

# OSTEOCHONDROSIS

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Lameness is the most frequent clinical problem in riding horses and the commonest reason for incapacity. In addition, two surveys of wastage in the Thoroughbred industry concluded that lameness was the major cause of loss (Jeffcott et al 1982 and Rossdale et al 1985). Against this background osteochondrosis, which was first reported in the horse by Nilsson in 1947 appears to have increased in incidence (Stromberg 1979; Knight et al 1985; Bramlage 1987; Wright and Pickles 1991). Although Jeffcott (1993) considers that osteochondrosis now affects between 10% and 25% of the horse population, its true incidence is unknown. Carlsten et al (1993) found radiological evidence of osteochondrosis in the metacarpophalangeal/metatarsophalangeal joint of 22% and tarsocrural joint of 11% of Swedish Standardbreds. The incidence in Thoroughbreds and Warmblood breeds appears to be significant but is unknown.

## Definitions

Olsson's (1978) original veterinary description of osteochondrosis as "defective endochondral ossification" has stood the test of time and remains the most accepted definition. McIlwraith (1987) described osteochondrosis as a disturbance of cellular differentiation in growing cartilage with persistence of the hypertrophic zone which subsequently undergoes necrosis. Since it is thought that the central lesion is a failure of differentiation of growth cartilage, Olsson (1978) and Jeffcott (1993) have suggested the term dyschondroplasia. Such comprehensive definitions suggest that osteochondrosis in animals is a generalised or systemic defect in endochondral ossification occurring in cartilage of the articular/epiphyseal complex and metaphyseal growth plates. It is also generally accepted and thus incorporated into the unifying theories of osteochondrosis that the process of endochondral ossification occurring at these two sites is similar.

The metaphyseal growth plates are discoid and occupy the space between the epiphysis and the diaphysis of most long bones. From the epiphyseal side to the diaphyseal side, these consist of zones of resting cells, proliferating cells, hypertrophic cells and a zone of calcified cartilage. Metaphyseal vessels invading the matrix of the hypertrophic zone permit mineralisation. Osteoid deposited in these spicules creates the

primary spongiosa of the metaphyseal bone and this, in due course, is remodelled to produce the diaphyseal cortex and medulla.

The process of endochondral ossification in the epiphysis is more complex. The immature epiphysis grows centrifugally. It has a centrally located centre of ossification and peripherally situated growth cartilage. This in turn is partially covered by articular hyaline cartilage which provides a low friction gliding surface and contributes to epiphyseal growth - hence the terms articular/epiphyseal complex.

In pigs the morphology of the epiphyseal growth cartilage is different from that in the metaphyseal growth plate and there are differences in the process of endochondral ossification occurring at these two sites (Brown et al. 1993).

Pool (1993) has proposed that there are two forms of equine osteochondrosis; primary (idiopathic) osteochondrosis which is an inherent defect in the cartilage model and secondary (acquired) osteochondrosis which is a disorder (from biomechanical, nutritional or other metabolic influences) superimposed on a normal cartilage model.

In an attempt to avoid terms with a specific aetiological or pathogenetic meaning the term developmental orthopaedic disease was coined at the 1986 American Quarterhorse Association meeting. This all-encompassing term is sometimes (inaccurately) used as a synonym for osteochondrosis and vice versa. However, the link between some developmental orthopaedic conditions for example flexural deformities and defective endochondral ossification is tenuous.

## Osteochondrosis in other species

Osteochondrosis is found when production pressures are applied to the breeding and rearing of animals. For example, Ekman and colleagues (1990) demonstrated osteochondrosis in domestic pigs but found none in mini pigs which are derived from wild boars and Reiland et al (1978) described osteochondrosis in broiler chickens but absent in Leghorns. It is possible that, for similar reasons, osteochondrosis is rare in ponies and feral horses.

In chickens osteochondrosis is mainly recognised in metaphyseal growth plates. The proximal tibia is most commonly affected and the term dyschondroplasia appears to describe well the clinical condition. It is most common in broiler chickens and the incidence is greatest in those lines which achieve the fastest growth rates. Avian dyschondroplasia has been described as consisting of an avascular mass of cartilage containing partially hypertrophied (transitional) chondrocytes. The morphology of these suggests that this is a consequence of aberrant chondrocyte differentiation (Thorp et al 1993).

