Osteoarthritis (Degenerative Joint Disease)-
An Update
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Osteoarthritis (OA), (previously known as degenerative joint disease) is a disease predominantly, but not solely, affecting the diarthrodial joints and results from an interaction of a number of complex mechanical and biological processes. The major characteristic of OA is progressive degradation and destruction of the articular cartilage. Knowledge of the etiopathogenesis has progressed significantly in recent years. The loss of articular cartilage represents a culmination of failure of the articular cartilage to withstand the cyclic trauma of athletic activity and this may be complicated by aging changes. Traumatic arthritis includes a number of conditions, but these can generally be divided into 1. synovitis and capsulitis and 2. instability causing injury such as intra-articular and collateral ligament injury, intra-articular fracture, subchondral bone disease and meniscal injury (stifle) and 3. osteoarthritis.

Pathways by which trauma can cause can an effect
The joint is an organ. There are a number of ways in which traumatic damage occurs. The possible pathways can be divided into abnormal forces on normal cartilage or normal forces on abnormal (diseased) cartilage as illustrated in Figure 1.
Abnormal stresses on normal cartilage can be created by heavy athletic activity, as well as loss of stability due to fractures or ligamentous tears with abnormal loading, as well as joint congruency changes. On the other hand, abnormal cartilage can be created within normal stresses when synovitis and capsulitis causes degradation of articular cartilage or there is pathologic change in the underlying subchondral bone.

**Principles of Therapy**

The aims of all therapeutic procedures are to prevent the progressive loss of articular cartilage. Many instances of early joint disease mainly manifest as synovitis and capsulitis and their appropriate treatment will delay or prevent the cartilage loss of OA (discussed below). On the other hand, timely and appropriate surgery for intra-articular fractures, osteochondritis dissecans (OCD) and other traumatic injuries to joints is also a necessary part of preventing OA.

**Newer definition of best treatments for osteoarthritis**

Various targets have been identified in recent years and confirmed to be of importance in the horse. Mediators of relevance are illustrated in Figure 2.

The principle factor of significance at the top of the inflammatory cascade in equine OA is interleukin-1 (IL-1). When considering therapies attention to inhibition to this molecule is critical.

**Advances in Therapies**

This is an update with new knowledge on some conventional therapies, as well as an introduction to newer biological therapies.

**Physical therapy and rehabilitation**

The advantages of rehabilitation protocols other than stall confinement or turn-out have become recognized in recent years. Experimental data is lacking, but currently a study is ongoing at the CSU Orthopaedic Research Center examining the value of underwater treadmilling in an experimental model of OA.

**Shock wave therapy**

Shock wave therapy has been used as a treatment for a number of conditions. Most recently the value of shock wave therapy has been demonstrated with experimental OA in the horse. The major usefulness is in decreasing the inflammatory response from synovial membrane and joint capsule, as well as symptomatic decrease in lameness.
Non-steroidal anti-inflammatory drugs (NSAID’s)

Generalized cyclooxygenase inhibitors such as phenylbutazone and flunixin meglumine have been used for a long time, but side effects in ponies, young foals and at larger doses in adults have been noted. More recently attention has been given to specific cyclooxygenase-2 (COX-2) inhibitors. These can potentially provide focused inhibition of inflammatory mediated cyclooxygenase production while preserving the normal physiologic COX-1 activities and thereby reducing side-effects. There is one licensed product in the US, Firocoxib (Equioxx™) and other products such as Meloxicam available elsewhere. Most recently the value of the topical liposomal-based 1% creme of diclofenac (Surpass™) has been demonstrated in an experimental model of synovitis. They were both symptom-modifying as well as disease-modifying effects and the topical use for 30 days provided more benefit than systemic phenylbutazone in another experimental group.

Intra-articular corticosteroids

More recent work has identified deleterious effects with methylprednisolone acetate (Depo-Medrol™), but marked beneficial effects from triamcinolone acetonide (Vetalog™) and betamethasone esters (Celestone™). They are still the most potent anti-inflammatory drugs and are still commonly used in combination therapies, primarily with hyaluronan (HA).

Hyaluronan

Hyaluronan (HA) has been used for a long time. Most recently however, experimental work in the CSU equine OA model demonstrated DMOAD effects, which supports the long-term value of this product. Marked acute anti-synovitis effects are not as obvious and this fits with clinical observations and supports the combination use with triamcinolone acetonide.

Polysulfated glycosaminoglycans (Adequan™)

Recent experimental work has differentiated value intra-articularly and intramuscularly. Intra-articular Adequan was recently shown to be highly beneficial for inhibiting acute inflammation in the synovial membrane and fibrous joint capsule in the CSU equine OA model. These experimental results confirm the clinical impressions of the ability of Adequan to markedly suppress severe synovitis in association with severe osteochondral fragmentation and exposure of subchondral bone. On the other hand, intramuscular Adequan has been tested in the experimental OA model and minimal effectiveness demonstrated. Use of Adequan on a ‘prophylactic’ based continues and it is certainly agreed that no harm is done. The beneficial effects still need to be demonstrated, but this is difficult.

Pentosan Polysulfate

Pentosan polysulfate is not available in the US, but it is available in many other parts of the world as Pentosan Equine™. This is an intramuscular product that has been demonstrated as beneficial in the CSU OA model implying superiority of this product to intramuscular Adequan.

Autologous condition serum (IRAP™)

This product is based on processing of autologous blood by incubating the blood for 24
hours in the presence of specially designed beads. Research has shown upregulation of interleukin-1 receptor antagonist/IL-1 ratio as well as upregulation of other growth factors to a lesser degree. After 24 hours of incubation the container is centrifuged and the supernatant used for 3-5 intra-articular injections. Testing in the CSU OA model has shown beneficial effects that were symptom-modifying and disease-modifying. The principle clinical use is post-surgery and also for OA that is no longer responsive to HA/Vetalog combination therapy.

*Platelet Rich Plasma (PRP)*

The use of PRP is based on the high growth factor content of platelets. The concentration of platelets allows for a growth factor rich medium and PRP has received considerable use in the treatment of tendon and ligamentous injuries. More recently the use of this product intra-articularly is being evaluated, but no controlled research is available.

*Gene Therapy with Interleukin-1 Receptor Antagonist (IL-1ra)*

Previous work by Frisbie showed that the use of gene therapy using an adeno-viral vector containing the equine IL-1ra gene could shut down experimental osteoarthritis in the horse. However, repeat injections of the vector caused immunologic responses and so work has continued in the development of a better vector. Work by Goodrich *et al* at CSU on an adeno-associated viral vector (aaV) is proving promising and there is hope that gene therapy will soon become a clinical reality.