

present throughout, but the increase in the concentration of the undissociated form consequent upon the decreased pH brings about prompt inhibition of respiration. Partial recovery occurs on restoration of the original pH level in the lower DNP concentration range. The control was not affected appreciably by the pH shift.

We have now shown on commercial yeast that a given total concentration of DNP will produce stimulation or inhibition of respiration depending upon the pH level, while the concentration of undissociated DNP is quite constant when optimal stimulation is evoked, and that change in acidity during a run will modify or reverse the effect of DNP on yeast respiration in a manner most directly explicable by changes in the concentration of undissociated DNP. We therefore conclude that in commercial yeast suspensions as in suspensions of pure yeast culture,⁴ DNP stimulates or inhibits yeast respiration only in the undissociated form. We know of no evidence to the contrary.

7957 P

Production of Superovulation in Normal Immature Rats by Injection of the Principle in Menopause Urine.

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The study of the effects of urine collected from a considerable number of normal women in the menopause and after castration has led us to regard the presence of lutein tissue in the ovaries of normal test rats as a common finding. The 24-hour specimens from such women were precipitated by alcohol, extracted with water and centrifuged. One-third of the powder thus obtained from each case was injected over a period of 3 days into a group of three 24 to 25 day old rats. (The remaining two-thirds was combined with synergist or pregnancy prolan in further tests for the active components of menopause urine, as will be seen in the following communication.) Autopsy was performed 96 hours after onset of injection. The urine of some of the patients was examined repeatedly; of the 20 women examined, the urine of 14 stimulated corpora on at least one occasion. Of a total of 88 tests, 20 showed corpus production.

We have, furthermore, been surprised to encounter ovarian weights of from 70 to 140 mg. in cases in which corpora lutea were

produced. There are many corpora in such ovaries—not the small crop characterizing pregnancy prolan. The histological picture of many of these corpora resembled that of the earliest stages of normal corpora just after shedding of the egg, and this fact together with the presence of distended oviducts led us to section the latter, where ova were encountered. In one case 83 eggs were found in 2 oviducts.

Smith and Engle¹ first reported experimentally induced superovulation in normal immature mice and rats after the implantation of rat anterior pituitary tissue. The phenomenon was again encountered by Leonard and Smith² on administering to hypophysectomized rats a mixture of the gonadotropic substances found in menopause and pregnancy urines respectively.

Irrespective of the interpretation or explanation adopted, menopause urine when administered alone is here shown to contain not infrequently a hormone or hormones capable of causing luteinization and, moreover, superovulation in normal immature test animals.

7958 P

Synergism or Augmentation Produced by the Addition of an Hypophyseal Synergist to Menopause or Castration Urine.

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Corpora lutea are frequently produced in immature test animals by the administration of menopause or castration urine alone; indeed, superovulation may result. It is to be admitted that the effect of the majority of such urines is characterized by the growth of follicles only in the test animals. Nevertheless, most of the latter urines also produce abundant corpora and moderately large ovaries in test animals when combined with an hypophyseal fraction (synergist) which by itself gives infantile ovaries in the 96-hour period. This phenomenon has been observed in 30 out of 34 tests on 20 castrate or menopause patients. The ovaries stimulated by this combination weighed from 50 to 150 mg.; the synergism reached as much as 290% and averaged 108%.

¹ Smith, P. E., and Engle, E. T., *Am. J. Anat.*, 1927, **40**, 159.

² Leonard, S. L., and Smith, P. E., *Proc. Soc. Exp. Biol. and Med.*, 1933, **31**, 283.