

In order to determine thiamin requirements more exactly we have also studied the amounts of cocarboxylase found in the blood of young infants. Preliminary results show that at an intake increasing from 42 to 56 units of thiamin per day during 9 weeks of study, one infant was not able to maintain the level of his blood vitamin, whereas a second infant did maintain the level of cocarboxylase in his blood when given an intake ranging from 49 to 58 units of thiamin per day over the same period. This second infant, however, was the best infant we have ever studied so far as utilization of nutrients is concerned, and it is probable that the minimum requirement for the average infant is above the level of 60 units of thiamin per day which these infants received. These blood data tend to substantiate the conclusion based on urinary excretion that 80 units of intake represent the minimum requirement. Further investigations are now under way to determine the lowest thiamin intake which is compatible with health, and also the optimal amounts of vitamin B₁ for the best development of the infant.

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Buccal Absorption of α -Estradiol in Propylene Glycol.

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In the treatment of estrogen deficiency states, it is frequently necessary to administer estrogens for prolonged periods of time.

The usual method of administration consists of subcutaneous or intramuscular injections. It would be highly advantageous if one could administer estrogens in effective amounts without submitting the patient to the annoyance of repeated injections. Although it has been shown that estrogens are absorbed through the skin and the intestinal tract, neither method is satisfactory for therapeutic purposes.

In the present communication, we wish to describe a method for administering estrogens which is both simple and effective. It consists of sublingual administration of α -estradiol in a propylene glycol solution.* The solution contains 0.5 mg of α -estradiol per cc of propylene glycol. Four drops are placed under the tongue and the patient is instructed not to swallow for five minutes. This can be done several times a day.

The present study was performed on a series of 8 women with

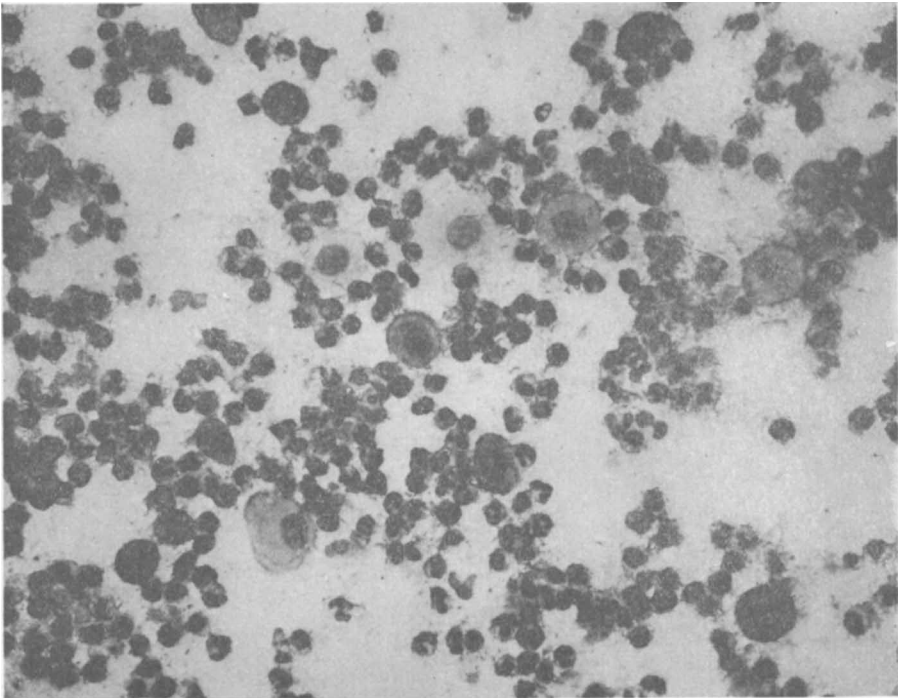


FIG. 1.

Patient S.B., age 54, menopause 6 years ago. Pre-treatment vaginal smear revealing marked degree of estrogen deficiency.

* For the materials used in this investigation, we are indebted to Dr. Edward Henderson, of the Schering Corporation, Bloomfield, N. J.

objective evidence (demonstrated by vaginal smears† and vaginal biopsies) of estrogen deficiency. The hormone was administered 3 to 6 times a day. Vaginal smears were taken daily and vaginal biopsies at intervals of 1 to 2 weeks.

Results. Characteristic vaginal smear changes indicating an estrogen effect were noted as early as 4 days after the beginning of hormone administration, with daily doses of 0.3 mg of α -estradiol (Figs. 1 and 2). Vaginal biopsies at the end of one week showed definite evidence of estrogen stimulation. No untoward effects were noted as a result of the propylene glycol absorption.

