Residual osteochondral debris represents a clinical problem associated with arthroscopic debridement and curettage of joint surfaces. At the Oregon State University Veterinary Teaching Hospital (OSU-VTH), during a period from January, 1983 to August, 1986, incidence of radiographically recognizable osteochondral debris in the carpal joints of postarthroscopic equine patients was excessive. Uncertainty exists regarding the fate and effects of this debris on the normal equine joint. Reports in human medical literature implicate osteochondral debris as both an inflammatory stimulus and a mechanical abrasive in the pathogenesis of osteoarthrosis. This study was designed to evaluate the fate and effects of surgically implanted autogenous osteochondral fragments, intended to mimic remaining operative debris, on various physical
and biochemical parameters of normal equine middle carpal joints over a six month time period.

Four autogenous osteochondral fragments, removed from the lateral trochlear ridge of the talus, were arthroscopically placed as loose bodies into a randomly selected middle carpal joint in each of 10 young horses (2 to 4 years old). The contralateral middle carpal joint, subjected to a sham procedure, served as control. Postoperative therapy was consistent with usual treatment of clinical arthroscopic patients. Lameness evaluation, radiographic examination, carpal circumference measurement, and synovial fluid analysis were performed preoperatively and at scheduled intervals postoperatively. After two months of confinement, the horses were subjected to an increasing level of exercise, intended to mimic a four month conditioning program. Animals were euthanatized at 1 month (1), 2 months (2), 4 months (1), and 6 months (6).

Gross and microscopic examination of remaining fragments, articular cartilage, and synovial membrane of each middle carpal joint was performed.

Clinically, increased joint circumference, effusion, lameness, and radiographic appearance of degenerative joint disease distinguished implanted from control joints over the six month period. Implanted joints were grossly characterized by grooved, excoriated cartilage surfaces and synovium which was thickened, erythematous, and irregular. Loose bodies became adhered to synovium at their subchondral bone surface within four weeks after placement into the joint. At four weeks, bone within fragments was undergoing necrosis, while cartilage was preserved. At eight weeks, fragments were radiographically inapparent, grossly evident as pale plaques on the synovial surface, and
composed of dense fibrous connective tissue.

Histologically, synovial membrane specimens from implanted joints demonstrated significant \( P < 0.05 \) inflammatory change two months after implantation. Mononuclear cells infiltrated the synovial layers. Significant physical damage \( P < 0.05 \) was apparent within the articular cartilage two and six months after surgery. Chondrocyte degenerative change was significant \( P < 0.05 \) six months after surgery. Generalized reduction in Safranin-O uptake was not apparent within each level of cartilage samples, but focal reduction in staining was readily apparent in cartilage layers adjacent to physical defects.

Synovitis, physical articular damage, and focal chondrocyte degenerative change resulted from a combination of 1) direct mechanical abrasion by the implants or implant-derived debris, 2) an induced effect of osteochondral debris on the synovium, 3) synovitis-induced cartilage degeneration, and 4) supraphysiologic loading associated with exercise.

In this study, osteochondral loose bodies of a defined size and shape were resorbed by the synovium within two months after joint implantation. These fragments directly and indirectly induced synovitis and significant articular cartilage degeneration. Methods to prevent and reduce residual postoperative debris and damage associated with its presence are discussed. Implementation of this methodology should reduce the potential for subsequent articular pathology.
Date thesis is presented  March 12, 1991

Typed by Susan C. Schamp and Lorie J. Kennerly for Michael J. Huber D.V.M.
DEDICATION

With much loving emotion, I dedicate this thesis to my family: Kate, Colin, and G.M.C., and my parents, Adolph J. and Dolores M. Huber.

What was initially for me has evolved for you.
ACKNOWLEDGMENTS

I would like to express my appreciation to Dr. Edward A. Scott, my major professor, who accepted me as a graduate student, and my project as a scientific endeavor ("Just because he could."). His encouragement was necessary; his personal and professional advice was helpful. Dr. Scott made me appreciate the value of this undertaking. His advice and philosophy will be lifelong for this "young man." Through his efforts, I have begun the transformation from surgeon to surgical scientist.

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Special thanks are extended to Dr. Wayne B. Schmotzer for his surgical assistance and gentle reminders to pursue fame; Dr. Thomas Riebold for his devoted expertise to anesthesia and support of my efforts; Dr. Barbara J. Watrous for radiologic interpretation of the highest caliber, and interest/encouragement with this project; and Dr. Stanley P. Snyder for performing extensive histologic evaluations. Associates as these, so accomplished in their specialty fields, induce one to maximally strive for the same notoriety.
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Finally, I would like to thank the members of my Graduate Committee: Dr. Erwin Pearson, Dr. Edward A. Scott, Dr. Bradford Smith, and Dr. Pamela C. von Matthiessen; for the time and scientific effort they have unselfishly donated guiding and scrutinizing my efforts toward completion of this project.

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THE FATE AND EFFECTS OF IMPLANTED AUTOGENOUS OSTEOCHONDRAL FRAGMENTS ON THE MIDDLE CARPAL JOINT OF HORSES

BY

MICHAEL J. HUBER, DVM

INTRODUCTION

The carpus is the collective name for the arrangement of bones forming a set of joints in the forelimb of the horse. It consists of seven, occasionally eight, and rarely nine carpal bones arranged in two rows forming three major joints that articulate between themselves, the radius proximally and the metacarpal bones distally (Ford et al., 1988; Shively, 1982). This joint is the only one in the horse through which vertical forces are thrust through one long bone, the third metacarpal, to another, the radius (Roberts, 1964). This arrangement results in increased susceptibility of the equine carpal bones to concussive trauma (Stashak, 1987). Factors such as fatigue, extreme speed, long distances, jockey position, poor racing surfaces, improper hoof trimming, and abnormal conformation may affect the normal congruous articulation of the carpal bones
during exercise. Loss of normal congruity and tremendous concussive forces generated during maximal exertion and fatigue-related hyperextension result in abnormal compression and shear of the dorsal surfaces of the carpal bones (Stashak, 1987; Turner and Colahan, 1987). Intra-articular fractures result from either single acutely traumatic events, or more commonly from the result of continued repeated trauma leading to pathologic alteration of bone structure, and subsequent separation (Rooney, 1977; Lindsay and Horney, 1981; Stashak, 1987).

Intra-articular osteochondral or "chip" fractures of carpal bones and distal radius have been reported in all breeds of race horses, hunters, jumpers, and other actively performing horses (Stashak, 1987; Auer, 1980; Lindsay and Horney, 1981; Schneider, 1979). Highest incidence of intra-articular carpal fractures occurred in the intercarpal or middle carpal joint (Speirs et al., 1986; Palmer, 1986; Lindsay and Horney, 1981; Park et al., 1970; Thrall et al., 1971). The dorsal articular border of the distal portion of the radial and intermediate carpal bones and the proximal aspect of the third carpal bone are the most commonly affected areas within the middle carpal joint (Bramlage, 1983; Speirs et al., 1986; Lindsay and Horney, 1981; Palmer, 1986; McIlwraith, 1987).

Intra-articular osteochondral fractures are accompanied by some degree of lameness (Stashak, 1987; Lindsay and Horney, 1981; Park et al., 1970; Dixon, 1981). Fracture instability and abrasive effects of opposing surfaces result in contact damage to adjacent articular cartilage. Cartilage damage liberates debris and enzymes which irritate the synovial lining and damage the remaining
articular cartilage (Bramlage, 1983). Lameness becomes a developed consequence of equine carpal fractures. Severity of lameness is dependent on the extent, location, and duration of fracture(s), as well as the presence and extent of degenerative joint disease (Stashak, 1987).

Although joint surgery is not a cure for all joint conditions, including degenerative joint disease, removal of osteochondral fragments from affected joints will reduce inflammation and degenerative changes. Recommended treatment for most large displaced osteochondral fractures of the equine carpus is removal of the fragment or fragments (Stashak, 1987; Bramlage, 1983; Auer, 1980; Lindsay and Horney, 1981). Several methods of fragment removal have been described (Stashak, 1987; Bramlage, 1983; Auer, 1980; Lindsay and Horney, 1981; McIlwraith, 1984a; McIlwraith, 1984b; Turner and McIlwraith, 1982; Jennings, 1984). Dorsal arthrotomy of the carpus was the method of choice through the 1970's. Arthroscopic surgery to remove osteochondral fractures has been popularized in the last decade. Advantages of arthroscopic surgery over arthrotomy techniques include reduced soft tissue trauma, improved visualization of lesions, earlier return to racing, reduced convalescent cost, and improved racing performance postoperatively (McIlwraith, 1984a; McIlwraith, 1984b; McIlwraith et al., 1987).

Arthroscopic procedures involving extensive curettage and debridement of articular cartilage and subchondral bone will invariably result in generation of loose debris within the joint (McIlwraith, 1984b). This debris can be recognized radiographically. Reports in human medical literature implicate debris as both
an inflammatory stimulus and a mechanical abrasive in the pathogenesis of osteoarthrosis (Evans et al., 1980a; Meachim et al., 1979). Synovial membrane cells have a tendency to engulf cartilaginous and bony particles (Evans et al., 1984; Meachim et al., 1979). This cellular activity results in metaplastic changes in the synovium, production of abnormal synovial fluid constituents, and synovitis (Tew, 1982). Cartilage particles also stimulate synovial cells or macrophages to produce neutral proteases resulting in the enzymatic depletion of cartilage matrix (Evans et al., 1981). Abrasive action of cartilaginous particulate matter results in further liberation of "wear" particles. Recently, the combination of intra-articular injections of homogenized autogenous cartilage particles, partial thickness cartilage biopsy, and exercise resulted in degenerative joint disease in horses (Hurtig, 1988).

Use of intraoperative radiographs, careful debridement, and efficient methods of lavage will result in minimal debris remaining within the joint after an arthroscopic procedure (McIlwraith, 1984b). At the Oregon State University Veterinary Teaching Hospital (OSU-VTH), during a period from January, 1983 to August, 1986, the overall incidence of radiographically recognizable osteochondral debris in the carpal joints of postarthroscopic equine patients was excessive. The primary objectives of this study were to evaluate the effects of implanted autogenous osteochondral fragments, intended to mimic operative debris, on the various physical parameters of normal joints over time (6 months). Four osteochondral fragments removed from the lateral trochlear ridge of the talus were placed under arthroscopic visualization into a middle
carpal joint via an egress cannula. A schedule of regular exercise, intended to mimic the onset of a conditioning program, was initiated during the latter stages of the postoperative period. The ultimate fate of implanted fragments and their effect on synovial fluid, synovial membrane, and cartilage surfaces was determined by this study.

This experiment was designed to provide some answers to a clinical problem. Implantation of osteochondral fragments was performed to mimic debris created during debridement of articular surfaces, which was not successfully lavaged from the joint at the end of the surgical procedure. Simple, direct questions to be answered by the experiment were: 1) What is the fate of the fragments; 2) What are the effects on the structures in the joint, and 3) If detrimental effects are noted, what would be the preferred method to deal with the debris or prevent its occurrence in future procedures.

Admittedly, I expected this experiment to confirm the accepted belief that osteochondral debris remaining within a joint following surgery was insignificant. A review of literature pertaining to the incidence, fate, and effects of intra-articular "loose bodies," and the results of this study provided surprising information which refuted my original postulate, and validated the significance of these fragments.
LITERATURE REVIEW

This review will first briefly describe the normal features of equine carpal bones, synovial lining, and articular cartilage; and subsequently review the incidence, pathogenesis, and treatment of fractures in this set of joints. Prevalence of degenerative change associated with intra-articular fractures dictates the need to summarize current concepts of degenerative joint disease, including inflammatory response of the synovial lining, development of articular lesions, and their potential for repair.

A review of the incidence, development, and fate of joint loose bodies and fragmented debris, both in the natural and experimental settings, should provide information regarding the reaction of articular structures to their presence, and their role in the pathogenesis of degenerative joint disease.

Anatomy of the Carpus

Diarthrodial or synovial joints consist of two or more articulating surfaces of bone covered by cartilage, a joint capsule, and a joint cavity (Clyne, 1987). The carpus is the collective name for the arrangement of bones forming a set of joints in the forelimb of the horse. It consists of seven, occasionally eight, and rarely nine carpal bones arranged in two rows, forming three major joints by virtue of their articulation between themselves, the radius proximally, and the metacarpal bones distally (Ford et al., 1988; Shively, 1982). The antebrachial
joint, acting as a ginglymus (Getty, 1975), is most proximal and is formed by the radius, fused ulna, and a proximal row of carpal bones. These bones are the os carpi radiale (radial carpal bone), os carpi intermedium (intermediate carpal bone), os carpi ulnare (ulnar carpal bone), and os carpi accessorium (accessory carpal bone) (Ford et al., 1988). The middle carpal joint, composed of numerous intracarpal joints (Shively, 1982), also functions as a ginglymus (Getty, 1975). It is formed by the proximal and distal row of carpal bones described from medial to lateral as os carpal II (2nd carpal bone), os carpal III (3rd carpal bone), and os carpal IV (4th carpal bone). Occasionally, os carpal I, and even more rarely, os carpal V are observed in the distal row. The carpometacarpal joint, a collective name for the plain joint formed by the distal row of carpal bones and metacarpal bones, os metacarpales II, III, and IV, represents the most distal joint of the collective carpus.

The antebrachial and middle carpal joints are the most mobile during flexion and extension of the carpus. The carpometacarpal joint has a much more limited range of motion during these activities.

Soft tissue and ligamentous support of the carpus is extensive. The fibrous layer of the joint capsule is common to all joints. Dorsally, this layer attaches to the articular margin of the radius proximally and the metacarpus distally and is referred to as the extensor retinaculum. The palmar fibrous layer is referred to as the palmar carpal ligament. Medial and lateral stability is conferred by the medial and lateral collateral carpal ligaments and an extensive number of ligaments between adjacent bones of the carpus (Getty, 1975).
Synovial membrane confines each joint. The antebrachial joint space is the largest in volume and does not communicate with the two distal spaces. The middle carpal joint space has medial and lateral palmar synovial pouches. It communicates with the carpometacarpal joints through a synovial fenestration between the third and fourth carpal bones. Additional communication routes between these two distal joints occur in 34% of a reported equine population (Ford et al., 1988).

**Anatomy of the Joint Capsule**

The joint capsule is composed of an outer fibrous layer and an inner synovial layer. Fibrous layers are continuous with the periosteum or perichondrium and are composed mostly of dense connective tissue (collagenous fibrils). In combination with the bony configuration of the joint, ligamentous and musculotendinous units combine to provide mechanical stability. This layer is well vascularized and richly innervated. In an inflamed joint, the fibrous layer represents a primary source of painful stimuli (Kellgren and Samuel, 1950).

Synovial membranes are highly vascular modified connective tissues comprised of a lining layer adjacent to the joint space called the synovial intima, and an outer supportive layer referred to as subsynovial or subintimal tissue. On its external surface, the subintimal tissue merges with the fibrous capsule of the joint. Grossly, the normal equine synovial membrane is white or yellowish-white on its internal surface. It is smooth and glistening except for areas where its two layers are formed into villi. Villi, often morphologically very diverse in both normal and disease states, increase the surface area and thus the functional
capability of the synovial membrane. Synovial villi are present in every joint. Their size and number increases with age (Ghadially, 1983). The gross and microscopic appearance of villi are altered in disease states.

The intimal layer is composed of two main cell types: type A and type B; and a third intermediate-type cell referred to as a C cell or AB cell (Ghadially, 1983). These cell types are differentiated ultrastructurally by differences in their internal cellular structure. Morphologically, type A cells resemble macrophages, and type B resemble fibroblasts. However, most authors feel the cells are not distinct, but are variants whose morphology depends on their functional activity (Ghadially, 1983). Type A cells are less common than type B in the equine synovial membrane (Johansson and Rejno, 1976).

Intimal layers are usually 1-4 cells thick, free of nerve endings, other than vasomotor autonomies (Freeman and Wyke, 1967; Halata and Groth, 1976), and are richly supplied with blood vessels and lymphatics. Synovial cells do not form a continuous layer, as spaces or gaps are seen between peripheral boundaries of adjacent cells. Interestingly, synovial intima shows no fundamental morphological differences from joint to joint or in different parts of the same joint, but subintimal tissues do. Subintimal cells can be categorized as adipose, areolar, or fibrous (Castor, 1960).

Synovial membrane functions include: phagocytosis, regeneration, regulation of synovial fluid content, and production of hyaluronic acid. Phagocytic activity of intimal cells has been repeatedly documented from in vivo and in vitro experiments demonstrating endocytotic uptake of particulate foreign
substances placed into the joint or in culture medium (Ghadially, 1983). Morphological response of individual intimal cells, and resultant cellular responses of the cells within the subintima vary depending on the type of foreign substance utilized. Clearly, in vivo, this response is protective with respect to the clearance of potentially dangerous foreign substances from the joint.

Synovial lining cells possess an ability to regenerate after synovectomy. Sequential studies have shown that 30 days after synovectomy, a new synovial membrane has reformed from primitive mesenchymal cells (fibroblasts and macrophages). Membrane continues to mature until 100 days postsynovectomy when it is indistinguishable from normal synovium when examined under the electron microscope (Key, 1925).

Regulation of synovial fluid content relates, in part, to the phagocytic nature of the synovial cells, abundant blood supply of the intimal layers, loose cellular junctions between synovial cells, and synovial cell production of hyaluronic acid. Synovial fluid is essentially a dialysate of blood plasma to which is added hyaluronic acid and a hyaluronate-lining protein produced by synovial cells (Swann, 1978a; Ghadially, 1983). Majority of synovial fluid forms as a result of simple diffusion through the matrix of the synovial intima without significant intervention of any cellular activity or active transport mechanisms. Size of diffusing molecules is limited by the intercellular spaces of the intima (McIlwraith, 1987). Presence of larger molecules such as fibrinogen and prothrombin within synovia is rare and inversely proportional to their molecular weights (Clyne, 1987). Joint capsule distension accelerates transynovial
exchange of all small molecules by increasing intercellular distance. In traumatic effusions, changes in composition and protein content of the synovial fluid have been associated with increased vascular permeability (Simkin, 1979) and increased protein synthesis by the synoviocytes (Roy et al., 1966).

Hyaluronic acid is a glycosaminoglycan (repeating-disaccharide units composed of sodium glucuronate and N-acetyl glucosamine) forming a polysaccharide with a molecular weight of 1-2 million daltons. Production of hyaluronate probably occurs in all cells of the synovial membrane (Ghadially, 1983). Evidence exists to support type A cell (Ghadially and Roy, 1969) and subintimal cell layer production of hyaluronic acid (McIlwraith, 1987). In synovial fluid, hyaluronic acid is organized into aggregates possessing a molecular weight of about 10 million daltons (Swann, 1978). Hyaluronic acid imparts viscosity to joint fluid. Aggregations of hyaluronate molecules arranged along the synovial cell layer act as a molecular "sieve" by virtue of their numerous ionic charges (Ogston and Phelps, 1961).

Hyaluronate acts as the boundary lubricant of the synovial membrane (McIlwraith, 1982). A theory of hyaluronic acid being the primary lubricating compound for the cartilage on cartilage interface has been disproved. Swan and Radin (1972) postulated, then subsequently isolated a specific lubricating glycoprotein, LGP-1 thought to be responsible for this function. Speculation still exists in support of a lubricating glycoprotein that binds with hyaluronate to lubricate the cartilage interface (Clyne, 1987).
Articular Cartilage Structure

Articular cartilage is an avascular, alymphatic, aneural tissue which covers articular ends of bones (Ghadially, 1983). Equine articular cartilage is hyaline in nature, composed of cartilage cells (chondrocytes) scattered in a matrix of collagen fibers and intercellular substance. Thickness of articular cartilage varies between joints, areas within joints, and between species. (Moss and Moss-Salentijn, 1983). Chondrocytes are the only living matter in cartilage, occupying about .01-.1% of the volume of the tissue. Histologically, chondrocytes are arranged in four zones or layers parallel to the surface. Superficially, the tangential layer is characterized by flat or ovoid chondrocytes and tangentially oriented collagen fibers. The intermediate or transitional layer contains larger chondrocytes which may be single or paired amongst obliquely-oriented collagen fibrils. Next, the radiate layer contains large chondrocytes arranged in vertical columns, separated by thicker collagenous fibrils also having a vertical arrangement. The calcified cartilage layer is composed of mineralized cartilage and few chondrocytes in various stages of degeneration. A histologically visible "tidemark" divides radiate layers from a the layer of calcified cartilage. The calcified layer rests on the underlying subchondral bone at a junction termed the "cement line."

Intercellular matrix is composed of collagenous fibrils in amorphous ground substance. Collagen fibers are tightly arranged parallel to the surface in the tangential zone, to withstand the shearing stresses concentrated near the surface. In deeper layers, collagen is arranged obliquely and vertically to
Collagen in articular cartilage is type II, accounting for about 75% of dry weight of immature cartilage, decreasing to about 50% in aged cartilage. Procollagen is synthesized and extruded by chondrocytes. Cleavage by extracellular procollagen peptidases and further cross-linkage between fibrils results in the final collagen fibers (Clyne, 1987).