Both articular/epiphyseal and metaphyseal osteochondrosis have been studied in pigs. Hill et al (1990) found morphological and histochemical differences between lesions at these two sites, which they considered to indicate that metaphyseal growth plate and articular/epiphyseal osteochondrosis are different entities. By contrast, the anabolic agents insulin-like growth factor (IGF) and transforming growth factor beta (TGF $\beta$ ) which are considered integral to chondrogenesis and endochondral ossification have been shown to be deficient at osteochondrotic foci of the articular/epiphyseal complex of pigs and the metaphyseal growth plate of chickens (Thorp et al 1993). This is the first demonstration of commonality in the molecular and cellular events between osteochondrosis of the articular/epiphyseal complex and the metaphyseal growth plate and also between species.

### **Aetiology**

The aetiology of osteochondrosis is unknown but it is currently thought to be multifactorial and may be a syndrome. The principal determining factors are considered to be: familial predisposition, growth rate, dietary imbalance and exercise.

### ***Familial predisposition***

Familial predisposition to the development of osteochondrosis is recognised in man, dogs, chickens and pigs. Significant heritability coefficients for some forms of osteochondrosis have been demonstrated in Standardbreds (Schougaard et al. 1990; Gröndahl and Dolvik 1992; Philipsson et al. 1993). The results of Philipsson et al. (1993) also suggested that predisposition to osteochondrosis in the tarsocrural and metacarpophalangeal/metatarsophalangeal joints were inherited independent of each other. Familial predisposition has been reported anecdotally in Thoroughbreds and is strongly suspected in the Warmblood breeds. It has been suggested also that there is a gender predisposition with males affected most often (Strömberg 1979) but more recent work has indicated a similar incidence in males and females (Gröndahl 1991; Sandgren et al 1993). It

has also been suggested that familial and gender disposition may occur as a result of foal size, growth rate and activity level. Similarly there have been suggestions of a relationship between the incidence of osteochondrosis and the age and/or parousity of mares but there is currently no objective evidence to support this (Sandgren et al. 1993). The above notwithstanding, selected breeding programs have thus far yielded disappointing results, highlighting the complex genetic nature of osteochondrosis.

### ***Growth rate***

Early descriptions of osteochondrosis in horses suggested that most affected animals were larger, more precocious and had greater growth rates than unaffected peers. Sandgren et al (1993) reported that Standardbreds with tarsocrural osteochondrosis were heavier and had greater average daily weight gain than unaffected animals. However, there was no such correlation with osteochondrosis of the metacarpophalangeal/metatarsophalangeal joints in the same animals. In addition recent work in Ireland (Jelan et al 1996) showed that there was no significant difference in growth rates between normal Thoroughbreds and those affected by developmental orthopaedic diseases including osteochondrosis.

There are anecdotal reports of interrupted growth rates in individual animals that have been followed by the development of various forms of osteochondrosis. Such interrupted development can be the result of concurrent disease of the foal or of the mare resulting in confinement of the foal and/or a change in nutritional status. The potential contribution to osteochondrosis is unknown.

It has been similarly suggested that selection of Thoroughbreds for precocity and management practices designed to produce yearlings for sale have contributed to development of osteochondrosis. However, there appears to be no difference in the incidence of osteochondrosis in animals produced for this market compared to those raised by owner breeders. In addition the incidence of osteochondrosis in animals produced for the show ring is low.

### ***Dietary imbalance***

Dietary imbalance has been the most commonly suggested aetiological influence on the development of osteochondrosis. The three principal areas of consideration have been caloric intake, copper deficiency and calcium/phosphorous imbalance.

### **Caloric intake**

High caloric intake has been implicated in the aetiology of osteochondrosis in all species.

Olsson (1978) and Strömberg and Rejnö (1978) both proposed high carbohydrate diets as predisposing to osteochondrosis in the horse. In 1984 Glade and Belling induced epiphysitis and osteochondrosis-like lesions by feeding 130% of the National Research Council recommended levels of carbohydrate and protein to foals. Glade (1987) subsequently proposed that high carbohydrate intake is deleterious to foals by disrupting co-ordinated thyroid hormone and insulin secretion after a grain meal. These hormone changes reduce the availability of nutrients to cells, resulting in a temporary limitation of chondrocyte energy metabolism and growth. Krook and Maylin (1988) suggest that such changes may also result in weakened osseous trabeculae. Ralston (1996) demonstrated post-prandial hyperinsulinaemia and hyperglycaemia in foals on a high carbohydrate diet. Temporary hypothyroxaemia was also demonstrated which could affect adversely chondrocyte maturation and extracellular matrix structure. Insulin and its derivatives have a direct effect on endochondral ossification acting as mitogens for chondrocytes and enhancing chondrocyte survival. Insulin also stimulates a rapid removal of T3 and T4 from the circulation; these are involved in the final stages of chondrocyte maturation. Savage et al (1993a) produced osteochondrosis-like lesions in 6 out of 12 foals fed 129% of the NRC levels for dietary energy. However, none of these studies have produced osteochondrosis in a form similar to that which is recognised clinically.

