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Local Effects on the Feather Papilla of Thyroxine and of Progesterone.* (21982)

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Shedding and renewal of plumage occurs in birds in well-defined association with sexual and seasonal events. Normally, the standing lifeless feather is gradually expelled from the mouth of the follicle as a new feather arises following an activation which is initiated in the resting papilla, an organ that uninterruptedly occupies the internal well of the follicle and which is the actual site of the externally manifest cyclical events. Seasonal inertia of the papilla is a familiar phenomenon in laboratories utilizing experimentally the regenerating plumage. Forcible removal of the standing feather causes a tearing of the apical tissue of the papilla with haemorrhage into the lumen of the follicle(1). The wound stimulus is sufficient to assure immediate activation of the papilla in the capon whereas in the cock and hen, regeneration usually fails outside of the environs of molt. We may speak at such times of a "quiescent papilla." The papilla has long been shown to respond by growth to oral or parenteral administration of thyroid substance(2; and many others). The dosage requisite for this reaction was less as the season of normal molt approached(3), showing the gradual course of natural changes which culminate in that event. Recently it has been established that progesterone, when given as a single intramuscular injection of a preparation having slow absorption from local depots (Reposito Progesterone), also will cause a general activation of the feather papillae in adult fowl(4). There was no hint in these experiments that progesterone action was here in any sense *via* a stimulation of the bird's thyroid; this was checked in the feather structure where excess thyroid has long been known to produce specific, readily recognized consequences(5; and many others). The similar end effects seem accordingly independently due to either progesterone or to thyroxine although some common intermediate participation is not ruled out.

This possibility suggested following the consequences of separate local applications of either of the two substances to the papilla;

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these observations are recorded here.

Methods. Adult hens bearing feather papillae in the various physiological states were used. The test substance was applied to an area of one side of the bird's body and as control the respective solvent was applied to an identically prepared site in the opposite location. Progesterone was administered as a single intradermal injection of 0.20 ml of a solution of 50 mg/ml in sesame oil or as a daily local application during 4 weeks of progesterone in ointment, 50 mg/g.† Thyroxine was prepared as a solution of 5 mg (Thyroxin crystals Squibb) in 1 ml distilled water plus 1 drop of a 4% sodium hydroxide solution. It was administered as a single intradermal injection of 0.2 ml or as a daily repeated local application in ointment during 4 weeks. One-half ml of the thyroxine solution was rubbed up in a small amount of a commercial vanishing-type cream, the procedure repeated as required. Progesterone in oil was also injected directly into the superior umbilicus of the large secondaries in the expectation that the cavity of the quill of the standing feather would provide a source of gradual supply to the underlying papilla. This proved negative. Previous experiments had shown thyroxine in the same situation to enter into the general circulation and this route to be unsuited to the purpose.

Results. Five birds were treated with progesterone in ointment and 5 with thyroxine in ointment; in 3 of each series, the application was made to simultaneously defeathered areas; in the other 2, application was to the skin spaces separating adjacent standing feather rows. No activation was elicited in the papilla in either circumstance. Thyroxine in some amounts, however, apparently penetrated the epidermal tissues as there were subsequently noted characteristic changes of pigmentation in regenerating feathers of distant location. Thyroxine was given by intradermal injection on 28 occasions, progesterone on 27 occasions. The birds used were prepared so as to afford the 3 classes of papillae to either test substance. Birds were defeathered in small areas to assure the additional stimulus of plucking; the immediately following injections were made between adjacent denuded follicles. In affecting the resting papilla, the site injected was between 2 rows of standing feathers. The birds considered to have quiescent papillae had been plucked about 2 months earlier and had not exhibited regeneration up to the date of this treatment. The data from these series are summarized in Table I. The compilations refer to the total number of feather germs which were regenerated in the immediate vicinity of the point of injection. Examination of Table I shows thyroxine in intradermal injection to effect local proliferation of all types of the papilla. Experimental activation in resting and quiescent states, where it is opposed to zero regeneration in the control side, could not be clearer. However, the augmentation of the stimulus brought to growth in preliminary defeathering is equally evident. The properties of progesterone in these respects are less distinct. As administered, progesterone was negative in the resting papilla and the records of the quiescent papilla must be discounted in view of the regeneration occurring in the control area. In defeathering, a greater number of regenerations occurred in progesterone treatment which may suggest an increasing importance as the seasonal inertia of the papilla lessens. It is evident that the papilla has an annual or biannual physiological cycle which may proceed at very different levels (*cf.* capon and sexes of fowl), and which is triggered to an external event, presumably some hormonal impulse or withdrawal. If

