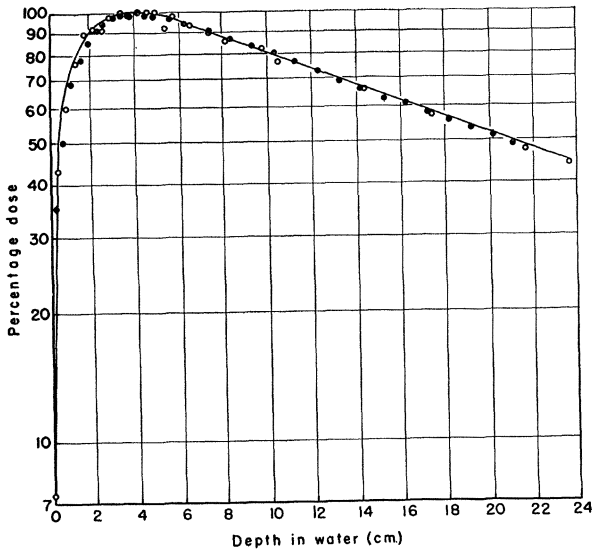

FIG. 2. Depth-dose distribution. Solid points are data obtained with ion chamber in water phantom with 5-cm field at 80-cm skin target distance. Hollow points are data obtained with a film phantom exposed under the same conditions.

distance. The surfaces were shaped by the use of a differential absorber in the x-ray beam consisting of a conical ensemble of fiber disks. No deviation greater than 2½% from perfectly flat isodose surfaces exists. The average of more than one ion chamber or film determination yields even flatter surfaces than those shown. The intensity of radiation 5 cm outside the geometrical edge of the beam is less than 1% of that within the beam.

The depth-dose distribution obtained with a 1-cm-diam beam falls off more rapidly at depths beyond 5 cm than with beams of larger cross-sectional area. The dependence of depth-dose on beam area is much less than the strong dependence which characterizes lower energies (*2*). A detailed analysis of these data is in preparation.

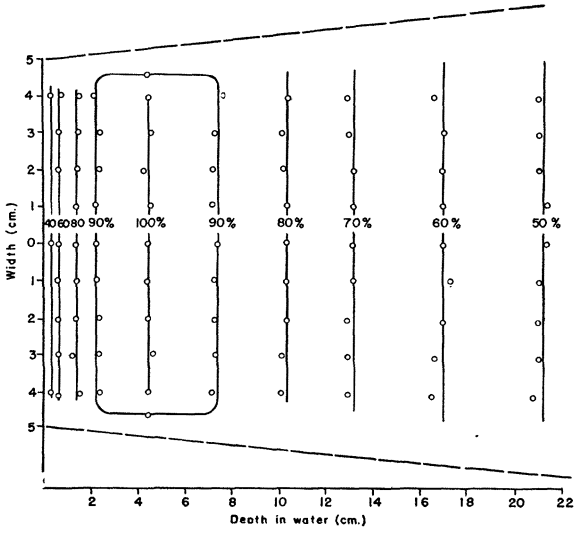

FIG. 3. Isodose distribution obtained in single operation of betatron with ion chamber in remote-controlled water phantom. Beam 10 cm in diam at 80-cm skin target distance filtered with hydrocarbon absorber.

References

1. QUASTLER, H. *Amer. J. Roentgenol.*, 1949, **61**, 591.
2. QUIMBY, E. H. *Radiology*, 1942, **38**, 268.

Antifolliculoid Activity of Vitamin A[1]

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Continued cornification of vaginal epithelium is considered to be a reliable early manifestation of vitamin A deficiency in female rats (*1*). Sherwood *et al.* (*9, 10*) reported that feeding large amounts of carotene suppressed the estrous vaginal smear picture in the normal rat; however, other workers administered high doses of vitamin A orally (*3*), or by injection (*2*), and found no inhibition of the vaginal response to estrogen. Recent studies on mice (*11*) tend to corroborate the observations of Sherwood *et al.*

Inasmuch as the liver is known to store and inactivate most of the ingested vitamin A (*5*) and probably much of the injected material, we doubted that these methods would result in making available a really high level of vitamin A to any particular target organ. A series of experiments have been conducted involving the intravaginal instillation of various substances by the method employed by Krichesky and Glass (*6*).

Bilaterally ovariectomized rats of an inbred strain were estrogenized by subcutaneous implantation of α-estradiol pellets.[2] After estrous (cornified) smears were obtained from the vagina, sesame oil, cod liver oil, and vitamin A alcohol in sesame oil and in acetone-sesame oil[3] were applied intravaginally in 0.05-ml daily doses, using a blunt 18-gage needle on a tuberculin syringe. Vaginal smears, taken daily during and subsequent to the period of administration of oil solutions, were stained with Wright's stain. The vaginal pictures were classified according to the dominant cell types seen: leukocytes, nucleated epithelium, nucleated vacuolated epithelium, precornified cells (i.e., with nuclear remnants), and cornified cells.

Table 1 demonstrates that topically applied vitamin A results in definite alteration of the keratinized picture produced by estrogen. The appearance of ovoid and round cells with vesicular nuclei, including many with large vacuoles in their cytoplasm, characterizes most smears after two or more days' treatment with vitamin A (Fig. 2). Some cornified and precornified cells were

[1] Aided by research grants from the University of California Board of Research.

[2] Generously supplied by Dr. W. H. Stoner, Schering Corporation, Bloomfield, N. J.

[3] Prepared from crystalline material produced by Distillation Products Industries, generously supplied by Dr. Philip L. Harris and C. J. Staud, Eastman Kodak Co., Rochester, N. Y.

