

pleural exudates made 45 minutes later showed abundant phagocytosis, and there was no difference in the phagocytic index between the normal and the intoxicated animals. Analyses at this time showed that the alcoholic content of the blood was never above 40 mg. higher than that of the pleural exudate, and both were as high or higher than the figures given in the literature for the blood level during human intoxication.

Differential counts in vital preparations of blood from both rabbits and patients in alcoholic stupor revealed no difference in the number of non-motile cells as compared with normals.

Conclusions. Alcoholic intoxication maintained at the point of stupor destroys resistance to pneumococcal infection in the rabbit. Even in animals rendered highly immune by the intravenous injection of antipneumococcal serum, intoxication deprives them of their immunity. The loss of resistance to the infection is due to the fact that intoxication profoundly inhibits the vascular inflammatory response as long as intoxication is maintained. Leucocytic emigration at the site of infection is negligible and the bacteria, therefore, proliferate uninterruptedly. Similar experiments show that ether-anesthesia has as marked an inhibitory effect on the inflammatory response as has alcoholic intoxication, and produces as marked a loss of resistance to infection.

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Pyrididium as a Source of Interference in Vitamin C Determinations.

CATHERINE F. GANNON AND TERESA MCGOVERN. (Introduced by Irving Wright.)

From the Department of Medicine, New York Post-Graduate Medical School and Hospital, Columbia University.

The method commonly employed for determination of vitamin C in the body fluids makes use of Tillmans¹ indicator, 2,6 dichlorophenol indophenol. This is not specific for the vitamin but under controlled conditions is practically so. Substances normally present in urine, namely cysteine, glutathione, and ergothioneine,² may

¹ Tillmans, J., Hirsch, P., and Jackisch, J., *Z. f. Untersuch. d. Lebensmitt.*, 1932, **63**, 241.

² Emmerie, A., and Van Eekelen, M., *Biochem. J.*, 1934, **28**, 1153.

reduce the dye, but Abbasy and coworkers³ have reported that the non-specific titer did not rise above 3 to 6 mg. per day for the average person. In many specimens from our patients, where vitamin C was excluded from the diet, total excretion of "vitamin C" varied from less than one to 4 mg. in 24-hour specimens. Such interference, therefore, seems to be unimportant in the majority of cases. We have found, however, that Pyridium, (phenylazo-diaminopyridine hydrochloride), a commonly used medication for disorders of the urinary tract, may constitute a serious source of error in blood⁴ and urine⁵ determinations of the vitamin.

In one instance, a patient's excretion following a test dose, 1000 mg. intravenously,⁶ of crystalline ascorbic acid,* decreased daily from 94 mg., to 32 mg., to 4 mg., and the next day the result obtained was 137 mg. On that day, however, 6 Pyridium tablets had been given in treatment of cystitis unrelated to the hypovitaminosis. The urine was diluted and titrated, and a distinct endpoint duplicated. This was the first apparent rise in excretion without increased intake in this subject. After the cystitis had disappeared a test dose of 1000 mg. orally and 6 Pyridium tablets were given for experimental purposes. The result obtained at a dilution of 1:40 was 385 mg., but after the specimen had stood in the refrigerator for 48 hours, the quantity present appeared to be 430 mg. In our experience the titer has increased on standing only in specimens which contained Pyridium.

A normal subject whose intake of vitamin C was regularly low and daily excretion less than 10 mg., apparently eliminated 40 mg. when given 4 Pyridium tablets. This exceeds the average for persons with adequate intake. After exclusion of foods rich in the vitamin for 4 days, a 24-hour urine contained 17 mg., and a blood specimen taken at 10:45 A. M. (following completion of the 24-hour sample of urine) 0.64 mg. per 100 ml. of plasma. At 11 A. M. two Pyridium tablets were taken. A blood specimen drawn 2 hours later showed highly colored plasma which, after protein precipitation, was pale yellow and gave a result of 0.77 mg. The 7 A. M. to 5 P. M. urine was highly colored, diluted 1:40 and indicated

³ Abbasy, M. A., Harris, L. J., Ray, S. N., and Marrack, J. B., *Lancet*, 1935, **2**, 1399.

⁴ Farmer, C. J., and Abt, A., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 1625.

⁵ Harris, L. J., and Ray, S. N., *Lancet*, 1935, **1**, 71.

⁶ Wright, I. S., Lilienfeld, A., and MacLenathen, E., *Arch. Int. Med.*, 1937, **60**, 264.

