Renin in the Uterus of Pregnant Mice
Immunocytochemical, Ultrastructural and Biochemical Studies*

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Summary. The distribution and content of renin in the uterus of pregnant mice (12–14 days of gestation) was studied by immunocytochemistry, electron microscopy and radioimmunoassay. The uterine renin concentration at this stage of pregnancy was four-fold higher than that of the nonpregnant uterus but still less than 0.1% of the kidney renin concentration. Renin was localized almost exclusively in the decidual and entodermal epithelial linings of the yolk sac (uterine) cavity near the marginal sections of the placenta. By electron microscopy granular and vesicular structures were observed in the renin containing epithelial cells. Chorioallantoic placenta, myometrium, decidua basalis and the antimesometral parts of the epithelial leaves of the uterine cavity did not contain renin. The specific localization of renin suggests a role in parturition or delivery of the placenta.

Introduction

The presence of renin-like activity in the female genital tract of various species has been the subject of intensive research (Eskildsen 1974; Skinner et al. 1968; Skinner et al. 1975). Recently, we have demonstrated by immunocytochemical techniques the presence and localization of two types of renin-producing cells in the nonpregnant uterus of the white mouse: epithelial cells at the luminal border of the endometrium and perivascular cells in the myometrium. The renin content of the uterus was found to vary with the hormonal cycle (Hackenthal et al. 1980).

In the pregnant uterus, marked species differences of renin-like activity have been reported (Bing and Farup 1966; Ferries et al. 1967); e.g. in rabbits, the uterine renin activity may exceed that of the kidney, whereas the pregnant

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uterus of rats and mice appears to contain only little renin (Eskildsen 1974). An attempt to demonstrate the synthesis of renin has been made in tissue cultures of the chorion and myometrium of the pregnant human uterus (Symonds et al. 1968). The cellular localization and the physiological role of this enzyme in the pregnant uterus remained, however, unknown. The aim of the present study was to identify and characterize by immunocytochemistry and electron microscopy the renin containing cells in the pregnant white mouse uterus.

Material and Methods

Pregnant white NMRI-mice were kept on a standard diet (Ssniff pellets and tap water ad libitum). On the 14–16th day of gestation the mice were anesthetized with pentobarbital and the uteri fixed by aortic perfusion – for immunocytochemistry with a solution of 37% formaldehyde containing 50% saturated picric-acid and 0.2% glutaraldehyde, for electron microscopy with a glutaraldehyde-formaldehyde fixative according to Forssmann et al. (1977). After perfusion, the fetuses were gently removed and the uteri including the placenta embedded for immunocytochemistry or electron microscopy (for details see Hackenthal et al. 1980). For immunocytochemistry paraffin sections (7 µm) were processed with an antimouse-renin-serum (dilution 1:1,000) according to the technique of Sternberger (1974).

Photographs were taken with a Zeiss photomicroscope II. For electron microscopy ultrathin sections were obtained with a LKB ultramicrotome, stained with uranyl acetate and lead citrate and studied with a Zeiss EM 10 electron microscope.

For the estimation of uterine renin, extracts were first dialyzed at pH 3.5 in the presence of peptidase-inhibitors, followed by pH 7.2 dialysis and incubation with rat angiotensinogen at pH 7.2. Angiotensin I formed was estimated by radioimmunoassay. Details of the procedure have been described previously (Hackenthal et al. 1980).

Results

In the schematic drawing of Fig. 1 which shows a cross-section of a gestation sac (at about the 14th day), the overall localization of renin-immunoreactive cells is depicted (black areas). Three different regions of the gestation sac (numbered 1–3 in Fig. 1) have been selected to describe our immunocytochemical and electron microscopic findings: 1) the smooth part of the visceral epithelium which is characteristic for the lateral (antimesometral) wall of the yolk sac and the decidua parietalis, the latter being separated from the former by the Reicherts membrane; 2) the villous part of the visceral entoderm which lines the yolk sac (uterine) cavity; and 3) the marginal section of the chorioallantoic placenta where the transitions occur from the visceral to the parietal yolk sac epithelium and the decidua parietalis.

Immunocytochemical Findings

In Fig. 2 a cross-section of the uterine wall together with the yolk sac is shown representing the Region 1 of Fig. 1. The cells of the smooth antimesometral part of the visceral entoderm are immunoreactive. In the antimesometral part