Abstract

Developmental orthopedic disease (DOD) is a broad topic in the horse. There are several categories of disease processes that fall under the realm of DOD including osteochondrosis (OC), osteochondrosis dessicans (OCD), subchondral cystic lesions, angular limb deformities, flexural deformities, physitis, cuboidal bone abnormalities, and juvenile osteoarthritis. Historically these issues have had a major financial impact on the equine racing and performance horse industries and veterinarians alike. The etiopathology of these processes is multifactorial.

There are many physiologic and phenotypic considerations with respect to disease manifestation such as body size, conformation, and growth rate. Exercise and body condition are variables that effect biomechanical stress on developing bone and cartilage. Environmental factors such as confinement versus pasture housing and availability of nutrients from pasture that may be deficient or low in necessary minerals can play a role in development of clinical abnormalities. Genetic and epigenetic relationships also are linked to expression of pathology.

Keywords: Equine, osteochondrosis, angular limb deformity, nutrition

Defining the problem

Osteochondrosis is a disease that results from the disruption of normal endochondral ossification of bone at the physes and epiphyses. This is an active process in juvenile animals that allows lengthening and thickening of bone. Osteochondrosis dessicans occurs within the epiphysis involving the articular cartilage. A core of cartilage is retained within the subchondral bone; this site undergoes necrosis and results in a defect in the articular cartilage that becomes a lesion in high motion, weight bearing surfaces within joints. Subchondral bone cysts occur if the defective endochondral ossification occurs at a deeper level within the bone than the articular surface. These lesions occur in high weight bearing areas and can also be secondary to trauma.

There are several known sites of predilection for the appearance of OC defects. Radiographic screening is the most common means of diagnosis. Radiographing both limbs is recommended as OCD lesions are frequently bilateral. Chronologically with respect to the timing of endochondral ossification OCD lesions should be present by seven to eight months of age. Spontaneous resolution of lesions may occur, but generally not after eight to ten months of age. The exception to this is OC of the sagittal ridge in the fetlock which may resolve later with conservative medical management.

The tarsus is one of the most commonly effected joints with lesions visible as young as three months of age. The three consistently named locations of problems within the joint are the distal intermediate ridge of the trochlea (DIRT), lateral trochlear ridge of the talus, and the medial malleolus of the tibia. The OC lesions at these sites usually appear as round, smoothly margined fragments with an underlying subchondral bone defect. Medial malleolus fragments are typically very small. Lateral trochlear ridge lesions may have more than one fragment and are fairly large involving a significant surface area of the ridge. Radiographically, it should be noted that “teardrop” fragments involving the medial trochlear ridge are considered incidental findings. This is characterized by focal dorsal flattening and small distal smoothly margined fragments. Distal intermediate ridge of the trochlea lesion fragments and those of the lateral trochlear ridge if displaced may be found distally, cranial to the talus or central tarsal bone.

Stifle OC may be visualized as early as five months of age. It should be cautioned that around four to five months of age the femoral trochlear ridges appear highly irregular and poorly defined on radiographs. The most common site of OCD is the proximal to middle third of the lateral trochlear ridge of the femur. Subchondral bone cysts occur more commonly on the medial femoral condyle.

Fetlock OCD of the sagittal ridge of MT3 or MC3 may affect all four limbs. A flexed lateromedial position gives the best diagnostic radiographic view as it removes superimposition. Often a
subchondral bone defect and flattening of the sagittal ridge are the only radiographic changes. Axial, proximal plantar or the palmar eminence of P1 lesions occur and are shown to have a hereditary component in Standardbreds. These may be seen prior to initiating training, but trauma has been proposed as an etiology as well.4

Shoulder lesions are less common but tend to carry a poor prognosis for soundness. Anatomically the humeral head is the site of pathology with or without secondary involvement of the glenoid cavity articular surface.3,4

Subchondral bone cysts appear as radiolucent round to oval lesions that are well circumscribed and may have a thin sclerotic edge. The stifle is the most common location but they are also found in the distal third of the metacarpal and metatarsal condyles, proximal or distal P1 and P2, and proximal P3. Computerized tomography and magnetic resonance imaging are very helpful to determine if there is communication to and involvement of the articular surface.4

