aureomycin revealed phytotoxic properties when tested by the author's phytopharmacological technique (*4*), as found in penicillin and streptomycin (*1*). Experiments now in progress with chloromycetin indicate similar properties.

The findings with aureomycin are of considerable practical clinical interest. There is undoubtedly a definite shortening of clotting time noted at the height of antibiotic therapy. While ordinarily nature provides a wide compensatory mechanism for prevention of thrombo-embolic accidents, still the coagulatory apparatus may be considered as in a metastable state, so that sudden physiological disturbances might precipitate thrombo-embolic accidents. Hence suitable prophylactic measures by use of anticoagulant drugs may be instituted.

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Body Retention of Carbon 14 from Labeled Sodium Bicarbonate[1]

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In view of the present wide usage of carbon 14 and the concern regarding possible radiation hazard involved, it is believed that certain data obtained on this subject are worth recording at this time. Bloom, Curtis, and McLean (*2*) and Armstrong, Schubert, and Lindenbaum (*1*) have previously published results indicating long term body retention of C^{14} from water soluble and insoluble carbonates. Brues and Buchanan (*4*) have reported some interesting results on the over-all metabolism of carbon dioxide.

The present experiments were designed to obtain quantitative data on $C^{14}O_2$ fixation, from which average body radiation could be calculated. Twelve mice were injected intraperitoneally with a solution containing 2.5 mg of $NaHC^{14}O_3$ and a total activity of 18 μc. The expired CO_2 from all animals was collected over varying intervals, and two mice were sacrificed for organ and tissue analysis at 24 hr, 48 hr, 1 week, 2 weeks, 4 weeks, and 3 months. The C^{14} assays were carried out on pooled blood, spleen, liver, kidney, lung, brain, small intestine, muscle, skin and hair, and bone samples. The procedures used in collecting expired CO_2 and excreta, oxidizing samples, and counting have recently been reported (*6*). The percentage of the total activity retained at a given time was calculated by difference (100% − expired and excreted C^{14}) for the first 24 hr; the activity retained after longer periods was calculated directly from organ,

[1] This work was carried out for the Atomic Energy Commission under a contract with the Office of Naval Research. Certain data reported herein were obtained in experiments carried out under a grant from the American Cancer Society on recommendation of the Committee on Growth, National Research Council.

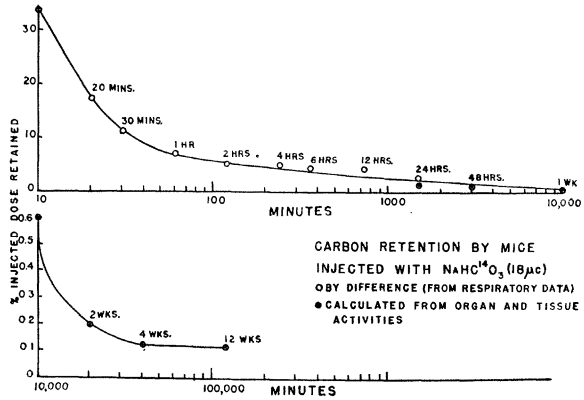

FIG. 1. Carbon 14 retention by mice injected with $NaHC^{14}O_3$.

tissue, and fluid weights, and specific activities. These results are presented in Fig. 1. If the amount of C^{14} in the body and the average energy of radiation are known, it is simple to convert such data to roentgen equivalent physical[2] (the basis for radiation tolerance calculations). With the assumption of even distribution, such calculations have been performed with regard to total body radiation and are presented in Table 1. To date we have

TABLE 1

BODY RADIATION OF MICE INJECTED WITH $NaHC^{14}O_3$ (18 μC)

Period	Body C^{14} content (integrated)		Body radiation	
	μc	% of injected dose	Total rep period	Average daily rep period
0–60 min	4.3	23.6	0.0250	
1–2 hr	1.12	6.2	0.0058	
2–4	1.00	5.6	0.0104	
4–6	0.92	5.12	0.0090	
6–12	0.86	4.77	0.0266	
12–24	0.54	2.93*	0.0333	
0–24	0.87	4.80	0.110	0.1101
24–48	0.21	1.15	0.053	0.027
1–7 days	0.18	1.00	0.1328	0.022
7–14	0.07	0.41	0.0636	0.009
2–4 weeks	0.03	0.16	0.0496	0.004
4–12	0.02	0.13	0.1613	0.003

* This value is an average of the 12-hr C^{14} level obtained by difference (100% − % expired) and the 1.37% found in the tissues at 24 hr.

Note: Tolerance does limit for a 24-hr exposure as set by Clinton Laboratories = 0.1 rep.

observed no outstanding selective accumulation of C^{14} from a gross anatomical standpoint.[3] It was observed that the rate of uptake and loss of C^{14} by the jejunum (a rapidly proliferating tissue) was significantly greater

[2] One rep or roentgen equivalent physical = 83 ergs/g of tissue. This dose is considered to produce no known effects on man when exposed indefinitely. Factor of safety is probably no more than 2 or 3 (*5*).

[3] The detailed results of these experiments, along with certain calculations as to rate constants having to do with carbon turnover, are being presented elsewhere.