TABLE I. Local Action on Feather Papilla of Thyroxine and of Progesterone.

Treatment	Papilla state	No. trials	Feather germs regenerated (No.) Treated side	Control side
Thyroxine (i.d.)*	Defeathered	15	119	59
	Resting	10	33	0
	Quiescent	3	10	0
Progesterone (i.d.)	Defeathered	15	96	58
	Resting	8	0	0
	Quiescent	4	9	10

* Intradermal.

† Progesterone was supplied generously by the Research Department of Ciba Pharmaceutical Products, Summit, N. J.

further studies should definitely prove progesterone to be locally negative in the feather papilla, this would show its systemic action to be upon some intermediate link. Since the bird's own thyroid is apparently unaffected by progesterone in circumstances where the substance is adequate for growth induction in the papilla, that gland is probably not the participant despite the very evident experimental effectiveness. In these aspects, the newly discovered role of progesterone casts some doubt on the concept that surges of thyroidal activity initiate the normal events of molt and suggests a revised approach to an important problem.

Summary. The respective local actions upon the feather papilla of thyroxine and of progesterone were examined. Application was made by intradermal injection to the immediate vicinity of the resting, quiescent and plucking-stimulated papillae. Thyroxine was effective in causing proliferation in all 3 circumstances; progesterone proved negative with this technic in the resting and quiescent states; it may have exerted a slight augmentation in the third.

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Fate of Ascorbic Acid in Early Radiation Damage.* (21983)

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There is a paucity of information regarding the role of ascorbic acid in radiation damage. In light of the reported involvement of ascorbic acid in the conversion of folic acid to citrovorum factor(1) and, thereby, in nucleic acid synthesis, its sensitivity *in vivo* to irradiation is of interest. Thus far, the study of ascorbic acid has been concerned chiefly with its changes in the adrenal gland(2). We have investigated a variety of rat tissues from the standpoint of the concentration and total organ content of ascorbic acid as well as organ weight after whole-body X-irradiation. These organs included cervical lymph nodes, thymus, liver, spleen, kidney, intestinal mucosa, testis, brown adipose tissue, muscle, adrenals, and brain. The results indicate a highly selective action of irradiation on tissue ascorbic acid.

Methods. Male Sprague-Dawley rats, weighing 125-200 g, receiving a stock Purina Chow diet *ad lib.*, were irradiated at a rate of 23 r/min with a 250-kvp X-ray machine at 15 ma with a 0.5 mm Cu plus a 1.0 mm Al filter and the HVL equal to 2.0 mm of Cu. The target distance was 34 inches from the table supporting the animals. At 4, 28, and 72 hours after irradiation, groups of 4 to 6 animals were sacrificed. The organs were dissected out, blotted, and weighed on a torsion balance. A 9-inch strip of small intestine was slit, washed, and scraped to provide a sample of intestinal mucosa. The tissues were homogenized in 10% trichloroacetic acid; all of the ascorbic acid was converted to the oxidized (dehydro) form and determined as the osazone by the method of Roe and Kuether (3). No differentiation of oxidized and reduced ascorbic acid was carried out. Typical control values and their variation are shown in Table I. The values for concentration, total ascorbic acid and organ weight for the experimental groups are reported as a percent of the control values.

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