Normal endochondral ossification

Normal endochondral ossification occurs in the axial and appendicular skeleton. Chondrogenesis is the result of accumulation and condensation of mesenchymal cells into cartilage, which then differentiate into chondrocytes. Next proliferation, hypertrophy, and ossification transform the chondrocytes creating bone at the diaphyseal and epiphyseal sites of ossification.7 This provides a constantly changing template for longitudinal bone growth that begins at the center of the avascular cartilage and radiates outward until the skeleton is ossified, leaving only articular surfaces.8 As endochondral ossification occurs, the bone and extracellular matrix is remodeled; this is controlled by factors including angiogenic factors such as vascular endothelial growth factor (VEGF) along the growth plate.7 If this process is disturbed in a young, dynamically growing individual, irregular ossification of the bone may occur, manifesting itself as osteochondrosis in the horse.9

Pathophysiology of OC and OCD

Damage to the micro-vasculature of the arterial supply of the articular epiphyseal growth cartilage has an important role in the early pathogenesis of OC. In fetuses there is a defined change in collagen structure from the proliferative to hypertrophic zones within the physis. The critical time period when this tissue is vulnerable is during the transition in the arterial source of vessels in the cartilage canals of the growth cartilage from perichondrial to vessels crossing the ossification center.1,10-12 This transition coincides with the time the lesions are known to occur in the hock and stifle joints. Biomechanical influences explain the mechanism of initiation of this type of pathology and the existence of predilection sites.1,12 This is supported by the inability to find OC lesions in fetuses.1,12,13

Treatment of OC and OCD

The question of treatment is circumstantial; many smaller lesions that are not accompanied by clinical signs such as lameness and joint effusion may not require treatment. Studies have shown that the long term effects on joint health and performance are minimal with the exception of the lesions that involve a large area of articular surface or involve fragmentation of the cartilage.1,3 Medical management options for OCD include rest, control of nutrient intake, administration of chondroitin sulfate and hyaluronic acid with the intention of providing matrix for cartilage repair. Selection criteria for medical management is that the lesion is <2 cm long and <5mm deep. The standard of care for OC with fragments, osteochondrosis desiccans, is typically arthroscopic surgery to remove the fragments. In the case of large OCD flaps the use of polydioxanone pins (PDS) to reattach fragments that maintained perimeter continuity with the attached cartilage and did not have excessive mineralization or fissures has been successful.3,13,14

Treatment of subchondral bone cysts, particularly in the femoropatellar joint involves debridement via arthroscopy plus or minus additional medical therapy.3 Subchondral bone lesions have been treated using intralesional injections of corticosteroid. Cancellous bone grafting has been performed but a six month follow up study revealed similar outcome for grafting versus surgical debridement.
Mosaic arthroplasty using osteochondral grafting has been successful for return to performance but has limitations for larger lesions with respect to rejection of the graft and it is a technically difficult procedure to perform. More recently developed techniques include the use of allogenic chondrocytes combined with human IGF-1 as a graft following surgical debridement. This was particularly effective for older horses with evidence of osteoarthritis. Mesenchymal stem cells in fibrin have also been used intralesionally after debridement.