Ground substance of cartilage is composed primarily of proteoglycan units and water. Proteoglycan macromolecules consist of numerous subunits or monomers. Subunits consist of a protein core with many attached glycosaminoglycans. Glycosaminoglycan is a chain of repeating disaccharide units, including chondroitin or keratin sulphate. Sulphate and carboxyl groups on these repeating units become arranged in solution and confer a high concentration of negative charges to the proteoglycan molecules. Subunits bind to hyaluronic acid by link proteins to form large aggregates with molecular weight up to 250 times that of a single monomer (Muir, 1980). The polyanionic charges of the proteoglycans repel each other, yet at the same time attract a hydration shell. Aggregates have large hydrodynamic size in solution, because a single monomer may entrain 50 mls of solvent per gram of solute (Myers and Mow, 1983).

Water, proteoglycans, collagen, and other cartilage components combine to impart cartilage its macroscopic properties. Collagenous fibrils have great tensile strength, but fail under compressive loads. Osmotic or swelling pressure is determined by the amount of water imbibed by the proteoglycans. Collagen withstand compressive forces (Clyne, 1987).
meshwork functions to retain and restrain the proteoglycans and their hydration shells, providing cartilage with its resilience and load-bearing properties. Cartilage is a tissue under tension; full tensional stress being borne by collagen fibrils when cartilage is in a non-loaded state. Tensile stresses are relaxed or relieved as soon as the tissue is loaded, as in weight bearing (Maroudas, 1980). Compressive loads are opposed by material swelling pressure.

Articular cartilage is avascular, its nutrition being derived from synovial fluid. Intermittent pressure created by interaction of opposing articular surfaces facilitates diffusion of fluid through cartilage, providing nutrition and the removal of metabolic by-products (Van Sickle and Kincaid, 1970).

Fractures of the Equine Carpus

Incidence of Fractures

Fractures of carpal bones are commonly reported in all breeds of racehorses. Most occur on the dorsal surface of this set of joints. Types of described fractures include: chip or osteochondral fractures involving one joint surface, slab fractures in which two joint surfaces are involved, and comminuted fractures. Chip fractures are classified as complete or incomplete, and displaced or nondisplaced. Slab fractures often occur in a frontal plane, but sagittal fractures have been described (Gertsen and Dawson, 1976; Palmer, 1986b). Slab fractures can also be further characterized by their degree of displacement.
Common sites of fracture within the carpus include the radial, third, and intermediate carpal bones, and the distal radius. Often, incidence of fracture type, site, and limb involvement (right or left), are correlated with the breed of racehorse. However, type of racing, direction, and type of gait more accurately account for these correlations. Various studies generally support the premise that the middle carpal joint is most often affected, yet in one large report radiocarpal joint fractures comprised a majority (McIlwraith et al., 1987).

Clinical diagnosis of fractures in the carpus is based upon history of lameness, clinical evidence of lameness, response to flexion tests, palpable pain, and joint effusion. Occasionally, synovial fluid analysis and intra-articular anesthesia may support a clinical diagnosis. Carpal radiography is necessary to confirm the presence, size, and location of fracture fragments. Secondary degenerative changes within a joint may also be radiographically apparent, although presence or absence of changes may not always correlate with findings of surgery or necropsy. Views taken from various angles are required for a complete and thorough radiographic exam; at least five different radiographic views are generally recommended. These include the dorsopalmar, lateromedial, dorsolateral-palmaromedial oblique, dorsomedial-palmarolateral oblique, and flexed lateromedial (Park et al., 1970; O'Brien et al., 1970; Burguez, 1984). Two additional views, 30° dorsoproximal-dorsodistal (30° flexed), and 60° dorsoproximal-dorsodistal (60° flexed), commonly referred to as the "skyline" views, have been recommended to diagnose and confirm nondisplaced slab fractures and to assist evaluation of trabecular pattern of the
third carpal bone (Fischer and Stover, 1987; DeHann et al., 1987).

Park et al. (1970) evaluated 149 individual fractures on 99 limbs in 73 Thoroughbreds and Quarterhorses. The middle carpal joint had the highest incidence of fracture frequency, and the radial carpal bone was most commonly affected. Fractures of the distal medial aspect of the radial carpal bone represented one third of all fracture types. The right carpus was more commonly affected than the left. Slab fractures also occurred more commonly in the right carpus. Similar fractures were present in 19.3% of both carpi in this group of the horses. The authors postulated that conformation and weight-bearing stresses played a prominent role in these fracture types.

In another report, fractures of the carpus were the cause of lameness in 57 of 90 carpal examinations (O'Brien et al., 1970). The distal radial carpal bone was most commonly affected in both Quarterhorses and Thoroughbreds, followed by the proximal aspect of the third carpal bone in Thoroughbreds. This study also demonstrated the radiographic appearances of intra- and extracapsular distension and its association with intra-articular pathology.

Larsen and Dixon (1970) reviewed 153 cases of carpal lameness in racehorses, and found fractures in 39 horses. The left carpus was most commonly affected, and the intermediate carpal bone most often fractured. Six of 39 horses reviewed had bilateral carpal fractures.

Conclusions regarding breed and site predilection were made by Thrall et al. (1971) in a review of carpal fractures in 371 horses undergoing carpal radiographic examination over a five-year period. They determined 56.7% of
Thoroughbreds radiographed had at least one chip fracture, compared to 29.7% of Quarterhorses studied. In Thoroughbreds, the most frequent fracture site was the distal radial carpal bone (31.7%), followed by the third carpal bone (20.3%). In Quarterhorses, the distal radial carpal bone was affected 42.1% of the time, followed by the distal end of the radius (18.4%).

Lindsay and Horney (1981) reviewed and reported 89 cases of carpal fracture treated by arthrotomy. Majority of horses were Thoroughbreds, and the left carpus was most commonly involved. The third carpal bone was most often fractured, followed by the radial carpal bone and distal radius. The right limb had an even distribution of radial and third carpal fractures. Chip fractures of the third carpal bone were more likely to occur on the left leg, whereas slab fractures were more common on the right. Postoperative results of this study indicated that fractures in the middle carpal joints had a reduced prognosis for return to successful racing; compared to fractures of the radial carpal joint.

Palmer (1986a) reviewed carpal fractures in 211 Thoroughbred and 75 Standardbred horses. The most common site for fractures in the Thoroughbred was the distal aspect of the radial carpal bone, with the majority located in the right carpus. Standardbreds were most commonly affected on the proximal aspect of the third carpal bone. Slab fractures in Thoroughbreds occurred more frequently in the right carpus. The majority of fractures in the left limb occurred in the radiocarpal joint. The author also described the presence of "opposing chip fractures" located on the distal aspect of the radial carpal bone and proximal aspect of the third carpal bone, and the distal radius and proximal
aspect of the intermediate carpal bone. Fourth carpal slab fractures in five horses were described by Auer et al. (1986). Three horses also had associated fractures of the intermediate carpal bone. Rotational moment at the time of weight-bearing impact was thought to be responsible for this unusual type of fracture.

Fischer and Stover (1987) described 12 cases of sagittal fractures of the third carpal bone. A 30° dorsoproximal-dorsodistal oblique projection was necessary to diagnose these fractures. Seven of the horses returned to their previous usage after being managed conservatively.

McIlwraith et al. (1987) published observations and results of arthroscopic surgery on 1,346 carpal chip fractures in 591 horses. Most of the horses were Thoroughbred or Quarterhorse racehorses. The distal radial carpal bone was the most common site of fracture for both breeds. This finding agrees with those of Thrall et al. (1971), Park et al. (1970), and Palmer (1986a), but contrasts with that of Wyburn and Gould (1974) where the third carpal bone was reported to be more commonly fractured. McIlwraith did not confirm a different incidence of fractures within the radiocarpal joints of the left and right forelimbs, but fractures of middle carpal joints occurred more frequently in the right forelimb.

Third carpal bone injury was assessed in a recent study by DeHann et al. (1987). They advocated at least seven views of the carpus, including two skyline views, in order to accurately assess the joints and evaluate the third carpal bone for radiographic appearance. Fractures and morphologic abnormalities were
confined to the radial fossa. The presence of bony sclerosis or osteolysis was considered to be a pathologic change in the bone.

The study involving the most animals reports a total of 1,852 horses with carpal fractures admitted to 14 veterinary teaching hospitals from 1979 to 1987 (Hayes, 1988). Third carpal bone fractures occurred most frequently in the Standardbred, comprising 79% of all fractures, with Thoroughbreds and Quarterhorses having third carpal fracture incidences of 44 and 32%, respectively, of all carpal fractures.

Schneider et al. (1988) classified 371 third carpal fractures in 313 horses into 8 different categories. Incidence of each type varied significantly between Thoroughbreds and Standardbreds. Over 10% of these fractures were identified only on the skyline radiograph, thus attesting to the importance of this view.

Pathogenesis of Equine Carpal Fractures

Trauma associated with repeated axial compression during exercise is responsible for intra-articular fractures. However, soft tissue fatigue, supraphysiologic exertion, detrimental racing surfaces, improper trimming, and conformational abnormalities represent factors which could alter the ability of the carpal joints to successfully transmit forces from the radius to the metacarpus without the risk of injury.

Individual carpal joints show some unique differences in mobility. The radiocarpal joint is a rotary hinged joint whose normal range of motion is
limited by the palmar joint capsule and the flexor muscles resisting overextension (Bramlage, 1983). Intercarpal joints are hinged, and by virtue of the palmar joint capsule and collateral ligaments are not prone to overextension. Numerous additional articulations exist between carpal bones. These are supported by intercarpal ligaments. Carpal bone arrangement and intercarpal articulations dissipate the axial weight-bearing load through medial to lateral displacement of the carpal bones, enabling some of the load to be accepted by the intercarpal ligaments. This anatomical feature enables force attenuation to occur during weight-bearing with the limb in full extension, reducing excessive bone impaction (Bramlage et al., 1988).

Carpal bones play a major role in the process of load dissipation. Articular cartilage was once thought to be the shock absorbing tissue of the joint. Recent studies have shown subchondral bone to be more important in absorbing load across a joint (Ghadially, 1983). Studies have been performed in the equine carpus which quantitate areas of stress concentration. Turner and Colahan (1987) have demonstrated, through in vitro use of pressure sensitive film, 25 areas of stress concentration within the carpal articulations. Sites of highest stress concentration were the dorsal articular aspect of the radial, intermediate, and third carpal bones. These sites correspond to areas of highest fracture incidence.

Efficiency of the intercarpal ligaments to dissipate axial compressive forces, and ability of palmar soft tissue structures to prevent joint overextension, require adaptation of these structures to the maximal stress of exercise.
Training induces physiologic adaptation. Failure of soft tissues and intercarpal ligaments associated with training results clinically in mild lameness and inflammation (heat, swelling) commonly referred to as "carpitis." Subtle inflammatory changes may be apparent radiographically on the dorsum of the carpal bones, and correspond to the areas of ligament and joint capsule attachment.

With training, cuboidal bones undergo a process of osteolysis and remodelling of trabecular pattern as an adaptation to stress. Failure to adapt at an adequate rate, compounded by continuing exercise, will result in fatigue damage, microcracking, interface debonding, and microfractures of the subchondral bone (Carter and Hayes, 1977). Indeed, surgically removed carpal fractures of an acute nature were found to have histologic changes similar to fractures of chronic duration (Pool, 1989). Adaptive changes within the carpal bones is the basis for reports on the radiographic and histologic changes seen in third carpal bones of horses subjected to race training (O’Brien et al., 1985; DeHann et al., 1987). O’Brien (1985) has recognized loss of osseous density and the development of sclerotic, irregular, trabecular pattern in third carpal bones of some horses. During the artificial situation of horses being subjected to continuous maximal exercise without adaptation, cumulative effects of mechanical stress may result in injury to the carpal bones (Bramlage et al., 1988).

* Pool RR, 1989 Personal Communication.
Acute trauma, in the form of maximal supraphysiologic exercise, can result in fractures. Specific areas of the carpus are more predisposed to this type of lesion. Likewise, chronic compressive loading results in progressive pathologic changes and fractures in other areas more susceptible to cyclic loading.

Fatigue of the joint capsule and palmar soft tissue allows overextension of the radiocarpal joint, which impacts the proximal row of carpal bones on the distal radius. Incidence of distal radial fractures is highest where a prominence on the craniolateral aspect of the radius impacts on the proximal aspect of the intermediate carpal bone. "Kissing" lesions of the intermediate carpal bone occur at a lower incidence.

The hinged intercarpal joint experiences the highest frequency of fractures in the distal aspect of the radial carpal bone and the proximal aspect of the third carpal bone. Chronic cyclic loading is a characteristic of this joint because of its tight fitting anatomy and lack of overextensibility. The radial carpal bone impacts the third carpal bone during loading of the limb in the close packed, extended position (Bramlage et al., 1988). Middle carpal joint stresses are greatest on the medial aspect of the outside limb when a horse is negotiating a turn. The medial position of the radial facet subjects it to larger forces during exercise, accounting for the highest incidence of fractures in this area of the third carpal bone.

Most studies report the highest incidence of carpal fractures to occur in younger horses. The racing population is skewed toward 2- and 3-year-olds. At
this age, skeletal immaturity and the speed at which these horses perform, predisposes them to carpal fractures (Schneider et al., 1988).

Difference in breed incidence of carpal fractures is thought to be related to their gait and length of race. Thoroughbreds have a higher incidence of fracture in the right forelimb. This relates to increased magnitude of stress on the medial side of the outside (right) leg when in the turn racing counterclockwise. Thoroughbreds also maintain the right lead at the end of racing, a time when fatigue, overextension, and exertion are characteristically maximal. At a gallop, each limb supports the entire weight of the animal at some point. Forces are maximal within this limb. Conversely, the Standardbred, at a trot or pace, has a gait that allows forces to be more balanced. There is always a rear leg supporting some of the horse’s weight when the front limb is loaded in the close-packed position (Schneider et al., 1988). On the turn, the medial aspect of the outside leg, and the lateral aspect of the inside leg, still experience higher forces, but the order of magnitude is less. Standardbreds have been found to have a higher incidence of third carpal fractures. Quarterhorses exhibit maximal exertion over a short distance, without the effect of turns. They are more susceptible to the distal radius fractures associated with acute trauma.
Pathophysiology of Intra-Articular Fractures

Intra-articular fractures can compromise joint stability, resulting in degenerative processes in the joint. Slab and comminuted fractures of carpal bones result in maximal joint instability, with resulting pain and loss of function (lameness). Degree of instability associated with small, discrete chip fractures appears minimal, prompting consideration of other mechanisms responsible for pain, lameness, and progression of degenerative signs within such joints.

Carpal chip fractures, even those involving minimal articular surface, have the potential to induce some degree of joint compromise. Pain and lameness result from direct and indirect synovitis and capsulitis. Cartilage, lacking nerve endings, plays an indirect pathophysiologic role. Fractures result in damage to adjacent and opposing articular cartilage, and the degree of displacement will correlate with extent of physical trauma. Fracture sites and damaged adjacent articular cartilage liberate debris and enzymes irritating to the synovium and cartilage surface (Bramlage, 1983; McIlwraith, 1987). Continued exercise will induce a self-perpetuating cycle of degenerative changes characterized by synovitis, capsulitis, and cartilage destruction.

Sources of pain associated with intra-articular fracture warrant attention. Osteochondral (chip) fractures are most often attached to the extensively innervated joint capsule, and movement associated with a loosely attached fragment stimulates local nerve endings. Osteochondral fractures, by definition, involve some degree of subchondral bone damage, and non-
myelinated nerves, present within subchondral bone, represent an additional source of direct pain (Pool, 1989). Increased subchondral bone pressures have been documented as a source of pain in the cuboidal bones of the equine tarsus (Sonnichsen and Svalastoga, 1985). Chronic pathology within the subchondral areas of the third carpal bone in association with chip fractures (Bramlage et al., 1988; Krook and Maylin, 1988; O'Brien et al., 1985; DeHann et al., 1987) may be indicative of increased bone pressure and associated pain.

Treatment of Carpal Chip Fractures

Surgical and nonsurgical methods have been used for the treatment of carpal chip fractures. Nonsurgical management involves supportive bandaging, stall rest and limited exercise over a 3-6 month period, radiographic monitoring of the healing process, and the judicious use of intra-articular therapy. Nonsurgical management of carpal fractures has been advocated for smaller fractures minimally displaced from the parent bone; the assumption being these type of fractures are more likely to heal and less likely to induce degenerative changes (Meagher, 1974). Healed fractures have the potential for refracture, while production of new bone and capsular damage exists within the affected joint (Bramlage, 1983). Final decision on the most acceptable method of therapy is dependent upon the size of the fragment, degree of displacement, amount of involved articular surface, presence and degree of degenerative changes within the joint, value, and future potential of the horse (Auer, 1980;
Meagher, 1974; McIlwraith, 1987). Fracture displacement may not significantly affect prognosis for future racing (Speirs, 1986) and may be inversely correlated to the resultant degree of degenerative joint disease (Auer, 1980).

Indications for surgical treatment of carpal osteochondral fractures are to restore athletic function, and prevent the further development of degenerative joint disease (Bramlage, 1983; McIlwraith, 1987). The technique of carpal arthrotomy and osteochondral fragment removal has been described (Stashak, 1987; Larsen and Dixon, 1970; Meagher, 1974; Wyburn and Goulden, 1974; Lindsay and Horney, 1981).

Future racing performance as a predictor of the success of arthrotomies in the treatment of carpal fractures has been reviewed by a number of authors. Stashak (1987) stated the prognosis for surgical treatment of selected carpal chip fractures was good; 75-80% of operated horses returning to successful racing. Wyburn and Goulden (1974) reported 25 of 32 horses (78%) started in at least 1 race after surgery, but decreased race earnings were reported for these horses. Lindsay and Horney (1981) reported 48 of 58 (83%) Thoroughbred horses subjected to arthrotomies to remove chip fractures returned to racing. Thirty of these 48 (62%) dropped in class, 12 (25%) returned to their original form, and 6 (12%) improved their previous level of performance. In these studies, fractures of the distal margin of the radial carpal bone and slab fractures of the third carpal bone appeared to have the least favorable prognosis. Chip fractures associated with the proximal margin of the radial carpal bone and the intermediate carpal bone had a better prognosis. These fractures demonstrated
less associated articular cartilage damage, subchondral bone changes, or periosteal new bone growth.

Dixon (1981) examined the effects of application of $^{60}$Co gamma radiation after carpal surgery on post-surgical racing performance. He compared two groups matched for age, sex, site of lesion, previous racing starts, and performance. Of 14 treated with carpal surgery alone, 71% returned to racing. Of the 26 horses in the irradiated group, 92% returned to successful work. The irradiated horses raced more often and placed more frequently when raced. Improved performance associated with irradiation was theorized to be attributed to reduced periostitis, fibroplasia, and neovascularisation.

Speirs and Anderson (1986) reviewed and compared the post-surgical racing records of 210 Thoroughbred racehorses to the performance of 840 matched controls. Operated horses were significantly inferior ($P < 0.01$) to controls in terms of number of races run and performance. Incidence of carpal arthritis was also more prevalent in operated horses. In this study, type of fracture and degree of displacement did not have a significant effect on assigned indicators of racing performance.

Retrospective studies on the racing performance of horses treated for slab fractures of the third carpal bone report a lower percentage of horses returning to racing. Martin et al. (1988) reported on 31 cases of third carpal slab fracture in which 21 (67.7%) raced again after recovery. Performance level of these horses was determined to be decreased 50% as judged by claiming value. Stephens et al. (1988) surveyed third carpal slab fractures in
Standardbred and Thoroughbred horses over a 7-year period. Post-fracture race records were obtained for 72 Thoroughbreds and 61 Standardbreds. Treatment method distribution was similar in both breeds. The effects of treatment on outcome were not significant. In Standardbreds, 77% of the horses raced after surgery, including all 38 horses with racing starts prior to fracture. In Thoroughbreds, 65% raced after surgery. Earnings per start declined in both breeds.

The value of carpal surgery has been assessed in various ways. Comparisons have been made based on treatment method (Wyburn and Goulden, 1974; Dixon, 1981; Pendergast, 1974), pre- and post-operative performance (Lindsay and Horney, 1981), sites of fracture (Lindsay and Horney, 1981), breed (Stephens et al., 1988), and post-surgical performance of treated horses and a control group (Speirs et al., 1986). Comparison of these studies to assess the value of surgery is difficult. An ideal study would include two matched groups of horses with similar lesions, differing only by the method of surgical treatment. Even if such a grouping were possible, additional variables include: 1) the degree of associated degenerative joint disease, 2) innate ability of the horse to perform ("heart"), 3) surgeon differences, and 4) postoperative rehabilitation. Failure to match or provide controls for these variables results in uncertainty. Retrospective studies remain the most available sources of information.

Desire to minimize soft tissue trauma and convalescence time has resulted in utilization of arthroscopic techniques for treatment of osteochondral
fractures of the carpus.

