Inflammation in the uterus: friend or foe?
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In this review presentation, we will first recall the Th1/Th2 paradigm, and as one of its consequences the view that inflammation per se is abortifacient. However, scratching under progesterone or progesterone + estrogen treatment, or mating with a vasectomised male, has been known since the 50s or 70s to induce décialisation, and has been used for long to transfer embryos, genetically modified or not, in foster mothers. Injection of NaCl, or oil, has also been used. The work carried after the discovery of immunotrophism lead to the discovery that CSFs were useful for implantation, but also to the Th1 /Th2 paradigm, for which inflammation and NK activation are “bad guys”. However, as early as 1990, it was realized that there was immediately post mating an influx of leucocytes and macrophages in the post mating, pre implantation uterus in mice and men (no reference to John Steinbeck novel). Impeaching this inflammation prevents implantation. This was followed by the works of Andrews and Wood group showing the presence at high titers of classical inflammatory cytokines in the pre implantation uterus. This became understandable when it was said “would there be life without LIF”, the 1st cytokine mandatory for implantation in mice, and whose status will be briefly discussed in other species, including of course human. The IL-1 controversy, the status of IL-11, and of TNF, and regulation by TWEAK will be discussed, as well as the new role for perivascular gamma interferon. However, excess inflammation or inflammation at the “wrong period” is either anti implantation (occult losses) or abortifacient, and this will be shown with high doses of TNF or gamma interferon and the dual status of IL-12 and IL-18 will be discussed. We will then turn to IL-17, and to NK hyper activation directly or in a transfer system, as well as the role of IL-17. We will be discussing animal models of endometriosis, and the anti implantation effects in several animal modes of endometriosis as well as for in vitro models of human implantation and finish by ..... evolution of pregnancy till eutherians in a reconsideration of the “Medawar paradigm”, with special interest on apparition of uterine regulatory T cells (u Tregs) in EUTHERIAN mammals.