Role of nutrition

Nutrition is a key component in normal bone and cartilage development. Often the problem lies with excess available nutrition and energy, particularly associated with carbohydrate availability and metabolism. Research has shown the necessity for adequate levels of trace minerals such as zinc and copper. Our understanding of the role of copper has been refined to learn that the adequate levels of copper in the foal’s liver at birth is related to the repair of cartilage lesions but not pathogenesis. Mare’s milk is very low in copper therefore ensuring that the mare receives adequate dietary copper during gestation is a part of nutritional prenatal programming. Lysyl oxidase is the copper-dependent enzyme necessary for normal maturation of connective tissue. In older foals it has been shown that low copper diets at 7-15 ppm result in increased incidence of osteochondrosis lesions. The NRC suggests a diet containing 125mg per day during late gestation. Zinc has an antagonistic effect on copper and it has been proposed that diets with excessive zinc could cause a secondary copper deficiency. Adequate protein intake for mares increases by about 20% in late gestation and from maintenance requirements during early lactation. The calcium to phosphorous ratio of the diet of the mare and foals is important. The ratio should be no less than 1:1 or there is risk of impairment of calcium absorption. It may result in skeletal abnormalities and in rare cases nutritional secondary hypoparathyroidism. Although quite high, it has been documented that the ratio in the diet of the growing horse may be as high as 6:1 if the phosphorous intake is adequate. The Ca:P ratio found in mare’s milk between 16-24 weeks lactation is between 1.8 and 2.5:1. One of the key difficulties producers face in balancing the diet appropriately is the variation in forage quality and content. Hay analysis is helpful if the source of the forage is consistent. Additionally, it is difficult to gauge the overall amount of energy and caloric intake for horses raised on pasture. All of the variables of nutrients in the diet, body condition, and the biomechanical stressors of excess weight could potentially have an epigenetic effect on the expression of genes associated with osteochondrosis.

Genetics of OC

There have been a number of studies to determine the factors that control OC in the horse, including predilection sites, predisposed breeds, heritability, and genetics. Low T3 and T4 levels that have been altered by insulin in a growing horse may be responsible for a lack of capillary penetration into the bone matrix that in turn gives rise to perceptible OC when compounded with the effects of mechanical exercise and environmental factors. Osteochondrosis can occur in a number of joints including the coffin joint, pastern, shoulder, hock, and stifle, with the fetlock being the most affected. Heritability in these joints varies across breeds, with the hock joint having the greatest heritability (typically presenting lesions from birth) at 0.3-0.4 in most populations and the stifte joint having the least heritability, as lesions were typically formed during the early stages of growth. In addition to this, both the metacarpophalangeal and metatarsophalangeal joints display medium levels of heritability. Although there has been no relation between birth weight and the appearance of OC in the growing horse, Warmblood foals presenting as OC positive appear to have a higher rate of weight gain in the third and fifth month of growth than foals that do not have any lesions present and are also taller at both the withers and the croup (withers 1.56 ± 0.004 m and croup height 1.60 ± 0.007 m in OC positive foals; withers 1.49 ± 0.004 m and croup 1.52 ± 0.03 m in OC negative foals) at the age of 11 months than OC negative foals. There do not appear to be consistent quantitative trait loci (QTL) shared across different breeds of horses, however next-generation sequencing of equine DNA and RNA samples may allow for a more
thorough understanding of the differences in the genetic regulation of OC. In a genome-wide association study (GWAS) on OCD conducted on Norwegian Standardbred horses, of 162 horses chosen for genotyping from 22 sires, it was determined that *Equus caballus* chromosomes (ECA) 5, 10, 27, and 28 were the ECA showing a moderate level of association with tibotarsal OCD. In this case, ECA10 possessed two single-nucleotides (SN), BIEC2-132748 and BIEC2-132753, which showed the most significant hits. Osteochondrosis dessicans in Thoroughbreds, however, is associated with ECA3, a suggestion of complex genetic inheritance of OCD lesions.

A number of QTL for palmar/plantar osteochondral fragments (POF) have been identified as well in Norwegian Standardbred trotters, with medial POF identifiable on ECA1, 2, 7, 9, and 31 and lateral POF identifiable on ECA7, 11, 27, and X. Medial POF occurs most frequently in these horses. Of 176 yearlings studied, 82 were POF-negative controls, 82 presented medial POF, 33 were diagnosed with lateral POF, and 21 had both. In another genome-wide OC study on 201 Dutch Warmblood horses, four significant SNP were discovered on chromosomes 3 (BIEC2-808543) and 10 (BIEC2-121323, BIEC2-121320, and BIEC20121337), which suggests a potentially novel susceptibility locus that is different from the loci associations in Norwegian Standardbreds and further indicates that there are both intricate genetic relationships to heritability as well as breed differences and environmental factors.

