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Excretion of Gonadotropic and Estrogenic Hormones in Urine During Normal Menstrual Cycle.

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None of the methods of bioassay for the urinary gonadotropins or estrogens is better than roughly quantitative. As long as definite standards of technic are not available the various absolute values claimed in the literature cannot be compared and no definite statements as to right or wrong can be issued. However, normal and abnormal fluctuations of these hormones during the menstrual cycle should be recognized with some degree of uniformity regardless of the absolute values obtained by the various methods. Our former belief in a single excretion peak of urinary gonadotropins during the menstrual cycle seems disproven by D'Amour, Funk and Liverman,[1] who showed as many as 3 excretion peaks in daily assays of urinary gonadotropins from normal women. Our previous conception of the premenstrual height of estrin excretion has been refuted by the careful investigation of Gustavson and coworkers,[2] who showed that as early as 5 days after the onset of menstruation a peak in estrin excretion curve can be found. This demonstrated that more data on the normal menstrual cycle of women are needed in order to establish the correlationship between the excretion of gonadotropic and estrogenic hormones. We have examined the urine of 3 healthy women during a complete menstrual cycle for gonadotropic and estrogenic substances and wish to report briefly on the results:

Method. Twenty-four-hour specimens of urine were collected from 3 women between the ages of 20 to 30 who by careful history did not show any evidence of menstrual disorders. In all 3 women menarche set in between 11 and 13 years, and menstruation occurred every 28 days, lasting from 4 to 6 days. There was no excessive flow, no menstrual pain or premenstrual tension. The specimens were kept on ice during collection and were assayed every 48 hours. Urinary gonadotropins were determined by the method of Levin and

[1] D'Amour, F. E., Funk, D., and Liverman, H., *Am. J. Obst. and Gynec.*, 1939, **37**, 940.

[2] Gustavson, R. G., Mason, L. W., Hays, E. E., Wood, T. R., and D'Amour, F. E., *Am. J. Obst. and Gynec.*, 1938, **35**, 115.

Tyndale,[3] using the uterine weight of immature mice as indicators. After precipitation with tannic acid had been completed, the remain-

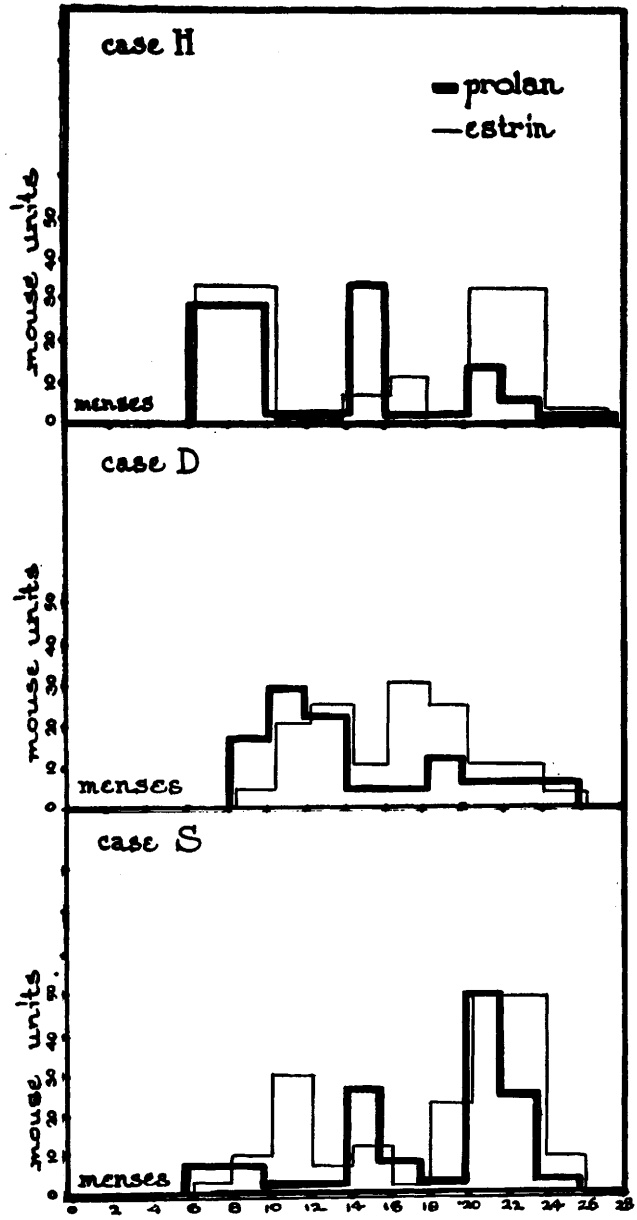

FIG. 1.

Curves of daily excretion of urinary gonadotropins and estrogens during the normal menstrual cycle.

[3] Levin, L., and Tyndale, H. H., *Endocrinology*, 1937, **21**, 619.

ing urine was acidified, hydrolized, and extracted with benzene, following the method of Smith and Smith.[4] The residue was dissolved in glycocol propionate and injected into immature white mice following the suggestion of Lauson, Heller, Golden and Sevringhaus.[5] We have repeatedly convinced ourselves that the tannic acid precipitates were free of any estrogenic substance.

Results. The curves depicting the cyclic excretion of estrogen and gonadotropin are pictured in Fig. 1. It appears that 1 to 3 peaks of prolan excretion may occur in a single cycle. The excretion of estrin either parallels or in some instances precedes the prolan excretion. Two distinct peaks have been observed in all our cases. In Patient D they were so close to each other that a separation may seem arbitrary. If we wish to deduce from the appearance of the hormone levels in the urine the time and incidence of ovulation, we must agree with Gustavson's statement that "the time of ovulation may vary considerably in different individuals, and that the corpus luteum may require varying periods of time to reach its full development and activity."

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Non-Identity of Gray Hair Produced by Mineral Deficiency and Vitamin Deficiency.

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The recent recognition of a specific organic food factor[1,2] necessary for the maintenance of the black fur of black or piebald rats has raised the question as to whether the phenomenon of graying noted by older workers[3,4,5,6] particularly in rats on an exclusive milk diet is due to this cause or is due to a specific mineral deficiency. Jukes and

[4] Smith, G. V., and Smith, O. W., *Am. J. Physiol.*, 1935, **112**, 340.

[5] Lauson, H. D., Heller, C. G., Golden, J. B., and Sevringhaus, E. L., *Endocrinology*, 1939, **24**, 35.

[1] Morgan, A. F., Cook, B. B., and Davison, H. G., *J. Nutrition*, 1938, **15**, 27.

[2] Lunde, G., and Kringstad, *Z. physiol. Chem.*, 1938, **257**, 201.

[3] Hartwell, G. A., *Biochem. J.*, 1923, **17**, 547.

[4] Kiel, H. L., and Nelson, V. E., *J. Biol. Chem.*, 1931, **93**, 49.

[5] György, P., *Biochem. J.*, 1935, **29**, 741.

[6] Gorter, F. J., *Z. Vitaminforsch.*, 1935, **4**, 277.