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Progesterone as a Diagnostic Tool During Equine Pregnancy

Progestogens are a class of steroid hormones largely responsible for sustaining the embryo and maintaining uterine quiescence. In horses, at least 10 known progestogens are present in maternal circulation during gestation. To date, only a few of them are known to be biologically active.

Progesterone, the most renowned of this class of steroid hormones, is the only one with clinical diagnostic application. During early pregnancy, progesterone is produced in the equine ovary by the corpus luteum (CL), and its concentrations remain elevated and peak between 60 and 120 days of gestation. From that point on, progesterone slowly decreases until it becomes nearly undetectable around 180 to 200 days of gestation. During late gestation, other progestogens produced by the fetoplacental unit are responsible for maintaining the pregnancy. These are first detectable by Day 60 of gestation and are completely capable of maintaining pregnancy from around 120 to 140 days of gestation until term.

Circulating progesterone has been used diagnostically to evaluate luteal function during early pregnancy. When the circulating progesterone (P4) concentration is above 1 ng/mL, this is considered consistent with the presence of luteal tissue, indicating that a follicle has ovulated, luteinized and is producing progesterone. When the circulating progesterone concentration is above 4 ng/mL, this is considered adequate to maintain pregnancy. There are a number of reasons for monitoring and supplementing endogenous progesterone with progestins (synthetic progesterones) during pregnancy, such as uterine infections, history of pregnancy loss, and luteal insufficiency.

A few important issues regarding laboratory techniques and progestogens require clarification. To date, all clinical veterinary diagnostic laboratories use immunoassays to measure circulating progesterone. The specificity of these tests is limited by the antibodies used in these assays. Due to the structural similarities among different progestogens present in late gestation, after Day 120 of gestation, antibodies are unable to differentiate between those different molecules and, therefore, can give false or inaccurate results. In addition, different progesterone antibodies will result in disparate amounts of cross reactivity; therefore, each progesterone assay will measure different amounts of progesterone, producing varying results between laboratories.

It is important to emphasize that the best clinical interpretation for any progesterone result is the one provided by the clinical laboratory that measured the progesterone, as they have reference ranges for their specific equine progesterone assay.

The specificity lacking in immunoassays and the inter-laboratory variations can be overcome with the use of liquid chromatography-mass spectrometry (LC-MS). This technique has allowed researchers to evaluate changes in different progestogens during late gestation and further elucidate links between placental compromise during late gestation and the changes associated with specific progestogens. It would be advantageous for clinical laboratories to switch to LC-MS to provide diagnostic panels of greater specificity and wider array of quantifiable progestogens.

In summary, current tests for progesterone in the mare are useful to evaluate the presence of luteal tissue (P4>1ng/mL) and to ensure that levels of circulating progesterone are adequate for maintenance of early pregnancy (P4>4ng/mL) until about 120 days of gestation. From that point until term, current clinical tests are somewhat unreliable due to the variety of progestogens present in maternal circulation. These limitations can be overcome with the use of LC-MS.

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