Excessive dietary crude protein was also suggested as a causative factor in the development of osteochondrosis by Glade and Belling (1986). However, this has not been substantiated by subsequent studies (Savage et al 1993a).

#### Copper deficiency

It has been known for some time that cattle deficient in copper develop epiphysitis. In 1987 an epidemiological study in Ohio and Kentucky linked copper deficiency and zinc excess (which inhibits copper absorption) with an increased incidence of development orthopaedic diseases in yearling horses (Knight et al 1985). Ceruloplasmin copper stimulates production of and is a co-factor for the enzyme lysyl oxidase which is necessary for collagen crosslinking. Poor collagen quality has been proposed as a possible primary lesion in osteochondrosis (Hurtig et al 1993).

Copper accumulates in the foetal liver early in gestation (Cymbaluk and Smart 1993). Mares milk is low in copper and this deficit is met by mobilisation of the foal's hepatic copper stores until solid food with an adequate level of available copper is consumed. Supplementation of mares with copper does not increase its level in milk (Breedveld et al 1987). The potential for copper deficiency is geographically variable

and dependent on the location of the animals and source of feed stuffs. Diagnosis of copper deficiency is difficult and reliable diagnostic criteria have not been defined. Excessive carbohydrate intake may also inhibit absorption of copper.

Severe experimental copper deficiency (1.7 ppm) was reported to produce flexural deformities and osteochondrosis by Bridges and Harris in 1988. These authors also demonstrated an increase solubility of type 2 collagen. Copper supplementation of pregnant mares and/or foals produced a reduced incidence of osteochondrosis in reports by Knight et al (1987), and Gabel et al (1987). However, supplementation did not eliminate the problems. Further experiments with diets marginal or deficient in copper (Hurtig et al 1991; Cymbaluk and Smart 1992; Glade 1992;) and marginal in copper with excessive zinc (Bridges and Moffit 1990) have reported lesions resembling osteochondrosis in the articular/epiphyseal complex and metaphyseal growth plate. In all cases the lesions produced by copper deficient diets were generalised (systemic) and not focal as seen in clinical cases of osteochondrosis.

A later study (Von Weeren et al. 2003) concluded that copper had a positive effect on the repair of osteochondrotic lesions, but not on their pathogenesis, which may explain some of the previous, apparently contradictory, results.

#### Calcium/Phosphorus imbalance

There is one report in which 5 of 6 foals fed excessive levels of phosphorus suffered osteochondrosis-like lesions (Savage et al 1993b). There is also one anecdotal report which suggests that osteochondrosis was induced in a group of weanlings which were confined and fed on a bran (high phosphorus) diet. Savage et al (1993b) also found osteochondrosis-like lesions in 2 out of 6 foals on a high calcium diet and 5 out of 6 foals on a high calcium and high energy diet. However these lesions were, as reported in other experimental studies, not typical of the clinical disease. In addition since dietary calcium and phosphorus levels are readily and regularly monitored on well-managed studs, imbalances are not generally considered to represent a major contribution to clinical cases of osteochondrosis. There have been suggestions that trace element and mineral deficiencies may be produced by periods of lush grass growth and predispose to osteochondrosis. Similarly, the depletion of maternal trace mineral stores by repeated pregnancy and lactation has also been implicated but neither have been substantiated to-date.

#### Exercise

van Weeren & Barneveld (1999) found that high intensity exercise of short duration appeared

to reduce the incidence of osteochondrosis in Warmblood foals. Bruin and Creemers (1994) reported the effects of varying levels of exercise on the incidence of osteochondrosis in Dutch Warmblood foals maintained on either low or high energy diets. The lowest incidence of osteochondrosis occurred in foals on a high energy diet which were receiving a high level of exercise while the highest incidence occurred in foals receiving a high energy diet but receiving a low level of exercise. These publications appear to suggest that exercise is a protective influence on the development of osteochondrosis and further studies have subsequently supported this hypothesis (Van Veeren unpublished data).

#### *Collagen metabolism*

There is increasing evidence that abnormal collagen metabolism plays an important part in the molecular mechanisms of osteochondrosis. However whether this is primary or secondary remains a debate. Nonetheless it forms an attractive hypothetical link between potential genetic, dietary and physical influences. (Van Veeren 2006).