*The crystalline ascorbic acid used in these studies was supplied through the kindness of Merck & Co., Inc., Rahway, N. J.

22 mg., while in the same period of the preceding day the excretion had been 6 mg. The 5 P. M. to 7 A. M. specimen was only slightly colored. When diluted 1:10 the result was 13 mg., as compared with 11 mg. during the same hours on the preceding day. The total 24-hour result was 35 mg., double that of the day before, the diet on both days being vitamin C-free. The usual dosage of 2 Pyridium tablets 3 times a day, which colors the urine very highly, was not given in this case, because of a complaint of nausea following the first two.

Pyridium was then added to urine specimens of known vitamin C content, and to standard solutions of crystalline ascorbic acid. In both the titer increased appreciably, as indicated in Table I.

TABLE I.

	Original Titer Ml. dichloro- phenolindophenol	Titer after Addition of Pyridium	
		Experimental Value	Corrected for dilution necessary to reduce color
Urine A	0.34	.44	(not diluted)
" B	0.21	.18	2.70 (dilution 15)
Standard A	1.13	.63	1.26 (" 2)
" B	1.24	.73	1.46 (" 2)
" C	1.36	.78	1.56 (" 2)

After addition of Pyridium, titration in the presence of its orange-amber color yielded results much higher than the original, and yet dilution to avoid color interference gave still higher values. In urine A, the addition of a dust-like particle of a powdered Pyridium tablet did not appear to alter the color of the specimen, but an increased titer resulted. In urine B, sufficient Pyridium was added to match the concentration in a specimen from a patient receiving this medication, and although practically colorless after being diluted 15 times, the titer was very close to that of the undiluted Pyridium-free specimen. Minute particles introduced into the standard solutions of ascorbic acid gave a very pale color which on dilution with an equal volume of water was barely perceptible. In all cases, however, the addition of Pyridium resulted in an increase of the titer with dichlorophenol indophenol.

The inability to obtain satisfactory results was noted in urine examinations as late as 3 days after Pyridium had been taken. Since varied efforts to remove Pyridium without loss of some of the vitamin C were unsuccessful, it would appear inadvisable to do this test by the present method on a patient who has had Pyridium medication within 5 days. Its presence may explain some apparently high ascorbic acid values unexpected from knowledge of the dietary of the individual.

In a study of the nutritional state of an individual in regard to vitamin C, many factors enter into an evaluation of analyses of the body fluids. Subnormal urinary values may sometimes be occasioned by loss in the sweat,⁷ or, in certain manifestations of kidney disease, by retention in the blood.⁸ The administration of salicylates⁹ has been reported to accelerate the excretion of the vitamin, while the metabolic demands of fever, particularly in pneumonia¹⁰ and tuberculosis,¹¹ may be responsible for a diminished output. That Pyridium medication may cause erroneously high vitamin C results is a possibility that should be considered.

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Progression of Different Nasally Instilled Viruses along Different Nervous Pathways in the Same Host.

ALBERT B. SABIN.

From the Laboratories of the Rockefeller Institute for Medical Research, New York.

In recent years much evidence has been accumulated to indicate that following nasal *instillation* many neurotropic viruses invade the central nervous system (CNS) by the olfactory pathway, and controversy has centered on whether these viruses progress along the perineural spaces or within the processes of the olfactory neurons themselves. Interruption of the olfactory pathway by surgical means has been shown to be capable of preventing poliomyelitis in monkeys induced by nasal instillation of the virus, in spite of the fact that all the other nerves connected with the nasal mucosa remain intact.¹ Similar interruption of the olfactory pathway in rab-

⁷ Lilienfeld, A., Wright, I. S., and MacLenathen, E., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 184.

⁸ Wright, I. S., and MacLenathen, E., *PROC. SOC. EXP. BIOL. AND MED.*, in press.

⁹ Daniels, A. L., and Everson, G. J., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 20.

¹⁰ Bullova, J. G. M., Rothstein, I. A., Ratish, H. D., and Harde, E., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 1.

¹¹ Martin, G. J., and Heise, F. H., *Am. J. Dig. Dis. and Nutr.*, 1937, **4**, 368.

¹ Schultz, E. W., and Gebhardt, L. P., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **31**, 728; Brodie, M., and Elvidge, A. R., *Science*, 1934, **79**, 235; Lennette, E. H., and Hudson, N. P., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 1444; Howe, H. A., and Ecke, R. S., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **37**, 125; Gordon, F. B., and Lennette, E. H., *J. Bact.*, 1938, **35**, 43.