**Arthroscopic Surgery for the Treatment of Carpal Osteochondral Fractures**

Arthroscopy involves the use of a small fiberoptic telescope inserted into a joint space through a stab incision to visualize the interior of the joint cavity. A constant flow of balanced electrolyte solution through the protective sleeve of the arthroscope distends the joint. Surgical instruments are inserted into the joint through a second stab incision. The surgeon must coordinate a view through the scope or video monitor with instrument manipulation in a process called triangulation.

In the last 10 years, equine arthroscopy has developed from being a diagnostic technique used by only a few veterinarians, to the accepted method of performing joint surgery (McIlwraith, 1990). One university veterinary teaching hospital estimates 90% of all joint surgery is performed arthroscopically (McIlwraith, 1984a). Techniques for removal of osteochondral fragments from the carpus, using arthroscopic surgery, have been described (McIlwraith, 1984; McIlwraith, 1990; McIlwraith and Martin, 1984; McIlwraith et al., 1987). Benefits of arthroscopic surgery include increased diagnostic accuracy, less tissue damage and improved cosmetic appearance of the joint, more complete irrigation of the joint and elimination of debris, decreased post-operative pain, ability to operate multiple joints concurrently, and improved performance after surgery. Earlier return to race training is considered to be another advantage of arthroscopic surgery over traditional arthrotomy techniques (McIlwraith et al., 1987).
Arthroscopic examination of carpal joints is indicated for diagnostic, prognostic, and treatment procedures of carpal joint injuries (McIlwraith, 1990). Although, arthroscopy is most commonly used for treatment of osteochondral fractures within equine carpal joints, diagnostic and/or surgical arthroscopy has been adapted for use in most joints of the equine appendicular skeleton.

In contrast to studies involving carpal arthrotomy, the number of retrospective studies on equine carpal arthroscopy are minimal. However, absolute case numbers reported in one study attest to the advantages of this technique. McIlwraith et al. (1987) and McIlwraith (1990) present the results of arthroscopic removal of osteochondral fragments from 1,000 carpal joints of 591 horses over a 3 1/2 year period. Incidences of fracture type and associated breed were presented. The author felt arthroscopic surgery was an effective technique for removing fragments, rating functional ability and appearance of the limbs as excellent. Postsurgical performance was able to be assessed in 445 of the operated horses. After surgery, 303 (68.1%) raced at a level equal or better than their preinjury level. If success was based upon a return to racing, success rate would be at least 88.6%. The authors were also able to correlate degree of cartilage damage present at surgery with ability to return to racing at an equal or improved level. They showed minimal articular defects were not the limiting factor in a horse's return to racing, and overall did not affect success rate. Horses with severe cartilage damage returned to compete successfully, but over a shorter overall time duration. This effect could be related to removal of offending fragments, and beneficial effect in joint function.
Degenerative joint disease (DJD), or osteoarthrosis, is defined as an intrinsic disorder of diarthrodial joints, hallmarked by varying degrees of destructive lesions within the articular cartilage. Additional structures involved in the genesis of the condition are the synovial membrane, synovial fluid, subchondral bone, and joint capsule with its periarticular attachments. Involvement of these other closely associated structures invariably results in some degree of joint dysfunction. Articular cartilage destruction may not be the initial abnormality in osteoarthrosis, but its demonstrable presence is a prerequisite for the eventual diagnosis of DJD.

Numerous reviews have been published regarding the pathogenesis of degenerative joint disease in the horse (MacKay-Smith, 1962; Raker, 1966; Betley, 1980; McIlwraith, 1982; McIlwraith, 1987; Clyne, 1987; McIlwraith and Vachon, 1989). More recent studies cite extensive in vitro experimental studies and extrapolate from studies involving the pathogenesis of the condition in humans. Despite an abundance of information, assignment of stepwise pathogenesis in the equine remains unclear. Difficulty associated with this task relates to the multiplicity of morphological events leading to joint dysfunction. Defining pathogenesis of degenerative changes associated with intraarticular
fractures may present a less difficult task, as it appears the story begins at, or prior to, the occurrence of intra-articular fracture. Even with such a defined incident, many questions still remain unanswered (Dyson, 1987).

McIlwraith and Vachon (1988) list intra-articular fractures as one category of primary joint problems leading to type 4 or secondary degenerative joint disease. By definition, osteochondral fractures involve some degree of articular cartilage damage. Extent of cartilage damage associated with carpal bone fracture is not well correlated to degree of clinical signs. However, cartilage damage may determine degree of degenerative change in other tissues of the joint which more closely correlate to clinical manifestations of osteoarthritis. If articular defects are minimal at fragment removal, they will not represent limiting factors to the horse’s return to racing. More severe cartilage damage appears to limit duration of racing career (McIlwraith et al., 1987).

Significance of intra-articular fractures should be considered from two different perspectives. Use-trauma is considered a central etiologic concept initiating degenerative joint disease (McIlwraith and Vachon 1989). Within this context, intra-articular fractures would be considered to occur secondary to trauma, and as such, may represent the initial event in a complex series of steps leading to DJD. However, it is possible the fracture represents an additional progression of a continuing series of chronic degenerative articular changes. Within this context, one must consider osteochondral fragments derived from fractured osteophytes (Clyne, 1987), and fractures of previously abnormal
subchondral bone and overlying cartilage secondary to excessive use-trauma; a so called pathologic fracture or, fracture secondary to chronic chondro-osseous necrosis (Krook and Maylin, 1988).

Cartilage damage associated with intra-articular fractures is possible through a number of mechanisms: 1) damage directly resulting from fracture extension into adjacent cartilage; 2) continued exercise and an unstable fragment (as a loose body or locally mobile in its fracture bed) resulting in mechanical abrasion of adjacent and opposing cartilage surfaces; 3) depending on size and location, fracture presence could lead to joint instability and degenerative trauma to specific areas of the joint; 4) release of small osteochondral, bony, or cartilaginous fragments from the fracture site could lead to direct mechanical cartilage damage (Hurtig, 1988) or damage secondary to induced synovitis (Chrisman et al., 1965; Hurtig, 1988; Evans et al., 1984; Clyne, 1987); 5) indirect cartilage damage secondary to the synovitis which may occur if the fracture fragment has significant attachment to the joint capsule (McIlwraith, 1987).

Biochemical Changes Associated with Degenerative Joint Disease

Integrity of matrix macromolecules imparts mechanical properties to intact articular cartilage (Hamerman, 1989). Direct trauma to chondrocytes results in a wide array of biochemical and structural changes. Structurally, although collagen content does not decrease in damaged cartilage, as measured
quantitatively by hydroxyproline content, variation exists in the quality of collagen produced by the chondrocytes. Damaged chondrocytes synthesize normal type II collagen chains, but also substantial amounts of type I collagen (Nimni and Deshmukh, 1973). Type I collagen, inferior as a functional component of articular cartilage, is associated with skin, bone and reparative fibrocartilage (Mankin, 1974). Weiss (1973) utilized electron microscopy to demonstrate increased diameter and variation in the normal distribution of the collagen fibers.

In animal models and human clinical cases, increased hydration of cartilage occurs early in the degenerative process. This finding relates to alteration in the normal network of collagen fibers and increased binding of water molecules to altered collagen (Mankin, 1974; Clyne, 1987; Hamerman, 1989). Changes in collagen network and dilution of proteoglycan content lead to functional deterioration of the matrix (Hamerman, 1989). Glycosaminoglycan loss may also be associated with leakage from a primary physical defect in cartilage (Maroudas et al., 1973). Investigators have detected decreases in at least one glycosaminoglycan in osteoarthritic cartilage; a decrease directly related to morphological severity of disease (McIlwraith, 1982). Increased chondrocyte production of proteoglycan represents an attempt to replace lost material, but newly synthesized proteoglycans are of lower molecular weight, have an altered glycosaminoglycan composition, and do not readily form aggregates (Clyne, 1987). Mechanical stress on abnormal cartilage produces more deformation, less elastic return, and increased contact pressure on the
subchondral bone (Radin and Rose, 1986), leading to fissures of cartilage surfaces (Hamerman, 1989).

Direct cartilage trauma results in increased production and release of lysosomal enzymes from chondrocytes. Increased levels of neutral metalloproteases were found in fibrillated cartilage (Martel-Pelletier et al., 1988). An acid cathepsin present in the lysosome has been shown to have powerful in vitro hydrolytic activity on the protein core of the proteoglycan. However, its greatest activity exists in the unphysiological range of pH 4, resulting in some question regarding its role in clinical disease. Collagenase activity has also been found in osteoarthritic cartilage (Ehrlich et al., 1978).

Although loss of proteoglycans and glycosaminoglycans can occur through the activity of cartilage-derived enzymes, it appears enzyme production from the synovial membrane may be more significant in enzymatic degradation of cartilage components (Torbeck and Prieur, 1979). Synovitis and capsulitis have commonly been implicated in etiological analyses of equine degenerative joint disease (McIlwraith, 1982; Clyne, 1984; McIlwraith and Vachon, 1988). Intra-articular fractures may induce inflammatory changes in joint capsule and synovium, indirectly by synovial response to liberated particles and chemical components of cartilage and subchondral bone, or directly by presence of significant capsular attachment to the fracture. Capsulitis and synovitis may have been occurring prior to the fracture. Inflammation in these structures may be responsible for the production of lysosomal enzymes, prostaglandins, superoxide and hydroxy radicals, and other chemical mediators associated with
degenerative processes involving glycosaminoglycan depletion and chondrocyte damage (McIlwraith and Vachon, 1988).

Lysosomal enzymes derived from cells of the synovial layer include collagenases, hydrolases, and neutral proteases. Enzymes are liberated into the synovial space and have potential to induce proteoglycan and glycosaminoglycan degradation within articular cartilage, or increase inflammatory response within synovium and affect synovial fluid components (Harris et al., 1972).

Prostaglandins, specifically prostaglandin $E_2$ (PGE$_2$), are produced in inflamed joints. Their source is synoviocytes or chondrocytes. Chondrocytes increased their production of prostaglandins when exposed to a media-derived factor of activated synovial fibroblasts (Evans et al., 1986). Prostaglandins are thought to cause a decrease in proteoglycan content of cartilage matrix by their ability to suppress glycosaminoglycan and proteoglycan synthesis, and their direct degradative effect (McIlwraith, 1982).

Inflamed synovial membrane also produces cytokines which have recently been implicated in osteoarthrosis (Hamerman, 1989). Interleukin-1 (IL-1), initially referred to as catabolin, is a soluble substance isolated from synovial cells. Its target cells within joints include other synovial cells and chondrocytes. Interleukin-1 can promote release of collagenase and PGE$_2$ by chondrocytes and synovial cells. It has also been shown to limit formation of Type II collagen in the chondrocyte. When IL-1 is added to in vitro explants of articular cartilage, proteoglycans are immediately released into the culture media (Hamerman, 1989).
Stimpson et al. (1988) demonstrated in vivo exacerbation of arthritis in rat joints previously sensitized to peptidoglycan-polysaccharide after injection of Interleukin-1. Increased response was characterized by a 50% incidence of early pannus formation and erosion of cartilage and subchondral bone.

Morris et al. (1990) identified IL-1 in the synovial fluid of 5 horses with osteoarthritis. This cytokine was implicated in induction and augmentation of inflammatory joint disease by stimulating release and activation of neutral proteases, collagenases, and prostaglandins from synoviocytes and chondrocytes.

A potential role for interleukin-1 in osteoarthrosis has been postulated. As a consequence of multiple factors contributing to articular damage, components of matrix, such as proteoglycans and collagen, enter joint fluid, are taken up by cells of the synovial lining, and induce release of interleukin-1 and other cytokines. These gain access to the cartilage where they promote metabolic functions in the chondrocyte deleterious to matrix integrity, and resultant perpetuation of a destructive cycle (Hamerman, 1989).

Another synovial cell cytokine, tumor necrosis factor a (TNF-a), has been shown to induce chondrocyte-mediated breakdown of matrix proteoglycans, and promote release of collagenase and prostaglandin E₂ by the chondrocytes and synovial cells.

Free radicals also have the potent ability to degrade hyaluronic acid, cartilage proteoglycans, and collagen. They are generated within the synovial space and articular cartilage secondary to inflammation (McIlwraith and Vachon, 1988).
Morphologic Appearance of Articular Degeneration

Intra-articular fractures have potential to incite enzyme systems, chemical mediators, and cellular responses leading to onset or progression of articular degeneration. Morphologic appearance of these changes will be briefly outlined.

Earliest gross pathologic signs of matrix degradation include discoloration, loss of cartilage consistency, and reduction in cartilage resiliency to pressure. Blister formation may follow. Superficial erosions or ulcers are considered to be partial thickness loss of cartilage. Erosions represent full thickness loss of cartilage. Exposure of direct contact on subchondral bone results in a polished, or eburnated bone surface. Wear lines represent partial thickness grooves of cartilage surfaces, oriented in the direction of joint motion. In experimental studies they can be induced by injection of cartilage particles (Hurtig, 1988).

Histologically, the essential lesion is disruption or damage of articular cartilage. Early fibrillation or flaking refers to a disruption of the surface layer (tangential). Fibrillation denotes damage to the tangential and radiate layers, and may be vertically or more commonly horizontally oriented. Deeper lesions manifest themselves as clefts through the full thickness of cartilage.

Cartilage degenerative change involves varying degrees of chondrocyte abnormality. Characteristic response is formation of chondrocyte clusters or chondrones adjacent to damaged cartilage. Clusters arise, not through cell
migration, but by accelerated mitotic index in the adjacent cells. Histochemical staining of degenerative cartilage matrix with safranin-O (Rosenberg, 1971) will demonstrate reduced staining intensity, representing depletion and reduced production of proteoglycan.

Two concepts regarding equine degenerative joint disease are consistent: 1) cartilage destruction is a characteristic finding, although it does not correlate well with clinical signs, and 2) involved articular tissues respond to inciting factors with stereotyped responses for each tissue.

Cartilage changes described as softening, discoloration, fibrillation and fissure formation, have been discussed. Subchondral bone, when subjected to repeated, increasing mechanical stress, will respond with increased osteoblastic stimulation in the form of appositional bone growth. This change has been termed sclerosis and can be recognized radiographically (O'Brien et al., 1985; DeHann et al., 1987). Focal full thickness loss of articular cartilage and direct contact of bone surfaces results in eburation, recognized upon direct visualization of the joint surface. Potential for subchondral cyst formation exists, but appears to be less common in the horse than man.

Circumferential remodeling and osteophyte formation represent proliferative changes of joint margins often associated with instability and subsequent recrudescence of periosteal or perichondrial osteogenic potential. Enthesophyte formation represents focal bone proliferation at the interface of joint capsule or other soft-tissue attachment to bone. Inflammation, usually secondary to trauma, incites this response. Joint capsule may demonstrate
villous hypertrophy, variable degrees of inflammation, fibrosis, and metaplasia of synovial fibroblast cells.

Synovial fluid changes have also been described in association with degenerative joint disease (Tew and Hotchkiss, 1981). Although not specific for DJD, synovial fluid may demonstrate elevated number of inflammatory cells, increased total protein, decreased hyaluronic acid concentration, and increased number of cartilage fragments.

Diagnosis of Degenerative Joint Disease

Clinical signs associated with degenerative joint disease will vary depending on joint involved, clinical entity or type of DJD (McIlwraith and Vachon, 1989), and duration of the condition (McIlwraith, 1982). Usually, there are varying degrees of the following: joint enlargement, reduced range of joint motion, pain after joint manipulation, and impaired function.

Regional nerve blocks or intra-articular anesthesia may be necessary to confirm the affected joint(s). Synovial fluid analysis may also provide additional confirmatory evidence (Tew and Hotchkiss, 1981), although this technique is limited in its specificity. Cartilage fragment analysis by ferrography (Tew, 1980; Evans et al., 1980b) or discontinuous density centrifugation, provides information regarding depth of the articular lesion, but is not able to accurately quantify the extent of articular damage.
Radiographic signs associated with degenerative joint disease of the carpus have been well documented (O'Brien, 1971; McIlwraith, 1987). Features which may be recognized include narrowing or loss of joint space, subchondral bone sclerosis or lysis, osteophyte formation, and periosteal proliferation.

Arthroscopy has been described as an additional diagnostic tool in assessing the degree of degenerative change relative to the cartilage surfaces and synovial membrane (McIlwraith, 1990).

Treatment of Degenerative Joint Disease

Treatment of degenerative joint disease in the horse has been extensively described (McIlwraith, 1987; Clyne, 1987; McIlwraith, 1982; McIlwraith and Vachon, 1988). Multiplicity of pathologic processes and lack of a complete understanding of the pathogenesis preclude provision of specific guidelines for treatment of the condition. McIlwraith and Vachon (1989) have divided principles of treatment into three general areas. The first principle is treatment or prevention of any primary cause. Intra-articular fractures must be removed or allowed to heal before resumption of training or successful application of additional therapies. Soft tissue inflammation (capsulitis or synovitis), potentially contributing to articular degeneration, must next be treated. Rest, physical therapy, anti-inflammatory agents, joint lavage, sodium hyaluronate, and polysulphated glycosaminoglycans may each provide improvement of the problem. Lastly, efforts must be directed toward improvement in the degree of
articular cartilage function. Limited ability of articular cartilage to repair, and lack of medications capable of stimulating this response, make this the most difficult goal. Benefits of medication and surgical modulation to promote cartilage healing are limited, prompting research into resurfacing of articular cartilage defects in order to restore normal joint function. Specific, current modalities are further described by McIlwraith and Vachon (1988).

A Summary of the General Response of Articular Cartilage to Various Forms of Injury

Data suggests under circumstances of chronic injury, chondrocytes are capable of mounting a significant reparative response and can replicate their DNA to form new cells. Chondrocytes in adult cartilage have the ability to increase their rate of matrix synthesis in response to injury (Mankin, 1982). The intrinsic repair of articular cartilage would thus appear to be possible.

Response to injury in vascularized mammalian tissues is phasic, beginning with necrosis, followed by inflammation, and finally repair. All phases are dependent upon vascular supply. As such, response of avascular articular cartilage to superficial or partial-thickness damage will vary from normal wound healing. Cartilage does undergo some degree of necrosis, with cell death and disruption of adjacent matrix at the site of injury. Inflammation of the articular tissue is absent. Lack of blood supply precludes the processes of transudation, exudation, and hematoma formation. A fibrin clot does not form and cannot
assume the role of a structural scaffold. Lack of cellular influx to the injured area, makes cell-mediated repair dependent on existing chondrocytes. These cells are capable of replication and matrix synthesis, but experimental studies have shown a limited potential for repair. If damage extends through cartilage to subchondral bone, all three phases of repair become possible.

Experimental production of superficial lacerations of articular cartilage in joints of animals has been a commonly repeated project. Mankin (1982) cites numerous studies which have identified relatively ineffectual healing response. Repair was characterized by abortive and disappointing attempts on the part of cartilage to add cellular and matrix elements. In mature animals, attempts never successfully healed the defect. Biochemical response, consisting of mitotic activity, matrix synthesis, and increased enzyme levels, remained elevated for up to 2 weeks after the traumatic injury. Long term follow-up of superficial injuries has shown no further healing of the defect, and yet only rare progression to osteoarthritis.

Deep lacerative injuries penetrating to subchondral bone evoke an exuberant healing response attributed to cellular and serum factor influx via the subchondral vasculature. Defects in cartilage ultimately fill with fibrocartilage which has been described as hyaline-like. Mitchell and Shepard recognized the hyaline nature of repair tissue reduced and became more fibrous over time (Mankin, 1982). Additionally, repair tissue may undergo degeneration, or demonstrate increased susceptibility to trauma. Ability to successfully fill a full-thickness defect is dependent on size of the defect (Convery, 1972).
Healing of Articular Cartilage Defects in the Equine

Number of studies devoted to healing of equine articular cartilage are minimal in comparison to the extensive number of studies performed in the rabbit and dog. Studies available in the horse compare healing of superficial and full thickness defects, effect of lesion size and location, and effect of exercise.

Riddle (1970) assessed healing of superficial and full thickness articular defects of the third carpal bone in ponies and horses. Superficial defects had not healed after 8 months. Proliferation of chondrocytes near the edges of the induced damage represented the only histological findings. At one month, full thickness defects were filled with granulation tissue extending into subchondral marrow spaces, and were grossly covered by synovial membrane adhering to the surface defect. Synovial adhesions were present at each examination interval up to 8 months. Early granulation tissue underwent metaplastic change to form fibrocartilage by 4 months, and imperfect hyaline cartilage by 8 months. Assessment of hyaline nature was based on gross and histologic findings. Discoloration and roughening of cartilage were noted on articular surfaces of carpal bones opposite created lesions by 4 months. Marrow spaces below full thickness defects were enlarged at 2 months and 4 months, while no changes were seen in the marrow below the partial defects. At 6 months, the subchondral trabeculae and marrow spaces were normal in appearance.
Kold et al. (1986) created four full-thickness cartilage defects (two linear and two elliptical) and four subchondral-cystic defects in the weight-bearing area of the medial femoral condyles of four ponies. Linear defects were present at 8 and 10 months after surgery. Healing of subchondral defects was characterized by loss of cartilage metachromasia (reduced proteoglycan staining), chondrones or chondrocyte clustering at the periphery, horizontal "matrix" flow, and formation of small cystic cavities in subchondral bone. Full thickness elliptical defects showed some macroscopic evidence of incomplete repair at the end of the study.

