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Factors supporting the clinical relevance of endometrial regeneration in the canine oestrous cycle

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In the course of the protracted oestrous cycle of the bitch the period of endometrial regeneration characterized by desquamation of the epithelial lining has been described in detail over 40 years ago\(^1\). This period starts with the completion of luteal regression by the end of the about 2 months luteal phase called dioestrus or metoestrus and has been shown to take further 2 to 2.5 months. Thus it occurs during ovarian rest, characterized by basal secretion of ovarian steroid hormones and has by this been added to the period of anoestrus by the majority of scientists. On the other hand, as the endometrium is still in the process of regeneration, other authors have defined this stage as the second part of metoestru\(^1\). In this case the period of anoestrus is characterized by both, ovarian rest and histological intactness of the endometrium. Studies on the cyclic regeneration of the canine endometrium are scarce which may result from the unawareness of these processes. However, from the clinical point of view this prolonged period should be kept in mind especially regarding hormonal manipulation of the oestrous cycle, either in a stimulating or an inhibiting way. We have focussed on steroid hormone receptor levels and proliferative and apoptotic processes during the period of cyclic endometrial regeneration. So far unpublished data on the quantity and distribution of oestrogen and progesterone receptors (ER and PR) revealed highest amounts of ER in the luminal epithelium (LE) and glandular epithelium (GE) of both the regenerating and completely regenerated endometrium (LE: 215.6 ±7.9 and 224 ±18.0; GE: 224 ±10.7 and 228 ±8.2). Corresponding mean estradiol-17α (E\(^2\)) concentrations were 21.3 ±8.0 pg/ml and 33.8 ±17.4 pg/ml, respectively. In GE scores of PR expression were significantly higher during endometrial reparation (138.6 ±17.4) than during anoestrus (30.4 ±21.1) (p<0.01) despite about equal progesterone (P\(_4\)) concentrations (0.4 ±0.2 ng/ml) in both oestrous cycle stages, indicating increased endometrial sensitivity towards exogenous progestins. Similar results have been published before\(^3\). In a recent study on proliferation (Ki-67) and apoptosis (Caspase-3, TUNEL) in the canine endometrium both these events could be linked to the remodelling processes during endometrial reparation. Despite basal levels of E\(_2\) (22.6 ±12.5 pg/ml) proliferating cells were found in similar amounts during endometrial reparation (1.68 ±0.75%) and anoestrus (1.67 ±0.49%) being significantly higher compared with mid luteal phase (0.24 ±0.11%) (p<0.05). The basal uterine glands showed increased rates of apoptosis during endometrial regeneration (1.16 ±0.2%) compared to late luteal phase (0.4 ±0.25%) and anoestrus (0.25 ±0.09%) (p<0.05). This increase occurring after completion of luteal regression seems to be independent from P\(_4\), as indicated by the P\(_4\) concentration of 0.47 ±0.34 ng/ml. From the clinical point of view these results indicate the need to distinguish the functional status of the canine endometrium during the period of ovarian rest into “endometrial reparation” and “intact endometrium”.