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Mechanism of Estrogen Effect on Nasal Mucosa in Atrophic Rhinitis; Successful Treatment with Prostigmin.

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Periodic changes in the appearance of the nasal mucosa during the menstrual cycle, have long been recognized. A consideration of this so-called "naso-sexual relationship" led Mortimer, Wright and Collip¹ to observe the effects of parenterally administered estrogenic substance upon the mucous membranes of the nose. The changes which they observed suggested the use of estrogens in the treatment of atrophic rhinitis. They reported clinical improvement in such cases, following the repeated application of oily solutions of estrone directly to the nasal mucous membranes. Blaisdell² arrived at the same therapeutic idea from the similarity in the pathology of atrophic rhinitis and of atrophic or senile vaginitis, and from the previously reported efficacy of local estrogen therapy in the latter condition. He also reported clinical improvement in atrophic rhinitis obtained by intranasal estrin therapy.

The local treatment of atrophic rhinitis with estrone has produced only mildly favorable or negative results in our hands. We were also impressed by the lack of any evidence of gonadal deficiency in most of our cases. Both these facts deprecated the importance of the "naso-sexual relationship", but did not offer any other explanation for such therapeutic results as were obtained with the estrogens. The situation was clarified by a recent study of one of us and coworkers,³ in which it was found that the various component phenomena of estrus may be classified into 2 categories:

1. The specific proliferative effects of estrin, and
2. Those effects which are secondary to hyperemia.

The latter effects can be reproduced by non-specific hyperemic agents such as yohimbin. However, when they result from estrin action, they are due to the acetylcholine-liberating properties of this hormone, as demonstrated by Reynolds.⁴ This suggested to us the probability that the benefit derived from intranasal estrone therapy

¹ Mortimer, H., Wright, R. P., and Collip, J. B., *Can. M. A. J.*, 1937, **37**, 445.

² Blaisdell, I. H., *Laryngoscope*, 1938, **48**, 699.

³ Hechter, O., Lev, M., and Soskin, S., *Endocrinology*, in press.

⁴ Reynolds, S. R. M., *J. Physiol.*, 1939, **95**, 258.

in atrophic rhinitis depended upon the incidental hyperemic effects of the hormone, rather than upon a specific sexual relationship. It also indicated the possibility that a mode of therapy especially directed towards a physiologic hyperemia of the nasal mucosa might give better results than those obtained with estrone, and at the same time avoid unnecessary exposure to this potent hormone. It seemed logical to try the local application of acetylcholine. But since this seemed not without danger, we decided to potentiate the naturally occurring acetylcholine in the nasal mucosa, by inhibiting the cholinesterase with a synthetic physostigmine-like substance which is commercially available.

To date we have treated 14 patients suffering from advanced atrophic rhinitis with ozena, for periods ranging from 2 to 6 months. Our procedure was to teach the patients to spray 0.25 cc of a 1 : 2000 solution of Prostigmin Methylsulfate* into each nostril, 4 times per day. To insure good contact of the medication with the mucous membrane they irrigated the nose with a mildly alkaline solution once or twice per day. All other therapy was stopped. Our results were far superior to those obtained with estrone or with any other recognized form of treatment. Without exception, all patients exhibited definite improvement within about 2 weeks, and progressed favorably thereafter. There was a decrease in crust formation and in the amount and character of the nasal discharge, the latter becoming less purulent and less tenacious. The ozena was controlled. The nasal, pharyngeal, and laryngeal mucosa lost its dry, blazed appearance and became moist and pink. Patients who had previously complained of great discomfort from pharyngitis and laryngitis sicca, were completely relieved. In a number of instances there was a definite space reduction in the nasal vaults, although not to within normal limits.

We have not, as yet, had the opportunity of observing the degree of permanence of the beneficial results when the treatment is stopped. However, the results would be eminently worthwhile even if treatment had to be continuous. We have not observed any untoward results or unpleasant side reactions from the daily use of the drug, in the specified amounts.

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