A number of experimental studies in animals and humans have been performed with regard to the possible toxicity of propylene

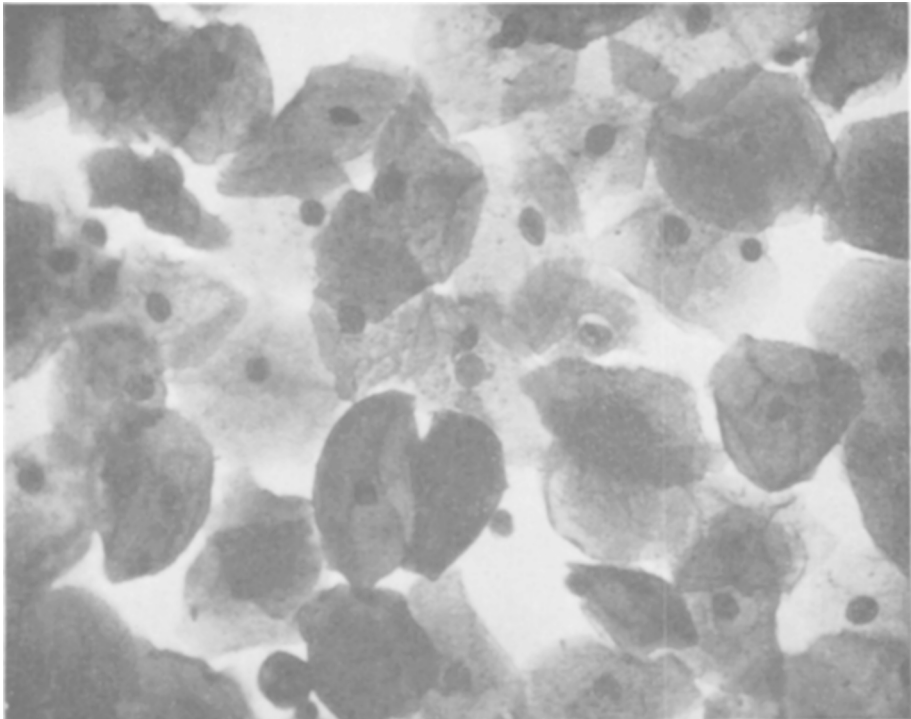


FIG. 2.

Vaginal smear taken 4 days after beginning of sub-lingual administration of α -estradiol in propylene glycol. Dose: .05 mg α -estradiol 6 times daily for 4 days = total of 1.2 mg = 14400 r.u. Smear reveals typical estrogenic effect.

†Vaginal smears prepared by the aqueous fuchsin technique.^{7,8}

⁷ Salmon, U. J., and Frank, R. T., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **33**, 612.

⁸ Geist, S. H., and Salmon, U. J., *Am. J. Obs. and Gyn.*, 1939, **38**, 392.

glycol.¹⁻⁶ The published reports, to date, agree as to the absence of toxic effects unless administered in large doses.

Discussion. A simple and economical method of administering estrogens for therapeutic purposes is described. This method consists of instilling several drops of a solution of α -estradiol in propylene glycol in the sublingual space. Definite morphologic evidence of absorption (demonstrated by characteristic estrogenic effects in the histologic sections of the vaginal mucosa and vaginal smears) was noted in all cases at the end of one week with daily doses of 0.2 and 0.3 mg of α -estradiol.

Although experimental studies appear to indicate that, in the small doses used, propylene glycol has no toxic effects, further studies should be conducted in order to determine what the effect of continued administration of these small doses would be. Should propylene glycol be found to be completely innocuous, this method of administration of estrogens offers great promise of simplifying and reducing the cost of estrogen therapy.

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Rumen Synthesis of the Vitamin B Complex.*†

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Work reported by McElroy and Goss¹ indicates the ability of sheep to synthesize several members of the vitamin B complex in

¹ Weatherby, J. H., and Haag, H. B., *J. Am. Pharm. Assn.*, 1938, **27**, 466.

² Laug, E. P., Calvery, H. O., Morris, H. J., and Woodard, G., *J. Indust. Hyg. and Toxicol.*, 1939, **21**, 173.

³ Hanzlik, P. J., Newman, H. W., Van Winkle, W., Lehman, A. J., and Kennedy, N. K., *J. Pharm. and Exp. Ther.*, 1939, **67**, 101.

⁴ Seidenfeld, M. A., and Hanzlik, P. J., *J. Pharm. and Exp. Ther.*, 1932, **44**, 109.

⁵ Hanzlik, P. J., Lehman, A. J., Van Winkle, W., and Kennedy, N. K., *J. Pharm. and Exp. Ther.*, 1939, **67**, 114.

⁶ Latven, A. R., and Molitor, H., *J. Pharm. and Exp. Ther.*, 1939, **65**, 89.

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¹ McElroy, L. W., and Goss, H., *J. Biol. Chem.*, 1939, **130**, 439.