

**Saturday, October 20, 2007**

**Is Canine Degenerative Cruciate Rupture  
a Consequence of Rheumatic Disease?**

**Peter Muir, BVSc, PhD; University of Wisconsin - Madison**

Rupture of the cranial cruciate ligament (CCL) in the stifle is one of the most important orthopaedic conditions of dogs and leads to a large economic burden. The cause of CCL rupture is not known. This ligament is equivalent to the anterior cruciate ligament (ACL) in the knee of humans. Most CCL ruptures in dogs are degenerative, and are not associated with accidental injury. Current surgical treatments, such as tibial plateau leveling osteotomy (TPLO), do not restore weight-bearing to normal and stifle arthritis typically gets progressively worse after surgery. A likely explanation for these findings is that current surgical procedures only treat dynamic stifle instability during weight-bearing, but do not treat passive instability during periods when the affected limb is not bearing weight, or other relevant pathological change. This presentation will review what is known about the cruciate rupture disease mechanism. Clinical Features: Affected dogs usually have a low-grade lameness initially, that precedes development of stifle instability and more severe lameness. Initial low-grade lameness and bilateral arthritis may persist for many months. At surgery, typical findings include palpable instability, indicating complete tearing of the ligament, and arthritic degeneration of the stifle. These findings suggest that degenerative cruciate rupture is a consequence of a pre-existing arthritic condition, with CCL rupture occurring progressively over time, such that in the early phase of the condition, the stifle is stable.

Joint Pathology: Moderate to severe joint inflammation, or synovitis, is typically seen, usually without full thickness cartilage loss. The synovium or joint lining contains a mixed population of inflammatory cells, which includes T lymphocytes, the inflammatory cell type that has a pivotal role in development of immune-mediated rheumatic arthritis conditions. These findings suggest that degenerative cruciate rupture is an oligoarthritis, which is defined as an inflammatory arthritis affecting  $\leq 4$  joints. The cell populations present within the stifle synovium suggest that inflammation is driven by a specific immunologic trigger. Relationship of synovitis to stifle instability: The classical paradigm for development of stifle arthritis in dogs with degenerative cruciate rupture suggests that synovitis is largely a consequence of degenerative cruciate rupture and development of stifle instability. This is supported by the fact that surgical cutting of the CCL in experimental dogs leads to synovitis. However, in dogs with mild lameness and a stable stifle, stifle arthritis is also found. These findings suggest that the inflammatory stifle arthritis that precedes development of joint instability is a key factor promoting progressing CCL weakening and eventual mid-substance rupture.

What are the key factors that promote degenerative cruciate rupture? Several factors may contribute to development of degenerative cruciate rupture. These include: (1) stifle anatomy; (2) altered ligament composition and metabolism in predisposed breeds; (3) age-related ligament degeneration; and (4) synovitis. Progressive CCL rupture is associated with up-regulation of ligament matrix turnover, fragmentation of matrix collagen, and loss of fibroblasts from the CCL tissue. Recent studies of the microscopic blood vessel supply to the CCL and the overlying synovial layer lining the stifle joint suggest that the ligament derives most of its nutrition from synovial fluid. Therefore, inflammation of the synovium adjacent to the CCL tissue may have a profound effect on ligament collagen metabolism. These concepts are supported by experimental studies in which induction of stifle synovitis caused

**Saturday, October 20, 2007**

significant degradation in the CCL tensile strength to 29% of control by 6 weeks. In control stifles, the typical mode of cruciate failure during biomechanical testing involved fracture of bony attachment sites; with induction of synovitis, the most common mode failure was mid-substance rupture. These findings suggest that the classical paradigm between synovitis and cruciate rupture needs to be updated and that the dogs with mild lameness, stable stifles and incipient cruciate rupture are typically affected with an oligoarthritis, with joint inflammation often affecting both stifles.

What causes stifle oligoarthritis in affected dogs? The immunologic trigger for canine stifle oligoarthritis is not known. This arthritis condition may be a form of autoimmune disease, in which immune defenses become directed to the patients own tissues. Autoantibodies to collagen may contribute to joint inflammation, but are not a primary causative factor. Translocation of bacterial material to the stifle is a common event and is associated with development of the cruciate arthropathy. Bacterial material is often detected in human joints affected with arthritis, although whether this is a cause or a consequence of the arthritis is controversial. In humans, it is well documented that specific variations in immune defense genes influence the risk of developing chronic arthritis. These data suggest that the presence of bacterial material within the stifle may be a key pro-inflammatory factor triggering chronic synovitis in dogs. Host-bacteria interactions likely involve genetic predisposition.

Future Directions: Improved understanding of the mechanism that leads to degenerative cruciate rupture in the dog will facilitate development of new strategies for diagnosis and treatment of stifle oligoarthritis, including ligament repair. Identification of clinically relevant markers for stifle oligoarthritis will improve diagnosis of the early phase of the arthropathy. Clinical trials will be required to determine whether antibiotics or disease-modifying anti-inflammatory therapy can reduce joint inflammation and the risk of progressive arthritis and the risk of degenerative cruciate rupture. Identification of at-risk dogs will be facilitated by determining whether specific genotypes confer susceptibility to stifle arthritis in the dog.

### **Biographical Profile**

**Dr. Peter Muir** obtained his veterinary degree in 1985 from Bristol University. After working in practice, he returned to Bristol obtaining a PhD in veterinary science in 1990. He then moved to the University of Sydney to undertake training in small animal surgery, obtaining a Masters degree in 1992. He completed his surgery training at the University of Wisconsin-Madison and became a Diplomate of the American College of Veterinary Surgeons in 1995. After periods on faculty at the University of California, Davis and the Royal Veterinary College, he returned to Madison as a faculty member, where he is an Associate Professor.

*Dr. Muir's research has been supported by the following grants:*

*2405: Inhibition of Collagenolysis in Canine Cranial Cruciate Ligament During Rupture*

*741: Polymicrobial Bacteria-Associated Inflammatory Stifle Arthritis/Degenerative Cranial Cruciate Ligament Rupture in Dogs*