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RECENT ADVANCES IN OSTEOCHONDROSIS RESEARCH

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Introduction

This presentation outlines recent advances in osteochondrosis (OC) through interpretative summaries of papers in the last four years, which record research work undertaken up to seven years ago. Only about 15 peer-reviewed papers have been produced in that time, and many are either case reports or the earliest work in new approaches to investigating pathogenesis. The amount of work conducted on OC is relatively sparse and insufficient to motivate a group of researchers interested in the disease to hold a planned meeting on osteochondrosis in 2004. A large amount of information was obtained from the study referred to as the EXOC study, which sought to determine if exercise in young horses would affect the incidence and severity of OC in warmblood foals. Other papers that provide information on OC management are also cited.

Hock and Stifle OC Have Different Progression and Regression in the First 11 Months of Life

The EXOC study was completed in 1999, and most findings have been published. All of the foals' sires (a total of eight) and 11 of the 43 dams had OC in the stifle (lateral trochlear ridge) or hock (intermediate ridge of tibia). The foals were randomly divided into three groups: box confined ($Group_{box}$), pastured ($Group_{pasture}$), or box confined and gallop exercised 6 days per week in a yard from 7 days of age ($Group_{training}$). The latter group was given 12-16 sprints to 24 days old, 24 sprints from 25-38 days, then 32 and 16 sprints on alternate days until 5 months of age. Thereafter, 24 (eight from each group) of the foals were euthanized, and the remaining 19 were all kept in a loose box with free access to a paddock.

All foals were radiographed monthly until 5 months and the remaining 19 until 11 months, and radiographic appearance classified as normal (0) through minimal, mild, moderate, and severe (4) changes of OC. The prevalence at various times was compared longitudinally.

Sixty-seven percent of tibial intermediate ridges had abnormal appearance at 1 month, 37% at 5 months, and 18% at 11 months, with lower severity of lesion with age. Regression of abnormal appearance was marked, progression was

uncommon, and normal appearance rarely became abnormal. Normal and abnormal appearances were permanent from 5 months on.

In the lateral trochlear ridge of the femur, abnormality was rare at 1 month, was present in 20% of stifles at 5 months, and then regressed to 3% at 11 months. Most abnormalities had become normal by 8 months, after which normal and abnormal appearances were permanent (Dik et al., 1999).

Exercise Did Not Cause OC Lesions

At 5 months of age, there was a mean of 5.5 lesions (a range of 1-14) in all foals, with tibiotarsal (1.9 lesions/foal), stifle (1.0), neck (1.0), and fetlock (0.6) joints being most affected. At 11 months, there were considerably fewer lesions (mean 3.7, range 0-7) in each foal, the most obvious decrease being in the stifle and the least in the hock. There was no statistically significant influence of exercise on the number of lesions, but lesions were more severe in $Group_{box}$. In the stifle, lesions were in the femoral condyle of boxed foals and in the trochlear ridge of exercised foals. It was concluded that, although exercise may affect the appearance and site of lesions, it does not appear to have an initiating role (van Weeren and Barneveld, 1999).

Altered Proteoglycan Metabolism in OC Cartilage is Result, Not Cause

Osteochondrotic and normal cartilage was harvested from foals at 5 and 11 months of age, and proteoglycan metabolism investigated by use of conventional techniques. Sulfur incorporation of OC was markedly less in osteochondrotic than normal cartilage in 11-month-old foals. Serum stimulation of proteoglycan synthesis was less in osteochondrotic than normal cartilage at 11 months, indicating reduced capability of chondrocytes from osteochondrotic cartilage, which was not due to the number of cells present as indicated by DNA content. Osteochondrotic cartilage from 5-month-old foals appears to be in a state of stimulation but chondrocytes are highly viable since they can be stimulated to similar metabolic levels as normal chondrocytes. Osteochondrotic cartilage from 11-month-old foals has a lower vitality and cannot be stimulated. The reduced and altered proteoglycan production at 11 months from lesions which have not regressed is likely to indicate that the changed synthesis reflects a result rather than cause of the OC lesions (van den Hoogen et al., 1999).

Horses Severely Affected with OC Have Lower Bone Mineral Density

In OC, the role of trauma is still contested. It has been suggested that normal forces on suboptimal bone, or higher than normal forces on normal bone, may

lead to microfracture and subsequent retention of cartilage. Showing that this occurs in normal life is difficult. In the EXOC study, mineral density was determined in the third carpal bone and in the distal radius. The data were analyzed in relation to the OC score of each animal, which was the sum of the number and severity scores of OC lesions in each animal. Of the four groups of OC scores, the highest (i.e., the most severely affected group of animals) had a significantly lower bone mineral density (BMD) than the other three groups. The implication might thus be that horses with severe OC may indeed have lower mineral density, which is a large determinant of bone's resistance to deformation. Further, OC is rare in the third carpal bone, which may indicate that the lower BMD found there was not localized. Although low BMD might be expected if OC or its sequelae caused lameness or recumbency, absolutely no such signs were evident. A further explanation is that of the 7 animals in the group with an OC score >20, four came from the 5-month-old $Group_{box}$, two were from the 5-month-old $Group_{training}$, and one was from the 5-month-old $Group_{pasture}$. None was from the 11-month-old foal group.

