characteristic blue fluorescence in sulfuric acid solution as the dihydrofollicular hormone and gives no depression of melting point when mixed with the latter. Furthermore, a small amount of a compound melting at 236° (uncorr.) which is more difficultly soluble in absolute methyl alcohol than the δ-hormone could be separated from the top fractions of the latter. The amount of the 2 last-named substances isolated was not sufficient for analysis and the preparation of derivatives.

The above findings establish for the first time the occurrence of estrogenic dihydroxy compounds in the urine of pregnant mares. Schwenk and Hildebrandt[2] have suggested that the dihydro-follicular hormone, which is about 6 times as active as theelin, may be the estrogenic substance actually circulating in the body fluids.* In this connection it may be pointed out that the only estrogenic substance which has been isolated in pure form from a mammalian organ, the emmenin obtained by Collip and his collaborators[3] from the placenta, has been shown by Butenandt and Browne[4] to be identical with theelol, the non-ketonic trihydroxy compound also present in human pregnancy urine. It is also conceivable that the very high degree of estrogenic potency reported by Zondek[5] for stallion's urine is at least partly due to the presence of substances of purely alcoholic character.

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Urinary Excretion of Vitamin C in Pneumonia.

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In previous work[1] on the tissues of laboratory animals we have

* The recent announcement of MacCorquodale, Thayer and Doisy at the 29th Annual Meeting of the American Society of Biological Chemists in Detroit, April 13, 1935, of the isolation from follicular fluid of dihydrotheelin (m.p. 173°, corr.) furnishes additional evidence for the correctness of this viewpoint.

3 Collip, J. B., *Can. Med. Ass. J.*, 1930, **22**, 212, 215, 761; Browne, J. S. L., *Can. J. Res.*, 1933, **8**, 180.

4 Butenandt, A., and Browne, J. S. L., *Z. physiol. Chem.*, 1933, **216**, 49.

5 Zondek, B., *Nature*, 1934, **133**, 209.

1 Harde, E., *C. R. de l'acad. des Sc.*, 1934, **199**, 618; Harde, E., and Philippe, *C. R. de l'acad. des. Sc.*, 1934, **199**, 738; Harde, E., and Benjamin, H. R., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 651.

found the vitamin C content to be reduced in many infections and intoxications. This suggested that cevitamic acid acted not only as an oxidative factor, in normal respiratory processes—but also had a neutralizing rôle in various pathological conditions other than scurvy.

Yavorsky, Almaden and King[2] examined human tissues from autopsy for their vitamin C content, and noted that generalized infections were more common among those having a low vitamin C content in their tissues. Worringer and Sala[3] reported scurvy in infants following diphtheria and pertussis.

Ten cases of pneumonia were examined on the Pneumonia Service of Doctor Bullowa at Harlem Hospital. The method of Hess and Benjamin,[4] and Birch, Harris and Ray[5] was followed using the dye 2,6,dichlorophenolindophenol. These authors noted that in normal individuals after the ingestion of large doses of vitamin C it was rapidly eliminated in great quantities in the urine. Recently Harris and Ray[6] found that when vitamin C was low in the diet individuals tend to excrete less vitamin C in urine than well-nourished ones. However, more reliable results as to the state of vitamin C saturation or unsaturation of the tissues can be obtained by examining the urinary excretion after administering large test doses of the vitamin. A normal excretion for adults per day the authors estimate as 15-30 mg.

The technique of Harris and Ray was followed as closely as possible. Occasionally, however, it has been impossible to get every specimen of urine in the 24 hours, and this has been noted in our calculations. Of the 10 cases 5 were given no saturation test.* Two of these were fatal cases. In the first, (a pneumococcus type I† pneumonia with empyema) in 3 specimens of urine voided 12 hours before death 8.6 mg. of cevitamic acid was excreted suggesting a normal output. In the second fatal case there was a lower excretion, 5 mg. in 20 hours. The calculation was inexact, a highly colored urine made the end point very difficult to determine.

2 Yavorsky, M., Almaden, P., and King, C. G., *J. Biol. Chem.*, 1934, **106**, 525.

3 Worringer, J., and Sala, A., *Rev. Franc. de Pediat.*, 1928, **33**, 806.

4 Hess, A. F., and Benjamin, H. R., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 855.

5 Birch, T. W., Harris, and Ray, *Biochem. J.*, 1933, **27**, 590.

6 Harris, L. J., and Ray, S. N., *Lancet*, 1935, 228.

* For the saturation test the patients were given large quantities of orange juice or pure cevitamic acid. This was generously supplied to us by Merck & Co. and Hoffman-LaRoche.

† In these cases we have found no definite correlation with the types of pneumococcus causing the disease, but the present data is insufficient.

In the 3 other cases, one excreted a normal amount, 30 mg. in 24 hours. In the second case a Pneumococcus type 3 complicated by a *Streptococcus beta* in the blood, the titration was so low as to be inexact, 1.9 mg. in 24 hours, (one specimen lost). Seven days later the patient was recovering and the amount excreted was 7 mg. in 12 hours. In the third case the excretion was 11 mg. in 24 hours only slightly lower than normal.

In 5 other cases saturation tests were made. One, a fatal case, 2 days before death had a normal content 13 mg. in 24 hours, 1 specimen missing. Given 350 mg. of cevitamic acid in the next 24 hours, resulted in no high peak of excretion—only 21 mg. excreted, the immediate "saturation" test being negative.

In the 4 other cases, one gave normal content over 12-hour period. He was "saturated" for 2½ days and then examined. Excretion was normal, 30.2 mg. per 24 hours, with no immediate saturation. Second case, recovering, in 12 hours only 5 mg. excreted. After 48 hours of hypervitamin C feeding saturation test was negative, 8 mg. in 15 hours. The 3rd case gave similar results. No exact calculation was possible, as a complete 24-hour specimen was not obtained. The urine titrated showed persistently low content. After 24-hour "saturation" no saturation had occurred.

Case 4. Examinations were commenced on the 19th day of the illness. Patient had been given a great deal of orange juice. The first titrations were but slightly below normal. After "saturation" for 48 hours there was no increase, 12.3 mg. Then 400 mg. of vitamin C were given—excretion was 14.10 mg. After continued saturation, 14.16 mg. excreted. It was only on the tenth day of the saturation that an overflow occurred—59.35 mg. was excreted in 10 hours. One sample was lost. In the next 6 hours the excretion was 36 mg., making a total in 16 hours of 95 mg. The patient was at this time recovering.

We have thus found in accord with Harris and Ray that by the saturation test a hypovitaminosis may be shown even though the titration of the urine alone might give normal values. Whether the deficiencies in the vitamin we have found in certain cases are due to the previous diet of the patients or to the intoxication of the pneumonia or to both factors we have not yet determined. We also note that certain of the lesions of the cardiovascular system in pneumonia suggest those found in scorbutic conditions.

The clinical results will be reported later.