veloped specific neutralizing and complement-fixing antibodies for the agent. Other patients in the epidemic with primary atypical pneumonia (PAP) or undifferentiated acute respiratory disease (ARD) also developed antibodies for the agent but those cases with proved influenza A' did not. A portion of the population maintains an antibody level against the new agent suggesting a rather general experience with it.

Confirmatory experiments. Certain of the basic observations presented in this report have been repeated by one of the authors (M.R.H.) in the laboratory of Dr. John H. Dingle at Western Reserve University. The RI-67 agent was taken to Dr. Dingle's laboratory and the cytopathogenic effect for HeLa cells was demonstrated in cultures prepared at Western Reserve University as well as in cultures taken from this laboratory. Neutralization tests with known positive and negative paired sera were also carried out using the cultures and reagents from the 2 sources and essentially identical results were obtained.

Addendum. Since the present manuscript was submitted for publication, Rowe et al. (PROC. SOC. EXP. BIOL. AND MED., 1953, v84, 570) *reported the recovery of an agent cytopathogenic for HeLa cells from cultures of human adenoid tissue. Tests performed in our laboratory and that of Dr. Huebner gave presumptive evidence of an immunological relationship between the RI-67 and the adenoid degenerative agent.*

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Received January 4, 1954. P.S.E.B.M., 1954, v85.

The Oxidation of Mannitol.* (20826)

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The value of mannitol, an isomer of sorbitol, as an adjunct to the diabetic diet has recently been reviewed by Olmsted(1). It was concluded that mannitol could not be of much importance as an adjunct to the diabetic diet, since 80% or more of the mannitol administered is excreted in the urine. These conclusions were apparently based on the data obtained by IV administration(2-6). Mannitol has also been known to form significant amounts of liver glycogen after oral administration(2,7), and under these conditions it is unlikely that mannitol can be excreted in the amounts indicated above. However, no posi-

* This investigation was supported in part by a research grant from the Division of Research Grants and Fellowships of the National Institutes of Health, U. S. Public Health Service.

TABLE I. Recovery of C^{14} after Administration of R.A. Mannitol.

	Hours of CO_2 collection	Experiment No. 1	2	3	4	5	6	7
		I.P. inj.		Oral feeding				Spleen injected
% administered radioactivity recovered in expired CO_2 (accumulative)	3	.4	0	3.5	.2	.5	.3	.5
	6	.8	.5	21	4	5	4	70
	9	1.1	1.7	35	11	13	12	71
	12	1.3	2.1	38	29	25	23	71
	18	1.6	2.4	46	42	54	47	71
	24	2.1	3.2	48	46	63	58	71
Urine		97	77	13	11	8	8	5
Stool						12	12	1
Total recovery		99	80	61	57	83	78	78
mg mannitol admin.		12	180	2	240	240	240	2
Animal wt, g		183	160	183	155	190	190	190

tive conclusions regarding the metabolic utilization of a substance can be obtained from liver glycogen data; for this, labeled material must be used. The differences in regard to the utilization of the sugar alcohol may be due to the technics employed in the administration. In order to clarify the overall metabolic fate of mannitol, we have studied its rate of oxidation and excretion after oral and IP administration. Mannitol uniformly labeled with C^{14} was employed.

Methods. Preparation of radioactive mannitol. Mannitol C^{14} was prepared by the catalytic reduction of C^{14} uniformly labeled glucose with Raney nickel in alkaline solution. The procedure is similar to that used for the preparation of sorbitol(8). The mannitol was purified by a series of crystallizations from water and finally from aqueous ethyl alcohol. The product was identified as mannitol by its M.P. (162°-163°C) and mixed M.P. (163°-164°C) with an authentic mannitol sample (164°C). In addition, the specific activity of a mixture of labeled mannitol and carrier mannitol did not change on repeated crystallization. *Animal treatment.* Non-fasted male albino rats were used. The mannitol was given intraperitoneally, orally, and in one experiment directly into the portal system by way of the spleen. For the latter experiment the spleen was exteriorized the day before the experiment. The methods used for collecting the expired CO_2 and for measurement of radioactivity are the same as that used for sorbitol(8).

