Regulation of immune cells in the uterus during pregnancy in ruminants

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ABSTRACT: Pregnancy results in a change in number and function of immune cells in utero that potentially affects fetal survival and uterine defense mechanisms postpartum. These changes are driven by local signals from the conceptus as well as from hormonal changes mediated by the placenta or maternal system. In sheep, for example, macrophages accumulate in the uterine endometrium during pregnancy (Tekin and Hansen, 2004). Use of a unilaterally pregnant model, in which pregnancy is surgically confined to 1 uterine horn, has revealed that accumulation of macrophages is due to systemic signals (numbers of cells in the nonpregnant uterine horn of the unilaterally pregnant ewe higher than amounts in uteri of nonpregnant ewes) and locally produced signals (number of cells in the uterus of unilaterally ligated ewes higher in the pregnant horn than in the nonpregnant horn; Tekin and Hansen, 2004). Gamma-delta T cells also accumulate in uterine epithelium during pregnancy as a result of unidentified systemic signals (Lee et al., 1992; Majewski et al., 2001). These cells may participate in growth of the conceptus, immunosuppression, or placental detachment at parturition. One of the key regulators of uterine immune function is progesterone. In sheep, progesterone can block tissue graft rejection in utero when injected to achieve concentrations too low to directly inhibit lymphocyte proliferation (Majewski and Hansen, 2002; Padua et al., 2005). Progesterone probably inhibits uterine immune responses in sheep indirectly by inducing secretion of a member of the serine proteinase inhibitor family called uterine serpin from the endometrial epithelium. Uterine serpin can block lymphocyte proliferation in vitro in sheep (Peltier et al., 2000) and natural killer cell-mediated abortion in vivo in mice (Liu and Hansen, 1993). Uterine serpin is also present in cattle, goats, and pigs, but its role in immune function in these species has not been documented. The relevance of changes in uterine immune function to the reproductive and immune status of ruminants has not been fully established. There is evidence for immunological causes of pregnancy loss associated with cloned fetuses (Hill et al., 2002) and with mastitis (Hansen et al., 2004), but it is not known whether inappropriate recognition of alloantigens on the conceptus is an important cause of pregnancy loss. It is also possible that downregulation of uterine immune function during pregnancy can lead to a postpartum uterus with a compromised capacity for preventing establishment of infectious disease. Thus, optimal immune function in utero requires a balance between the need to maintain effective immune surveillance and effector mechanisms with the requirement that immunological responses leading to conceptus demise are minimized.

Key words: uterus, pregnancy, immunology, ruminant

LITERATURE CITED


Liu, W.-J., and P. J. Hansen. 1993. Effect of the progesterone-induced serpin-like proteins of the sheep endometrium on natu-