was able to produce chronic hypertension by renal ischemia after excision of one adrenal, denervation of the other and mechanical destruction of its medulla. This type of hypertension, therefore, apparently is independent of epinephrine secretion from the adrenals. Rogoff and Wasserman tested bloods from a small group of patients with hypertension (obtained through the courtesy of Dr. R. W. Scott at Cleveland City Hospital) and were unable to detect epinephrine in the specimens. Stewart[7] had previously reported a similar negative result.

These experiments lead to the conclusion that increased secretion of epinephrine from the adrenals, as a probable factor in causing persistent hypertension, lacks support of adequate quantitative experimental evidence. Our evidence is against the physiological concept which is a basis for the clinical procedure of surgical interference with the adrenal glands as a therapeutic measure for the relief of hypertension.

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Effects of Thyroxin and Female Hormone on One Phase of Saddle Feather Development.

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The c-isochrone has been defined by Fraps and Juhn[1] as the locus of points in the regenerated feather representing a given level of cell division around the annular collar of the feather germ. This locus appears as a constant configuration in each vane-half of the grown feather and is symmetrical with respect to a common transverse shaft level. If the barbs of either vane-half are in parallel array (at any uniform angle with the shaft), the c-isochrone is a straight line from shaft to margin, equidistant on shaft and a given barb from the point of union of that barb with the shaft. In Fig. 1, for example, barbs are laid out at right angles to the shaft, AB (apex of the feather at A), and the c-isochrone must form in this particular construction an angle of 45° with the shaft. Since the apex of the

[7] Stewart, G. N., *J. Exp. Med.*, 1911, **16**, 502.

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[1] Fraps, Richard M., and Juhn, Mary, *Phys. Zool.*, 1936, **9**, 319.

feather forms first, an apical-most c-isochrone, *Am* of Fig. 1, drawn from apices of the two barbs uniting at their bases to form the shaft (when these are in alignment with the shaft) identifies elements represented in the collar at the onset of feather growth. Successive c-isochrones taken at regular intervals in apico-basal order determine similarly the number of barbs simultaneously represented in the collar of the germ and are the source of other data treated by Juhn and Fraps[2] in the formation of a number of developmental relations. The subcutaneous injection of thyroxin or female hormone into the Brown Leghorn male or capon causes, among other things, marked changes in the contours of certain feathers, notably those of the saddle tracts. What appeared to be a limiting effect of thyroxin on contour was taken by Fraps and Juhn as evidence for the constant configuration of the c-isochrone itself, a deduction resting entirely upon the existence of an open ventral field† in saddle feather germs. It was suggested that this ventral field does not differentiate into definitive barb primordia in the normal saddle feather germ, but that it does so following injection of thyroxin in sufficient concentrations. The present paper records the results of further c-isochrone analyses, including previously unreported modifications effected by female hormone. The germinal relations corresponding to the c-isochrone measures reported here are described elsewhere.[3]

The limiting effect of thyroxin on contour (and associated variables) is a convenient basis of comparison of other modifications. Let Fig. 1 represent a section from one vane-half of a normal saddle feather upon which certain hormone modified contours are superimposed. The part of the figure shown in heavy lines to give the contour *Amnop* represents approximately the main vane region of the unmodified saddle feather (by main vane region is meant that part of the feather from apex to levels at which down or "fluff" is produced). Changes in spacing of barbs on the shaft do not alter the relative magnitudes of interest here and are not shown in the figure.

Following a single injection of 10 mg. thyroxin in aqueous solution, the saddle feather of the male or capon takes on approximately the contour outlined by *ost* of Fig. 1. The c-isochrone drawn from *d* and intersecting the normal contour at *o* indicates barb levels

[2] Juhn, Mary, and Fraps, Richard M., *Phys. Zool.*, 1936, **9**, 293.