#### **Conclusions**

Recent work has identified lesions of osteochondrosis in animals as young as 3 days of age. It is therefore considered unlikely that osteochondrosis can be explained as post-natal nutritionally induced dyschondroplasia. Dietary excesses and imbalances appear clinically to relate more closely to osteochondrosis of the metaphyseal growth plate than osteochondrosis of the articular epiphyseal complex. Current interest in the development of the latter is being directed toward influences on the pregnancy mare.

#### **Pathogenesis**

Osteochondritis dissecans (OCD) and subchondral bone cysts are considered to be the principal manifestations of osteochondrosis affecting the articular/epiphyseal complex. Physitis (physolysis; epiphysitis; physeal dysplasia) is thought to result from osteochondrosis affecting the metaphyseal growth plate.

In addition, osteochondrosis is implicated in the development of angular and flexural limb deformities, cervical vertebral malformation/malarticulation and juvenile arthrosis. There have been suggestions that cuboidal hypoplasia, proximal phalangeal fragmentation and the development of some carpal chip fractures are also related to osteochondrosis. It is possible that there is no clear demarcation between the two forms of osteochondrosis suggested by Pool (1993) but rather a merging of conditions which are currently thought of as failures of stress adaptation and those which results

from defective endochondral ossification. This concept that subclinical abnormalities in endochondral ossification may predispose to injury by the production of bone which is of suboptimal quality has been supported by Krook and Maylin (1988) and Kaneko et al (1993) who suggests that osteochondrosis is an important predisposing factor to subsequent bone fracture in horses in training.

Classical osteochondritis dissecans tends to occur on articular surfaces which are not consistently subjected to axial load. It is theorised that retained hypertrophic cartilage undergoes necrosis and that applied physical stresses produce fissures and flaps. However, this is not consistent with the clinical appearance of most lesions. Bramlage (1987) and Hurtig et al. (1993) have suggested that the primary defect is at the transition of mineralised cartilage to bone and that overlying articular cartilage is affected secondarily. De Moor et al (1972) demonstrated separation in the subchondral bone in histological examination of clinical cases. In many affected animals there is also extensive degeneration of underlying bone but it is not yet understood if this is a primary feature or a secondary phenomenon. McIntosh and McIlwraith (1993) reported osteolysis within already ossified epiphyses which is at variance with the defective endochondral ossification theory of osteochondrosis.

Other lesions, which are currently classified as manifestations of OCD, are more difficult to explain with current theories of pathogenesis. Fragments from the dorsal articular margin of the distal intermediate ridge of the tibia are frequently covered by apparently normal hyaline cartilage and can have subchondral bone of good mechanical quality. They are separated from the parent bone by a distinct fissure containing fibrous tissue or fibrocartilage. This has led some authorities to suggest that such lesions may result from fractures of the articular/epiphyseal cartilage that subsequently undergoes endochondral ossification. A similar explanation may be offered for fragmentation associated with the dorsoproximal and plantaroproximal margins of the proximal phalanx (Dalín et al 1993).

Longitudinal studies documenting the clinical and radiological course of OCD are sparse. It is generally claimed that detached osteochondral fragments cannot heal. However, there is increasing awareness that subchondral defects can increase in size, decrease in size or disappear in young animals. The cut-off point with which healing can occur appears to vary between joints; lesions in the femoropatellar joint have been seen to heal up to at least 14 months of age.

There are two principal theories, regarding subchondral bone cyst formation. The first suggests that these are focal areas of defective endochondral ossification in the articular/

epiphyseal complex which collapses. Growth of the epiphysis (condyle) around this site produces a cyst cavity. Watkins (1992) suggested that subchondral bone cysts are located primarily in areas under substantial, continuous compressive loads (in contrast to OCD lesions which tend to occur in areas subjected to shear forces). The second theory suggest that focal defects in articular cartilage and/or subchondral bone may, under the influence of compressive load, degenerate permitting inflow of synovial fluid and formation of a cyst. The characteristic fibrous pseudosynovial tissue which fills developmental subchondral bone cysts is difficult to explain with either theory. It is possible that this is poorly differentiated mesenchymal tissue but it could be a chronic inflammatory response. Again, there is a dearth of longitudinal information with respect to the pathological course of subchondral bone cysts. In some sites, for example the medial condyle of the femur, healing appears to be limited whereas in other sites, for example, the metacarpal condyles, the converse is true.

