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Artikel: The fundamental and long-lasting role of the placenta in the production of healthy horses

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Infections of the CNS do not elicit the same immune response as seen at other sites of the body. Medawar and colleagues, pioneers in transplantation immunology, already found in the late 1940's that allogeneic graft material was not rejected from sites such as the central nervous system, the eye, the fetal-maternal interface, and the gonads, while the same tissue was vigorously rejected from other sites of the body. These tissue sites of the body with a deviation in their immune response were called 'Immune Privileged Sites'. Functionally, this mechanism provides a MODULATORY role in drive and progress of an immune and inflammatory response within the CNS, which protects this organ system from excessive inflammation and its detrimental effect on the CNS's poor regenerative capacity. Studies in people have demonstrated the presence of certain substances within the central nervous tissue, and the cerebrospinal fluid as a mirror of central nervous metabolism with an immune suppressive effect on macrophages and lymphocytes. It had been demonstrated that Interleukin-10, Transforming Growth Factor-β (TGF-β), a-Melanocyte Stimulating Hormone (a-MSH), and Vasoactive Intestinal Peptide (VIP) play a crucial role in modulating and suppressing the immune response within the CNS.
Further research will provide tools and strategies to influence inflammation associated with central nervous infection, providing a better and guided response compared to established treatment methods. Immune responses could then be activated with interferons or soluble receptors, or suppressed with one of the recombinant factors as mentioned above, which provides us as clinicians with tools to steer and manipulate an immune-mediated inflammatory response at such vulnerable sites as the CNS.

The fundamental and long-lasting role of the placenta in the production of healthy horses

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The diffuse epitheliochorial nature of the equine placenta demands the presence of a healthy and fully functional endometrium lining the maternal uterus with which it can interdigitate to form the complex and extensive microcotyledonary interchange that provides adequate sustenance for the fetal foal throughout gestation. Anything which interferes with either the quality of the extent of this essential materno-fetal exchange of nutrients and waste products will obviously limit fetal growth and development, especially during the period of the fetal growth spurt in the final weeks of gestation.

The presence of twin conceptuses in the uterus is perhaps the most obvious example of placental underfunction leading to fetal starvation and abortion. The twin placentae simply compete for the available area of endometrium to which they may attach and the fetus that achieves the lesser area of placental contact becomes nutritionally disadvantaged as gestation proceeds. If the degree of disadvantage is too great, the undernourished fetus simply starves to death. If this occurs prior to about 5 months of gestation the products of pregnancy are often resorbed by the mare and the small mummified twin is found in the afterbirth of what otherwise appears to be a normal, well-grown singleton foal at term. But if fetal death occurs after 5 months, separation of the dead fetus' placenta from the endometrium initiates mammary development, milk secretion and prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) production in the uterus which, in turn, induces abortion of both the dead and living twin fetuses.
A second, all-too-common cause of placental underfunction in equine pregnancy stems from the range of degenerative changes which develop in the mare's endometrium with increasing age and parity to give the syndrome known widely nowadays as endometrosis. These changes include erosions of the lumenal epithelium and thinning of the *Stratum compactum,* untoward accumulations of mononuclear cells in the stroma, fibrous degeneration and encapsulation of the endometrial glands to give functionless "gland nests", and blockage of lymph drainage channels to give lymph-filled cysts that protrude into the uterine lumen or form multiple lymphatic lacunae throughout the endometrial stroma. By gross inspection combined with light and electron microscopic examinations of placental development in young, fertile mares versus old sub-fertile mares exhibiting varying degrees of endometrosis, we have shown that the endometrium in the older animals is much less able to respond to the growth factors, hormones and other stimuli emitted by the rapidly growing trophoblast of the fetal allantochorion. Accordingly, the degree and overall extent of septal development which the endometrium can make in forming the interdigitation between fetal and maternal epithelial layers is diminished, with a consequent reduction in the weight and general growth charactristics of the fetus (*Bracher* et al., 1996). And this placental "runting" of the fetus is followed by the birth of small, under-privileged foals after a prolonged gestation period (i.e. dysmaturity).
A third example of under-function of the placenta and its effect on fetal and postnatal growth in the mare was shown originally by the classical experiments of Walton and Hammond (1938) when they reciprocally crossed Shire horses and Shetland ponies using artificial insemination. As expected, the foal born from the Shetland pony mare inseminated with Shire horse semen was much smaller (i.e. approximately half the weight) of that born form the Shire mare inseminated with Shetland pony semen. But most importantly, the great difference in size between these two foals remained unchanged in

adult life, thereby indicating that, in the horse and other equids, "runting" sustained *in utero* persists until adulthood, regardless of post-natal nutrition.

