

Failure of Acetylsalicylic Acid to Affect Excretion of Ascorbic Acid (Vitamin C) in Urine.*

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Daniels and Everson¹ have recently reported that the intake of acetylsalicylic acid increases the urinary excretion of vitamin C in children. Such an action of this drug would be important but to us it seemed unlikely that acetylsalicylic acid had this effect. During a 4-months study of the vitamin C excretion of several subjects kept on a fairly constant intake of the vitamin the drug was taken on several occasions by various subjects without apparent effect on vitamin C excretion.² During this time the output of vitamin C remained quite constant, except for intentionally produced variations. Although slight unexplained variations in excretion occasionally occurred, in no instance could they be related to administration of the drug, despite close observation to relate unexplained variations to such factors.

The authors referred to above, state that acetylsalicylic acid "as such or combined with urine" does not react with the 2,6 dichlorophenolindophenol indicator commonly used. It is not clear, however, that they include the conjugation products of salicylates which may be present in the urine and might conceivably give a false reaction for ascorbic acid.

We have studied the effect of ingested acetylsalicylic acid on the excretion of ascorbic acid in 4 subjects. In view of the ease with which ascorbic acid is destroyed by gentle means, such as mild heat or bubbling oxygen through solutions,² it was intended to subject the specimens to such procedures with the idea that a failure to reduce the apparent content of vitamin C would indicate that the specimen contained substances which gave a false reaction for the vitamin and were responsible for the apparent increase in the latter. It was realized that failure to reduce the apparent content would not necessarily eliminate the possibility that conjugation products were responsible for the apparent increase in vitamin. It happened, how-

* This study was aided by a grant from the Division of Medical Sciences of the Rockefeller Foundation.

¹ Daniels, A. L., and Everson, G. J., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 20.

² Authors' unpublished data.

ever, that this part of the study was unnecessary because no increase in vitamin C excretion in the urine, real or apparent, after the taking of acetylsalicylic acid, was found.

The subjects were 4 young, healthy adults, 2 men and 2 women. They were given a vitamin C-free diet† before and during the ex-

TABLE I.
Influence of Acetylsalicylic Acid on Urinary Excretion of Vitamin C (Ascorbic Acid).

Subject	Date Jan., 1937	—Ascorbic Acid—		
		Intake mg.	Output (urine) mg.	
1. J.B.Y.	7	50	27.34	
	8	50	27.39	
	9	50	28.98	
	10	50	22.14	
	11	A.a.* 0.6 gm., 9:45 a.m.	50	33.99
	12	A.a.* 1.3 gm., 10 a.m.	50	24.11
	13		50	28.91
	14	A.a.* 1.3 gm., 10 a.m. 1.3 gm., 1:45 p.m.	50	28.48
2. M.B.C.	6	50	39.24	
	7	29	29.08	
	8	50	27.25	
	9	50	28.34	
	10	50	37.41	
	11	50	23.10	
	12	A.a.* 1.3 gm., 10:15 a.m.	38.51	26.65
	13	50	24.12	
3. H.F.	6	50	15.00	
	7	50	15.98	
	8	50	12.21	
	9	50	8.12	
	10	50	13.44	
	11	A.a.* 0.6 gm., 9 a.m.	50	15.37
	12	A.a.* 1.3 gm., 10:30 a.m.	50	12.05
	13	50	14.14	
4. M.G.C.	6	50	22.98	
	7	50	20.02	
	8	50	16.35	
	9	50	20.78	
	10	50	17.31	
	11	A.a.* 0.6 gm., 9:30 a.m.	50	16.12
	12	A.a.* 1.3 gm., 10 a.m.	50	18.66
	13	50	20.05	
14	A.a.* 1.3 gm., 9 a.m. 1.3 gm., 1:15 p.m.	50	18.57	

*Acetylsalicylic acid.