This indicates that horses in the most severely affected OC group were young and had been confined, at least to some degree, possibly indicating a reason for lower BMD. Boxed horses would develop less muscle or use muscle less and exert less force on their limb column; thus they are likely to have lower BMD (Firth et al., 1999).

Comparison of Distribution, Severity and Number of OC Lesions in Various Studies

The lesions encountered in four crops of pasture-raised foals in New Zealand have revealed the same lesions originally found in one of them (Pearce et al., 1998a). No other manifestations of the DOD complex were observed. In 21 pasture-fed 5-month-old Thoroughbreds, there were 1.6-3.3 lesions/foal; the most commonly affected site was the talar condylar ridge followed by the proximal humerus, though the lesions were not severe and so small as to be apparently innocuous. No intervertebral lesions were noted. The lesions were more numerous, the site order was different, and the severity of the lesions was greater in studies in Ohio (Knight et al., 1990), Canada (Hurtig et al., 1993), and The Netherlands (van Weeren and Barneveld, 1999). It is unclear if the differences are due to the variances in management system, nutrition, breed, and exercise possibilities at pasture.

Different Patterns of Decline in Liver Copper Concentration in Thoroughbred Foals

Serial liver biopsies were taken from foals soon after birth to 160 days of age. In seven of the foals, the normal decline in liver copper concentration was evident,

as previously documented (Pearce et al., 1998c), and declined from a high mean (+/- SD) liver copper concentration at birth (374 +/- 130 mg/kg DM) to adult values (21 +/- 6 mg/kg DM) by 160 days of age. In three foals the decline was slower than in the other seven and at 160 days of age the mean concentration was 162 +/- 32 mg/kg DM. The differences between each of eight biopsies ($P < 0.01$) and between "normal" and "accumulator" foals ($P < 0.002$) were significant (Gee et al., 2000).

IGF and Collagen Changes in Osteochondrotic Cartilage are Related to Healing

Specimens were harvested and snap frozen from OC-affected immature horses and age-matched controls, either at surgery or necropsy. PCR was used to determine expression of IGF-1, and TGF-ß1, which was greater in cartilage from horses with OC, significantly in the case of IGF-1. Using rabbit polyclonal antibodies against human IGF, the site of localization of IGF-1 was shown to be just beneath the tangential zone and in the deepest cartilage layers of osteochondrotic cartilage. In situ hybridization showed increased type I collagen in deep layer fibrocartilage repair tissue and fibrous tissue in the osteochondrotic cleft. The increased expressions are most likely to be a healing response and are not etiologically significant (Semevolos et al., 2001).

Copper May Contribute to Repair of Early OC Lesions

The possible role of copper in OC in pasture-raised Thoroughbred remains unresolved, despite the alteration of foal copper status by oral administration of copper to pregnant mares (Pearce et al., 1998b,c). The very fact that the lesions were few and subtle may reduce the ability of researchers to determine if copper status does or does not affect lesion number and severity.

Therefore, the concentration of copper in foals known to be prone to OC was examined. Liver biopsies were taken from warmblood foals at 4 days and 5 months after birth, and liver copper concentration determined. For each foal, the liver copper concentration was related to the OC status of the foals as determined by scoring of stifle and hock OC lesions in radiographs taken at 5 and 11 months of age. The liver copper concentration was similar to those in Thoroughbred foals in previous studies (Gee et al., 2000; Pearce et al., 1998c) and declined to adult levels by 5 months. The reduction in number and severity of radiographically detectable lesions was similar to that previously described (Dik et al., 1999). Radiographic score was not related to liver copper concentration at birth. The foals with the lowest liver copper concentrations had a worsening OC score between 5 and 11 months. Foals with the highest 50% of liver copper concentrations had an improvement in score by 11 months in OC of the stifle but not the hock. This

evidence supports copper being less involved in the cause of OC, and more in the repair of early OC lesions (van Weeren et al., 2003).

Injectable Copper Does Not Alter Foal Copper Status

Oral copper administration to late pregnant mares at pasture is labor intensive, and parenteral administration was investigated. The effects of copper supplementation by two injections of copper edetate given to mares in late gestation were determined by assessing liver copper concentration of their foals at birth. The injections did not improve copper status as shown by no significant difference in liver copper concentration of foals from mares that had received copper injections compared to those that had received saline injections (Gee et al., 2000).

Body Composition in Thoroughbred Foals

High-energy diets, overfeeding, and high growth rates are often cited as associated factors in the pathogenesis of OC. However, there is little basic nutrition work in Thoroughbred horses on which to begin determining what nutritional factors may be directly related to developmental orthopedic disease. Therefore, body composition was examined in 5-month-old Thoroughbreds using ultrasound, condition scoring, and bioelectrical impedance. Of the partial empty bodyweight, fillies had significantly more fat and higher percentage fat than did colts. Live animal condition scores, particularly rib condition scores, were closely related to fat mass and concentration, but condition scores were only slightly higher in fillies than colts. Ultrasound measurement of rump fat thickness was significantly correlated with condition score and explained 71% of variation in body fat mass. Impedance is difficult to measure in vivo (Gee et al., 2003).

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