† The *ventral field* here denotes the ventral collar region of the regenerating feather germ at the opposed faces of which barb apices arise (see Fraps[3]). The ventral triangle (Lillie and Juhn[4]) is considered a special case in the present discussion.

[3] Fraps, Richard M., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 206.

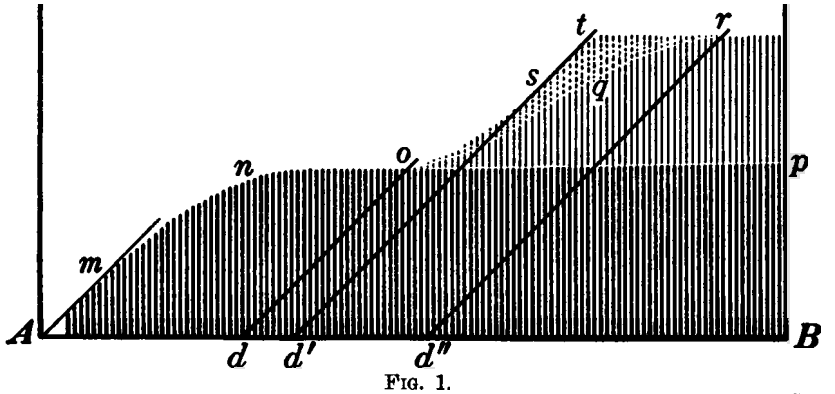

FIG. 1.

Section of one vane-half of a saddle feather from male or capon Brown Leghorn with contours induced by thyroxin and female hormone superimposed. The diagram is simplified by omission of certain striking effects which do not enter directly into relations considered here (see Juhn and Fraps,[5] Fraps and Juhn[1]). Barbs are at right angles to the shaft, *AB*, with feather apex at *A*. Contour of normal saddle feather, *Amnop;* following thyroxin injection, *ostr;* following female hormone injection, *oqr*. The diagonals *Am*, *do*, *d't*, and *d''r* are c-isochrones defining in the order given the apical barb formation, the level of initial hormone effect (for both curves), the level of simultaneous reaction to thyroxin, and the level of maximum female hormone effect.

simultaneously represented in the collar at the time of initial thyroxin effect. All barb apices and barb segments basal to this locus originated or were grown following thyroxin effect. Considering only the origin of barb apices, the effect of thyroxin falls into 3 distinct phases. From *o* to *s*, Fig. 1, the number of apices formed per mm. axial growth of the germ increases rapidly; the measure of this effect is most simply seen as the number of barb apices lying between successive c-isochrones, supposing these to be drawn into the figure at small uniform intervals basal to c-isochrone *do*. The second phase of effect is indicated in Fig. 1 by the alignment of barb apices between *s* and *t* along the locus of the single c-isochrone, *d't*. The third phase is marked by an abrupt break in the number of apices formed per mm. axial growth of the germ and appears basal to *t* in the figure.

Assuming the accuracy of the c-isochrone relationship, the first phase of thyroxin effect means that increasing numbers of barb apices are formed in the ventral field with increasing thyroxin concentration. The second phase signifies the simultaneous formation of a greater or lesser number of primordia at a critical level in thyroxin concentration. This phase is apparently analogous to formation of barb apices at the feather apex (*A* to *m*, Fig. 1); Lillie and Juhn[4] have presented evidence indicating that these

[4] Lillie, Frank R., and Juhn, Mary, *Phys. Zool.*, 1932, **5**, 124.

apical-most barb primordia are of simultaneous origin in the germ. The third phase (basal to *t*) must occur if the ventral field has been suddenly and completely occupied with barb primordia, since barb primordia can now arise only from the faces of the usual ventral triangle as this is restored following formation of a primordium by growth from the base of the feather germ. This interpretation of events is supported by examination of germs in process of regeneration (Fraps[3]).

