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Conceptual Orientation: A Unique Phenomenon of the Equine Pregnancy

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Abstract

There is a clear fact that the reproductive system of the domestic animals is subjected to rhythmic changes throughout the life of the animal and that make them unique among other body systems. The intimate relationship between the fetal membranes and the conceptus represent the cornerstone for the dynamic changes during the gestation period. Estrogen, progesterone and other ovarian steroids exerts a strict control over the function of the hypothalamus and the pituitary gland. Orientation occurs between the time of fixation and the appearance of the irregular shapes. Factors are believed to interact during orientation are thick (three-layered) and thin (two-layered) portions of the yolk-sac wall; asymmetrical encroachment from thickening of the upper turgid uterine wall on each side of the mesometrial attachment; and the massaging action of uterine contractions. The interaction of these factors results in the thickest portion of the yolk sac wall (embryonic pole) rotating to a ventral position (anti-mesometrial). It can be suggested that orientation is a unique phenomenon of the equine conceptus. Much speculation has been suggested about its significance but the fact that it is still unclear what is the exact role of this phenomenon during the early life of the equine fetus.

Keywords:

Mare; Early pregnancy; Fetal mobility; Fetal orientation; Fetal fixation

What is meant by Orientation of the Conceptus?

Orientation is defined as the rotation of the embryonic vesicle so that the embryo proper comes to lie on the ventral aspect of the yolk sac [1] or refers to the position of the embryo proper at the periphery of the vesicle relative to the position of the mesometrial attachment [2,3].

When the Orientation Phenomenon Initiated?

The equine conceptus is unique among domestic farm animals in that it is mobile from day 6 after ovulation when it enters the uterus until day 16 when it lodges at the base of one uterine horn [4,5]. In mares, the embryonic pole of the vesicle is antimesometrial after completion of orientation. Its pattern differs among species but not in the same species [6]. The equine embryo proper is detected as early as Day 19-22 of pregnancy and usually present at the ventral aspect of the conceptual swelling [7]. It is speculated that orientation occurs before the embryonic mobility stops. Thus, simulated embryonic vesicles rotated or rolled during the embryonic mobility [8]. These observations indicate that orientation occurs between the day of fixation (Day 16) and the earliest reported day of ultrasonic identification of the embryo proper (Day 19). The direction in which the embryonic disk faces relative to the mesometrial attachment after orientation is completed contributes to species differences in the pattern of development of the fetal membranes and the site of attachment of the umbilical cord [3,4]. Physical interactions between the embryo and the uterus play a critical role in the events of early pregnancy [2]. The equine conceptus is mobile within the uterus from the time it can be detected ultrasonically (Day 9) until fixation (mean = Day 16). This mobility, an interaction between uterine contractions and the embryonic vesicle, is postulated to be important in preventing uterine–induced luteolysis. Fixation, the cessation of mobility, is believed to occur as a result of the increasing of size of the embryonic vesicle combined with increasing resistance to vesicle movement due to the development of uterine tone. It has been postulated that increasing uterine tone, thickening of the uterine wall dorsal to the embryonic vesicle and uterine contractions orient the embryo between the time of fixation and Day 19. Luteal progesterone is an important factor for embryonic mobility, fixation, orientation and survival during early pregnancy in mares [8,9]. Fixation of the early conceptus in Days 16 to 17 apparently is caused by the uterine tone and thickening of the uterine wall as well as rapid growth of the conceptus [5]. Increasing uterine tone may explain why the vesicle changes shape as pregnancy advances. Fixation generally occurs in the caudal portion of the uterine horn near the bifurcation (corpus cornual junction). In post-partum mares, the previously gravid horn provides less restriction, and thus the conceptus generally fixes in the opposite uterine horn. Fixation occurs with greater frequency in the right horn in maiden and barren mares [10].

Uterine Tone during Early Pregnancy

Ginther [5] noted that a pronounced thickening of the uterine wall and an increase in uterine tone begins to occur in pregnant mares by day 15-17, reaching a maximum by day 25. At approximately the time that uterine tone begins to increase, or shortly thereafter, the embryonic bulge becomes visible or palpable. The uterine tone is maintained until approximately day 50 in the non-involved portions of the gravid horn and throughout the non-gravid horn and uterine body.