Recently, we have extended the Walton and Hammond study to further examine the interacting effects of maternal size and fetal genotype on the physical and physiological development of the placenta, by using between-breed embryo transfer to create 8 Pony-in-Thoroughbred, 8 Thoroughbred-in-Pony and 4 each of control Pony-in-Pony and Thoroughbred-in-Thoroughbred pregnancies. The concentrations of a range of hormones were measured in maternal blood throughout gestation, the placentae were all weighed, measured for area and biopsied at multiple sites for histological assessment, and the foals themselves were weighed, photographed and subjected to measurement of 13 different body dimensions from birth to weaning at 5 months of age.

Hormone levels measured throughout gestation (eCG, progestagens and total conjugated oestrogens) were essentially similar in the 4 types of pregnancy except that progestagen concentrations in the Pony mares carrying Thoroughbred fetuses were appreciably higher in the last few weeks, thereby indicating an increased level of fetal stress in these animals. The mares all foaled spontaneously between days 322 and 348 of gestation, except two (one Pony-in-Thoroughbred and one Thoroughbred-in-Pony) which aborted, respectively, at days 275 and 299 of gestation, and one (Thoroughbred-in-Thoroughbred) which died accidentally on day 149. In descending order, foal weight, placental weight and placental area at birth were all higher in Thoroughbreds born from Thoroughbreds, than ponies born from Thoroughbreds, than Thoroughbreds born from ponies, than ponies born from ponies. In addition, there were good correlations between maternal weight and foal weight, placental weight and foal weight, and placental area versus foal weight, across all 4 types of pregnancy.

The birth weights of the Thoroughbred-in-Thoroughbred and Pony-in-Pony foals and their postnatal weight and heigth gains were within the normal ranges for their breed. However, the Pony-in-Thoroughbred foals were much heavier at birth (37 ± 4.6 kg n = 7) than their Pony-in-Pony counterparts (24 ± 3.8 kg n = 7), and they reached mean weight and height advantages over the latter of 38 kg and 6 cm at weaning. The Pony-in-Thoroughbred foals all showed normal leg joint and long bone development despite their "luxurious" intrauterine environment and the potentially excessive milk supply available to them from their large surrogate mothers. In contrast, the 7 Thoroughbred-in-Pony foals were lighter at birth (32 ± 6.1 kg n = 7) than their Thoroughbred-in-Thoroughbred counterparts (55 ± 6.6 kg n = 3) and although they grew at a faster rate than the lattter, they still registered mean weight and height disadvantages of 23 kg and 4.5 cms (n = 5) at weaning. Two of these Thoroughbred-in-Pony foals were carried and reared by two larger, cob-type Pony surrogate mares. They showed more rapid catch-up growth than their 3 other group mates, possibly due to a greater milk supply, and they both developed valgus of the kneejoints which required surgical intervention ("stapling") to correct.

Conclusions: Like the examples of twin pregnancy and mares with endometrosis, and in support of the earlier findings of Walton and Hammond (1938) and those of Tischner (1987), the results of our recent study have also shown that maternal size significantly affects fetal growth, presumably by means of limiting the area of uterine endometrium available for attachment of the diffuse epitheliochorial placenta. They indicate that breeders should take into account the relative body sizes of the sire and dam when making their mating plans and they should cull ruthlessly from their breding herd older mares with endometritic changes in their uteri.

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Videoendoskopische Hysteroskopie bei der Stute

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Die Endoskopie des Uterus (Hysteroskopie) ist eine nützliche Spezialuntersuchung bei Abklärung einer Fruchtbarkeitsstörung bei der Stute, da sie eine direkte Visualisierung des Uteruslumens ermöglicht. Mit entsprechender Ausrüstung (Elektrokauter oder Laser) können zusätzlich transendoskopische Therapien (Separation von Adhäsionen, Entfernung von Zysten) durchgeführt werden.

Die Indikation für eine Hysteroskopie ist speziell bei güsten Maidenstuten, Stuten mit der Anamnese einer traumatischen Geburt und bei Stuten mit Verdacht auf intrauterine Adhäsionen gegeben. Die Bergung eines «verlorengegangenen» Uterustupfers kann ebenfalls eine Indikation darstellen.

Geeignet ist ein Endoskop (fiberoptisch oder Videoendoskop) mit einer Mindestlänge von 90 cm. Übliche Laryngo- oder Bronchoskope für Pferde sind geeignet, sofern sie eine gute Lichtquelle besitzen. Die Endoskop-Einheit muss die Möglichkeit der Luftinsufflation bieten, und eine Einrichtung zum Absaugen der eingepumpten Luft nach Abschluss der Untersuchung ist empfehlenswert. Ausserdem empfiehlt sich die Verwendung steriler Teflonkatheter, die durch den Arbeitskanal des Endoskopes eingeführt werden können und die eine Probenentnahme für zytologische und mikrobiologische Untersuchung erlauben.