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ACTH PENETRATION IN THE ADRENAL CELL

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1. Although the study of the adrenal subcellular distribution of ^{3}H-ACTH might turn out to be a useful tool for investigation of the kinetics of intracellular interactions of ACTH, interpretation of currently available data has to be very conservative. So far Dr. Müller and I obtained no proof that intracellular radioactivity is ^{3}H-ACTH, *i.e.*, that ACTH gets into the cell. Indirect indications in favour of this arise from studies of adrenal A.-V. differences of perfused ^{3}H-ACTH. Though absolute values were not obtained for technical reasons, A.-V. differences were significantly higher ($p < 0.0125$) in hypophysectomized than in sham-operated rats, the possible interpretation being that adrenal receptors might be blocked in the latter group by endogenous ACTH. The work of Dr. Lowenstein *et al.* (Part 2, pp. 343-344) appears to be in support of the idea that some peptide hormones can reach the nuclei of their target glands.

2. Nuclear fractions as prepared by homogenisation and differential centrifugation may well contain microsomal contaminations attached to the nuclei and also cell membrane fragments. Since microsomal radioactivity disappears rapidly and ^{3}H-ACTH is unlikely to stick to cell membranes for two hours *in vivo*, contribution of radioactivity to nuclear fractions from these contaminations should not be so substantial as to explain the increasing nuclear radioactivity with time.

3. Some adrenal effects of ACTH have been obtained after long term hypophysectomy,

when virtually no response of corticosterone secretion to ACTH administration was evoked. These include:

stimulation of adrenal blood flow (Staehelin *et al.*, 1965)
stimulation of adrenal ascorbic acid release (Staehelin)
stimulation of adrenal 3′5′ cyclic AMP production (Butcher and Sutherland, Part 1)
stimulation of adrenal amino acyl transferase (Scriba and Kluge, 1968)

From this dissociation of activities it appears that some adrenal effects may be independent of the steroidogenic action of ACTH and thus possibly different in mechanism and in cellular receptor.