The equine uterus is flaccid during and immediately after estrus increases in tone until mid-diestrus, decreases in tone until Day 10 or 11, and then, if the mare is pregnant, gradually increases in tone and becomes turgid [11-15].

The increase in the uterine tone associated with a decrease in the uterine diameter and continues until Days 25-30. The gradually increasing uterine tone and decreasing uterine diameter together with increasing conceptus diameter apparently combine to result in fixation of the conceptus. This hypothesis is compatible with the following: 1) earlier fixation and greater uterine tone in young mares than in old mares, 2) higher frequency of fixation in the most involuted horn postpartum, 3) the larger the embryo on Day 14, the sooner fixation occurs, 4) fixation when the diameter of the conceptus is similar to the distance between the inner opposite walls of the myometrium of the turgid horns and 5) fixation a day later in horses than in ponies [12].

Dynamic Relationship between Vascular Perfusion and the Conceptus

In a study on the dysorientation during pregnancy in the mare [4,5], it was reported that the most important vascular changes observed were: 1) Transient changes in endometrial vascular perfusion accompany the embryonic vesicle as the vesicle changes location during embryo mobility. 2) The continued presence of the vesicle in the same horn for an average of 7 min stimulated an increase in vascularity of the endometrium of the middle segment of the horn during mobile phase. 3) After fixation, endometrial vascularity was progressively higher in the following sequence: horn without the vesicle, horn with the vesicle, and area of endometrium surrounding the fixed vesicle. 4) After fixation, an early vascular indicator of the future position of the embryo proper was discovered by color-Doppler imaging and consisted of a colored spot in the image of the endometrium close to the wall of the embryonic pole. In addition to the observed vascular changes, morphological changes also were observed. They are related to asymmetrical encroachment of the uterine wall, resulting from differential thickening of the upper turgid uterine wall at the mesometrial attachment, in which is normally observed in mares after embryonic vesicle fixation [12,13]. The thickening of the endometrium was studied during mobile phase and after fixation, and the thickness of the endometrium at the mesometrial aspect of the vesicle divided by the thickness at the antimesometrial aspect was termed the encroachment ratio. The most important morphological changes observed were: 1) Differential dorsal thickening of the endometrium that surrounds the embryonic vesicle began during the later days of the mobility phase. 2) After fixation, the differential dorsal thickening or endometrial encroachment upon the vesicle increased rapidly and was more than four times thicker than ventrally by 3 days after fixation. 3) The increase in vascularity began before the increase in the encroachment ratio in the endometrium at the site of future fixation. 4) The increase in the encroachment ratio between 1 and 3 days after fixation was more rapid than during -4 to 0 days before fixation. 5) Embryonic vesicle dysorientation was associated with a flaccid uterus and defective encroachment of the dorsal endometrium. 6) Asymmetric enlargement of the allantoic sac spontaneously corrected the dysorientation of the embryo proper in mares with apparently normal uterine tone and endometrial encroachment, so that orientation of the umbilical cord attachment was at a normal position near 12 o'clock [11].

The function of the increase of the uterine tone has not been defined. However, there are close temporal associations among the development of the increased uterine tone (Days 15-25), fixation of the conceptus (Day 16-17), the vesicle expansion plateau (Days17-24), the onset of loss of the spherical shape of the conceptus (Day17), and the postulated time of vesicle orientation on Days 17-20. The blastocyst enters the uterus on either side with equal frequency in barren and lactating mares, as indicated by the side of ovulation; however, entry occurs more frequently on the left side in maiden mares [14]. Regardless of the side of entry, the early conceptus is highly mobile and moves back and forth within and between horns many times each day until approximately day 15. The spherical form of the vesicle favors mobility. As uterine tone increases, the endometrial folds impinge upon the vesicle causing increasingly exaggerated irregularities in shape of the conceptus and a plateau in vesicle expansion [11]. These processes combined with the increased uterine tonicity on each end of the embryonic enlargement prevent further intrauterine movement. Fixation occurs in the caudal portion of a uterine horn and with greater frequency in the right horn in barren mares and maiden mares; however, the pattern of vesicle mobility and fixation are altered in postpartum mare, so that the embryo is less likely to become fixed in the formerly gravid horn. Because of the uterine turgidity, the vesicle does not enlarge on Days 18-26 when viewed in a cross section of the horn. During this time, a compensatory increase in conceptus length occurs along the longitudinal uterine lumen and accommodates the increasing growth of the conceptus. Uterine contractions continue after fixation, and may a play a role in orientating the embryonic vesicle. Continuous ultrasonic viewing indicates that shape of the fixed embryo is continually altered by uterine contractions [14]. It has been postulated that orientation occurs between the time of fixation and the appearance of the irregular shapes.

