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Induction of Pseudopregnancy in Rat by Silver Nitrate on Nasal Mucosa.

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Physiologic relationship of nasal and genital regions has been described chiefly by Fliess¹ and Brettauer.² Recent studies have been made by Collip and his collaborators.³ Suggestive clinical observations by one of us (Rosen) stimulated a series of laboratory experiments in an effort to establish evidence of a specific naso-genital mechanism. Results reported herein are taken from a large and varied group of experiments.

Adult female albino rats, from an inbred colony, were used. They were isolated from males, fed a diet of hospital table scraps supplemented with greens, Pabulum, powdered milk, and cod liver oil. The regularity and the nature of the sexual cycles of all the stock females were determined from vaginal smears. Only rats with regular 4 or 5 day cycles were used. After the observation of 4 to 6 consecutive regular cycles, treatment consisting in the application of silver nitrate solution to the mucosa of the conchae was started. The silver nitrate solution was applied in one group with a fine cotton applicator; in a second group, by instillation of 0.05 cc. AgNO₃ using a tuberculin syringe. The time of treatment was: (a) during the proestrus and estrus of 2 consecutive cycles, a total of 6 days with interruption by 2 rest days, and (b) during diestrus, proestrus, estrus and diestrus, a total of 6 days application. This second type of treatment was more generally used. Certain animals received 10%, others 20% and still others 50% (gm., %) solutions during entire treatment period; others received progressively increased doses of 10, 20, 50% for 2 days each. Two control studies were made by (a) using NaCl (0.9%) and (b) applying silver solutions to the buccal mucosa. All cases, experimental and control, were treated under light ether anesthesia.

A group of the animals which experienced a post-treatment prolongation of the diestrous phase was autopsied during diestrus and

¹ Fliess, H., 1897, Leipzig and Wien.

² Brettauer, J., *Am. J. Obs. and Dis. Women and Children*, 1911, **64**, No. 2.

³ Mortimer, H., Wright, R. P., Collip, J. B., *Canadian M. J.*, 1936, **35**, 503.

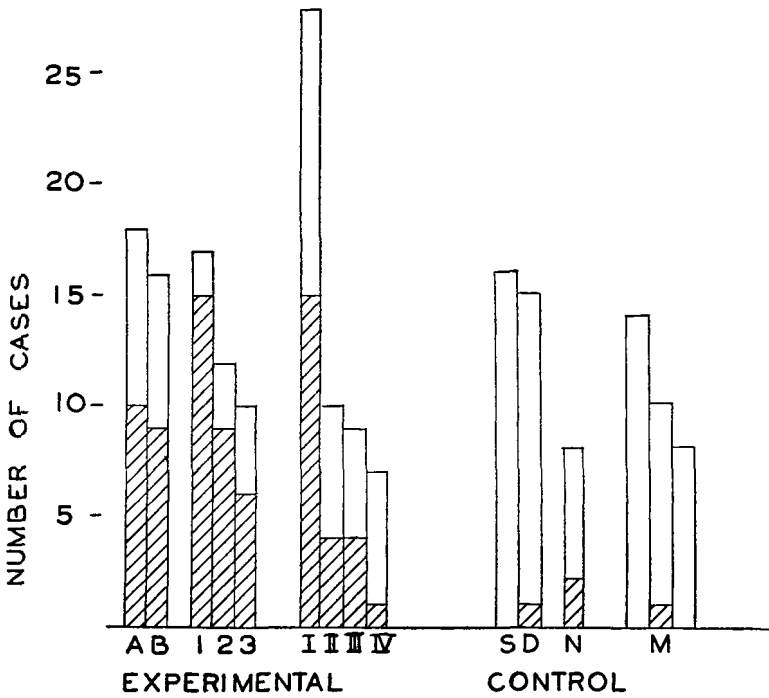


FIG. 1.

Graph shows number of cases in each series and positive responses (cross-hatched).

Experimental—A, B = 2 groups receiving 10, 20, 50% progressively, 2 days each, with cotton applicator.

1, 2, 3 = 3 groups treated as A, B but with instillation by catheter.

I, II, III = 50, 50; 10, 20; 10, 50% respectively, with cotton applicator, on two consecutive estrus periods.

IV = 10% with applicator for 6 consecutive days.

Control—S, D = Nasal application with dry catheter for 6, 4 days.

N = Nasal application 0.9 NaCl, for 6 days.

M = Buccal application of 10, 20, 50% progressively, 2 days each concentration.

the ovaries examined; a second group was operated on the 4th or 5th day of leucocyte phase and the uteri were traumatized with silk thread loops (longitudinal—Shelesnyak⁴) to provoke deciduoma formation.

Of 186 animals included in this study, 127 were treated intranasally with silver nitrate. The weighted average length of 1400 cycles was 4.1 days. Prolonged cycles ranged from 8 to 21 days. Of the 127 experimental animals, 69 (or 54%) cases experienced post-treatment prolongation of leucocyte phase. One technique of treatment induced 30 positive reactions of 59 trials (77%). Three cases evinced a decidual reaction in the traumatized uterus. Of the

⁴ Shelesnyak, M. C., *Am. J. Physiol.*, 1933, **104**, 693.

69 controls 4 cases of prolongation occurred; 3 of them 8-day cycles and one a 13-day. Three of these 4 prolonged cycles were in cases which received nasal manipulation but no silver salt.

The findings establish the existence of a naso-genital relationship whereby nasal stimulation elicits an ovarian response, a diestrual prolongation. On the basis of luteal ovaries and decidual reactions in traumatized uteri, this prolongation must be considered pseudo-pregnancy.

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9417

Is Antibody-Globulin "Denatured" by Its Combination with Antigen?

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It has frequently been stated that antibody becomes "denatured" when combined with its antigenic or haptenic counterpart. "Denatured" is one of our slippery words which has a loose rather than a definitive signification. Perhaps "lessened solubility" most commonly expresses what is meant by denaturation. Shibley¹ has recorded the remarkably identical electrophoretic behavior of thermally denatured normal globulin and of bacteria thoroughly coated with antibody-globulin. But, that antibody-globulin has not really lost its natural (and very labile) qualities as a result of its combination with antigen, is shown by the facts that dissociated antibody retains its specific combining characteristics, and immune sera produced by injecting antibody-antigen complexes not only reflect the species-specificity of the serum,² but also the particular features of different kinds of antibody, *e. g.*, that of antipneumococcal serum is antigenically somewhat different from diphtheric antitoxin³—each having been combined with its antigen before injection into the antibody-producing animal.

To compare, in another way, the properties of specific globulin-antigen compounds and thermally denatured globulin we have mixed

¹ Shibley, G. S., *J. Exp. Med.*, 1929, **50**, 825.

² Braun, H., *Z. f. Immunitätsf.*, 1909, **3**, 53.

³ Ando, K., Kee, R., and Komiyama, T., *J. Immunol.*, 1937, **32**, 181.