† The diet consisted of thoroughly cooked meat, cooked eggs and milk, cereals, dried fruit, dried vegetables and butter.

perimental period, to which was added 50 mg. of ascorbic acid daily in the form of orange juice (titrated daily). Twenty-four hour specimens were collected from 8 a. m. to 8 a. m., each individual specimen being examined directly after voiding except in the case of the one or 2 night specimens, which were preserved in 10% of 2N sulphuric acid. After a preliminary period of 5 days to determine the usual daily excretion, acetylsalicylic acid was given in amounts of 0.6 to 2.6 gm. (10 to 40 grains a day), the smaller amounts being taken in a single dose in the morning, the larger in divided doses within about 4 hours. The ascorbic acid content of the urine was determined by the 2.6 dichlorophenolindophenol method as described previously.³

The results as shown in Table I indicate that the ingestion of acetylsalicylic acid in amounts as great as 2.6 gm. (40 grains) had no significant effect on the excretion of ascorbic acid in the urine. Neither a significant increase nor decrease occurred in any subject and the slight variations which occurred were no greater than those during the preliminary period. All of the urine specimens following administration of the drug showed a positive test for salicylates (ferric chloride) and occasionally reduced Benedict's solution slightly. It may be added that the excretion of ascorbic acid was of the same order as that observed on other occasions under like conditions, the same persons having served as subjects in previous experiments.

Certain differences between our experiments and those of Daniels and Everson should be noted. Their subjects were children, ours were adults. It is possible that children behave differently from adults in these circumstances, particularly in the presence of fever. Our subjects were afebrile. Their subjects were fed weighed diets and the vitamin C content of the food as well as of the added orange juice was determined. Our diets were not weighed nor the vitamin C content, except that of the orange juice, determined but the nature of our diets was such that an equally constant vitamin intake was obtained and the difference in this respect, if any, should have tended to increase the variation in urinary excretion in our experiments. The vitamin C intake of Daniels and Everson's children varied from about 70 to 102 mg. per day. This is considerably greater in proportion to body weight than our subjects received. Children require more of the vitamin in proportion to weight but our subjects received at least the generally accepted maintenance

³ Youmans, J. B., Corlette, M. B., Akeroyd, J. H., and Frank, H., *Am. J. Med. Sci.*, 1936, **101**, 319.

requirement for adults, and were in a good state of vitamin C nutrition at the start of the experiment. We believe that these conditions constitute, if anything, a better test of the effect of acetylsalicylic acid on vitamin C excretion. Our experiments indicate that the ingestion of acetylsalicylic acid in daily doses of 0.6 to 2.6 gm. (10 to 40 grains) does not increase (nor decrease) the excretion of vitamin C in the urine in adults.

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Ascorbic Acid in Gastric Juice.*

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The literature on vitamin C contains numerous reports on the presence of ascorbic acid in various body fluids and tissues. However, we could find no information on whether vitamin C was present in gastric juice. The fact that normal gastric juice is the most acid of all body secretions suggested that an analysis be made.

First, the gastric juices of dogs were analyzed and later human gastric juice. Nine dogs which had been starved 24 hours were used. Their stomachs were washed with 200 cc. saline and then aspirated. Histamine was given subcutaneously and one hour later the gastric juices were drawn. These fluids were immediately filtered and 25 cc. portions were titrated against the 2-6 dichlorophenolindophenol indicator prepared as described by Bessey and King.¹ The dye was standardized against a standard ascorbic acid (Hoffmann La Roche) solution made up just before analysis, using 25 mg. of the vitamin C per 100 cc. 5% acetic acid. The samples of gastric juice from 9 dogs showed a range of from 0.33 to 1.51 mg. of vitamin C per 100 cc. of gastric juice with an average value of .692 mg.

With a view to ascertaining which part of the gastro-intestinal tract contained the greatest amount of the ascorbic acid, the following analysis was done. The mucosae of the stomach, duodenum,

* Aided by Landon Research Fellowships.

The authors wish to express their appreciation to Dr. H. M. Trusler and Dr. R. N. Harger for their kind assistance.

¹ Bessey, O. A., and King, C. G., *J. Biol. Chem.*, 1933. **103**, 687.