TABLE 1

EFFECT OF INTRAVAGINALLY APPLIED VITAMIN A SOLUTIONS ON THE ESTROGENIZED VAGINAL SMEAR TYPE

Animal group	Treatment	No. of animals	Days of treatment	Total dosage in ml	No. of animals with vaginal smear type :*		
					L, NVE, NE	NE, PC, C	PC, C
Ia	Cod liver oil (780 I.U./ml)	10	2	0.10	0	0	10
	Sesame oil	4	2	0.10	0	0	4
Ib	Cod liver oil	10	16	0.80	0	2	8
	Sesame oil	4	16	0.80	0	0	4
IIa	Vit. A in acetone-sesame oil (25,000 I.U./ml)	17	4	0.20	14	3	0
	Acetone-sesame oil	6	4	0.20	0	1	5
IIb	Vit. A in sesame oil (30,000 I.U./ml)	20	6	0.30	15	5	0
	Sesame oil	10	6	0.30	0	1	9
IIc	Vit. A in sesame oil (50,000 I.U./ml)	10	8	0.40	7	3	0
	Sesame oil	4	8	0.40	0	1	3

* L = leukocytes, NE = nucleated epithelium, NVE = nucleated vacuolated epithelium, PC = precornified cells, C = cornified cells.

also generally present in these smears, but in greatly reduced numbers. The rats treated with sesame oil, on the other hand, showed no appreciable inhibition of the estrogen-induced keratinization (Fig. 1).

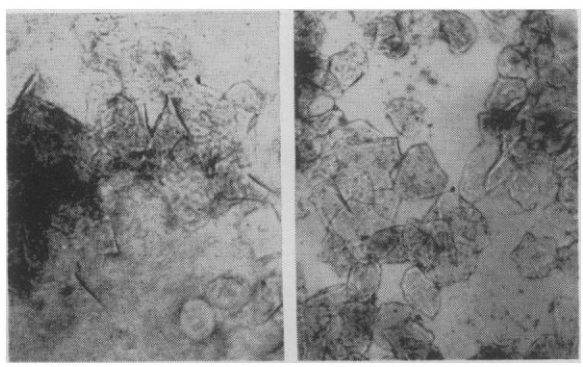

FIG. 1. *Left,* vaginal smear from estrogenized castrated rat (group IIb), before administration of sesame oil (Wright's stain. Magnification 87 ×). *Right,* vaginal smear from same animal, after intravaginal application of 0.05 ml sesame oil daily for 6 days (Wright's stain. Magnification 87 ×).

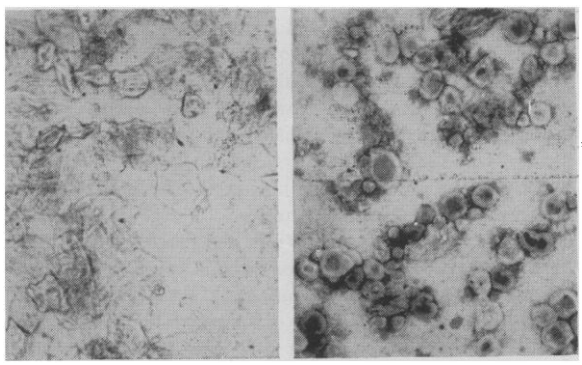

FIG. 2. *Left,* vaginal smear from estrogenized castrated rat (group IIb), before administration of vitamin A (Wright's stain. Magnification 87 ×). *Right,* vaginal smear from same animal, after intravaginal application of 0.05 ml vitamin A alcohol in sesame oil (1500 I.U.) daily for 6 days (Wright's stain. Magnification 87 ×).

The absence of a definite effect from cod liver oil is probably due to the relatively small amounts of vitamin A available in the doses administered, and possibly to the nonspecific keratinization-favoring effect of certain materials, such as cholesterol (*6*), present in cod liver oil.

The data herein presented may support the contentions of some earlier investigators (*4, 8*) who related all epithelial metaplasia and keratinization, at least in the rat, to the same basic etiologic factor (local vitamin A inadequacy), regardless of the initiating agent. The general metabolic role of vitamin A in favoring the synthesis by epithelial cells of glycoproteins (mucin) over fibrous proteins (keratin), as suggested by Mason and Ellison (*7*), is further indicated here.

A histologic study of the vaginal reaction to various locally applied oil solutions, including vitamin A in oil, along with data supplementary to those summarized herein, will be reported elsewhere.

References

1. ABERLE, S. B. D. *J. Nutrition,* 1936, **6**, 1.
2. BRODY, H. and GOLDMAN, S. *Endocrinology,* 1941, **29**. 164.
3. BURRILL, M. W. and GREENE, R. R. *Endocrinology,* 1941, **28**, 765.
4. CRAMER, H. *Dtsch. med. Wschr.,* 1942, **68**, 809.
5. HADFIELD, G. and GARROD, L. P. *Recent advances in pathology.* Philadelphia: Blakiston, 1942. P. 139.
6. KRICHESKY, B. and GLASS, S. J. *Endocrinology,* 1947, **41**, 196.
7. MASON, K. E. and ELLISON, E. T. *J. Nutrition,* 1935, **9**, 735.
8. MCCULLOUGH, K. and DALLDORF, G. *Arch. Path.,* 1937, **24**, 486.
9. SHERWOOD, T. C., BREND, M. A., and ROPER, E. A. *J. Nutrition,* 1936, **11**, 593.
10. SHERWOOD, T. C., DEPP, O. R., and BIRGE, G. P. *J. Nutrition,* 1937, **14**, 481.
11. THORBORG, J. V. *Acta endocrinologica,* 1948, Suppl. 2, 1.