

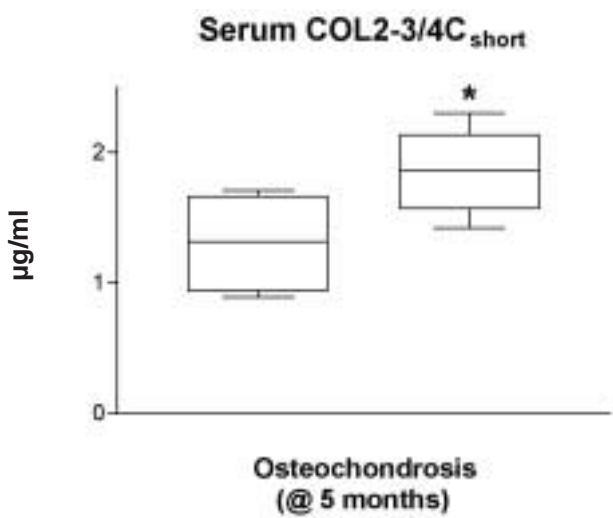
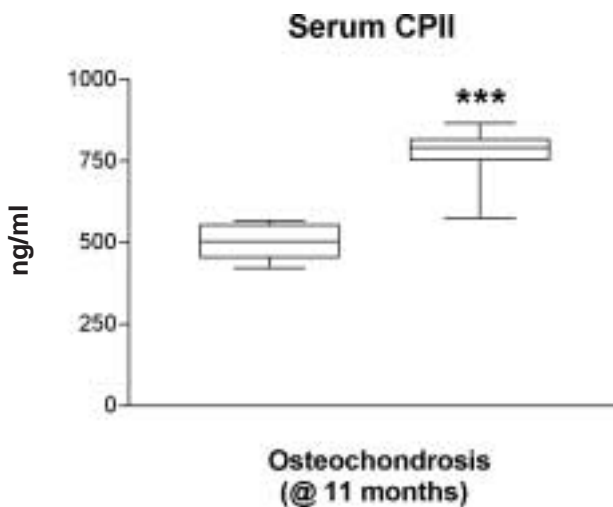
**Blood Tests to Identify Alterations in Skeletal Tissue Turnover in Developmental Orthopaedic Disease in Horses**

**Summary:** This study shows that the blood levels of certain biomarkers of collagen turnover, especially during the first 11 months of life, are significantly elevated in those foals with increased number and severity of OC lesions, many of which are not evident on radiographs. Free pasture exercise was the best for maintaining steady serum levels of the biomarkers of collagen turnover. This supports the conclusion, based on previously performed biochemical studies of articular cartilage taken from these same foals, that pasture exercise is the best for developing healthy cartilage resistant to injury. This study also demonstrates the strength of using serum assays for specific markers of skeletal tissue metabolism for monitoring development at the molecular level and for allowing early intervention if abnormalities are detected.

Osteochondrosis (OC) is an important developmental orthopaedic disease (DOD) affecting a large number of different joints in the young, growing horse, and it is a significant cause of economic burden to the equine industry. It is a multifactorial disorder with genetic traits, mineral and hormonal imbalances, toxins, dietary factors, growth rate, conformation, trauma and exercise all being implicated to some degree. OC is essentially a disturbance in endochondral ossification, a process in which cartilage is gradually converted into bone and is responsible for bone elongation in the growing horse. This process, like most metabolic processes, involves the release into the animal's circulation of molecules that are the byproducts of tissue turnover. Dr. Clark Billingham, with Megan McGraw and Dr. Wayne McIlwraith from the Orthopaedic Research Center and Drs. Pieter Brama and Rene van Weeren from Utrecht University, worked to try to identify which molecules, specific for bone and cartilage metabolism, may be of value in screening the serum of foals during their first year of life for the presence or potential of developing OC and for predicting the severity of OC when present.

The results of this study suggest that there is abnormal collagen turnover in osteochondrosis in the horse. By measuring the serum levels of specific molecular markers of collagen metabolism, one may be able to identify foals with OC lesions and to predict those that will develop into more severe and debilitating lesions as the horse matures. In particular, it appears that elevations in the serum levels of a marker of type II collagen synthesis, CPII, during the first year of life, is a consistent indicator of foals that have or will develop classic and persistent OC lesions (Figure 1). As well, elevations in the serum levels of the general collagen degradation biomarker COL2-3/4C<sub>short</sub>, particularly during the first 5 months of life (Figure 2), suggest there is increased collagen destruction in OC at a

time when there is the highest incidence of horses with lesions. It was interesting to note that there were significantly lower serum levels of 234CEQ, a marker specific for the breakdown of type II collagen, the collagen of articular cartilage, in foals from 0-5 months of age with more severe OC. This



assay was developed in our lab by Dr. Billingham. This suggests decreased degradation of cartilage collagen, which suggests the observation in many OC lesions of the focal retention and thickening of cartilage. That OC is perhaps more a disturbance of collagen metabolism is further strengthened by the finding of no significant differences in serum levels of any of the noncollagenous markers analyzed in this study between foals with low and high OC severity scores.

An evaluation of the serum levels of these biomarkers in the foals, grouped by type of exercise, was also performed. It was shown that the foals having free exercise in pasture with their dams had the fewest alterations in serum levels of the biomarkers of collagen metabolism. Forced training and stall confinement from 0-5 months negatively affected collagen turnover by increasing the degradation of type I collagen and decreasing the synthesis of type II collagen, as shown by significant changes in levels of COL2-3/4C<sub>short</sub> and CPII, respectively, compared to serum levels in the pastured foals. These results suggest that allowing foals pasture exercise during the first months of life is the most beneficial in terms of normal skeletal development.

In summary, this study shows that the blood levels of certain biomarkers of collagen turnover, especially during the first 11 months of life, are significantly elevated in those foals with increased number and severity of OC lesions, many of which are not evident on radiographs. It was shown in a related

study involving these foals that a significant number of these OC lesions regress after 5 months of age. Therefore, our observation of prolonged elevation in serum levels of these same biomarkers in foals with OC lesions up to 11 months of age, suggests screening foals for these biomarkers until at least one year of age. It is also important to note that the serum levels of these markers of collagen turnover are affected by exercise, especially during the first 5 months of life. Free pasture exercise was the best for maintaining steady serum levels of the biomarkers of collagen turnover. This supports the conclusion, based on previously performed biochemical studies of articular cartilage taken from these same foals, that pasture exercise is the best for developing healthy cartilage resistant to injury. This study also demonstrates the strength of using serum assays for specific markers of skeletal tissue metabolism for monitoring development at the molecular level and for allowing early intervention if abnormalities are detected.

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#### **Publications**

Billingham RC, Brama P, McGraw M, Van Weeren R and McIlwraith CW. Alterations in serum levels of biomarkers of collagen metabolism in equine osteochondrosis. Proceedings of the 48th Annual Meeting of the Orthopaedic Research Society, 2002. 151.