Articular defects associated with created cysts were partially filled by fibrous or fibrocartilaginous tissue extending into subchondral bone. Although incomplete, the authors felt the defects were attempting to heal by formation of a morphologically adequate joint surface. Failure of this task was related to presence of the defect on a weight-bearing surface, and pressure effects associated with joint fluid. Inadequate healing response indicated a need to utilize cancellous bone grafts to treat condylar cysts in weight-bearing areas.

Size and location of full-thickness articular cartilage defects have a significant effect on the degree of healing and type of healing response. Grant (1975) created different sized osteochondral defects in carpal bones of ponies, and compared healing response of treated and X-irradiated defects. All defects failed to show complete healing by 67 weeks, being composed of a mixture of fibrous and fibrocartilaginous tissue derived from subchondral bone. Increased superficial fibrous tissue was associated with defects contacted by synovial
adhesions. Specimens examined after 17 and 28 weeks demonstrated replacement tissue of a cartilaginous nature, with fewer synovial adhesions, than those examined at 54 and 67 weeks after surgery. Within a few defects, hyaline-like tissue was detected in the inner portion of the healing response.

Microscopically, typical changes associated with attempts to heal cartilage defects were noted. Proliferation and cloning of chondrocytes and a zone of necrosis were detected adjacent to defects. Matrix flow was detected but played a minor role in the healing process. Replacement tissue in defects was found to lack metachromasia throughout the duration of the study.

Convery et al. (1972) created a series of defects of increasing diameter in weight-bearing surfaces of the medial femoral condyle of ponies. Smallest lesions (3 mm) were filled within 3 months by fibrous and fibrocartilaginous tissue. By 9 months, one lesion could be detected and was composed of hypercellular cartilaginous tissue. Defects greater than 9 mm were not completely healed by 9 months. Repair tissue consisted of an irregular mixture of fibrous tissue, fibrocartilage, hypercellular cartilaginous tissue, and occasionally bone. Progenitor cells were derived from subchondral bone. Irregularities or "kissing lesions" on the surface of the tibial plateau were detected opposite all created defects. Poorest healing response, lameness, and marked synovial reaction were associated with the largest (21mm) created lesions. Matrix flow did not appear to be an important healing mechanism.

Hurtig et al. (1988) evaluated the effects of lesion size and location on repair of equine articular cartilage by studying large (15 mm²) and small
(5 mm$^2$) full-thickness lesions in weight-bearing and non weight-bearing areas of the radiocarpal, middle carpal, and femoropatellar joints. Smallest lesions filled by one month with poorly organized fibrovascular tissue which matured over the next 4 months. Basis for repair was attributed to matrix flow and migration of elements from the subchondral bone (extrinsic repair). Matrix flow was most evident within stifle defects, accounting for a significant reduction of lesion size during the early healing period. Statistically better healing occurred in small weight-bearing lesions compared to large, or non-weight-bearing lesions. As in the study by Grant (1975), synovial adhesions, or perichondrial pannus, interfered and were detrimental to healing of lesions near the dorsal rim of carpal bones.

Large lesions demonstrated good initial repair at 2 1/2 months, but at 5 months, clefts developed between repaired tissue and subchondral bone. Replacement tissue in these defects was inadequate when subjected to weight-bearing forces. The authors encouraged complete removal of the zone of calcified cartilage in order to provide maximal involvement of extrinsic mechanisms for repair, and to enhance attachment of repair tissues to subchondral bone. The technique of quantitative microdensiometry, after safranin-O staining, determined mean proteoglycan levels, within the defects, to be 75% normal at nine months.

Fischer et al. (1986) induced 6.5 mm osteochondral defects on the weight-bearing and non weight-bearing surfaces of the trochlea of the talus. Fibrocartilaginous repair tissue filled defects. Non weight-bearing defects
healed faster and more completely. This result is in contrast to findings by DePalma (1966) and Hurtig et al. (1988). Most likely, response varies between animal species, physiologic load, joint involved, type of joint motion, location of the lesions, and defect size.

Numerous studies have attempted to define the role of joint motion and weight-bearing on cartilage healing. Superior repair of rabbit articular was reported in association with continuous passive motion during the postoperative period (Salter et al., 1980). French et al. (1988) attempted to define effects of exercise on repair of defects created in third and radial carpal bones of the equine carpus. Differences, although not significant, were related to increased thickness and quality of repair tissue in exercised horses. Their study found no differences in healing ability based on defect size or location. Limitation of synovial adhesion incidence to one animal was attributed to animals being actively exercised during the study. Repair tissue was found to be composed of fibrous tissue and fibrocartilage. Long term quality of repair, or further metaplastic change was not able to be assessed in the 13-week duration of the study.

**Surgical Modification of Cartilage Healing**

It is generally accepted superficial defects in articular cartilage do not heal, and full-thickness defects which invade the line of calcified cartilage into subchondral bone repair through metaplasia of granulation tissue originating from the subchondral area (McIlwraith and Vachon, 1988). Yet, conversion of superficial defects to full thickness lesions in order to promote healing appears
to be a practice which is being abandoned. Potential for incomplete healing and recognized deterioration of replacement tissue justify these doubts (McIlwraith and Vachon, 1988). Effect of small partial thickness defects on joint function appears minimal relative to the functional morbidity associated with extensive curettage. One surgeon feels debridement of solid areas of partial-thickness hyaline cartilage to induce fibrocartilage is contraindicated (McIlwraith and Vachon, 1988; McIlwraith, 1990). Variability of healing response between joints and limited knowledge of cartilage healing in other joints limits application of this statement to the equine carpus and stifle.

Full-thickness defects should be curetted deep enough to remove the tidemark, leaving perpendicular edges of cartilage and subchondral bone. Bevelling cartilage edges in canine scapulohumeral joints resulted in increased degenerative change within the joint, larger final defect size, and increased frequency of fibrillation and erosion of apposing articular surface (Rudd et al., 1987). In horses, failure to remove the tidemark resulted in incomplete filling of defects, and defective bonding of repair tissue to subchondral bone (Hurtig et al., 1988; French et al., 1988).

Presence of sclerotic subchondral bone below a focal defect, or associated with osteoarthritic cartilage, may necessitate the need for removal of the subchondral bone plate (spongialisation) or its penetration with holes (subchondral drilling or forage), to provide an avenue for pluripotential cells to affect repair (Mitchell and Shepard, 1976; Furukawa et al., 1980).
Vachon et al. (1986) demonstrated the value of cancellous bone as a source of repair tissue for healing of full-thickness cartilage wounds in the equine third carpal bone. Subchondral drilling (forage) of full-thickness defects resulted in significant increase in surface area coverage, and thickness of the fibrous and fibrocartilaginous repair tissue. Non-drilled defects demonstrated only partial fibrous repair. However, after 21 weeks, none of the created defects were completely healed. This observation could have related to lesion size and inadequate healing time, but realistically, inability of third carpal bones to completely heal probably relates to high density of the subchondral bone and role of high-impact forces within this joint. Presence of induced third carpal defects resulted in apposing cartilage defects on the radial carpal bones of each horse.

Shamis et al. (1989) evaluated the effects of subchondral drilling on repair of partial thickness cartilage defects of equine third carpal bones. Repair was incomplete in all cases after 21 weeks, but there was significant production of fibrocartilage in drilled defects. New tissue was not able to anchor itself to partial thickness cartilage remnants, indicating poor functional stability of repair tissue. Subchondral drilling may be a method to improve healing of large partial thickness defects in which full-thickness curettage may be counterproductive.

Allografts as a Potential Treatment for Cartilage Defects

Periosteum and perichondrium possess a chondrogenic layer of undifferentiated mesenchymal cells which, when placed in a synovial
environment, can differentiate into chondroblasts capable of forming hyaline-like cartilage (McIlwraith and Vachon, 1988). Continuous passive motion has been shown to induce hyaline cartilage production in free intra-articular periosteal autografts in rabbits (O'Driscoll and Salter, 1984). Implanted periosteal grafts were used to resurface full thickness defects in stifles of rabbits subjected to either immobilization (4 weeks), continuous passive motion (2 weeks), or cage rest. Duration of the study was one year. Grafts subjected to continuous passive motion showed significantly less gross degenerative change, and significantly better healing quality, type of tissue, freedom from articular degenerative changes, and no degeneration in cartilage adjacent to the defects (O'Driscoll et al., 1988).

To assess potential for neochondrogenesis in horses, Vachon et al. (1989) placed free periosteal and perichondrial autografts as loose bodies into the tarsocrural joint. Neochondrogenesis was observed in 5 of 6 periosteal grafts and in 1 of 6 perichondrial grafts. The chondroid tissue of the periosteal grafts was significantly greater in amount, and had morphologic and matrical-staining properties similar to hyaline cartilage. However, the same authors (Vachon et al., 1991) demonstrated periosteal autografts did not improve healing of osteochondral defects of the distal portion of the radial carpal bone. In contrast to previously reported chondrogenic potential of intra-articular free periosteum, repair tissue was fibrous in nature. Reasons for failure probably involve trauma to chondrogenic cambial cells of the implant, and the negative effect of synovial adhesions on repair tissue.
Rationale for use of osteochondral allografts to resurface joint defects is based on the assumption articular cartilage of grafts will survive, while the avascular osseous component will be replaced gradually by creeping substitution from the host (Oakshott et al., 1988). Use of fresh osteochondral allografts has been described in human clinical cases (Meyers et al., 1989; Zukor et al., 1989). Methodology is still investigational, but results are promising. The most common clinical application is treatment of osteochondral defects of the distal femur, or for replacement of traumatically compromised weight-bearing portions of the knee. Success rates of 75% were reported for a trauma group (McDermott et al., 1985), and another study involving 59 patients (Meyers et al., 1989). Treatment of osteochondral defects of the distal femur with fresh allografts in 24 patients not responding to previous arthroscopic arthroplasty resulted in improvement in all 10 patients whose follow-up was greater than 2 years (Garrett 1986). Reports of failures also exist (Oakeshott et al., 1988; Kandel, 1985). Failures were related to donor-recipient matching, patient selection, age, timing, and technique. Poorest prognosis for success was associated with patients suffering from chronic degenerative arthritis, secondary to trauma. Viable hyaline cartilage was noted in 12 of 18 failed grafts.

Stevenson et al. (1989) demonstrated fresh-tissue-antigen matched osteochondral allografts were most successful and least likely to result in long term complications in the dog.

Complete clinical reports of osteochondral allograft transplantation in the equine are rare. Sullins et al. (1987) detailed experimental use of cancellous
cores and periosteum to promote healing of created 14 mm cartilage and subchondral bone defects of the medial femoral condyle. Improved radiographic filling of the bone defect, and a more uniform cartilage covering were described. Practicality of this procedure may be doubtful at present (McIlwraith and Vachon, 1988). However, the success of "pressfit" allograft cores in human femoral condyle defects may offer some encouragement for investigation of this treatment for specific application in the horse. A study by Hurtig (1989) indicated resurfacing of equine third carpal bones was more successful using osteochondral shell autografts. Fresh allografts induced an immune reaction leading to capsular inflammation and poor incorporation into the recipient site.

Intra-Articular Loose Bodies

Free osteochondral debris secondary to fracture or remaining after curettage of joint surfaces represent specific types of loose bodies. Evaluation of literature provides information regarding eventual fate of these fragments, and potential pathology associated with their presence.

Origins of Loose Bodies

The first historical account of a loose body was by Ambrose Pare, who in 1558 reported on removal of an almond-sized "stone" from the knee of a patient. So surprising was his find, the account was described in his chapter on monstrosities. Alexander Munro noted in 1726 that a loose body had a
corresponding defect in the condyle of the femur. He postulated in 1738 loose bodies might be derived from the articular ends of bones (Fischer, 1921). Koenig in 1887 described formation of osseous loose bodies by a process he considered sui genesis and which he named accordingly osteochondritis dissecans (Freiberg and Woolley 1910).

Loose bodies are defined as free, nonattached fragments within a joint, tendon sheath, or synovial bursa (Milgram, 1977a). They are composed of one or a combination of materials derived from any of these structures. Loose bodies composed of cartilage, cartilage and bone, metaplastic synovial villi, or tissue of meniscal origin are most commonly described, and have been associated with degenerative joint disease, traumatic osteochondral fractures, synovial osteochondromatosis, osteochondritis dissecans, rheumatoid arthritis, neurotrophic arthritis, and tuberculous arthritis (McGinty, 1982; Pattee and Snyder, 1988).

Classification and Incidence of Loose Bodies

Often, origin of loose bodies cannot definitely be understood solely from an analysis of history, radiographs, and operative findings. Usually histopathology is necessary to categorize these fragments in order to understand pathogenesis of individual cases.

In the largest study reviewed, Milgram (1977a) reports 119 human cases in which one or more loose bodies were found at surgery. He defined the term "nidus" as referring to the structure of original loose body that was cast free into the joint cavity. Because morphology and composition of loose bodies free
within a joint will evolve over time, histological structure of the nidus becomes the "fingerprint" on which to base classification.

Milgram classified his series of loose bodies into three different categories. The first type were loose bodies secondary to osteochondral fractures. Often, history of joint trauma existed, and at surgery a defect was apparent from which the loose body arose. Degenerative and/or destructive disease of articular surfaces resulted in a second type of loose bodies. Lastly, intra-articular loose bodies have been recognized in patients with proliferative disorders of the synovium, yet grossly normal articular surfaces. The most common entity is synovial osteochondromatosis.

Identification and characterization of three different types of cartilage; articular, osteophytic, and lobular, within nidi of loose bodies, provided basis for determination of fragment origin. Loose bodies which contained articular cartilage with minimal degenerative change were classified as osteochondral fractures. Degenerative changes within articular cartilage were characterized by proliferation of chondrocytes in various clones, matrix degeneration, and loss of mucopolysaccharide staining. Bodies whose nidi consisted of this type of cartilage, or "osteophytic" cartilage, were considered to be the result of degenerative arthritis. Fragments which contained what Milgram described as lobular cartilage were considered to be secondary to synovial osteochondromatosis, a condition characterized by cartilaginous metaplasia of the synovial fibroblast cells. Even though bone matrix within any of these types of free bodies was necrotic, morphology of the remaining bone often provided
additional information regarding the original tissue, prior to it becoming avascular and free within the joint.

Having developed classifications based on cartilage type, Milgram further characterized each category. Loose bodies secondary to osteochondral fractures were composed of nidi consisting of articular cartilage, or articular cartilage with attached subchondral bone. Articular cartilage was found within the nidus of every fracture specimen studied. Loose fragments consisting solely of bone became attached to the synovium, resorbed, and did not persist as loose bodies. Such findings become relevant with regard to other implantation studies.

Milgram identified three primary mechanisms by which nidi for loose bodies were generated in arthritic joints. The first type of nidus was associated with fragmentation of a joint surface. Structures contained degenerative articular cartilage with subchondral bone or fragments of sclerotic bone. Degenerative articular changes were thought to occur prior to fragmentation from the joint surface. Osteophyte formation and subsequent fracture represented a second mechanism. Fractured osteophytes were the most expected type of nidus associated with degenerative arthritis. Production of the third nidus type was a process similar to osteophyte formation. Metaplastic response within synovium resulted in denovo development of chondral or osteochondral nodules. Number of nodules were few, distinguishing it from synovial osteochondromatosis.

In his discussion, Milgram felt free bodies which arose secondarily from joints with degenerative arthritis may be the most common type of
osteochondral loose body, yet were not recognized as such because of their propensity for absorption by the synovium.

Fisher (1921) reviewed the etiology and pathology associated with loose bodies composed of cartilage or cartilage and bone. He, like Milgram, categorized his cases into three groups; loose bodies associated with arthritic joints, non-arthritic joints, and those secondary to synovial chondromata. He commented on ability of cartilage cells to survive nourished by synovial fluid, yet osteocytes and bone tissue were always found to be dead and necrotic. Fibrocartilaginous growth was responsible for size increase in loose bodies. Osteogenic function occurred in those fragments developing vascular supply through adhesion formation. His simple classifications, morphological and histological descriptions, and drawings are extremely accurate when compared to similar studies produced much later in the century.

Causes of and changes in loose bodies arising from articular surfaces is the topic of an extensive paper by Phemister (1924). He discounts trauma as a cause for the free bodies, as he notes chip fractures with fresh fracture surfaces never remain free within a joint, but become attached and resorbed by the synovium. Those fragments which survived as loose bodies showed no fracture surface, but were always found with a fibrous covering over their surfaces, formation of which antedated liberation of the body in the joint. He also documented the ability of the loose body to induce irritation and subsequent proliferative reaction in the joint capsule.
Hauser (1942) reports on four cases of loose bodies derived from meniscal fragments in the knee joint of human patients. Alterations in the synovial fluid and intra-articular synovial friction were postulated to result in smoother edges and symmetrical shape. Surfaces became laminated and fragments resembled loose bodies derived from other clinical cases.

Barrie (1977) studied 100 specimens of loose bodies from the human knee joint. Of these, 35 consisted of detached osteoarthritic spurs or metaplastic synovium, 4 of meniscal fragments, and 56 derived from the articular surface of the joint. Freshly detached osteochondral fragments developed typical morphologic changes in the articular face, sides and base of fragments. Original articular surface underwent minimal change, characterized by loss of superficial matrix, cell de-differentiation, and cell division resulting in a layer of fibroblastic activity. Fragment sides experienced morphological and chemical changes resulting in rounding in shape and external covering by fibrocartilage. If the base was cartilaginous, it responded much like the sides, whereas if made of bone, the marrow cells died, with subsequent production of fibrocartilage by transformed cells. As surfaces became coated with new growth, central areas underwent complex changes consisting of varying combinations of cell hyperplasia, dechondrification, and unmasking of collagen preceding the onset of necrosis and calcification. Degenerative changes were expected, as chondrocytes only remain viable for a distance of 3 mm from the surface. Secondary remodelling was described and attributed to osteoclast-like cells. Signs of surface erosion were most marked in those bodies sequestered in synovial
pouches. Osteoclastic differentiation may be related to oxygen tension, which would increase closer to the synovium. Intrinsic and extrinsic enzyme systems are responsible for loss of cartilage matrix.

Milgram (1977c) and Perry et al. (1988) described synovial osteochondromatosis as benign proliferation of cartilaginous bodies resulting from metaplasia of synovial fibroblasts. Bodies remained attached to the synovium, or become loose bodies. In either situation, fragments became ossified, calcified, or both. Milgram felt resorption of fragments was as frequent as production, but noted resorption only occurred after attachment to the synovial membrane.

In a continuation of his paper on loose body classification (Milgram 1977a), Milgram (1977b) discussed the common sequence of morphologic alterations which occurs, regardless of origin, within all free osteochondral loose bodies in synovia-lined joints. As did Fisher (1931), he documented the existence of proliferation, surface resorptive activity, and degenerative calcification in loose bodies remaining in joints longer than 6 months. He also reaffirmed most fresh osteochondral fragments never form loose bodies, but become attached and resorbed by either macrophages or osteoclasts in the synovial lining.

Mori (1979) reported on the incidence of visible debris within 732 knee joints examined by arthroscopy since 1961. Forty six (6%) of the joints had recognizable debris at surgery. Debris was classified arthroscopically into four types: 1) precipitation of fibrin (14 cases), 2) degeneration and necrosis of villi
(20 cases), 3) articular cartilage desquamation (9 cases), and 4) metaplasia of villi (3 cases). He postulated precipitation of fibrin was associated with active synovitis as seen in acute cases of rheumatoid arthritis, and more rarely in cases of tuberculosis. Degeneration and necrosis of villi was associated with cycles of remission and recurrence of acute inflammation, a pathogenesis specific to rheumatoid arthritis. Debris associated with desquamation of articular cartilage results from repeated synovitis inducing degenerative softening and necrosis of articular cartilage. Villous metaplasia was the name given to the presence of small miliary bodies composed of a eosinophilic staining debris, devoid of cartilage cells, but similar to that seen in synovial osteochondromatosis.

Hendel and Halprin (1988) reported finding an unusually large loose body (1.5 x 2.5 cm) within a sealed suprapatellar pouch in the knee of a 20-year-old male patient. They postulated the loose body was the result of an osteochondral fracture, secondary to trauma, one-year previously. It was separated from the joint by a plica of tissue between the suprapatellar pouch and the femoropatellar joint. No histology was performed on the loose body, but it was suspected to have increased in size over the one-year period. No other abnormalities nor degenerative changes were noted within the joint.
Experimental Studies Involving Joint Loose Bodies

In the early 1920's, conclusions regarding behavior of cartilage and bone free in the joint space were theoretical deductions based on information gained from human pathological material. Animal studies by Hildebrand, Barth, and Rimann found it impossible to produce permanent loose bodies in joints by detaching fragments of cartilage and bone, as all fragments became adherent and absorbed by the synovial layer (Phemister 1923).

