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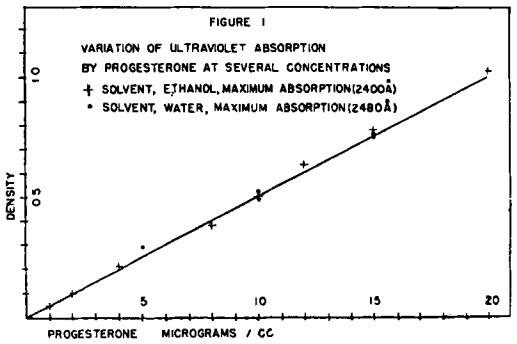
Solubility of Progesterone in Water and in Saline.*

ARTHUR L. HASKINS, JR. (Introduced by Willard M. Allen.)

From the Department of Obstetrics and Gynecology, Washington University School of Medicine, Saint Louis, Mo.

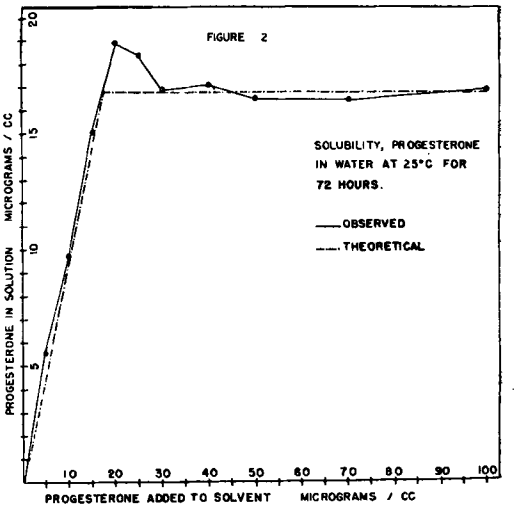
During the course of studies concerning the metabolism of progesterone, it became expedient to determine the solubility of this hormone in distilled water and in 0.9% aqueous saline. Because of the paucity of published data in this regard and its application to both *in vitro* and *in vivo* metabolic studies of progesterone, the findings are reported at this time.

The progesterone used in this study was synthetic alpha-progesterone, melting point of 128°C, and with characteristic ultraviolet absorption band at 2400 Å when dissolved in 95% ethyl alcohol. The Beckman

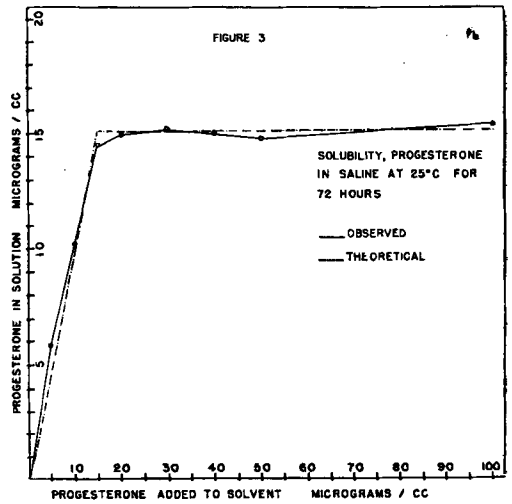


spectrophotometer, with 1 cm square fused silica absorption cells, was used in making all ultraviolet absorption observations. Fig. 1 illustrates the relation of concentration of progesterone in solution, to ultraviolet density obtained. It is apparent that progesterone whether in aqueous or alcoholic solutions follows Beer's law.

Into chemically clean 10 ml volumetric flasks, various concentrations of progesterone in 1 ml of 95% ethanol were introduced. The concentrations varied from 50 μg/ml to 1000 μg/ml. These alcoholic solutions were evapo-

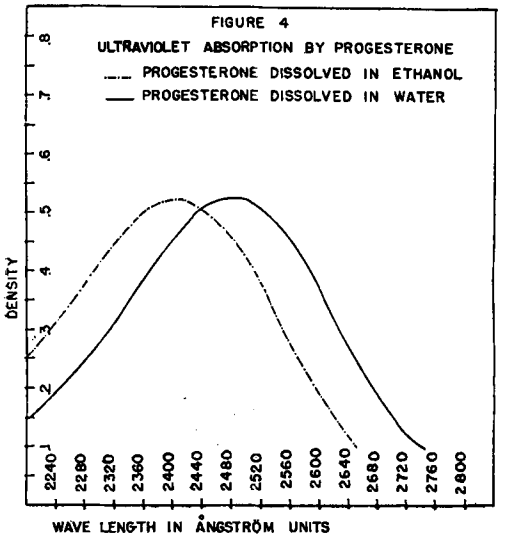


rated to dryness on a steam bath. To the residue was added 2 ml of the intended solvent, either distilled water or aqueous NaCl (0.9%). This mixture was returned to the steam bath for 30 minutes, then removed, cooled, and diluted to a 10 cc volume with the appropriate solvent. The flasks were then placed in a closed room with mean tempera-



* United States Public Health Fellow in Obstetrics and Gynecology.

ture of 25° C until spectrophotometric readings were made at 24, 48, 72 and 168 hour intervals on the supernatant fluid. The solubility of progesterone thus obtained is presented in Fig. 2 and Fig. 3. It should be noted that equilibrium between the progesterone and its solvent was obtained at 72 hours and that the solution concentration remained constant to 168 hours. The slight irregularity in solubility noted in Fig. 2 is thought to represent supersaturation.



An incidental finding noted during these solubility studies was the shift of maximum ultraviolet absorption by progesterone from 2400 Å when dissolved in 95% ethanol to 2480 Å when dissolved in water. This shift occurred quite independently of the pH of the solution. Ultraviolet absorption curves are presented in Fig. 4 to illustrate this finding.

As will be noted in Fig. 2 and Fig. 3 the average solubility of progesterone in distilled water at room temperature for 72 hours was found to be 16.8 μg per ml and in 0.9% aqueous saline, 15.1 μg per ml, under identical conditions.

The solubility of progesterone in aqueous media as found in this experiment is at variance with that reported by Forbes and Hooker[1] of 6-9 μg per ml in saline. These results should not be construed as a marked disagreement since the smaller recorded solubility was based on bioassay primarily and the limited quantitative accuracy of bioassay is admitted.

Summary. The solubility of crystalline progesterone in aqueous media was determined spectrographically. Progesterone was found to have an average solubility at room temperature of 16.8 μg per ml in distilled water and 15.1 μg per ml in 0.9% aqueous saline.

[1] Forbes, T. R., and Hooker, C. W., *Science*, 1948, **107**, 151.

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Cell Proliferation Accelerating and Inhibiting Substances in Normal and Cancer Blood and Urine.*

EARL R. NORRIS AND JOHN J. MAJNARICH.

From the Department of Biochemistry, University of Washington, Seattle.

The rate of cell proliferation of bone marrow cells and of normal tissue cells cultured *in vitro* is accelerated by normal blood serum and inhibited by blood serum from cases of neoplastic disease, pernicious anemia, aplastic anemia and leukemia.[1] These pathological blood sera and normal blood sera counteract the effect of each other in a manner similar to the counteracting effect of xanthopterin and antixanthopterin[2] on cell proliferation *in*

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[1] Norris, E. R., and Majnarich, J. J., *Am. J. Physiol.*, 1948, **153**, 483.

[2] Norris, E. R., and Majnarich, J. J., *Am. J. Physiol.*, 1948, **152**, 652.