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Title: (Use Normal style (Times New Roman 12). Only capitalise the first letter of the first word. No full stop at the end of the title) The equine placenta – a vital clue to neonatal problems

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For the mare owner there are few things as exciting and wondrous as the birth of a foal. However, as the onlookers are busy checking and assessing the new arrival little thought is spared for the placenta despite the fact that this temporary, but complex, organ has had responsibility for ensuring that the fetus is sufficiently developed and mature to make the transition from an intra- to an extra-uterine existence. If a foal is compromised or dies at or soon after birth the placenta may well be submitted to a pathology laboratory for examination. However, for most other births, apart from a cursory check for completeness the placenta is usually discarded unexamined. Yet there is much to be gained by a careful examination of this remarkable organ, with anomalies in both gross and microscopic structure providing clues to its functionality during fetal life. Some abnormalities may be are indicative of problems that influence neonatal health whereas others are suggestive of uterine pathology.

It is important to remember that the placenta at term represents the final stage of its development and throughout the 11 month gestation period it has adapted to meet the demands of the growing fetus. In early pregnancy a transitory yolk sac placenta exists, which bears little resemblance to the placenta seen at term. The yolk sac imbibes secretions from the mare's endometrial glands (histotroph), to provide essential nourishment for the embryo. However, the yolk sac soon becomes unable to fulfil the escalating nutritive requirements of the conceptus and it is gradually replaced by the allantochorion, to provide the definitive placenta which supports the fetus to term. The allantochorion forms an increasingly complex interdigitation with the maternal endometrium to produce the vast number of microcotyledons which function essentially to bring the fetal and maternal capillary beds into close proximity and thereby facilitate haemotrophic nutrition. Between this myriad of microcotyledons lie absorptive areas called areolae which facilitate the up-take of histotroph throughout gestation. In addition to nourishing the growing fetus the placenta also functions as an endocrine organ that secretes a variety of hormones to orchestrate essential events in both placental and fetal development.

Critical developmental windows exist *in utero* for the development of most fetal organs and body systems. Hence, incorrect or inferior placentation at any stage of gestation will have implications for the development and well-being of the fetus, either at the time of placental perturbation or later in gestation. Poor placentation also impacts overall growth of the fetus and low birthweight in many species is often associated with an increase in the incidence of problems in early life and disease in later life. In the mare the area of the allantochorion is correlated positively to foal birthweight and shortfalls in this parameter, occasioned either by poor development of the microcotyledons or a reduction in the area of functional endometrium in contact with the microcotyledons, invariably results in reduced foal birthweight. Although research has shown that placental area in the horse is influenced by maternal size, age, parity and genotype, other factors are also likely to play important roles. For example, the nutritional status of the pregnant ewe can modulate placental development and, although such a relationship has not been established convincingly in the horse, pregnant Thoroughbred mares that suffered severe weight loss occasioned by *Streptococcus equi* (Strangles) infection in mid-gestation showed alterations in placental and fetal development at term that correlated positively to the amount of weight lost previously.

Aberrations in the overall shape of the allantochorion and untoward changes in its linear dimensions can also reveal uterine abnormalities since the allantochorion provides a map of the uterus and it illustrates the amount of 'space' the fetus had to develop in. A recent study indicated that foals born with flexural limb deformities showed changes in their placentae that were indicative of uterine narrowing. However, it was unclear if these changes reflected uterine constriction as the underlying cause of the flexural deformities or were the consequence of diminished movements or mal-positioning of the fetus occasioned by the deformities.

Stretching, or even frank tearing, of the allantochorion gives an indication that it has been subjected to undue force during delivery. This can occur when the cervical star fails to rupture in a timely manner. Likewise, a complete cervical star with rupture of the allantochorion further back in the body region may imply that the placenta is thickened or it has separately prematurely. Both conditions have implications for fetal health.

The position, length, vasculature and degree of twisting of the umbilical cord is of particular importance since the cord carries all the fetal blood to and from the allantochorion. Hence, any shortfalls or variation in its morphology will impact directly levels of nutrients and oxygenated blood going to the fetus. Cord length is a good illustration of the impact cord morphology can have on the fetus; short cords predispose the foal to premature rupture of the cord during delivery and *intra-partum* anoxia (oxygen starvation), while long cords increase the risk of fetal strangulation, twisting of the cord with resulting obstruction of blood flow and necrosis of the placenta at the cervical pole. Even the under-researched amnion, the curious hippomane consisting of a concentric layers of allantoic debris and the usually well-hidden remnant of the yolk sac, can all provide valuable information about the foal's intrauterine existence.

Careful examination of the placenta at term provides a unique opportunity to learn more about the uterine existence of a foal and 'what went wrong' in individual animals with problems. More importantly, in a species that is bred primarily to perform as an athlete, continued research into the structure and function of this incredible organ will enable optimisation of mare management during gestation to, in turn, optimise fetal wellbeing *in utero* and the birth of a viable and robust foal with good athletic potential.