uterus is almost twice that of the pseudopregnant uterus by 09:00h on the morning of day 5 of pregnancy in the rat, i.e. some 4–6h before the blastocyst makes contact with the epithelium. By contrast, DNA synthesis, almost absent in the pseudopregnant uterus, does not commence until 5–6h later, after contact has been made. These early changes appear to be associated with the induction of decidualization, since they do not occur in uteri containing unfertilized ova, but appear 6–8h after artificial induction of decidualization in the pseudopregnant uterus.

Thus by the early morning of day 5 in the pregnant rat, the stromal cells are synthesizing increased quantities of specific proteins, increased quantities of RNA and probably a new RNA species, and are able to respond to a deciduating stimulus. If this does not occur, regression of cell metabolism takes place, and the cell becomes unresponsive even to trauma, a state which may involve either a blocking of specific regions of DNA or possibly a degradation of DNA itself.

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Endocrinology and Biochemistry of Uteroglobin and other Proteins involved in Blastocyst Development

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Analysis by means of acrylamide-slab-gel and disc-gel electrophoresis, immunodiffusion and immunoelectrophoresis has revealed that genital-tract secretions in the female are composed of a number of proteins. Several of these are identical to blood serum proteins, but others are considered to be organ- or pregnancy-specific for oviducal or uterine secretions. There exists a selective transport of serum proteins into the genital-tract lumen. On the other hand there are 'unique' proteins, which have been identified immunologically, that are not present in blood plasma and which reflect the particular secretory activity of the epithelia of the oviduct and uterus. Special attention must be drawn to uteroglobin, the predominant uterine secretion protein in the rabbit. This protein was first described by myself (Beier, 1966, 1967) as an immunologically identical component of uterine secretion and of the blastocyst fluid. Independent reports on this protein came from Krishnan & Daniel (1967). Since then a large amount of information on uteroglobin (mol.wt. 15000) has been accumulated by several investigators [for references, see my review (Beier, 1976)].

In the rabbit, biochemical investigations have identified at least nine different proteins in endometrial secretion; among these, seven clearly show the characteristics of glycoproteins. There is a high N-acetylsialic acid content in uterine pre-albumin (mol.wt. 50000), of glucose in uterine post-albumin (mol.wt. 20000), and a large quantity of galactose in uterine β-glycoprotein (mol.wt. 100000). These proteins are taken up by the developing blastocyst from its intra-uterine environment (Beier & Maurer, 1975). However, there is no clear-cut information on the biological function of these uterine proteins.

Obviously, ovarian steroids regulate the steady-state of genital-tract proteins, their metabolism, and their involvement in reproductive processes. The effect of an experimentally stimulated hormonal imbalance in the maternal endocrine
Disc-electrophoretical separation was carried out in Tris/glycine buffer, pH 9.0, and staining was with Amido Black ALB, albumin; β-GPF, β-glycoprotein fraction; UGL, uteroglobin; UPR, uterine pre-albumin.

system yields variations in the relative proportions of the intra-uterine protein fractions, and failure of the maternal reproductive system to deliver these secretion proteins at the appropriate time to constitute the proper environment for the developing embryonic system, the blastocyst (Beier, 1974). Progesterone administration to ovariectomized or intact female rabbits leads to secretion of uterine secretion proteins, one of which, uteroglobin, reaches concentrations up to 2 mg per uterine-wash fluid (Beier, 1968). Incubation of isolated uteri in vitro has shown that uteroglobin represents about 50% of the synthesized and secreted proteins of the endometrium of animals treated sequentially with oestradiol and progesterone but only about 3% of the secretion proteins of the endometrium treated only with oestradiol (Beato & Arnemann, 1975). Progesterone regulates the synthesis of uteroglobin and its precursor protein in endometrial epithelial cells. The translation of uteroglobin mRNA in cell-free systems has been demonstrated by Beato & Nieto (1976) and Bullock et al. (1976).

The involvement of uteroglobin together with the other endometrial secretion proteins in blastocyst development is demonstrated by experiments using asynchronous egg transfer and delayed-secretion rabbits as recipient foster-mothers. The appropriate uterine environment is not only beneficial for normal development and implantation,
but essential (Beier, 1974). Culture studies in vitro with single protein fractions as supplements to the medium, or with non-fractionated uterine secretion proteins, indicate that single fractions (as uteroglobin) are not regulating blastocyst development alone, but it is evident that a regulatory system of several components is acting here (Maurer & Beier, 1976).

Blastocysts of delayed-secretory uteri do not expand and show herniations of trophoblast cells after breaking of the zona pellucida (Beier, 1974). Identical pictures are obtained when blastocysts are developing in vitro without uterine proteins in their culture environment. Presumably blastocyst development, including radial expansion and dissolution of the mucin coat, does require the action of uterine secretion proteins in combination or in a cascade-like reaction chain, similar to the event leading to fibrin formation or fibrinolysis.

With regard to its role within a system that is composed of proteinase–proteinase-inhibiting activities the analysed trypsin-inhibiting activity of uteroglobin should be elucidated, to shed more light on the biological significance of this challenging protein component.

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Uterine Secretions in the Cow and Sheep

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The cow and sheep produce very little uterine secretion except for about 24h during oestrus. Our information to date on the chemical composition of the ruminant uterine fluid is based almost entirely on the examination of material rinsed from the uterus after slaughter (Heap, 1962; Roberts & Parker, 1974a). Each uterus when rinsed yields some 5–10mg of protein, although up to 25mg can sometimes be recovered in early pregnancy. The greater part of these proteins (~98%) is identical with the serum proteins from the same animal, but they are not necessarily present in the same relative proportions as they are in blood (Hunter, 1974). In addition, some enzymes are present at very high activity in the uterine fluid of the cow, notably phosphatases (Schultz et al., 1971) and β-N-acetylhexosaminidase (Roberts & Parker, 1974b). Sorbitol was found

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