Menstruation and endometrial regeneration occur during every normal reproductive cycle in women and some old world primates. Many of the cellular and molecular events of menstruation have been identified by correlative or in vitro studies, but the lack of a convenient model for menstruation in a laboratory animal has restricted functional studies. In this study, a mouse model for menstruation first described by Finn in the 1980s was modified for use in a commonly used inbred strain of mouse. A decidual stimulus was applied into the uterine lumen of appropriately primed mice and leukocyte numbers and apoptosis were examined over time following progesterone withdrawal. Endometrial tissue breakdown was initiated after 12-16 h and by 24 h the entire decidual zone had been shed. Reepithelialization was nearly complete by 36 h and the endometrium was fully restored by 48 h. Leukocyte numbers increased significantly in the basal zone by 12 h after progesterone withdrawal, preceding stromal destruction. Stromal apoptosis was detected by TUNEL staining at 0 and 12 h but decreased by 16 h after progesterone withdrawal. Matrix metalloproteinases (MMP) -3, -7 and -9 were also detected during tissue breakdown and repair. This mouse model thus mimics many of the events of human menstruation and has the potential to assist in elucidation of the functional roles of a variety of factors thought to be important in both menstruation and endometrial repair.