Results and discussion. The data given in Table I show that mannitol, when given parenterally, is excreted to a large extent in the urine, which is in agreement with numerous previous reports. The high urinary excretion after parenteral injection is balanced by a low rate of oxidation of about 2-3%. On the other hand, oral feeding of the sugar alcohol leads to oxidation values of about 50% of the injected radioactivity. These divergent results regarding mannitol utilization, obtained by the two methods of administration, indicate either that the mannitol is oxidized, initially at least, only by the liver or that mannitol is acted on by the intestinal flora before absorption from the intestinal lumen. In the latter case the metabolic utilization of fed mannitol is due to the absorption of conversion products of bacterial action. In order to differentiate between these two possibilities, mannitol was injected directly into the portal system by way of the spleen. In this experiment (Exp. 7), 71% of the mannitol was oxidized, indicating that the liver is the most likely site of mannitol oxidation and that bacterial action in the intestinal tract does not play a measurable role in the oxidation. One must assume from these results that mannitol cannot be oxidized by tissues other than the liver and also that the kidneys have a low renal threshold for the sugar alcohol. In parenteral injection a large fraction of the material is subjected largely to the excretory action of the kidneys before it is made available to the liver, and it is rapidly excreted, due to the low renal threshold, before it can be oxidized. In oral feed-

ing practically all of the material must pass first through the liver before it is put into the general circulation; hence the oxidation values of 48-63% are obtained. It is of interest to note that Dominguez, Corcoran and Page(4) in evaluating the use of mannitol in renal function concluded from their studies that the utilization of mannitol in humans, although small after IV injection, is presumably metabolic.

Although metabolites are routinely given parenterally in many experimental studies in order to by-pass the intestine, it is obvious from the results reported here that data obtained from parenteral injection should be examined with comparable data obtained after oral administration for a true evaluation of the metabolic pathway.

Summary. Radioactive mannitol has been administered to rats with the following results: 1. When given orally, about 50% of the mannitol carbon is recovered in the expired CO_2 in 12 hours. 2. With intraperitoneal injection, the mannitol is largely recovered in urine with only 2-3% of the mannitol carbon recovered in the expired CO_2. 3. By injection directly into the portal system by way of the spleen, oxidation comparable to or greater than that obtained by oral administration is obtained. It is concluded from these results that mannitol can be oxidized by the body if it is administered by a route that makes it first available to the liver, as in oral feedings.

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Received January 4, 1954. P.S.E.B.M., 1954, v85.

Urinary Oxalate Excretion by Man Following Ascorbic Acid Ingestion.* (20827)

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Oxalic acid has long been known to be a product of the *in vitro* oxidation of ascorbic acid(1-5). *In vivo,* Scheinkman(6) showed that ascorbic acid ingestion by guinea pigs resulted in increased urinary oxalate. Burns *et al.*(7) found that one of the end products of the metabolism of radioactive 1-C^{14}-L-ascorbic acid administered to guinea pigs was urinary oxalate. Since large doses of ascorbic acid are being prescribed by physicians(8,9), an investigation of the effect of ascorbic acid on the urinary oxalate excretion of man is warranted. This study is concerned with that investigation.

Procedure. In the first experiment, 11 healthy adult males on their regular diet collected 24 hour control urine samples. Each subject then ingested, in addition to his regular diet, 3 g of pure ascorbic acid at each mealtime (9 g/day) for 2 days, collected a 24 hour urine sample on the second day and another 24 hour control urine sample one week later. The results indicated that there was increased oxalate excretion with the daily ingestion of 9 g of extra-dietary ascorbic acid. A second experiment was conducted to determine at what minimum dosage of supplementary ingested ascorbic acid an increase in urinary oxalate occurred. Forty adult males were placed into groups ingesting different amounts of ascorbic acid ranging from 0.25 g to 8 g (divided into 3 doses as in the first experiment) daily for one week at the end of

* Supported in part by a grant from Hoffmann-LaRoche Inc., Nutley, N. J.