The increasing length of barbs the apices of which have formed in the ventral field is clear if we suppose that successive barb apices arise serially in strict dorso-ventral order around each half of the collar. This supposition is in accord with observations of Lillie and Juhn[4] on completion of collar complements following formation of the limited apical primordia of simultaneous origin. Many saddle feathers show striking contour modifications in the region basal to *n* of Fig. 1 following thyroxin injection. These changes are due to changes in frequency with which barbs join the shaft (Juhn and Fraps,[5] Hardesty,[6] Fraps and Juhn[1]), and have no effect upon differentiation of apices in the ventral field.

Injection of thyroxin in 1 to 5 mg. doses (single injections) produce modifications ranging from slight convexities in contour to fairly extensive shifts toward (but never attaining) the contour *ost* of Fig. 1. In general, then, thyroxin appears to cause differentiation of the ventral field in proportion to amounts injected over rather wide limits, with simultaneous differentiation of the entire field into definitive barb primordia as a limiting condition of effect.

Curve *oqr* of Fig. 1 represents the approximate contour of a saddle feather following modification by injection of female hormone (1st to 3rd days, 400 r.u. daily; 4th to 6th days, 800 r.u. daily; 7th to 9th days, 1200 r.u. daily). The c-isochrone *do* indicates the level of initial hormone effect, c-isochrone *d''r* the level of maximum hormone effect. The total number of barbs cut by *d't* is of the same order as the number cut by *d''r*, indicating that maximum effects of thyroxin and female hormone are approximately equivalent on the ventral fields in these 2 instances. Thyroxin, however, produces its maximum effect (following 10 mg. injections) much more rapidly, as is seen by comparing growth increments *dd'* and *dd''*, Fig. 1. Whether sufficiently high concentrations of female hormone can reproduce the rapidity of effect obtained following thyroxin injection (10 mg.) is not known at present.

[5] Juhn, Mary, and Fraps, Richard M., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 1185.

[6] Hardesty, Mary, *J. Exp. Zool.*, 1935, **71**, 389.

The effects obtained with female hormone in saddle feathers of the Brown Leghorn male or capon are of particular significance in view of the fact that the same hormone in equal or greater concentrations produces in breast feathers negligible or very slight effects that can be referred to the ventral fields (or ventral triangles) of these feathers. This difference in reactivity of feathers from the 2 tracts must involve, in some part at least, differences in the ventral fields of the germs if the interpretation of effects followed here is sound. Observational evidence for the existence of the postulated differences is given elsewhere (Fraps[5]).

Hardesty[6] has reported the presence of additional barb primordia in breast feather germs of the guinea fowl within 24 hours after injection of thyroxin (4 mg.). Thyroxin may produce a similar (though probably not extensive) effect in certain regions of breast feathers of the Brown Leghorn; however, the lack of appreciable reaction to female hormone in Brown Leghorn breast feathers points rather to characteristic species differences in the 2 birds, as do many other observations recorded by Hardesty.

It is more than likely that changes in growth vectors, in the size of barb primordia, in the slopes of barb primordia at the ventral limits of the collar, and perhaps in other factors contribute in part toward effecting results described in this paper. These changes, however, could not account for the approximation to simultaneity in origin of a certain number of barb apices; the simultaneous formation of primordia thus remains the critical datum indicating the existence of an open ventral field in normal saddle feather germs of the Brown Leghorn male or capon. Assuming the validity of this critical relationship, the increasing order of effect with increasing hormone concentrations (both thyroxin and female hormone) indicates further that the ventral field is subject to threshold differentials increasing in dorso-ventral order. Lillie and Juhn[7] have compared the properties of the ventral field or triangle ("formative center") with the properties of the primitive streak or blastopore in the formation of the axis of the embryo. The application of c-isochrone procedures to the regenerated feather appears to make possible the accurate quantitative analysis of this "organizer" and its field with respect to its reaction under varying general physiological conditions.

[7] Lillie, Frank R., and Juhn, Mary, *Science*, 1937, **86**, 38.