Warmblood horses tend to have a very high occurrence of OC in the coffin joint, whereas Standardbreds have the highest occurrence of lesions in the pastern joint. In the shoulders and hocks, they are seen in Quarter Horses frequently; Standardbreds also have a high occurrence of hock fragments, but they rarely appear in their shoulders. Dutch Warmblood horses also historically have a high incidence of lesions in the hock joint, with the distal end of the talus lateral trochlear ridge, the distal tibia medial malleolus, and the distal intermediate ridge of the tibia at the cranial apex all representing various predilection sites. Ponies, conversely, are typically not affected by OC to the extent that horses are.

**Angular limb deformities**

There are a number of different types of presentations of angular limb deformities (ALD) ranging from slight deformities with the ability to potentially resolve over time to those requiring less passive forms of intervention. There are two main forms of ALD; if the limb deviates laterally from the site of the deformity it is referred to as being valgus, whereas a limb that deviates medially is referred to as varus. Common conformational areas in which these deformities occur include the fetlock as well as both the carpal region and tarsal region in the foal. Mild fetlock valgus (5°), carpal valgus less than 15 degrees, and slight tarsal valgus in foals have been found to typically correct on their own given time and do not need intervention; conversely, fetlock varus, carpal varus deformity, and tarsal varus often require intervention or corrective surgery. It is important to diagnose these angular limb deformities early in life. If there is a physical deformity as well as an articular deformity present, intervention is necessary, but once ossification reaches the cartilage periphery, the deformity is considered uncorrectable; this typically occurs at around four months. These deformities are often bilateral, although they can present as unilateral, and in some studies show a linkage to both genetic and physical factors including both breed and size.

**Treatment of angular limb deformity**

Much of the correction of angular limb deformities relies on foot balance adjustment made on a regular basis, every two to four weeks by a skilled farrier. Foals grow hoof at a rate of 15mm per month which is much greater than adults at 9 mm per month. Many of the mild valgal conformation imperfections will correct as the foal grows and the chest broadens. With valgal conditions there is more weight bearing on the medial side of the hoof capsule which pushes the hoof capsule laterally and the medial heel bulb proximally. Foal feet not only grow distally but also expand. The expansion occurs proximally which gives the foot a tapered shape. This places the weight more on the dorsal aspect of the foot. Mild rasping of the heel increases the weight bearing surface area and moves it to the rear of the foot. Trimming to include a round or square toe will promote better break over easing stress on the toe. Aggressive trimming can lead to distortion of the hoof capsule. The use of glue on shoes and extensions...
to extend the weight bearing surface in the direction of axial alignment in moderate to severe cases helps to prevent deformity of the foot. Confinement is recommended for severe cases to reduce the risk of damage to the growth plates.  

Surgical procedures are reserved for moderate to severe cases. Common techniques are the placement of single transphyseal screws, and the screws and wires technique. Correction of the deformity occurs by creating pressure across the growth plate which reduces chondrocyte proliferation and hypertrophy leading to decreased longitudinal bone growth. A second procedure is required after the desired correction has been achieved to remove the hardware to avoid overcorrection. Periosteal transection with or without periosteal elevation on the convex side of the deformity is another corrective method. The timing of physeal closure must be considered in the treatment approach. Fetlock deformities must be addressed sooner, typically between four to six weeks of age as MC3 and MT3 physes functionally close at 12 weeks of age. Carpal conformation should also be evaluated concurrently with fetlock issues as offset carpi tend to impair effective correction of fetlock varus. Radial physeal closure occurs much later thus carpal deviations may be surgically addressed at several months of age. However, the highest rate of growth at the distal physis is from birth to ten weeks of age. Carpal valgus of up to 4 degrees are considered normal in the horse.

Conclusions
Developmental orthopedic disease will continue to persist as a complex issue in the horse. Progress has been made to manage clinical manifestations with a better understanding of dietary needs as well as continually improving medical and surgical techniques. Genetic associations with specific locations of osteochondrosis lesions and breed correlations may give breeders another selection tool when considering pairings. Ultimately, the goal is to produce a horse that is a functional athlete. Promoting client understanding of which lesions are relevant to function versus those that should be considered a cosmetic defect should be a focus of veterinarians as it is in the best interest of the horse. Many imperfect physical specimens have accomplished great athletic feats.

References