Efforts of Haas (1926) to protect bone fragments in fenestrated tubes were to no avail, for the fragments became adherent and resorbed by synovium. Harbin and Moritz (1930) enveloped implanted autogenous fragments in a colloidin membrane prior to placing them in canine stifle joints. In all cases which the membrane remained intact, formation of a fibrous capsule resulted in increased size. Other fragments had attached to synovium within three weeks.

Bennett et al. (1932) studied repair of articular cartilage and reaction of normal stifle joints of adult dogs to "joint mice." In one group, fragments of articular cartilage were replaced as a loose bodies into the joints from which they were derived. In another series a fragment consisting of articular cartilage and subchondral bone was returned to the joint cavity. The associated pathology was examined at 4, 12, 20, and 28 weeks duration. At 4 weeks post-operatively, 3 of 4 cartilage specimens were recovered. One fragment was free in the joint, while the others were attached to the synovium. Cartilage cells within the free fragment were viable, but had assumed the appearance of
fibroblasts on their superficial surfaces. Other cartilage implants were found attached to the synovial membrane of the fat pad below the patella. None of the attached cartilage fragments became vascularized, and did not show extensive changes in size. Increased joint effusion was only evident at four weeks postimplantation.

By 12 weeks, joint mice initially composed of hyaline cartilage and subchondral bone had undergone complete bone necrosis. Marrow spaces were filled with fibrous tissue which resembled cartilage. Hyaline cartilage remained viable in its entirety, lacking degenerative change in cells or matrix. The entire loose body was surrounded by a narrow layer of proliferating fibroblasts. All loose bodies had attached to the synovium by 20 weeks, but cartilage matrix was still preserved. No fragments were detected by 28 weeks post-implantation. Synovium was not inflamed, but was hypertrophic. The authors postulated attachment of the fragment to the synovium may occur more commonly in smaller joints.

Bailey and Selle (1959) implanted large (6mm x 8mm) cores of bone into knee joints of young and old rabbits, which were evaluated at six weeks, two months, and six months. Radiology and autoradiography using $\text{H}_2\text{S}^{35}\text{O}_4$ were utilized to assess growth and viability of fragments. Size of fragments prevented migration within the joint space. Seventeen of 18 specimens were evaluated. All specimens showed an increase of weight attributed to fibrous tissue proliferation, on the bony surface of the fragment. Juvenile rabbits demonstrated almost twice the amount of weight increase when
compared to adults. Hyaline cartilage remained viable, but bone was necrotic. The investigators concluded: 1) loose body increase in size was attributed to fibrous tissue proliferation on the bony side of the fragment, 2) necrosis of bone was observed within two months, 3) hyaline cartilage was viable, but did not show any growth, and 4) loose bodies were able to incorporate $^{35}$S into their cartilage, and it must have been absorbed via the synovial fluid as no synovial attachment existed.

Agins et al. (1986) recognized a potential risk of arthroscopic meniscectomy to be retention of debris of meniscus origin within the joint. He and his co-workers designed a prospective study which analyzed fate of loose bodies of meniscal origin after placement into canine knee joints. Carefully measured fragments were cut from a meniscus which had been removed from the arthrotomized right stifle joint. Six meniscal fragments were placed into the medial compartment of the left stifle using a 3 mm arthroscope. The groups of dogs were sacrificed at 3 weeks and 12 weeks post-implantation. At 3 weeks, 16.7% of the free fragments were completely degraded, 16.7% were absorbed by the synovium, and 66.6% were loose, located between synovial folds. Fragments still present within the dogs' stifle at 3 weeks had altered gross morphology. Those with distinct edges and sharp corners were roughly the same size as at the time of implantation. Other fragments were changed in both shape and size. They were round and showed an average reduction of 46% in length and 30% in width. Histologically, fragments had a surrounding capsule consisting of fibroblasts.
At 12 weeks, only 2 of 30 fragments were found in five dogs. The other 28 fragments were degraded. Fragments found were oval shaped and showed a 57% reduction of length and a 70% reduction in width. The 2 retrievable fragments consisted of fibrous tissue. One had dystrophic calcification at 12 weeks.

Origin of fibroblasts which proliferated on the exterior of the fragments, was not obvious but the authors felt they could have originated from synovium. In contrast, Bennett et al. (1932) showed fibroblasts could differentiate from chondrocytes in articular cartilage. Synthetic activity of these cells is supported by nutrition derived from synovial fluid. Degradation of meniscal loose bodies was attributed to enzymatic digestion, mechanical abrasion, and synovial phagocytosis.

**A Summary of Loose Body Dynamics**

**Size**

Most fresh osteochondral fragments extruded into joint cavities never form loose bodies, but become attached and resorbed by cells of the synovial lining (Milgram, 1977b; Bennett et al., 1932; Lloyd-Roberts, 1953). Tendency for synovial attachment was first reported by Ito in 1924 (Bennett and Bauer, 1924). Prior to synovial adhesion, fragments become reduced in size as a result of enzyme degradation, fibrillation secondary to mechanical damage within the joint, and bone necrosis, resulting from a lack of blood supply and inadequate nutrition from the synovial fluid (Milgram, 1977a; 1977b; Hauser, 1942; Phemister, 1923; Barrie, 1978). Bone necrosis is apparent within two months of
fragmentation (Bailey and Selle, 1959; Agins, 1986). Histologically, free fragments acquire an external layer of fibroblastic cells from four to 12 weeks (Milgram, 1977b; Bennett et al., 1932). These cells are derived from either the synovium (Agins, 1986) or by endogenous metaplasia of the superficial chondrocytes of the fragment (Bennett et al., 1932). Barrie (1978) felt external cells of the loose body assume a resorptive role upon loose body adherence to synovium. Change in function may be related to increasing oxygen tension as the fragment becomes vascularized or spatially closer to capsular blood supply. From 4 weeks to 28 weeks, fragments will become completely engulfed and resorbed by macrophages or osteoclasts in the synovial lining (Bennett and Bauer, 1932; Fisher, 1931; Phemister, 1923). Inflamed synovium appears to be more efficient in its resorption of fragments (Milgram, 1977b). Although rare, new bone formation was detected in some reattached loose bodies (Fisher, 1931). Exceptional osteochondral fragments may remain free within the joint, undergoing distinctly different changes within its internal and external structure. These changes become a basis for conclusions regarding behavior of cartilage and bone within joint spaces. Proliferative changes on the surfaces of loose bodies have been described (Bailey and Habel, 1960; Bennett and Bauer, 1932; Fisher, 1931; Habin and Moritz, 1930; Phemister, 1924). Phenomena of cartilage proliferation, surface resorptive activity, and degenerative calcification appear to occur in all older osteochondral loose bodies remaining free within the joint cavity, regardless of origin and composition (Milgram, 1977b). After at least six months of liberation within a joint space, 92% developed proliferative
changes. Fibrocartilaginous layering began on surfaces of necrotic bone, and expanded in a semi-circular pattern. Extent of layering was a good indicator of fragment age. Resorption by osteoclast-like cells causes both gross and microscopic pitting in the surface of the loose body.

Nutrition of cells forming superficial layers is dependent on the synovial fluid (Fisher, 1931; Harbin and Moritz, 1930; Milgram, 1977b). As newer layers of cartilage prevent deeper diffusion, cellular necrosis with potential for secondary calcification occurs within the older, deeper tissues. Cartilage depth greater than three millimeters exceeds the diffusion capacity of normal synovial nutrients (Barrie, 1978).

Loose bodies secondary to osteochondrosis behave in a different manner. Degree of indirect inflammatory reaction associated with osteochondrotic lesions may be minimal, unless numerous small fragments are constantly being liberated into the joint. Reduced synovial inflammation, joint spaces with large synovial recesses, and delayed release of the free fragment from parent bone may reduce effects of enzymatic degradation, mechanical trauma, and synovial entrapment. Some osteochondrotic fragments have demonstrated documented fibrocartilaginous enlargement on their surfaces (Levine and Kant, 1988). Stromberg and Rejno (1978) in an extensive study of osteochondrosis in horses stated avulsed cartilage can be resorbed by the synovium, remain static in a state of partial attachment to adjacent cartilage, or undergo changes related to increased density, spherical contouring, and smoother edges.
Migration and Localization of Loose Bodies

Minimal documentation exists regarding whether loose bodies have a tendency to consistently locate in specific areas of various joints. Phemister (1923) observed fresh osteochondral fractures never remain free in joints; rather they attach to synovial membrane of joint recesses. Reduction of fragment mobility would appear to be a prerequisite for synovial adhesion. Mobility may be a factor for persistence of aged free bodies.

Bennet and Bauer (1932) noted all loose bodies implanted into canine stifle joints eventually became attached to the synovial membrane below the patella. McGinty (1982) commenting on the removal of loose bodies from human knees, stated the most common locations for loose bodies are the lateral suprapatellar recess and the posteromedial compartment. Dandy (1984) observed loose bodies arising within joints find their way to the posteromedial compartment through the intercondylar notch or via the medial gutter. Vachon et al. (1988) illustrated propensity for implanted periosteal and perichondrial autografts to locate in the cranial synovial recesses of the equine stifle joint.

Gravity (Lloyd-Roberts, 1953), joint size, and degree of joint motion appear to be important factors determining the final resting spot for fragments. Additionally, although not recognized in the literature, there may be some difference in propensity for a fragment to become attached to villous versus non-villous synovium.
Studies Involving the Role of Bony and/or Cartilaginous Debris in Joint Disease

**Fragment Induced Arthritis**

Presence of cartilaginous or bony debris in association with various human arthritides is not uncommon. Often debris will be free within the synovial fluid, or intimately enfolded or attached to synovial lining of the joint. Whether fragments represent causal entities, or merely occur secondary to the inflammation and destruction occurring within synovium and on articular surfaces, remains an unanswered question. Similar findings, although with far less frequency, have been reported in certain species of animals. Concern exists regarding roles played by minute osteochondral, bony, or cartilaginous fragments released secondary to osteochondral fractures. They have potential to cause direct mechanical cartilage damage (Hurtig, 1988) or damage secondary to induced synovitis (Chrisman et al., 1965; Evans et al., 1984; Clyne, 1987; Hurtig, 1988). It is appropriate to consider incidence of debris, and its *in vivo* and *in vitro* effects.

**Incidence of Articular Debris**

Debris recognized grossly and ultrastructurally in association with human arthritic joints provides the majority of information concerning the role of these potential irritants. Muiriden (1970) examined 100 open biopsies of patients diagnosed as having rheumatoid arthritis. Presence of cartilage and bone fragments, seemingly derived from the destructive processes within the synovial
cavity, existed in over half of the samples, and were significantly related to the duration of disease. Fragments were found to be present on the surface, particularly in the crypts or folds of the villous membrane, and at various levels within the synovial stroma. Fragments undergo slow digestion within the synovium, and have the potential to induce synovial proliferation and capsular fibrosis.

Evans et al. (1982) utilized the technique of ferrography to evaluate its application in recovery and analysis of wear particles from synovial fluid. Results were compared to findings of arthroscopic examination. Size of wear particles increased with the severity of mechanical erosion of the articular surface. Ferrographic retrieval and microscopic exam proved to be a more sensitive monitor of cartilage erosion than arthroscopic examination.

Hotchkiss et al. (1982) utilized micropore filtration of synovial fluid to recover cartilaginous debris from the synovial fluid of 70 patients undergoing arthroscopic surgery. Correlation existed between arthroscopic evaluation of the articular surfaces and presence of cartilaginous fragments. Patients with moderate to severe fibrillation of articular surfaces demonstrated significantly more fragments per sample, and clustering of chondrocyte nuclei in the fragments.

Dieppe et al. (1984) described 12 cases of an acute, destructive arthritis associated with aggregates of apatite crystals (calcium pyrophosphate dihydrate) free within the synovial fluid or deposited within the synovium. Synovial biopsy revealed synovial cell hyperplasia, imbedded fragments of calcific material, and
minimal inflammatory cell infiltrate. The authors acknowledged, along with others (Cheung et al., 1981; Halverson et al., 1982) bone fragments may accelerate joint damage by interacting with synovial macrophages, causing release of destructive factors and inducing synovial cell proliferation. Apatite crystals were only one factor involved in the pathogenesis of the joint destruction.

Salisbury and Nottage (1985) described four stages of pathologic change associated with human rheumatoid articular cartilage degeneration. Pathology of stage III was characterized by the presence of full-thickness meniscal tears and free-floating fragments of meniscal and articular debris. Articular damage was characterized by erosions with sharp, vertically oriented sides. Defects were postulated to be mechanical in origin and secondary to the free fragments loose within the joint. Radiographic appearance did not correlate to degree of damage within the joint, as 75% were radiographically normal, while 25% showed signs of minimal reduction in joint space. Synovial inflammation correlated to the amount of debris observed within joints. Clinical improvement of pain and effusion was noted following removal of joint debris. The authors concluded resultant debris from cartilage degeneration mechanically abrades articular surfaces.

In an elaborate study utilizing monoclonal antibodies to determinants on Type II collagen, Klareskog et al. (1986) demonstrated presence of numerous cartilage fragments within synovial tissue of patients with osteoarthritis. Fewer fragments were associated with rheumatoid arthritis. Presence of additional
determinant sites may increase the potential antigenicity of fragmented articular cartilage, accounting for accumulation of T lymphocytes within synovium adjacent to the fragments.

Witter et al. (1987) utilized specific antibodies to further characterize the types of proteoglycan degradation products in the synovial fluid of patients with rheumatoid arthritis, juvenile rheumatoid arthritis, and osteoarthritis. Fragments were detected in all fluids. The authors postulated different fragments are probably the result of enzymatic degradation by proteinases originating from chondrocytes, synovial cells, and polymorphonuclear leukocytes in inflamed joints.

Fewer reports of fragment-associated arthritis are present within the veterinary literature. Tew and Hackett (1981) isolated wear fragments from equine joints using a filtration technique, and compared their findings to visual examination of the joints at necropsy. A strong positive correlation existed between presence of cartilage lesions and cartilage fragments.

Heinegard et al. (1985) utilizing a canine model of induced osteoarthritis, determined proteoglycan levels significantly increased in synovial fluid as the arthritic condition progressed. Their methodology was postulated to be useful to follow progression of articular cartilage destruction, and in the evaluation of various forms of therapy.

As the exact pathogenesis of degenerative joint disease has not been elucidated, role and chronological appearance of synovial debris cannot be determined. Arthritogenic potential of this material is not in question, rather
magnitude and chronology of its role in the overall degenerative process remains a matter of debate between research labs. Evaluation of clinical presentations alone limits the ability of scientific community members to further elucidate pathogenesis of various forms of arthritis. Experimental studies, both in vivo and in vitro, hold the most potential for further elucidation of the role of fragments within the degenerative sequence.

**In vivo Experimental Studies**

Hulten and Gellerstedt (1940) demonstrated fragments of allogenic and autogenic cartilage introduced into joints became engulfed and digested by synovium. Lloyd-Roberts (1953) showed particles of bone or cartilage injected into the stifles of rabbits produced synovial hyperplasia. Chrisman et al. (1965) injected 20 mg of autogenic costal cartilage particles into canine knees and, after 6 months demonstrated synovitis, stiffness, and osteophytosis. Articular damage was not found.

Evans et al. (1984) were able to induce experimental arthritis by intra-articular injection of allogenic cartilaginous particles into rabbit stifle joints. One month of injections resulted in modest effusion, without marked histologic changes. By 2 months, injected joints became slightly swollen and warm. Moderate synovitis, with mononuclear infiltrate, was confirmed histologically, and there was a marked increase in production of neutral proteinases and acid hydrolases. Articular cartilage was histologically normal. By 3 months there was marked loss of metachromasia in superficial layers of cartilage. Synovitis was more severe, and enzyme levels became maximally stimulated. Enhanced
intrinsic collagenolytic activity was present in samples of articular cartilage. At 5 months, repeated injections exacerbated all conditions. Clinically, the limbs were painful. Cartilage damage progressed from a loss of proteoglycan staining to the presence of longitudinal fissuring, discoloration, and pitting. Other than evidence of capsular swelling at 3 months, no radiographic changes occurred within the first 5 months. Four months later, osteophytes were present in the stifles of one group. This study provided direct evidence particles of articular cartilage are arthritogenic. Loss of metachromasia preceded mechanical disturbances. The authors were able to rule out the presence of an immune response to intact fragments of cartilage. Since this is the least antigenic type of collagen, an immune response to peptide fragments may not have been apparent. Mechanical damage by particles may expose previously hidden antigens, inducing wear particle mediated enzyme release of cleavage peptides capable of inducing the immune system. After five months of injections, reactions became self-perpetuating. Joint lavage to remove wear particles resulted in relief of clinical signs.

Boniface et al. (1988) recognizing ability of cartilage wear particles to activate synoviocytes and chondrocytes resulting arthritic degeneration, desired to assess the response of synoviocytes to purified cartilage proteoglycans injected into rabbit stifle joints. Twice-weekly injections provoked synovial hypertrophy, synovitis, erosion of the articulating surfaces, loss of cartilage metachromasia, and elevated production of neutral collagenase and gelatinase from both synoviocytes and chondrocytes. Synoviocytes were also found to produce a
factor related to interleukin-1, which provoked the activation of chondrocytes. Changes produced by the injections were consistent in all rabbits.

Hurtig (1988) injected autogenous cartilage particles into middle carpal and fetlock joints of horses to create a model of naturally occurring degenerative joint disease. Injected joints developed persistent joint effusion, and were noticeably larger in circumference than control joints. Monthly analysis of synovial leukocyte and total protein levels remained within normal limits for both groups. At post mortem, joints subjected to cartilage particles had more wear lines and areas of cartilage thinning than controls. Capsular fibrosis and synovial membrane hyperplasia were marked in the treatment group. Histologically, injected joints showed a loss of the superficial cartilage layer, clustering of chondrocytes, loss of matrix staining (reduced proteoglycan concentration), and wear lines. Synovial villi contained abundant vasculature and stromal connective tissue. Cartilaginous debris had been engulfed by synovial cells. Joint capsules were markedly hyperemic, containing large areas of fibroplasia. Mechanisms by which the particles induced degenerative joint disease could not be determined from this study. Degree of cartilage damage was postulated to be associated with either particle induced synovitis or leukocytic enzyme-mediated proteoglycan depletion. Joint lavage to remove wear particles, and intra-articular medication to reduce the activity or effect of degradative enzymes were concluded to be valid modalities for treatment of fragment associated degenerative joint disease.
In vitro Experimental Studies

In vitro studies using cell cultures from constituents of the diarthrodial joint allowed further characterization of the specific mechanisms involved with fragment-induced arthritis. Mauer and Schumacher (1979) incubated hydroxyapatite crystals with human polymorphonuclear leukocytes and viewed the response using light and electron microscopy. The apatite crystals were readily phagocytized by the cells. Degranulation, loss of cytoplasmic density, and necrosis were apparent in the cultures.

Evans et al. (1981) postulated "wear" particles of cartilage shed into joints may incite release of enzymes capable of degrading cartilaginous matrix. Destructive activity would facilitate release of more particles, triggering a self-perpetuating cycle of tissue destruction which may be important in the pathogenesis of degenerative arthritis. Cartilaginous wear particles retrieved from synovial fluid aspirates of human diarthrodial joints stimulated production of proteolytic enzymes in cultures of human mononuclear phagocytic and synovial cells. Enzymes from synovial cells induced release of glycosaminoglycans and hydroxyproline (a component of collagen) from cartilage. Activation of synovial cells and macrophages by wear particles in vivo may be involved in the pathogenesis of degenerative joint diseases.

Mohr and Wessinghage (1981) examined ultrastructural characteristics of synovial samples from 65 patients with osteoarthritis. They concluded detritus synovitis occurs in association with cartilage and osseous destruction in osteoarthritis. Fragments became engulfed within synovium. The authors
speculated fragments are a sequel to destruction of the joint, and do not represent the primary stimulus for joint degeneration in this condition.

Cheung et al. (1981) and (1983) demonstrated production of collagenase, neutral protease and prostaglandins from cultured rabbit chondrocytes and canine synovial cells in response to the addition of calcium-pyrophosphate-dihydrate and hydroxyapatite crystals. Production of these mediators was considered a nonspecific sequel of endocytosis of the particulate matter.

Dogterom et al. (1985) demonstrated *in vitro* proteoglycan release associated with cartilage and synovial co-culture is a result of synovial enzymes acting directly on the matrix rather than chondrocyte-mediated breakdown.

May et al. (1988) and (1989) in an attempt to characterize cellular mechanisms underlying development of degenerative joint disease secondary to intra-articular fractures, treated cultured equine synovial cells with different concentrations of bone fragments, and measured PGE$_2$ levels post-incubation. Significantly elevated concentration of PGE$_2$ were associated with higher dose and larger size of fragments. The study proved the ability of equine synovial cells to produce PGE$_2$, a potent mediator of inflammatory processes, in response to bony debris.

