



PROGESTERONE PRIMER

Patrick M. McCue

DVM, PhD, Diplomate American College of Theriogenologists

Progesterone is one of the key reproductive hormones in the mare. It is the hormone that takes a mare out of heat after ovulation and it is absolutely required for the maintenance of pregnancy. The goal of this article is to review sources and blood levels of progesterone in non-pregnant and pregnant mares and to discuss supplementation of mares with exogenous progesterone to maintain pregnancy.

The large preovulatory follicle of the mare is filled with follicular fluid and contains a single oocyte or egg. Cells lining the follicle produce the hormone estradiol- 17β (an estrogen) that stimulates behavioral estrus or heat. Ovulation is the process during which the follicle ruptures and releases the follicular fluid and egg. The egg is transported down the oviduct where fertilization may occur if the mare had been bred. After ovulation, the collapsed follicle fills up with blood and the cells lining the former follicle invade the blood clot. Over the next few days the cells organize into a structure called the corpus luteum (CL) and begin to produce the hormone progesterone and the mare goes out of heat. Progesterone levels first rise above baseline levels (greater than 1 ng/ml) by 12 to 24 hours after ovulation. Levels of progesterone reach a plateau of 5 to 10 ng/ml between days 5 and 14 after ovulation in the nonpregnant mare. Concentrations then decline rapidly to less

than 1 ng/ml after prostaglandins are released from the uterus 13 to 15 days after ovulation. The absence of progesterone and the increase in levels of estrogen produced by the next dominant follicle cause the mare to return to estrus.

If the mare is pregnant, a critical event termed maternal recognition of pregnancy occurs which prevents release of prostaglandins and destruction of the corpus luteum. Consequently, progesterone production by the ovarian corpus luteum continues in the pregnant mare. Pregnant mares begin to form additional or secondary corpora lutea by day 40 to 45 of gestation. Secondary CL's are unique to the mare and are stimulated to develop in response to the hormone equine chorionic gonadotropin (eCG) produced by endometrial cups of the placenta. Progesterone levels in blood increase markedly due to the presence of secondary corpora lutea and reach peak levels at 2 to 3 months of gestation. Production of progesterone by the ovaries subsequently declines over the next few months.

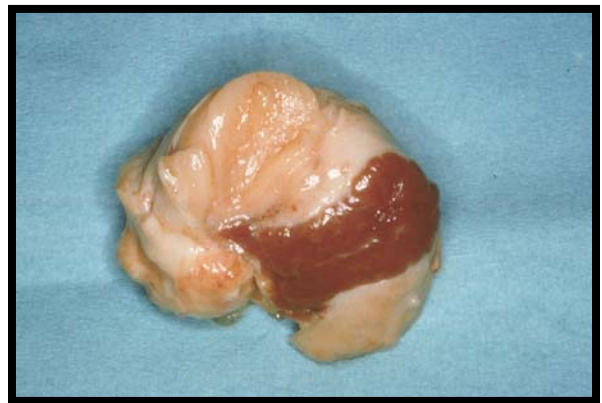
The placenta begins to produce progesterone between day 70 and 90 of pregnancy. By day 90 to 100, the placenta produces sufficient progesterone and other progestins to maintain pregnancy without any ovarian support. Concentrations of progesterone

measured in blood are only 2 to 3 ng/ml during the second half of gestation. This is much lower than levels during the first 3 months of pregnancy.

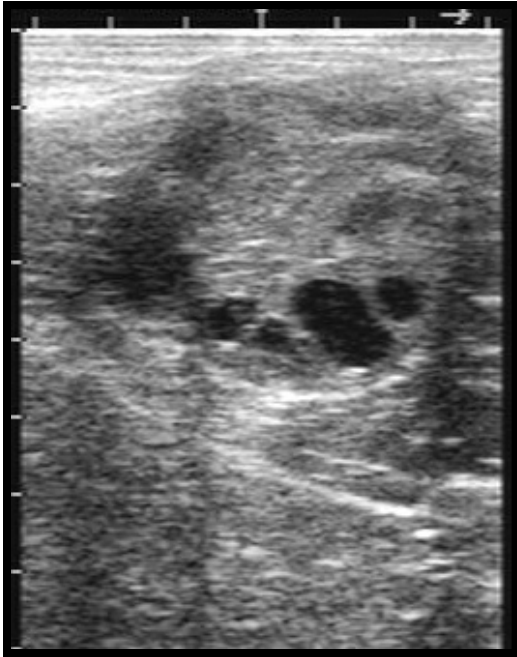
Blood samples are often collected from pregnant mares to determine if progesterone levels are adequate to maintain the pregnancy. Interpretation of blood progesterone levels must take into account the month or stage of pregnancy. Early in pregnancy progesterone levels above 4.0 ng/ml are considered adequate to support pregnancy. Mares with concentrations below 4.0 ng/ml may be at some risk of pregnancy loss and supplementation may be warranted. As noted previously, progesterone levels are commonly between 2 and 3 ng/ml from mid-pregnancy to term and supplementation based on 'low blood levels' is usually not warranted.

Progesterone supplementation in pregnant mares has become very common in the last 5 to 10 years. Mares are often administered exogenous progesterone without any knowledge of their natural blood levels of progesterone. Administration of progesterone is typically used as 'insurance' in an effort to help maintain a valuable pregnancy. Unfortunately, there is little scientific evidence to support the theory that giving extra progesterone to a normal mare will either increase the pregnancy rate or decrease the incidence of pregnancy loss. However, anecdotal reports do suggest that some mares with a history of repeated pregnancy loss will stay pregnant when supplemented with progesterone.

Several types of progesterone products have been used in an attempt to maintain pregnancies in mares. The synthetic progestin altrenogest or Regumate[®] is the only product that will consistently maintain pregnancy in a mare that does not produce sufficient quantities of her own progesterone. Administration is usually initiated within a few days after ovulation and is continued until day 120 of pregnancy, at which time production of progesterone by the placenta is adequate to maintain pregnancy. Supplementation may be discontinued at an earlier date, such as day 50 to 60 of pregnancy, if natural or endogenous blood levels of progesterone are determined to be adequate. Administration of Regumate[®] will not interfere or cross-react with natural progesterone on a blood test. Alternative medications, such as injectable hormones used to prevent pregnancies in women (i.e. medroxy-progesterone or Depo-Provera[®]) have been shown in controlled clinical trials to be ineffective in maintaining pregnancy in mares. Consequently, the use of these alternative products cannot be recommended.



Photograph of a corpus luteum within an ovary



Ultrasound photograph of a corpus luteum