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Potency Evaluations of the Human Chorionic Gonadotropic Preparations.

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There are 7 preparations of the gonadotropic principle of human pregnancy urine in common use at the present time. All of these are standardized in rat units. However, each manufacturer defines his unit differently, using various criteria as a basis.

Estrous type of vaginal smear, follicular maturation and luteinization, and change in ovarian weight are some of the criteria employed. The age of the test animals, the time elapsed during the assay, and the number of injections, are also variables.

Since different quantities of the human urinary gonadotropic material are required to produce these criteria, and since an older test animal is more easily brought to maturation than a younger one, the commercial human urinary gonadotropic units are not comparable by definition alone.

D'Amour and D'Amour[1] have attempted to make an effective comparison of these units, employing ovarian weight as a criterion. We have adopted the estrous type of smear in 21-day-old rats as the criterion in our assays. All our animals were females of the Sherman strain, and at least 10 rats were utilized for each assay. All available human urinary gonadotropic products were then assayed by this method.*

Daily injections of 0.5 cc of the test material were given subcutaneously for 3 consecutive days, and the animals were tested for the estrous type of smear at 120 hours following the initial dose. Their ovaries were examined grossly for evidences of maturation. A result was considered positive if at least 50% of the animals had an estrous type of smear.

If the number of rat units of the test substance first employed was insufficient to give a positive result, a greater number of units was injected into each of the next group of 10 rats. If the first test was positive, the number of rat units was reduced until the

[1] D'Amour, M. D., and D'Amour, F. E., *J. Pharm. and Exp. Therap.*, 1938, **62**, 263.

* All products were bought from a reputable pharmacist.

TABLE I.
Production of the Estrous Type of Vaginal Smear.

Preparation	Lot No.	Total Dose, R.U.	No. of rats used	No. of rats in estrus	% of rats in estrus	Relative potency
Antuitrin-S	3203307	3.0	9*	9	100	
"	"	2.25	10	8	80	
"	3220458	1.5	10	5	50	
"	"	1.0	10	1	10	1.00
A.P.L.	RB556	3.0	10	1	10	
"	"	4.0	10	4	40	
"	"	4.5	10	5	50	0.33
Entromone	10981	3.0	10	0	0	
"	"	6.0	10	0	0	
"	"	9.0	10	0	0	
"	"	12.0	10	0	0	0.00†
Follutein	65467	1.5	10	6	60	
"	"	1.0	10	1	10	1.00
Korotron	CN415	1.0	10	1	10	
"	"	1.5	10	3	30	
"	"	2.0	10	0	0	
"	"	2.5	10	1	10	
"	"	3.0	10	9	90	
"	8204	1.0	10	0	0	
"	"	1.5	10	0	0	
"	"	2.0	10	0	0	
"	"	2.5	10	2	20	
"	"	3.0	10	1	10	
"	"	4.0	10	3	30	
"	8900	5.0	10	10	100	‡
Placestrin	27	1.5	10	0	0	
"	"	3.0	10	0	0	
"	"	6.0	10	0	0	
"	"	7.5	10	0	0	
"	"	10.0	10	0	0	0.00†
Pregnyl	§	3.0	10	7	70	
"	"	1.5	10	7	70	
"	"	1.0	10	3	30	1.00

*One of the 10 rats died in this assay.
†These products were found to be impotent in the dosage employed.
‡The marked variations in potency of individual ampules make it impossible to rate this product.
§Lot number not noted.

minimum amount necessary to produce a positive result was ascertained. In all doubtful cases the experiment was repeated.

All these preparations were tested for the presence of estrin which would invalidate results based on an estrous type of smear. None of the assayed products contained any estrogenic material.

These results suggest that the potencies of the human urinary gonadotropic rat units employed by the manufacturers vary greatly. To remedy this situation a uniform standard should be adopted.† This has already been accomplished with the estrogenic preparations.

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Protecting Action of Procaine Against Ventricular Fibrillation Induced by Epinephrine During Cyclopropane Anesthesia.

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There is much evidence indicating that several anesthetic agents sensitize the heart so that the addition of small amounts of epinephrine may cause ventricular fibrillation. Oliver and Schafer[1] were first to observe this as a frequent complication during chloroform anesthesia, and Levy[2] elaborated on the reaction. More recently, Meek, Hathaway and Orth[3] have shown that the same effect may be produced in the dog during cyclopropane anesthesia. Experimental data accumulated by Kochman and Daels,[4] Mautz,[5] and Beck and Mautz[6] serves to establish that procaine applied locally to the heart reduces irritability of the myocardium as evidenced by augmentation in intensity of stimulation necessary to produce extra-systoles or ventricular fibrillation. Hermann and Jourdan[7] have reported that following subcutaneous injections of procaine a larger dose of epinephrine is necessary to produce ventricular fibrillation during chloro-

† Since the completion of these experiments, the League of Nations Health Organization has set up an international unit for the human chorionic gonadotropin. It is designated as 0.1 mg of a standard preparation of a gonadotropic extract from human pregnancy urine. This unit is supposed to produce an estrous type of smear in 21-day-old rats.

1 Oliver, G., and Schafer, E. A., *J. Physiol.*, 1895, **18**, 230.

2 Levy, A. G., *J. Physiol.*, 1911, **43**, 3.

3 Meek, W. J., Hathaway, H. R., and Orth, O. S., *J. Pharm. and Exp. Therap.*, 1939, **61**, 240.

4 Kochman, M., and Daels, F., *Arch. Internat. Pharm.*, 1908, **18**, 41.

5 Mautz, F. R., *J. Thoracic Surg.*, 1936, **5**, 612.

6 Beck, C. S., and Mautz, F. R., *Ann. Surg.*, 1937, **106**, 525.

7 Hermann, H., and Jourdan, F., *C. R. Soc. de Biol.*, 1931, **106**, 1153.