Olson et al. (1988), performed *in vitro* and *in vitro* evaluation of the effects of wear particles created from seven different artificial ligaments. All fragments induced significant elevations of collagenase, gelatinase, and chondrocyte activating factor (Interleukin-1) from rabbit synovial cell cultures. *In vivo*, wear particles accumulated in the periarticular synovial folds and
induced moderate to severe macrophage infiltration within synovium. In both
circumstances, response was dose-dependent. Carbon and bovine xenograft
wear particles produced highest levels of enzymes.

Synovial Response to Articular Debris

Microscopic examination of synovial samples from human osteoarthritic
joints at surgery or autopsy reveals strong correlation of synovial inflammation
and presence of articular debris (Lloyd-Roberts 1953; Dieppe 1976; Goldenberg
et al. 1982; Altman and Gray 1983; Gordon et al. 1984). Attached cartilage and
bone fragments were recognized on the synovial surface or in the subsynovial
tissues. Free and attached fragments had the same appearance and staining
characteristics as degenerate cartilage from the articular surface of an
osteoarthritic joint. Opinion varies amongst medical researchers concerning
interpretation of findings. Questions regarding the role of fragments as inducers
of osteoarthritis, or arising secondarily have not been answered. Although
Dieppe (1976) felt fragments were capable of inducing inflammation in the
synovial membrane in patients with osteoarthritis, leukocytic infiltration was not
a consistent finding. Goldenberg et al. (1982) documented necrosis of adjacent
synovial villi associated with cartilage fragments, but confirmed leukocytic
synovial infiltration in only three of 15 patients with confirmed joint debris.
Altman and Gray (1983) stated biopsy of arthritic joints at arthroscopy revealed
modest synovitis in conjunction with synovium-entrapped cartilage debris.
Revell et al. (1988) utilized histological and monoclonal antibody techniques to examine synovial membrane samples from patients with osteoarthritis. Samples demonstrated detritic fragments of bone and cartilage embedded within synovium. Inflammatory infiltrate was not associated with fragments. Bony debris was more often associated with fibrin deposition at the synovial surface. Observations of human synovial inflammatory response contrast to findings in horses. Mononuclear cell (lymphocytic) infiltration of synovial tissues was consistently observed in samples from carpal joints subject to intra-articular implantation of cartilaginous debris (Hurtig 1988), osteochondral allo- and autografts (Hurtig 1988a), periosteal resurfacing grafts (Vachon et al. 1991), and filipin (McIlwraith and Van Sickle 1981).

Regardless of species, intra-articular fragments were always associated with synovial cell hyperplasia, villous proliferation of synovial lining, congestion and erythema (Hulten and Gellerstedt 1940; Lloyd-Roberts 1953; McIlwraith and Van Sickle 1981; Hurtig 1988, 1988a; Vachon et al. 1991). Removal of the inciting stimulus will result in reversal of synovial hyperplasia and associated signs within four weeks (McIlwraith, 1981). However, prolonged synovial inflammation will result in irreversible subsynovial fibrosis. Hulten and Gellerstedt (1940) demonstrated repeated injections of bone debris into rabbit joints induced capsular fibrosis. Repeated injections of cartilaginous fragments resulted in capsular fibrosis of equine middle carpal joints.

From in vivo and in vitro studies, it would appear fragments of cartilage and/or bony origin have the ability to produce a primary inflammatory and
subsequent degradative response within the joint. Variation of induced response relates to species, joint involved, cartilage fragment size and number, and duration of insult.

Summary

Free fragments within a joint induce cartilage surface damage from direct mechanical injury or secondary to fragment-induced synovitis and resultant deleterious cartilage effects. Fragments have been implicated as initiators of a secondary inflammatory response as occurs in other arthritic diseases (Mears et al., 1978). They initiate production, release, and activation of leukocytic lysosomal enzymes. Fragment-induced activation of synoviocytes, results in production and activation of numerous enzymes, and release of chemical mediators. Proteinases, collagenases, and gelatinases can be assayed in media containing activated synoviocytes, and possess degradative and inflammatory capabilities. Powerful mediators of inflammation, Interleukin-1 and Prostaglandin E₂, are capable of activating chondrocytes, synoviocytes, and macrophages, resulting in local cellular changes, release of additional degradative enzymes, and further articular degradation and synovial inflammation. Variation in degree of severity and clinical course of primary or secondary processes may result in the ultimate fate of fragmented debris, or loose bodies.
Morphologically, effect of enzymes and mediators becomes apparent. Synovium becomes consistently hyperplastic, a condition which may be reversible, but which could later lead to permanent subsynovial fibrosis. Cartilage matrix degradation and chondrocyte death secondary to enzyme release and cellular activation will lead to early loss of matrix staining (metachromasia), fibrillation, deeper erosion, and eventual loss of normal function; characteristics hallmarking degenerative joint disease.
MATERIALS AND METHODS

Ten adult horses of either Quarterhorse or Thoroughbred breeding (average weight 420 kg) between 2 and 4 years of age (mean 2.4 years) were purchased from external sources for this study. Selection and subsequent inclusion in the study required the horses be free of lameness and any clinical abnormalities found by routine physical and lameness examination. Four standard radiographic views of both carpi (dorsopalmar, lateromedial, dorsopalmar lateromedial oblique, and dorsopalmar mediolateral oblique) were performed to ensure radiographic normalcy of the carpus (Watters J.W., 1981). All animals were dewormed, vaccinated for encephalitis and tetanus, confined to an 8-10 acre pasture with water and improved pasture grasses, and fed free-choice alfalfa or grass hay. Prior to performance of the surgical procedure, each animal was moved to a 12 foot x 12 foot box stall within the hospital complex. Lameness exams, carpal circumference measurements, and arthrocentesis of each middle carpal joint were performed prior to the surgery.

Surgical Procedure

Both carpi and the right tarsus were clipped circumferentially, and scrubbed for 6 minutes with povidone-iodine surgical soap. A sterile gauze roll

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b Eqvalan Paste®, MSD Agvet/Merck and Company, Rahway, N.J.

c Encevac T®, Haver/Mobay Corp., Shawnee, KS.

d Prepodyne Surgical Scrub, AMSCO Medical Products, Erie, PA.

E Cling gauze, Professional Medical Products, Glenwood, SC.
soaked in povidone iodine solution $^f$ and a three inch adhesive bandage $^g$ were applied over both carpi and the tarsus. Horses were fasted 12 hours prior to surgery.

Each horse was pre-medicated with intravenous acepromazine maleate $^h$ (0.05 mg/kg), induced with 300-450 ml of 0.4% thiamylal $^i$ in 10% guaifenesin $^j$ intravenously, oral-tracheally intubated and maintained with halothane $^k$ in oxygen mixture. Horses were padded in left-lateral recumbency, presurgical bandages removed, and both carpi and the right tarsus were aseptically prepared and draped for surgery. One middle carpal joint was randomly selected for implantation of osteochondral fragments. The opposite middle carpal joint served as a sham control.

A. Arthrotomy

A 5 cm skin incision was made on the lateral aspect of the hock directly over the lateral trochlea of the talus, 1 cm lateral and parallel to the long digital extensor tendon. Subcutaneous tissues and joint capsule were incised to expose

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$f$ Prepodyne solution, AMSCO Medical Products, Erie, PA.

$g$ Elasticon®, Johnson & Johnson, New Brunswick, NJ.

$h$ Promace®, Fort Dodge, Fort Dodge, IA.

$i$ Biotal®, Boehringer Ingelheim, St. Joseph, MO.

$j$ Glyceryl guaiacolate®, Aceto Chemical, Flushing, NY.

$k$ Fluothane, Fort Dodge, Fort Dodge, IA.
the tibiotarsal joint. Tissues were retracted with blunt Weitlaner retractors\(^1\) to expose the lateral trochlea of the talus (Fig 1A). A 5.5 mm (7/32 inch O.D.), depth calibrated Michele trephine\(^m\) was used to remove two cores of articular cartilage and subchondral bone from the trochlear ridge (Fig 1B). Core samples were trimmed and divided to yield 4 hemicylindrical fragments measuring 3.0 mm in depth, 2.0 mm in the largest width, and 4.0 mm in length (Fig 2). Average total weight and calculated volume for all four fragments were 140 mgs and 75.42 mm\(^3\), respectively. In all cases, fragment composition was articular cartilage and subchondral bone in approximately a one to two ratio of thickness. Fragments were maintained in sterile gauze sponges saturated with balanced electrolyte solution\(^n\) until implantation. The tibiotarsal joint was lavaged with balanced electrolyte solution to remove any debris. Joint capsule was reapposed with 2/0 polydioxanone\(^o\) in a simple, continuous pattern. Subcutaneous tissue was reapposed in a similar manner and the skin incision was closed with interrupted horizontal mattress sutures of 2/0 nylon.\(^p\)

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\(^1\) Weitlaner retractor, Miltex, Lake Success, NY.

\(^m\) Michele Trephine, Miltex, Lake Success, NY.

\(^n\) Lactated Ringers Injection U.S.P., Kendall McGaw Laboratories, Irvine, CA.

\(^o\) PDS\(^\circ\), Ethicon, Sommerville, NJ.

\(^p\) Ethilon\(^\circ\), Ethicon, Sommerville, NJ.
Fig 1A. Surgical exposure of the lateral trochlea of the talus (LTT). (IR = Intermediate ridge of the distal tibia).
Fig 1B. Cores of articular cartilage and subchondral bone were removed from the lateral trochlea of the talus with a Michele trephine.
Fig 2. Osteochondral cores were divided to yield four hemicylindrical fragments 3.0 mm in depth and 4.0 mm in length. (a = articular cartilage; b = subchondral bone)
B. Arthroscopic Procedure

The arthroscopic procedure was performed according to standard protocol (McIlwraith, 1984b; McIlwraith et al., 1987). Two 1.0 cm skin incisions were made over the middle carpal joint, 1.5 cm lateral and medial to the common digital extensor tendon of the randomly preselected experimental carpus. The middle carpal joint was distended with 20-25 cc of balanced electrolyte solution and a sharp obturator within the 4.0 mm arthroscopic sleeve was used to penetrate the subcutaneous tissue and joint capsule of the middle carpal joint. This joint was entered lateral or medial to the extensor carpi radialis tendon; whichever approach was dorsal for the surgeon. Sharp obturator removal followed with placement of a blunt obturator, allowing the arthroscopic sleeve to be positioned further into the joint. The blunt obturator was replaced by an arthroscope, egress flow established, and the middle carpal joint was examined fully as previously described (McIlwraith, 1984b; Hurtig et al., 1985). Abnormal findings were noted within the surgical report. Following arthroscopic examination, an egress cannula was placed through the incision made opposite the arthroscopic entry portal of the experimental leg. Joint lavage utilized alternating distension and collapse until a full liter of cold

q 4 mm arthroscopic sleeve, Richard Wolf Instruments, Inc., Rosemont, IL.

r 2.7 mm O.D. 25° telescope, Richard Wolf Instruments, Inc., Rosemont, IL.

s Dyonics Infusion Cannula, Andover, MA.
buffered isotonic fluids\(^1\) had been flushed. The four previously harvested osteochondral fragments were individually placed, under arthroscopic visualization, into the middle carpal joint through the egress cannula. A blunt obturator was used to advance them through the cannula into the joint. The egress cannula was removed and fragment placement was again verified by direct arthroscopic visualization. A similar procedure was performed on the opposite middle carpal joint, but osteochondral fragments were not implanted. Skin incisions were closed with 2/0 nylon in a cruciate pattern. All operative areas (carpi and tarsus) were covered with sterile non-adherent dressings.\(^u\)

**Post-Operative Care**

Horses were medicated with 2 grams of phenylbutazone\(^v\) intravenously one hour after recovery from anesthesia and were maintained on this medication orally at 1 gram twice daily, for the following three days. Bandages were changed on the third post-operative day and replaced as needed for 7 days. Skin sutures were removed after 10 days. All animals were maintained in a 12 foot by 12 foot stall for one month. Passive flexion was initiated twice daily after day 10 and continued for 20 days as described (McIlwraith, 1984b). Table 1 summarizes signalment, duration, implanted limb, and exercise provision for each horse. After one month, one horse was euthanatized. Nine other horses

\(^1\) Lactated Ringer Injection plus 2 cc/liter of 8.4% sodium bicarbonate solution.

\(^u\) Telpha, The Kendall Co., Boston, MA.

\(^v\) Butazolidin, Coopers Animal Health, Inc., Kansas City, KS.
were moved to outside paddocks for an additional month of confinement. Two of these horses were euthanatized prior to onset of exercise. Evaluations, measurements, and sampling were performed according to Table 2.

**Exercise Regimen**

The remaining seven horses were begun on an exercise program two months after surgery (Table 3). Initial 4 weeks of exercise included daily walking (approximately 1.5 m/sec) on a mechanical walking device w (hot walker) for 20 minutes in a clockwise direction and 20 minutes counterclockwise. Following this period, remaining horses were given 2 full months of daily exercise on either a longe line or a mechanical walking device at a trot and canter, 60 minutes per day, 6 days per week. During the final month, the horses were exercised every other day at a walk and a trot for 60 minutes on a mechanical walker.

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w Hot to Trot, Cleveland, OH.
TABLE 1  Summary of horse signalment, duration of study, implanted limb, and exercise provision for each animal.

<table>
<thead>
<tr>
<th>Duration of Study (Mo.)</th>
<th>Horse</th>
<th>Breed</th>
<th>Sex</th>
<th>Age (yr.)</th>
<th>Implant Limb</th>
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<td>L</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>QH</td>
<td>G</td>
<td>2</td>
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</tr>
<tr>
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<td>7</td>
<td>QH</td>
<td>M</td>
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<td>R</td>
<td>+*</td>
</tr>
<tr>
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<td>1</td>
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<td>G</td>
<td>3</td>
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<td>3</td>
<td>L</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>TB</td>
<td>G</td>
<td>3</td>
<td>R</td>
<td>+</td>
</tr>
</tbody>
</table>

TB = Thoroughbred  
Q = Quarter horse  
A = Arabian  
G = Gelding  
S = Stallion  
M = Mare  
L = Left  
R = Right

t = 4 months  
* = 2 months  
+ = Exercised  
- = Not exercised
<table>
<thead>
<tr>
<th>Evaluation intervals</th>
<th>Pre-Op*; Post-Op†; Monthly</th>
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</thead>
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<tr>
<td>Lameness evaluation</td>
<td>Pre-Op; Post-Op; Monthly</td>
</tr>
<tr>
<td>Circumference measurement</td>
<td>Pre-Op; Post-Op; PSM-1; Euthanasia</td>
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<tr>
<td>Arthrocentesis</td>
<td>Pre-Op; Post-Op; PSM-1; Euthanasia</td>
</tr>
<tr>
<td>Radiographic exam</td>
<td>Pre-Op; Post-Op; PSM-1; PSM-2;</td>
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<tr>
<td>Euthanasia/Post mortem§</td>
<td>Euthanasia</td>
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<tr>
<td></td>
<td>PSM-1 (4); PSM-2 (2, 5); PSM-4 (7);</td>
</tr>
<tr>
<td></td>
<td>PSM-6 (1, 3, 6, 8, 9, 10)</td>
</tr>
</tbody>
</table>

PSM = Post Surgical Month
* = Pre-Operative
† = Post-Operative - Within two weeks post surgery
§ = Numbers in parenthesis indicate identity of horses
TABLE 3  Exercise protocol, horses involved, and daily distance for months three through six.

<table>
<thead>
<tr>
<th>Month</th>
<th>Exercise</th>
<th>Horse</th>
<th>Distance km/day (miles/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSM-3</td>
<td>Walk (1.5m/sec.)</td>
<td>1, 3, 6, 7, 8, 9, 10</td>
<td>3.6 (2.25)</td>
</tr>
<tr>
<td></td>
<td>40 minutes daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSM-4,5</td>
<td>Trot (4.0m/sec.) and canter (5-6m/sec.)</td>
<td>1, 3, 6, 8, 9, 10</td>
<td>14.4 - 21.6 (9 - 13.5)</td>
</tr>
<tr>
<td></td>
<td>60 minutes daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSM-6</td>
<td>Walk/trot</td>
<td>1, 3, 6, 8, 9, 10</td>
<td>2.72 - 7.2 (1.7 - 4.5)</td>
</tr>
<tr>
<td></td>
<td>60 minutes every other day</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PSM = Post Surgical Month
Evaluation

Lameness Evaluation

At regular intervals (Table 3), horses were observed for detectable lameness while trotted on pavement in a straight line in hand, and when longed in a circle in either direction. Responses to deep palpation, a 2 minute carpal flexion test, and range of motion were determined. If lameness was detected, site of involvement was identified by a combination of perineural and intra-articular anesthetic injections (Schmotzer and Timm, 1990).

Joint Enlargement

Degree of synovial effusion was evaluated visually and assessed by measurement of middle carpal joint circumference. A bovine scrotal circumference tape \(^x\) was placed around the carpus over the middle carpal joint with the horse standing in a fully weight-bearing position. Positioned over the palpable synovial fossae of the middle carpal joint, a small bubble level \(^y\) was used to verify the tape position being parallel to the ground surface and circumferentially perpendicular to the leg. Measurements were recorded with the tape tightened to firm contact with the skin.

Synovial Fluid Sampling and Evaluation

Synovial fluid was obtained aseptically from both middle carpal joints at indicated intervals (Table 2), placed in EDTA vacutainer tubes \(^z\) and submitted

---

\(^x\) Intermountain Veterinary Supply, Seattle, WA.

\(^y\) Hopkins Mfg. Corp., Emporia, KS.

\(^z\) Becton, Dickinson and Co., Rutherford, NJ.
for immediate analysis. Appearance, color, and volume of fluid was recorded.

White cell count, \(^{\text{aa}}\) differential cell count (Wrights Stain), total solids measurement as an index of total protein, \(^{\text{bb}}\) and mucin clot forming ability (MCFA) \(^{\text{cc}}\) were determined.

Synovial fluid samples were submitted to an independent laboratory \(^{\text{dd}}\) for assessment of hyaluronate sodium concentration and presence of cartilaginous fragments prior to euthanasia.

**Radiographic Examination**

Carpal radiographs were performed and evaluated as indicated (Table 2). Four standard views, were utilized. Radiographs were evaluated for (1) soft tissue swelling, (2) effusion, (3) location, size, and number of fragments, and (4) degenerative changes suggested by osteophyte production, reduction of apparent joint width, subchondral bone sclerosis, joint surface irregularity, and enthesophyte formation.

---

\(^{\text{aa}}\) Coulter counter, ZBI, Coulter Electronics, Inc., Hialeah, FL.

\(^{\text{bb}}\) TS Meter, American Optical Corp., Scientific Instrument Division, Buffalo, NY.

\(^{\text{cc}}\) Add 0.5 ml of fluid to 2.0 ml of 2.5% glacial acetic acid.

Rating:

- Good - compact clot, clean fluid
- Fair - soft clot, turbid fluid
- Poor - viable clot, cloudy fluid
- Very Poor - no clot, flocculent fluid

\(^{\text{dd}}\) Chesapeake Biological Laboratories Inc., Baltimore, MD.
Post Mortem Exam

At previously described intervals, animals were humanely destroyed using an overdose of sodium pentobarbital. Carpi were removed by making transverse bandsaw cuts proximally through the radius, and distally through the third metacarpal bone. Removal of skin was followed by exposure of middle carpal joints by circumferentially incising dorsal attachments of the joint capsule to the proximal row of carpal bones. Cartilage surfaces were described and photographed to document abnormal findings. Synovial lining was evaluated for color, thickness, and surface irregularity in both villous and non-villous areas of the dorsal and palmar capsule. All areas of synovium were grossly examined for presence of osteochondral fragments. If fragments were detected, size, orientation, location, and sites of attachment within the joint were recorded.

Preparation of Microscopic Samples

Using a rotary saw, 3 mm x 20 mm frontal slabs were cut across weight-bearing surfaces of the radial, intermediate, and third carpal bones in specifically determined locations (Fig 3). Osteochondral slabs were fixed in 10% buffered formalin, decalcified in 10% formic acid for 72 hours, trimmed, embedded in paraffin, and sectioned at 5 microns. Careful attention was given to assure the microtome blade cut through articular cartilage perpendicularly (Hurtig et al., 1988). Sections were stained with hematoxylin and eosin, a

---

a Sleepaway, Fort Dodge, Fort Dodge, IA.

b Variable speed rotary tool, Sears Roebuck & Co., Chicago, IL.

g Gill(R)-3 hematoxylin, Shandon, Pittsburgh, PA.
Fig 3. Surface profiles of bones comprising the middle carpal joint. Sampled frontal areas are outlined by the dashed lines on the radial (C_R), intermediate (C_I), and third (C_3) carpal bones. (Cu = ulnar carpal bone; C_2 = second carpal bone; C_3R = radial facet of third carpal bone; C_3I intermediate facet of third carpal bone; C_4 = fourth carpal bone.
and 0.1% safranin-O in 0.02 M phosphate buffer (pH=6) for 10 minutes. Safranin-O sections were stained simultaneously by the same histochemist in an effort to standardize staining intensity (Hurtig et al., 1988; Kiviranta et al., 1984; Kiviranta et al., 1985).