Embryonic Mobility

During the embryo-mobility phase, regardless of the side of ovulation, the embryo can be anywhere in the uterine lumen from the tips of either horn to the cervix. The mobility phenomenon in mares allows the embryo to contact all parts of the uterine lining. In this manner, the relatively small spherical embryo is able to block luteolysis despite the relatively large uterus [15]. There are indications that the conceptus produces a substance that acts as an antiluteolysin at the ovarian level [16,17].

Embryo Fixation

Discovery of the phenomenon of embryo mobility and fixation is a research milestone because it provided the rationale for hypothesis on the following perplexing phenomena: 1) occurrence of fixation almost always in the caudal portion of one uterine horns, 2) lack of agreement between side of ovulation and side of fixation, 3) more frequent embryo fixation in postpartum mares in the most involuted horn, 4) greater incidence of unilateral than bilateral fixation in mares with twins, especially when the vesicles are of unequal size and 5) ability of small conceptus to block the uterine luteolytic mechanism throughout a relatively large uterus [17]. Fixation occurs on mean Days 15 in ponies and 16 in horses. Fixation usually occurs near a flexure in the caudal portion of one of the uterine horns. It has been postulated that fixation occurs at this site, despite continuing uterine contractions, because the flexure is the greatest intra-luminal impediment to continued embryo mobility. The sonogram shows that in cross section of the uterine horn the vesicles tended toward a guitar-pick or irregular shape. The apex of the vesicle is orientated dorsally and the smooth rounded base is orientated ventrally. The irregular shapes after fixation

is normal and should not be taken as a sign of abnormal development. The shape change is attributable to uterine turgidity and thickening of the dorsal uterine wall especially on each side of the mesometrial attachment [18].

The occurrence of fixation is consistently in the caudal portion of a uterine horn may be attributed to the sharp curvature or flexure of the horns at this point [19]. Fixation of the early conceptus on Days 16 to 17 apparently results from increased uterine tone and thickening of the uterine wall as well as the rapidly expanding growth of the conceptus. This may explain why the vesicle changes in shape as pregnancy advances. Fixation usually occurs in the caudal portion of the uterine horn near the bifurcation (the corpus-cornual junction). In post-partum mares, the previously gravid horn provides less restriction and thus the conceptus usually fixes in the opposite uterine horn. Fixation occurs with greater frequency in the right horn in maiden and barren mares [10]. The sharp curvature may impede the continued intraluminal mobility of the growing vesicle. Similarly, in postpartum mares the flexure at the caudal portion of the formerly non-gravid horn may be a greater impediment to vesicle mobility than that of the formerly gravid horn. As the conceptus grows the tenseness of the yolk sac wall decreases, allowing the yolk sac membranes to conform to the irregularities of the uterine lining. However, the strength of the yolk sac wall becomes greater for the dorsal uterine wall, especially on each side of the mesometrial attachment, than for the ventral wall [15]. The greater strength of the yolk sac at the embryonic pole coupled with the greater impingement of the uterus on each side of the mesometrial attachment cause the conceptus to become rotated or positioned by Day 20 so that the embryo is distal and the bilaminar omphalopleure is adjacent to the mesometrial attachment cause. The resulting orientation is firm and serves to hold the conceptus in place till permanent attachment occurs. Since the fetal umbilical cord eventually reaches the outer wall of the allantochorion at the site of the bilaminar omphalopleure, orientation of the yolk sac vesicle on Days 17-20 results in a close and persistent spatial relationship between the site of umbilical attachment and the mesometrial attachment [15]. On Day 18, the embryonic vesicle begins to lose its spherical form, and the image of the vesicle may be oblong, triangular (guitar-pick shape), or irregular. In one study, roughly triangular forms began to appear on Day 17 (11%), increased in frequency until Day 20 (61%) and then decreased in frequency. When first detectable, the embryo is on the ventral aspect of the embryonic vesicle indicating that orientation has occurred. Regardless of the mechanisms involved in orientation, the ultrasonographer should be thoroughly familiar with the changing shapes of the conceptus and the expected orientation of the embryo.

