

in size, and colloid increased in amount, the sections produced progressively blacker records. It is interesting to note in the figures of the thyroid of the 5.0 mm body length tadpole that of the adjacent sections, the one containing more colloid contained also much more radio-activity, revealed by a striking difference in the radio-autographs.

It is clear, therefore, that in this frog function by the thyroid can be demonstrated very early after formation of follicles within each of the 2 primitive, still yolk-laden, lobes. It should be remembered that the iodine in the serial sections which produced the radio-autographs had remained in the thin section even after immersion in aqueous and alcoholic solutions, in alcohol-ether, and xylene. The iodine is, therefore, quite likely in an organic linkage, probably as thyroglobulin.

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Origin and Differentiation of Epithelium of Urinogenital Sinus in the Opossum.

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Previous results have shown^{1, 2} that administration of estrogens to young opossums during early pouch life produces extreme hyperplasia and cornification of the lining of the urinogenital sinus and structures associated developmentally with the sinus. The related structures are the *neck* and *trigone* region of the bladder, and the *sinus horns* (dorso-lateral diverticula of the sinus which received the gonoducts and subsequently contribute extensively to the *lateral vaginal canals*). The sinus epithelium undergoes intense squamous metaplasia with continuous shedding of keratinized layers after estrogen treatment, closely resembling the adult vagina at estrus. Similar results are reported by Moore.³

Where other epithelia of the urinogenital tract join the sinus the former do not respond, and the transition is abrupt. The response was, therefore, considered specific for sinus epithelium. In 20-day

¹ Burns, R. K., Jr., *Proc. Soc. Exp. Biol. and Med.*, 1939, **41**, 270.

² Burns, R. K., Jr., *J. Morph.*, 1939, **65**, 497.

³ Moore, C. R., *Physiol. Zool.*, 1941, **14**, 1.

young such transitions occur where the gonoducts join the sinus horns, and at the borders of the trigone; at the external meatus, however, the sinus lining continues indistinguishably into the epidermis, and at all levels of the sinus the metaplastic mucosa shows the same close resemblance to skin that characterizes the adult mammalian vagina.

In younger specimens, treated from 10 to 14 days, the reaction is less advanced and a progression is clearly seen. Hyperplasia is most extreme and cornification most advanced in the neighborhood of the meatus and in the lower sinus. Both conditions diminish toward the bladder. In the *sinus horns* and in the *trigone*, stratified squamous epithelium from the sinus can be seen actively eroding and replacing the primitive linings of these areas. Appearances clearly indicate an invasion of this tissue from below, with the process greatly accelerated by hormone action.

Since the sharply limited and specific nature of the cornification response indicates a common origin of the tissues involved from the sinus; and since the characteristic histological features are evoked in the order mentioned, the original derivation of the cornifying epithelium from the ectodermal portion of the cloaca is suggested. Early development decidedly favors this view: the ectodermal cloaca or uro-proctodeum is rather deep in the opossum⁴ and a core of ectodermal epithelium extends toward both anal and urogenital divisions of the cloaca, as the cloacal membrane breaks down approximately 12 hours before birth. The urethral plate is likewise a potential source.⁵ The sinus is very shallow at this time and entering tissue would at once lie at a level just below the sinus horns. Shortly after birth the linings of sinus and ectodermal cloaca appear continuous and identical; and pigmented, keratinized cells (like those of the epitrichium) already occur in the lower sinus. At the base of the bladder 3 kinds of epithelium may be distinguished: (1) a thick, many-layered tissue lines the sinus as far as the bladder neck; (2) the trigone area is covered by simple, cuboidal epithelium continuous with that of the mesonephric duct; (3) the bladder proper and the sinus horns are lined by an irregular epithelium of so-called transitional type. The last-mentioned appears to represent the primitive cloacal endoderm. In older experimental animals, as we have seen, the linings of sinus horns and trigone are replaced by stratified squamous (cornifying) epithelium from the sinus; and the primitive cloacal endoderm appears to be restricted eventually

⁴ McCrady, Edw., Jr., *J. Morph.*, 1940, **66**, 131.

⁵ Barnstein, N. J., and Mossman, H. W., *Anat. Rec.*, 1938, **72**, 67.

to the bladder. Elongation of the canal plus active ingrowth readily explain the presence of the invading tissue at the horn level in older stages (and later still in the lateral vaginal canals).

Recently Zuckerman,⁶ reviewing an extensive literature, has reached the same conclusions with regard to a common origin from the urinogenital sinus for tissues sensitive to estrogens; and Raynaud's results on the cat⁷ deserve particular mention since he reports cornification of urethra and trigone. Zuckerman also raises, but does not decide the question of ectodermal contribution to the sinus. This is an old problem, never conclusively attacked, but now fairly clearly answered in the opossum.

Summary and Conclusions. 1. Those epithelia in the urinogenital tract of the opossum which respond to estrogens by squamous metaplasia and cornification, have a common origin from the lining of the urinogenital sinus. 2. The sinus epithelium itself is apparently derived at an early stage of development from the ectodermal cloaca or uro-proctodeum, and perhaps in part from the urethral plate. 3. The primitive cloacal endoderm is eventually restricted to the bladder proper. 4. A common ectodermal origin best explains the histological and physiological likenesses of the tissues involved, and the occurrence of stratified squamous epithelium in the lower urinogenital tract of mammals generally. Early development in higher mammals needs reinvestigation with respect to this point. 5. The use of hormones (particularly estrogens) in the immature organism is a valuable method of precociously differentiating tissues not so readily delimited in normal development of the urinogenital tract.

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Decomposition of Urea by Proteus.

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At the Third International Congress for Microbiology St. John-Brooks and Rhodes¹ suggested a simplification of the taxonomy of the *Proteus* genus. On the basis of maltose fermentation and indol

⁶ Zuckerman, S., *Biol. Rev.*, 1940, **15**, 231.

⁷ Raynaud, A., *C. R. Soc. Biol.*, 1937, **126**, 215.

¹ St. John-Brooks, R., and Rhodes, M., *Third International Congress for Microbiology, Report of Proceedings*, 1939, 167.