Sagittal sections of the joint capsule were removed from predetermined sites in the dorsal villous, dorsal nonvillous, and palmar synovial areas, fixed in 10% buffered formalin, trimmed, embedded in paraffin, sectioned at 5 microns, and stained with hematoxylin and eosin.

Grossly recognizable osteochondral fragments were removed with surrounding tissue, fixed in formalin, embedded in paraffin, sectioned at 5 microns to process separately in hematoxylin and eosin and safranin-O as previously described.

**Microscopic Evaluation**

All histologic sections were coded and evaluated microscopically without examiner knowledge of the implanted joint. Synovial samples from each middle carpal joint were evaluated and scored with regard to (1) proliferation of synovial cells and villi, (2) depth of inflammation, and (3) degree of inflammation. Categories were scored (0 = absence of change, 1 = mild change, 2 = moderate change, 3 = severe change). A tabulated total was used as an index of synovial inflammation for each joint. Character of inflammatory cell infiltrate, intimal cell appearance, and presence of capsular fibrosis, granulation tissue, fibrin deposition, or adhesion formation were qualitatively noted by the examiner (Appendix).
Osteochondral slab samples were evaluated for: (1) articular cartilage morphology; (2) matrix staining with Safranin-O at three depths (superficial, intermediate, deep); and (3) degenerative articular changes. A modified scoring system (Yovich et al., 1987) was used to quantitate these results. Additional parameters examined included subchondral bone morphology, integrity of the tidemark, and chondrocyte changes involving chondrone formation, or degree of cellularity (Appendix).

Sections of retrieved fragments were evaluated for size, distribution of cartilage and bone, Safranin-O staining intensity, cellular infiltration, attachment orientation and morphology, and chondrocyte changes. Results were recorded for each identified fragment (Appendix).

**Statistical Analysis**

A paired t-test at the 5% significance level was applied to analyze parametric differences between the implanted and nonimplanted middle carpal joints, with respect to limb circumference, synovial white blood cell count, synovial protein concentration, index of synovial inflammation, cartilage matrix staining, articular cartilage morphology score, degenerative articular change, and hyaluronate sodium concentration.
RESULTS

Postoperatively, recovery from anesthesia occurred without complication in all ten horses. Incisions healed primarily, and complications were not observed with or following surgical procedures.

Information regarding effusion, lameness, mucin clot activity, and radiographic results for each horse throughout the duration of the study is summarized in Table 4.

Clinical Exam

Mild to moderate degree of soft tissue swelling and palpable heat of both dorsal carpal areas was observed in all horses after surgery. Within 3 days, this anticipated inflammatory reaction had subsided. From two weeks to the second post-surgical month (PSM-2), it was possible to visually determine the implanted carpus in five of nine horses (2, 5, 8, 9, 10), based on a difference in the degree of middle carpal joint effusion. At 6 months (PSM-6), effusions were evident in the implanted middle carpal joint in five of six horses (3, 6, 8, 9, 10).

Lameness Exam

Horses 3, 7, 8, and 10 developed lameness at PSM-1. Pain originated from the implanted joint. Examination 30 days later at PSM-2, revealed persistence of the lameness associated with the implanted middle carpal joint in two horses (3, 7). Horse 7 was not lame by PSM-3, but horse 3 was consistently lame to PSM-6.
<table>
<thead>
<tr>
<th>Duration (Month)</th>
<th>Horse</th>
<th>PSM-1 Effusion</th>
<th>Lameness</th>
<th>Radiology*</th>
<th>PSM-2 Effusion</th>
<th>Lameness</th>
<th>Radiology*</th>
<th>PSM-4 Effusion</th>
<th>Lameness</th>
<th>Radiology*</th>
<th>PSM-6 Effusion</th>
<th>Lameness</th>
<th>Radiology*</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
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<td>+</td>
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<td>-</td>
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<td>5</td>
<td>+</td>
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<td>+</td>
<td>-</td>
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<td>+</td>
<td>-</td>
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<td>+¹,²</td>
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<td>-</td>
<td>+²</td>
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<td>+</td>
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<td>+¹</td>
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<td>+</td>
<td>+</td>
<td>+¹</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>+</td>
<td>+</td>
<td>+¹</td>
<td>+¹</td>
<td>-</td>
<td>+¹</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+¹</td>
</tr>
</tbody>
</table>

+ = Lameness, effusion, or radiographic changes present
- = No lameness, effusion, or radiographic changes present
* = Radiographic changes
1. Soft tissue swelling
2. Degenerative changes
† = Mucin clot activity fair
# = Mucin clot activity poor
**Limb Circumference**

Circumferential limb measurements at middle carpal joints increased post-operatively in all horses. Significant increase in limb circumference ($P < 0.05$) was detected in implanted joints 2 weeks after surgery. No significant differences were detected at subsequent intervals, but implanted joints remained larger in the majority of horses. Mean differences for each time period are tabulated in Table 5 and plotted in Figure 4. In horses maintained until PSM-6, limb circumference increased an average of 1.1 cm in the control joints versus an average of 1.91 cm in experimentals.

**Radiological Exam**

**Soft Tissue Changes**

At the initial postoperative exam, mild soft tissue swelling, associated with synovial effusion, was detected radiographically over the dorsal carpus in both experimental and control knees of all horses, except for horse 4. Marked soft tissue swelling was described in two of the implanted carpi (horses 9, 10).

Two months post-operatively (PSM-2), mild bilateral swelling was detected in horses 3, 5, and 7. Mild unilateral soft tissue swelling was apparent in implanted carpi of horses 2, 8, 9, and 10.

Six months postoperatively, five of six horses (3, 6, 8, 9, 10) had increased effusion in the implanted middle carpal joint. Horse 1 showed no soft tissue swelling in either joint.
### TABLE 5  Mean differences in circumference measurements at each time interval.

<table>
<thead>
<tr>
<th>Time (Month)</th>
<th>n</th>
<th>Mean Difference</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre op (0)</td>
<td>10</td>
<td>0.12</td>
<td>.115</td>
</tr>
<tr>
<td>Post op (.5)</td>
<td>10</td>
<td>0.53*</td>
<td>.163</td>
</tr>
<tr>
<td>PSM-1 (1.0)</td>
<td>10</td>
<td>-0.12</td>
<td>.216</td>
</tr>
<tr>
<td>PSM-2 (2.0)</td>
<td>9</td>
<td>0.31</td>
<td>.208</td>
</tr>
<tr>
<td>PSM-3 (3.0)</td>
<td>7</td>
<td>0.32</td>
<td>.131</td>
</tr>
<tr>
<td>PSM-6 (6.0)</td>
<td>6</td>
<td>0.80</td>
<td>.286</td>
</tr>
</tbody>
</table>

SE = Standard Error

* = Significant Difference (P < 0.05)
Fig. 4. Plot of mean difference and standard error of limb circumference measurements at each measured time interval. (From Table 5)

(* = significant difference P<0.05)
Degenerative Changes

Degenerative changes were detected relatively early in the post-operative period; the majority occurred in implanted middle carpal joints. Described changes included superficial periosteal reaction, narrowing of the middle carpal joint space, osteophyte production, and presence of enthesophytes.

One month post-operatively, horse 1 demonstrated a superficial periosteal reaction on the dorsum of the third carpal bone of the implanted (left) middle carpal joint.

Two months post-operatively, signs of degenerative change and soft tissue swelling were detected in the implanted middle carpal joint of three additional horses (2, 5, 7). Findings included exostoses on the intermediate and third carpal bones (horse 2), and osteophyte production on the dorsal aspect of the radial carpal bone (horse 5). Horse 7 appeared to have the most profound degenerative changes, consisting of enthesophyte formation on the radial carpal bone, periosteal reaction on the third carpal bone, and narrowing of the middle carpal joint space. Changes remained consistent over four months when the horse was euthanized.

At PSM-6, mild degenerative changes were detected in the implanted middle carpal joint of horse 3. Changes, consisting of osteophyte production of the intermediate carpal bone, were not evident prior to this time.

Osteochondral Fragment Dynamics

Postoperatively, radiology confirmed presence of implanted osteochondral fragments in all horses. Fragments were located either within the dorsal
synovial space or the lateropalmar synovial pouch of the middle carpal joint. If less than 4 fragments were seen, one of the other fragments was inordinately larger than expected suggesting two fragments in close proximity. Particulate debris, thought to represent crushed fragments, was detected in four of ten joints.

At PSM-1, osseous densities were apparent in all implanted joints except one. Number and size of detected fragments were decreased. Osteochondral fragments were present in the lateropalmar pouch of the middle carpal joint in eight of ten horses. Three horses had osteochondral fragments in both dorsal and lateropalmar aspects of the joint. All fragments implanted in one horse were situated on the dorsal aspect of the joint.

Two months postoperatively, one horse demonstrated a single radiographically detectable fragment, reduced in size and density, on the dorsal aspect of the joint. Fragments were not apparent radiographically in any horses at four or six months.

**Synovial Fluid Assessment**

*Color and Clarity*

Preoperative appearance of synovia for all horses was straw colored and clear. At PSM-1, three of ten horses had abnormally appearing fluid aspirated from the implanted carpus. At PSM-2, seven of nine horses demonstrated a visible difference between pairs of synovial fluids. In all cases, fluid from the implanted joint lacked normal clarity and had an orange or light red coloration, different from iatrogenically-induced hemorrhage. At PSM-6, one horse
demonstrated a lack of clarity in synovial fluid from the implanted joint.

**Total Protein Concentration**

Synovial protein concentrations ranged from 0.249 gm/dl to 4.7 gm/dl. Significance testing for differences between paired values for individuals at a given time demonstrated a significant increase ($P < 0.05$) in implanted joints at PSM-2. Mild elevations of protein, although not significant between paired samples, were noted in three of six animals after the onset of exercise.

**Synovial White Blood Cell Count**

Total white blood cell (TWBC) counts of synovia from middle carpal joints ranged from 100 cells to 3,300 cells. Greatest increase of cell numbers occurred between PSM-1 and PSM-2. In all cases highest white cell counts were detected in implanted joints. Significant difference between paired samples was detected only at PSM-6, with implanted joints demonstrating significantly higher ($P < 0.05$), although not elevated, levels of white cells. Normal distribution of cell types was found in all samples (Tew, 1980).

**Mucin Clot Forming Ability (Table 4)**

Mucin clot forming ability (MCFA) was rated good in all specimens collected before the surgical procedure. Three of nine samples taken from the implanted middle carpal joint showed a reduction in the MCFA from good to fair at PSM-2. At PSM-6, MCFA was reduced in four of six horses; three were graded fair, and one as poor. All sham operated joints showed normal MCFA.
Hyaluronate Sodium Concentration

Hyaluronate sodium concentrations, irrespective of time, ranged from 0.581 to 0.956 mg/ml in implanted joints, and from 0.565 to 0.942 mg/ml in sham operated joints. No significance was detected between differences of implanted and nonimplanted hyaluronate concentrations at PSM-2 and PSM-6.

Cartilage Fragment Analysis

Results of cartilage fragment analysis and clinical interpretation by an independent laboratory are presented in Table 6. Six of ten horses demonstrated existing cartilage damage at euthanasia. Minimal articular degeneration was evident through PSM-2. Samples from the implanted joint of the horse examined at PSM-4 indicated substantial cartilage damage. Of six horses sampled at PSM-6, four implanted joints demonstrated substantial cartilage damage, based on the types of cartilage recovered. Cartilage fragments identified were consistent with articular damage within the superficial, first (resting), and second (proliferative) layer. Samples from control joints were determined to be normal.

Gross Pathological Exam

Extensive changes were noted within implanted middle carpal joints at gross examination (Table 7). Findings contrasted sharply those in nonimplanted joints. Abnormal findings involved cartilage surfaces, synovium, and morphology of detected fragments.
TABLE 6  Summary of cartilage fragment analysis for each horse.

<table>
<thead>
<tr>
<th>Horse</th>
<th>Duration</th>
<th>Implanted</th>
<th>Control</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>1</td>
<td>3 S</td>
<td>3 S</td>
<td>No significant erosion</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>3 S-1 I</td>
<td>4 S</td>
<td>Articular lesion</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>4 S-1 I</td>
<td>3 S-1 I</td>
<td>No extensive lesion</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td>3 S-5 I-5 II</td>
<td>4 S</td>
<td>Substantial cartilage damage</td>
</tr>
<tr>
<td>1</td>
<td>6</td>
<td>3 S</td>
<td>2 S</td>
<td>No significant damage</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>4 S-3 I-2 II</td>
<td>3 S-2 I</td>
<td>Substantial cartilage damage</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>5 S</td>
<td>5 S</td>
<td>No significant erosion</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>5 S-5 I-5 II</td>
<td>3 S-1 I</td>
<td>Substantial cartilage damage</td>
</tr>
<tr>
<td>9</td>
<td>6</td>
<td>3 S-2 I</td>
<td>4 S</td>
<td>Mild articular damage</td>
</tr>
<tr>
<td>10</td>
<td>6</td>
<td>5 S-2 I-1 II</td>
<td>5 S</td>
<td>Significant cartilage damage</td>
</tr>
</tbody>
</table>

* = Number and layer of origin of fragments
S = Superficial
I = Resting
II = Proliferative
### TABLE 7  Summary of gross pathological changes for each horse.

<table>
<thead>
<tr>
<th>Horse</th>
<th>Duration</th>
<th>Cartilage</th>
<th>Synovium*</th>
<th>Fragments*</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>1</td>
<td>+</td>
<td>++</td>
<td>(4 - 3 palmar; 1 dorsal)</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>++</td>
<td>+</td>
<td>(3 - 2 palmar; 1 dorsal)</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>++</td>
<td>+</td>
<td>(2 palmar plaques)</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td>++</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>6</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>++</td>
<td>+ (adhesion)</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>++</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>6</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>6</td>
<td>++</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

† Graded severity of tissue changes:

0 = No gross abnormalities
+ = Mild degree of abnormality
++ = Moderate to severe abnormality

* Synovial changes included discoloration, thickening, villous irregularity.

# Number of fragments detected and their location in the joint.
One Month (PSM-1):

One horse (4) was examined. Joint capsule of the implanted (left) side was thickened and hyperemic on its dorsal and palmar aspects. Articular changes were minimal, consisting of linear scoring on articular surfaces of the intermediate carpal bone. Lesions were not detected in the nonimplanted joint, or either carpometacarpal joints.

Three implanted osteochondral fragments were detected within synovium caudal to the palmar aspect of the third carpal bone. Two fragments were measured to be approximately half their original size. A third fragment was similar to original size at implantation. An additional fragment was located in the palmar lateral pouch adjacent to the fourth carpal bone. It was no smaller than original dimensions. Fragments were adhered at their osseous surfaces to synovium.

Two Months (PSM-2):

Two horses (2, 5) were examined. Synovial surfaces of implanted joints were thickened and erythematous dorsally in villous areas. Articular surfaces of implanted joints were characterized by sagittally orientated linear excoriations. In horse 2, two fragments were attached to synovium on the palmar lateral aspect of the joint, while a third was located dorsally, enveloped within nonvillous synovial lining. The dorsal fragment was detected radiographically. Size of fragments was reduced 75% from original dimensions, and attachment surface was not able to be ascertained. Two small surface plaques, considered to be sites of fragment resorption, were intimately attached to the synovium of the
lateral palmar pouch in horse 5. Radiographically, these densities were not detectable. Gross abnormalities were not detected in either the nonimplanted middle carpal joint or adjacent carpometacarpal joints.

Four Months (PSM-2):

Horse 7 was the only animal examined at this interval. The left (nonimplanted) middle carpal joint showed no gross changes. The right middle carpal joint demonstrated marked thickening (twice control) of the dorsal synovial layer. Linear "paint-brush" cartilage defects were present over the articular surfaces of all bones comprising the middle carpal joint. No fragments were grossly detected at PSM-4.

Six Months (PSM-6):

Of six horses examined (1, 3, 6, 8, 9, 10), four exhibited mild synovial thickening and discoloration, but no attendant cartilage damage within the control joint.

Abnormalities were detected in all synovial membranes and most articular surfaces of each implanted middle carpal joint. Dorsal and palmar synovium was found to be discolored, severely thickened, and irregular in all horses except horse 10, whose synovial layer was discolored, but not thickened. Horse 3 had synovial adhesions to focal cartilage defects on the dorsal rim of the radial and second carpal bones.

Gross articular cartilage damage ranged from none (horse 6) to severe. Mild linear scoring in a sagittal plane was present on articular surfaces in horses 1 and 9. Horses 8 had moderate to severe changes characterized by cartilage
irregularity, linear scoring in a sagittal plane, and excoriation of the cartilage surfaces. Two horses (3, 10) demonstrated severe focal cartilage damage. Third and intermediate carpal bones appeared to be most affected.

Implanted osteochondral fragments were not detected. Detectable abnormalities were not detected in the carpometacarpal joint.

**Histologic Evaluation**

At one month, all fragments recovered from the implanted joint of horse 4 had developed connective tissue attachments from the synovium to the bony side of the implant. Blood vessels were occasionally recognized within this connective tissue attachment. Fragments demonstrated viable articular cartilage, dead or dying bone, and bone resorption at the synovial interface. Size reduction was apparent in two fragments.

Osteochondral implants underwent size reduction, and complete necrosis of cartilage and bone components by two months postimplantation. Synovial plaques, thought to be resorbed fragments, consisted of vascularized dense fibrous connective tissue. Two nodules, recovered from different animals, demonstrated small fragments of necrotic cartilage and bone within their interior. Cellular infiltrate, consisting of scattered lymphocytes, plasma cells, and hemosiderin-laden macrophages, was also present in these nodules. Fragments were not recovered from implanted joints at four or six months after surgery.

Table 8 summarizes microscopic abnormalities in synovium and cartilage samples.
### TABLE 8  Summary of microscopic changes for each horse.

<table>
<thead>
<tr>
<th>Duration</th>
<th>Horse</th>
<th>Synovium Score</th>
<th>Synovial Findings</th>
<th>Cartilage Morphology Score</th>
<th>Safranin-O Score</th>
<th>Degenerative Articular Score</th>
<th>Chondrone Formation</th>
<th>Hypocellularity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>3</td>
<td>Multifocal inflammation fibroblastic response</td>
<td>2</td>
<td>3 - 3 - 3</td>
<td>1</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>2</td>
<td>Macrophages; granulation tissue; hemosiderophages</td>
<td>2.5</td>
<td>2.5 - 3 - 3</td>
<td>1</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>1</td>
<td>Edematous villi</td>
<td>1</td>
<td>2.5 - 3 - 3</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>1</td>
<td>Macrophages; focal inflammation</td>
<td>3</td>
<td>1.5 - 2.5 - 3</td>
<td>3</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>1</td>
<td>Mineralized debris in synovium</td>
<td>2</td>
<td>2 - 3 - 3</td>
<td>2.5</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>1</td>
<td>Lymphocytic infiltration</td>
<td>2.5 focal</td>
<td>1.5 - 3 - 3</td>
<td>2</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>1</td>
<td>Macrophages; amorphous debris</td>
<td>1</td>
<td>2.5 - 3 - 3</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>1</td>
<td>Lymphocytes, plasma cells</td>
<td>4 focal</td>
<td>1.5 - 3 - 3</td>
<td>3.5</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>9</td>
<td>0</td>
<td>Minor changes</td>
<td>2</td>
<td>2.5 - 3 - 3</td>
<td>2.5</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>1</td>
<td>Lymphocytic infiltration</td>
<td>1</td>
<td>2.5 - 3 - 3</td>
<td>1</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

* Synovial Score:  
  0 = Normal  
  1 = Mild  
  2 = Moderate  
  3 = Severe  

* Safranin-O Staining. Superficial - Intermediate - Deep:  
  0 = No matrix staining  
  1 = Slight  
  2 = Moderate  
  3 = Normal  

† Cartilage Morphology Score:  
  0 = Normal  
  1 = Surface frayed  
  2 = Horizontal fibrillation  
  3 = Vertical fibrillation  
  4 = Cartilage erosion  

§ Degenerative Articular Score (all focal):  
  0 = Normal  
  1 = Minor loss of chondrocyte nuclear staining  
  2 = Eosinophilic chondrocyte nuclei and empty lacunae  
  3 = Empty lacunae and disorganized matrix  
  4 = All chondrocytes necrotic, loss and/or collapse of matrix
Paired synovial samples of horse 7 contrasted sharply. Synovium from the implanted joint was characterized by a moderate to severe degree of synovial cell and villous hyperplasia. Mild to moderate superficial inflammatory response ranged from solitary to multifocal areas within synovial villi. Foci consisted of aggregations of lymphocytes, plasma cells, and occasional hemosiderin-laden macrophages (hemosiderophage). Synovium from the dorsal villous area demonstrated profound villous thickening associated with inflammation and fibroplasia. Synovium from the control joints lacked inflammatory reaction.

Physical changes in articular cartilage of implanted joint were limited to superficial fraying, with no deeper pathology. Chondrocyte degenerative change ranged from minor loss of nuclear staining to presence of empty lacunae and disorganized matrix.