Orientation

Meanwhile, McKinnon et al. [10] reported that Orientation is defined as rotation of the embryonic vesicle so the embryo proper is on the ventral aspect of the yolk sac. On Day 14, the vesicle is highly mobile and the embryo is probably not orientated. Shortly after the end of the mobility phase (Days 15 to 17), the dorsal uterine wall begins to enlarge and encroach on the yolk sac. Increasing uterine tone enhances encroachment. The disproportionate thickening and encroachment of the uterine wall on the vesicle, in addition to the massaging action of uterine contractions, cause the vesicle to rotate so the thickest portion of the yolk sac (embryonic pole) assumes a ventral position. Hypertrophy of the uterine wall is especially prominent on each side of the dorsal mid-line location of the apex of the triangular-shaped vesicle and the thinness of the uterine wall ventrally. The embryo is first detected by ultrasonography within the vesicle at Days 19 to 25 and is most commonly observed in the ventral position. The growth or expansion profile of the equine embryonic vesicle is peculiar because of a distinct plateau between approximately Days 18-26. During this time, the image of the in situ vesicle does not change significantly in size whether measured by vertical or horizontal dimensions or by area. This phenomenon has been attributed to resistance by uterine wall to vesicle orientation. Although the vesicle is not increasing in size during this time, profound morphological changes are occurring. Three factors are believed to interact during orientation: 1) thick (three-layered) and thin (two-layered) portions of the yolk-sac wall; 2) asymmetrical encroachment from thickening of the upper turgid uterine wall on each side of the mesometrial attachment; and (3) the massaging action of uterine contractions. The interaction of these factors results in the thickest portion of the yolk sac wall (embryonic pole) rotating to a ventral position (anti-mesometrial). It is not clear, however, whether the localized thickening of the endometrium adjacent to the thin-walled portion of the yolk sac occurs before, during or after orientation; the cause of the thickening has not been determined. Once fixation and orientation are established, increasing uterine horn turgidity, cranial and caudal to the vesicle, prevents the vesicle from dislodging longitudinally in the uterine lumen. The orientated position apparently is aided by adhesiveness and cross ridging of the endometrial folds, [10]. In mares, transient changes in endometrial vascularity accompanied conceptus location changes during the mobility phase. Continued presence of the conceptus in the same horn (7-min average) stimulated an increase in vascularity. After fixation, endometrial vascularity was higher in the endometrium surrounding the fixed conceptus, than in other areas of the ipsilateral horn, or in the opposite horn. Differential dorsal thickening of the endometrium preceded embryonic orientation. An early vascular indicator of the future position of the embryo proper was discovered. Orientation of the embryonic vesicle occurred immediately after fixation. Embryonic dysorientation was associated with a flaccid uterus and defective encroachment of the dorsal endometrium. Asymmetric enlargement of the allantoic sac spontaneously corrected dysorientation. The dorsal endometrium at the fixed conceptus site was edematous and richly vascularized, exhibiting a high density of blood vessels and endometrial glands [15-20]. It can be suggested that orientation is a unique phenomenon of the equine conceptus. Much speculation has been suggested about its significance but the fact that it is still unclear what is the exact role of this phenomenon during the early life of the equine foetus.

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