There are a number of theories regarding the pathogenesis of osteochondrosis of the metaphyseal growth plates. These include failure of cellular differentiation, reduction or obliteration of metaphyseal blood flow, physical trauma, inadequate mineral substrate, inadequate matrix production, and failure of local or systemic triggers of cartilage mineralisation or osteoid production. The theory which is currently most popular suggests that the primary defect is poor cellular differentiation in the hypertrophic zone of the growth plate. The second theory suggests that metaphyseal blood vessels are vulnerable to trauma due to the lack of a protective bony plate, as occurs in the epiphysis. It is postulated that excessive compression of the physis results in reduction or obliteration of metaphyseal blood flow. The proliferating zone continues to divide but, with reduced endochondral ossification, there is widening of the compressed physis. When the physis is too thick to be sustained by the epiphyseal vessels, there is necrosis at the hypertrophic/mineralised cartilage interface. Trauma in the form of compressive injuries may produce an increase in activity in the proliferating zone (as predicted by the Heuter-Volkman law of physeal growth) with resultant failure of endochondral ossification to keep pace with this activity and hence the clinical, radiological and pathological features of metaphyseal growth plate osteochondrosis. Alternatively the radiological widening of the metaphyseal growth plate may not be due to retained cartilage and/or failure of endochondral ossification but rather to metaphyseal fractures. Inadequate supply of mineralised substrate is now a less accepted theory of pathogenesis. Inadequate matrix production, principally collagen may explain some of the mechanical features of affected tissue and certainly provides a potential aetiological link with other (soft

tissue) developmental orthopaedic diseases through the copper-dependent enzyme lysyl oxidase. It is possible that osteochondrosis of the metaphyseal growth plate is a syndrome in which a dyschondroplastic growth plate may be damaged by physiological loading or a normal growth plate may become osteochondrotic under abnormal loading conditions.

Osteochondrosis of the metaphyseal growth plate always resolves although radiological closure may be delayed. Secondary and/or associated problems such as limb deformities may persist and there may be altered limb contour at the level of the physeal line. It has never been explained how osteochondrosis of the metaphyseal growth plate is able to resolve. It is not known whether zones of dyschondroplasia subsequently undergo endochondral ossification or whether these areas are resorbed and there is infilling from adjacent tissue.

None of the theories of the pathogenesis of osteochondrosis have yet reconciled the currently accepted generalised or systemic aetiologies with a site-specific nature of the clinical disease. There is only one study which has shown any relationship between clinical osteochondrosis of the articular/epiphyseal complex and metaphyseal growth plate (Sandgren et al 1993) and the general consensus is that these conditions affect primarily different animals.

### **Clinical manifestations**

The lateral trochlear ridge of the femur is the commonest site of clinical OCD in Thoroughbreds. This is followed by the distal intermediate ridge of the tibia, the distal lateral trochlear ridge of the talus, the proximal articular margins of the proximal phalanx, the dorsal sagittal ridge of the third metacarpal bone, the medial malleolus of the tibia, the patella, the glenoid of the scapula and humeral head and the femoral condyles. In the Warmblood breeds the commonest site for clinical OCD is the distal intermediate ridge of the tibia and this is followed by the plantar processes of the proximal phalanges, the extensor process of the distal phalanx and the medial malleolus of the tibia. The distal intermediate ridge and medial malleolus of the tibia and lateral trochlear ridge of the talus are the most common sites in Shire horses. In Thoroughbreds OCD is also found commonly in the articular facets of the cervical vertebrae where it may be related to arthropathy, subsequent impingement on the spinal canal and hence be part of the Wobbler syndrome.

The clinical signs associated with OCD are dependent on the site of the lesion, their severity and the age of the animal. Many horses are affected at bilaterally similar sites although the severity of the lesions is frequently asymmetric. Most lesions are detected in investigation of lameness and/or joint distension. However,

a significant number are discovered on radiographic examination of animals prior to purchase or as part of a preventative medicine programme. Sometimes foals and yearlings are presented because studs have noticed postural changes, for example, animals becoming more upright with a tendency to develop flexural deformity.

The radiological features of OCD are again dependent on the site of the lesions, their severity and the age of the animal. Irregular, articular margins are usually poorly defined in young animals but are later seen as smoothly marginated defects. There may be varying degrees of subchondral lucency which is usually most marked in young animals. Defects in more mature individuals are frequently marginated by subchondral sclerosis. Articular defects in young foals may later contain radio-dense fragments and in some cases these may detach. In this event fragments may be detected remote from the parent osteochondrotic focus.

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