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This Week's Citation Classic™

Steelman S L & Pohley F M. Assay of the follicle stimulating hormone based on the augmentation with human chorionic gonadotropin.
Endocrinology 53:604-16, 1953.
[Fundamental Res. Dept., Armour Labs. and Res. Division, Armour and Co., Chicago, IL]

This paper describes a simple, specific method for the bioassay of the follicle stimulating hormone (FSH) based upon the augmentation of the ovarian weight response to FSH with human chorionic gonadotropin (HCG). [The *SCI*® indicates that this paper has been cited in over 1,010 publications since 1955.]

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"As a result of the findings of Hench[1] that cortisone was useful in the treatment of rheumatoid arthritis, the Armour Laboratories began the production and sale of ACTH as an alternative therapy. Literally hundreds of pounds of porcine pituitaries were processed each week. As a result, there was potentially available a large quantity of pituitary by-products from which one could recover hormones. It was found that the residue, after extraction of the ACTH and posterior pituitary hormones, contained gonadotropins (predominantly follicle stimulating hormone [FSH]).

"After reviewing the literature, it was readily apparent that there was no simple, specific assay for FSH. In order to purify FSH, we needed a better assay. After examining many possible methods in a variety of animals, we decided that the interaction between FSH and LH on ovarian weight was the most promising. By administering a large excess of LH (as human chorionic gonadotropin [HCG]), it was shown that any LH contamination in the sample would not affect the ovarian weight response to FSH. Many variables were examined including normal *vs.* hypophysectomized rats, dose of HCG, frequency of administration, interfering hormones, etc. As a result of these exploratory studies, a simple, specific assay for FSH was developed using immature female rats. In the development of the method, Florence Pohley, a statistician, analyzed each experiment. When we arrived at a workable procedure, it was found that the response was not a function of the logarithm of the dose as is the case in almost all bioassays. The slope ratio method for calculation of potencies was utilized and was described in detail in the publication. Several other investigators have conducted extensive mathematical analyses of the dose response curve and confirmed our original data [personal communications]. However, most investigators now use the log dose calculation method employing a narrower portion of the dose response curve. More recent studies indicate that by using 40-50 IU of HCG, the frequency of administration can be reduced.

"With a good assay method in hand, the purification of porcine FSH progressed rapidly and the product was eventually tested in humans and animals and found to be active. It was marketed for animal use. We were able to prepare, in 1952, many grams of a purified FSH (264-151-X) which was well characterized with regard to contamination with other hormones. This preparation was widely distributed to investigators and was used as a reference standard until the National Institutes of Health began preparing and distributing purified hormone preparations.

"The paper has been frequently cited because the method was used to bioassay pituitary preparations as well as human and animal biological fluids. Until radioimmunoassays became commonplace, the method was the simplest, most sensitive, and specific available."

1. **Hench P S, Kendall E C, Slocumb C H & Polley H F.** The effect of a hormone of the adrenal cortex (17-hydroxy-11-dehydrocorticosterone: compound E) and of pituitary adrenocorticotropic hormone on rheumatoid arthritis. *Proc. Staff Meetings Mayo Clinic* 24:181-97, 1949.
(Cited 260 times since 1955.)