Synovial samples from implanted joints were significantly ($P=0.04$) inflamed and hyperplastic. Synovium from the implanted joint of horse 2 was characterized by synovial cell and villous hyperplasia, superficial inflammation consisting of macrophages and lymphocytes, nodules of granulation tissue, and fibrin on synovial surfaces. Within these nodules were scattered hemosiderophages and macrophages. Samples from the implanted joint of horse 5 were less inflamed, having a mild to moderate degree of synovial cell and villous hyperplasia. Dorsal villi were edematous.
Degeneration of cartilage morphology was significantly increased (P=0.03) in implanted joints. Features included fraying, groove formation, and erosion. Sections from the intermediate and third carpal bones were most commonly affected.

With respect to chondrocyte changes, joints examined at two months were not significantly different (P=.205), exhibiting minor loss of nuclear staining in occasional sections.

PSM-4

Synovial samples from the implanted joint of horse 7 at four months exhibited mild to moderate hyperplasia, with focal inflammatory response consisting of proliferating fibroblasts, lymphocytes, and hemosiderophages surrounding irregular fragments of necrotic bone. The control joint showed mild hyperplasia in the dorsal synovial area.

Focal articular erosion was commonly described lesion in the implanted joint. The nonimplanted joint demonstrated normal articular morphology.

Profound chondrocyte degenerative change was associated with the implanted joint. Each sample exhibited focal chondrocyte necrosis and loss or collapse of matrix near cartilage erosions. Chondrone formation and focal hypocellularity were always present adjacent to the erosions.

PSM-6

Six months after surgery, synovial samples demonstrated no significant difference (P=0.09). All horses, except two (1,9), had mild to moderate synovial hyperplasia in one or more synovial samples; the dorsal synovial area always
being affected. Implanted joints differed from controls by presence of cellular infiltrates consisting of lymphocytes, plasma cells, and macrophages within the synovial villi.

Physical damage to the articular surfaces was significantly more severe (P=0.03) in implanted joints. Damage ranged from minimal surface fraying (6,10) to multiple areas of erosion (8). Surface grooves extended deeper into the cartilage layers with a more gentle slope to the sides of the erosion.

Chondrocyte degenerative change, classified as moderate to severe in four horses, was significant (P=0.02) in implanted joints at six months. Severely affected cartilage was characterized by empty lacunae, necrotic chondrocytes, and disorganized or lost matrix. Changes occurred adjacent and below erosions, and consisted of chondrone formation, hypocellularity, and local reduction in matrix staining.

**Safranin-O Staining**

At two months, distribution and intensity of safranin-O stain in articular cartilage was not significantly different between implanted and control joints for superficial (P=0.5), intermediate (P=0.5), and deep or radiate (P=0.5) layers. No difference was detected in degree of safranin-O uptake between joints for each cartilage layer (P>0.3 for all layers) at six months. Reduction in stain intensity was detected more frequently in the superficial layer of cartilage from implanted joints at each assessment period. Only on rare occasion was reduced stain uptake evident in the intermediate layers; deep (radiate) layers always stained maximally.
Table 9 provides a complete summary of the frequency of abnormalities associated with investigated parameters of the implanted joint.
### TABLE 9  Frequency of horses having abnormalities associated with various parameters of the implanted joint.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PSM-1</th>
<th>PSM-2</th>
<th>PSM-4</th>
<th>PSM-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effusion (circumference)</td>
<td>5/10</td>
<td>5/9</td>
<td>4/7</td>
<td>5/6</td>
</tr>
<tr>
<td>Lameness</td>
<td>4/10</td>
<td>2/9</td>
<td>2/7</td>
<td>1/6</td>
</tr>
<tr>
<td>Mucin Clot Abnormal</td>
<td>3/10</td>
<td>0/2</td>
<td>0/1</td>
<td>4/6</td>
</tr>
<tr>
<td>Radiographic Changes</td>
<td>3/10</td>
<td>4/9</td>
<td>1/1</td>
<td>5/6</td>
</tr>
<tr>
<td>Cartilage Fragment Analysis Abnormal</td>
<td>0/1</td>
<td>1/2</td>
<td>1/1</td>
<td>4/6</td>
</tr>
<tr>
<td>Gross Cartilage Damage</td>
<td>1/1</td>
<td>2/2</td>
<td>1/1</td>
<td>5/6</td>
</tr>
<tr>
<td>Gross Synovial Changes</td>
<td>1/1</td>
<td>2/2</td>
<td>1/1</td>
<td>5/6</td>
</tr>
<tr>
<td>Grossly Visible Fragments</td>
<td>1/1</td>
<td>1/2#</td>
<td>0/1</td>
<td>0/6</td>
</tr>
<tr>
<td>Microscopic Synovial Abnormalities</td>
<td>1/1</td>
<td>2/2*</td>
<td>1/1</td>
<td>4/6</td>
</tr>
<tr>
<td>Microscopic Cartilage Abnormalities</td>
<td>1/1</td>
<td>2/2*</td>
<td>1/1</td>
<td>5/6*</td>
</tr>
</tbody>
</table>

* = Significant at P<0.05  
# = One synovial plaque
DISCUSSION

This study represents an analysis of the clinical, radiographic, and pathological changes associated with implantation of osteochondral fragments in middle carpal joints of horses. The middle carpal joint was selected because it represented the joint most commonly found to have radiographically recognizable debris after arthroscopic surgery for intra-articular fractures.

Horses from two to four years were utilized to reflect clinical population, minimize incidence of previous articular pathology, and to standardize response. Implants were intended to mimic debris remaining after arthroscopic procedures involving extensive curettage of articular surfaces. Implant size was exaggerated to allow development of conclusions over the long term. Number of fragments implanted was within observed ranges of counted fragments in clinical cases.

After arthroscopic examination and implantation of fragments, the horses were subjected to routine postoperative protocol consisting of stall rest, passive flexion, paddock confinement, and a gradual return to increasing levels of exercise in order to mimic the typical situation for clinical cases (McIlwraith, 1990). Termination of the study after six months provided adequate time to assess fate of fragments, and presence of synovial or articular pathology.

Recognition of osteochondral debris in a significant number of cases necessitated developing conclusions regarding its fate and effects on joint structure and function. Lack of prospective studies on osteochondral loose bodies in horses, and questions regarding the occasional trauma-induced loose
body prompted this investigation.

The majority of prospective and retrospective studies investigating origins and development of loose bodies indicate most fresh osteochondral fragments extruded into joint cavities never become loose bodies, but become adherent and gradually resorbed by cells of the synovium (Phemister, 1924; Harbin and Moritz, 1930; Bennett et al., 1932; Lloyd-Roberts, 1953; Milgram, 1977a, 1977b). Attachment to synovium may occur more readily in smaller joints (Bennett et al., 1932). In dogs, synovial adherence occurred in the stifle joint by three to four weeks (Harbin and Moritz, 1930; Bennett et al., 1932).

In this study, fragments were adhered to the synovium within four weeks, displaying mild degradation. Each fragment was adhered at its bony surface. The reason for this is unknown, but the irregular subchondral surface may better stimulate and allow more efficient adherence by the synovium. Necrotic bone within the implant may produce local factors capable of activating synoviocyte adherence, and stimulation of phagocytic function.

Propensity for loose bodies to locate in specific areas has been noted by numerous authors (Phemister, 1923; Bennet and Bauer, 1932; McGinty, 1982; Dandy, 1984; Olson et al., 1988; Vachon et al., 1989). Loose fragments in this study predominately located in the palmar area, usually within the lateral palmar pouch. Occasionally a fragment located dorsolaterally in the middle carpal joint. Loose bodies, being more dense than synovial fluid are subject to the force of gravity, and will usually locate in the more distal aspect of the joint (Lloyd-Roberts, 1953; Dandy, 1984). Fragment dimension, joint size, and degree
of joint motion also affect final location of loose bodies or debris. Loose bodies did not demonstrate a propensity for adherence to villous areas of synovium.

Prior to synovial adhesion, fragments may become reduced in size as a result of fibrillation secondary to mechanical damage within the joint, bone necrosis resulting from inadequate nutritional support or altered synovial fluid composition, or enzymatic degradation (Milgram, 1977a; 1977b; Hauser, 1942; Phemister, 1923; Barrie, 1978; Agins et al., 1986). In our study, crushing of original implants between opposing articular surfaces resulted in radiographically apparent reduction in size, and production of smaller fragments within the joint of four horses in the early postoperative period. Additional, less apparent mechanical abrasion undoubtedly occurred between the implant, synovial, and articular surfaces prior to synovial attachment.

At one month, osteocytes and trabeculae were undergoing necrosis, while chondrocytes remained viable. Earlier investigations of loose bodies in other species confirm synovial fluid is capable of sustaining chondrocyte longevity, while bone in the absence of blood supply, will undergo necrosis (Fisher, 1921; Bennett et al., 1932; Baille and Selle, 1959; Barrie, 1978). In agreement with previous studies (Bailey and Selle, 1959; Agins et al., 1986), our implants demonstrated bone and cartilage necrosis and resorption within two months of implantation. Cartilage necrosis was attributed to altered synovial composition.

Free osteochondral fragments may undergo superficial loss of matrix from the cartilage, chondrocyte de-differentiation, and acquisition of an external layer of fibroblastic cells (pseudocapsule) at four to eight weeks (Bennett et al., 1932;
Origin of these cells is unknown, but may be from the synovium (Agins et al., 1986) or by endogenous metaplasia of the superficial chondrocytes of the fragment (Bennett et al., 1932). Formation of an external layer of fibroblasts was apparent on loose bodies examined at one and two months. Source of this "pseudocapsule" is not readily apparent because implants were adhered to synovium at each examination interval. Cellular morphology in our sections appeared to be metaplastic chondrocytes. However, at the earliest evaluation period (1 month), the pseudocapsule failed to cover the entire circumference, and demonstrated more cellular layers closer its attachment to the synovium. This finding suggests the capsular cells may be differentiated from the synovial intima.

From one to two months, adhered fragments demonstrated "scalloping" of the surface of necrotic bone adjacent to the synovial attachment. Barrie (1978) felt external cells of loose bodies assume a resorptive role upon adherence to the synovium. Change in function is possibly related to increased oxygen tension. Fragments have been shown to become completely engulfed and resorbed by macrophages or osteoclast-like cells in the synovial lining (Bennett and Bauer, 1932; Fisher, 1931; Phemister, 1923). Inflamed synovium appears to be more efficient in resorption of fragments (Milgram, 1977b).

Proliferation and enlargement of implants did not occur in this study. The exceptional osteochondral fragment may remain free within the joint, and undergo proliferative changes (Phemister, 1924; Habin and Moritz, 1930; Fisher, 1931; Bennett et al., 1932; Bailey and Habel, 1960; Milgram, 1977b).
Proliferation of new cartilage layers, surface resorptive activity, and degenerative calcification appear to occur in all older osteochondral loose bodies remaining free within the joint cavity regardless of origin and composition (Milgram, 1977b). Fibrocartilage production over surfaces of the loose body will be responsible for any size increase. Usually, fibrocartilage production initiates on the bony surface, and gradually forms successive overlapping layers to eventually surround the original nidus (Milgram, 1977b). Original cartilage cells will remain viable centrally, until their depth approaches 3 mm, a distance preventing adequate diffusion of synovial nutrients. Internally, cell necrosis will occur and dystrophic calcification may become apparent (Agins et al., 1986).

At the outset of this experiment, I had anticipated implants would become adherent to the synovium and gradually resorbed without inducing significant pathology. In contrast to my thoughts, and studies involving other species (Bennett et al., 1932; Harbin and Moritz, 1930), loose body implantation in the horse subjected to normal postsurgical protocol does not appear to be without associated pathology. Indeed, the implants, although resorbed early in the study, resulted in significant synovitis and articular damage.

Osteochondral fragments, either original implants, or micro- and macroscopic debris from abraded articular cartilage, resulted in signs consistent with synovitis early in the postoperative period. Effusion, lameness, increased limb circumference, and radiographic abnormalities represent clinical signs of acute, induced synovitis (McIlwraith et al., 1979). Increased synovial protein, and reduction of mucin clot forming activity are additional signs consistent with
synovial inflammation in the horse (Van Pelt, 1962; 1974).

One month after surgery, four of ten horses were lame. Acute synovitis, and mechanical irritation and interference by implants most likely account for this finding. Reduction to one of six horses lame at PSM-6 is related to lack of macroscopic fragments, reduction in the degree of synovial inflammation, and pathologic findings being limited to the articular cartilage.

Exostosis and osteophytosis was apparent in implanted joints in four of nine horses. This finding occurred earlier than reported by Vachon et al. (1986) or Riddle (1970). Osteophytosis represents a nonspecific response to cartilage or joint capsule damage. Cartilage defects stimulate increased metabolic activity of the cells at the periphery of a joint surface (French et al., 1989). Endochondral ossification within these areas results in osteophyte formation (Vachon et al., 1986).

Histopathological findings included granulation tissue, fibrin deposition, synovial thickening, hyperemia, and cellular infiltration. Development of an equine model of osteoarthritis by injections of filipin (McIlwraith et al., 1979) or autogenous cartilage fragments (Hurtig, 1988) resulted in similar findings. Fibroblastic proliferation, apparent in synovial samples at four months, represents a nonspecific response to synovitis (McIlwraith and Van Sickle, 1981). Exercise or joint movement may exacerbate this finding (French et al., 1989).

Synovial cell and villous hyperplasia accounted for grossly apparent synovial thickening, and was a consistent finding in synovial sections examined. Specific features distinguished implanted joints. Cellular infiltrates of
lymphocytes, macrophages, and occasional plasma cells were apparent within the synovium at each exam period. Cells were confined in solitary or multifocal groupings. In one study, mononuclear infiltration of the synovium was also a prominent feature in six of eight pony joints subjected to filipin (McIlwraith and Van Sickle, 1981). Lymphocytic infiltrates may indicate a possible immune response, as similar cells are found in patients with rheumatoid arthritis, and cartilage damage may liberate potentially antigenic material. Yet, in vivo immune reactions to components of cartilage have not been documented (Evans et al., 1984). Recent studies on human osteoarthritis, a condition supposedly devoid of synovial inflammation, have documented an inflammatory form of synovitis characterized by lymphoid and macrophage infiltration (Goldenberg et al., 1982; Revell et al., 1988). Evans et al. (1984) documented synovitis with synovial infiltration of lymphocytes and other mononuclear cells in rabbit joints subjected to injections of cartilaginous fragments. Agins et al. (1986) felt the presence of mononuclear infiltration in the synovium is consistent with osteoarthritis created by debris phagocytized and degraded by synovial cells. Olson et al. (1988) demonstrated similar focal histologic change of mild synovial hypertrophy and mononuclear infiltration after one injection of artificial wear particles. Generalized infiltrative synovial response may require high concentrations of particles (Hurtig, 1988).

Reversal of the degree of lymphocyte infiltration was apparent within the first month of the stabilization period of an osteoarthritis model (McIlwraith and Van Sickle, 1981). Focal infiltrative response seen in implanted joints in
this study remained apparent through the sixth month. Salisbury and Nottage (1985), in their study of synovial changes associated with rheumatoid arthritis, observed degree of synovial infiltration correlated to amount of debris present in the joint. In absence of macroscopic fragments, perhaps the presence of microscopic wear particles, as confirmed by cartilage fragment analysis, were responsible for maintaining cellular infiltration.

Hemosiderophages are macrophages which have previously phagocytized erythrocytes, resulting in the presence of readily apparent pigments in their cytoplasm. They have been reported in inflamed joints after injections of filipin (McIlwraith and Van Sickle, 1981) or monoiodoacetate (Trotter et al., 1989). In this study, they were probably induced by synovial trauma associated with the implanted fragments, or by some degree of hemarthrosis secondary to synovial fluid aspiration.

Dorsal synovial hyperplasia, less severe in control joints was apparent bilaterally in the middle carpal joints of each exercised horse. Reason for this is unknown, but a similar finding thought to be associated with exercise has been postulated (French et al., 1989). Increased severity in implanted joints relates to concurrent fragment-induced synovitis.

Throughout the study, it was apparent osteochondral fragments induce articular cartilage damage. At PSM-2 and PSM-6, significant damage was noted in the physical character of the cartilage. Degenerative changes within the chondrocytes were significant at PSM-6. Recent work has shown damage to articular surfaces can result from direct mechanical abrasion when macroscopic
particles are crushed between articular surfaces (Hurtig, 1988). Physical
cartilage damage was apparent early in this study; directly induced from
mechanical abrasion by macroscopic particles. Damage presented grossly as
multiple grooves or striations from dorsal to palmar in the same direction as
joint movement. Similar wear lines have been reported in association with
degenerative joints or fragment induced arthritis (Hurtig, 1988; McIlwraith,
1987; Salisbury and Nottage, 1985). In our study, the original implants, debris
from crushed or abraded implants, and liberated fragments from abraded
articular surfaces represent macro-and microscopic irritants capable of producing
articular damage and synovitis (Meachim, 1979; Evans et al., 1980; Hotchkiss et
al., 1982; Hurtig, 1988).

Studies have shown osteochondral fragments or debris may induce
cartilage damage secondary to the induction of synovitis. Fragment phagocytosis
by synoviocytes induced metaplastic changes in synovial membrane (activation),
variation in synovial fluid composition, and synovitis (Meachim, 1979; Evans et
al., 1980; Tew, 1982). Macrophages can produce enzymes after binding to, but
not necessarily engulfing debris in a process called "frustrated phagocytosis"
(Olson et al., 1988). Synoviocytes and macrophages respond to fragments by
producing neutral proteinases, collagenases, and acid hydrolases capable of
inducing glycosaminoglycan or proteoglycan degradation within the articular
cartilage (Chrisman et al., 1965; Evans et al., 1984; Clyne, 1987). Production of
prostaglandins, interleukin-1, and tumor necrosis factor-a from stimulated
synoviocytes and macrophages will result in cartilage damage by their ability to
stimulate degradative enzyme systems in other synoviocytes, and suppression of collagen, glycosaminoglycan, and proteoglycan synthesis in chondrocytes (McIlwraith, 1982; Evans et al., 1986; Hamerman, 1989; Morris et al., 1990). Differences in physical morphology and degenerative chondrocyte change evolved over six months. Early superficial grooving as a result of macroscopic fragments were characterized by vertically oriented sides, adjacent superficial surface fraying, and minimal chondrocyte pathology. By six months, grooves extended deeper into the cartilage layers with more gentle slope to the sides. Local loss of glycosaminoglycan staining and significant chondrocyte pathology were discovered adjacent to grooves. Histological evidence of chondrone formation, erosions extending to the tidemark, hypocellularity, and local matrix loss are observations consistent with changes seen in focal degenerative arthritis (McIlwraith and Van Sickel, 1981). Additionally, cartilage fragment analysis at six months revealed increased number and depth of fragments recovered. This debris represents material derived from cartilage surfaces undergoing degeneration, as the original implants had been previously resorbed. As has been reported (Mori, 1979), continuous low grade synovitis, secondary to fragment induction, could have compromised cartilage function through resultant chemical mediators. Accentuation of existing cartilage damage resulted when exercise was initiated.

Generalized reduction of glycosaminoglycan content, based on Safranin-O staining, was not evident in the cartilage layers as has been previously reported in degenerative joints (Hurtig, 1988; McIlwraith and Van Sickle, 1981). Reduced
stain uptake was apparent focally, immediately adjacent to physical defects. Defects on the cartilage surface represent areas of glycosaminoglycan leakage, and account for a local reduction in safranin-O uptake adjacent to the groove (Maroudas et al., 1973). Effect of synovitis-induced cartilage damage was not generalized, but could have predisposed to additional pathology, upon initiation of exercise, in those areas already mechanically damaged.

Lack of gross synovitis or cartilage damage within any of the carpometacarpal joints indicates macroscopic particles either did not find enter this distal communicating joint, or failed to induce cartilage damage. Limited synovial space may enhance rapid adherence and resorption of fragments. Degradative enzyme activity originating from the middle carpal joint was either not present in high enough concentration to evoke damage, or inherent joint immobility prevented any manifestation of direct or enzyme-induced cartilage damage resulting from exercise. Microscopic pathology could have existed in these joints, but failure to submit appropriate sections would account for lack of recognition. Studies by Hurtig (1988), McIlwraith and Van Sickle (1981) describing induced osteoarthritis in middle carpal joints fail to mention whether changes were noted in the distal communicating joint.

In summary, osteochondral fragments of the size utilized in this study, after implantation into the middle carpal joint, appear to induce direct cartilage damage prior to fragment adhesion to synovium. This study contrasts to models of osteoarthritis in horses and other animals in which chemical abnormalities secondary to induced synovitis preceded mechanical disturbances in the
cartilage. In our study, mechanical damage occurred initially, followed by
synovitis which further exacerbated and maintained cartilage damage.

Fragments will usually locate in the palmar aspect of the joint,
specifically the lateral palmar pouch, or occasionally dorsally. They attach to
the synovium at their bony surface within one month after implantation. At that
time, cartilage morphology is essentially normal, still obtaining adequate
nourishment from the synovial fluid, but bone cells and trabeculae are already
in an advanced state of necrosis. Fragments are partially surrounded by cells
resembling fibroblasts. These cells may be metaplastic chondrocytes, or
synovium-derived connective tissue cells.

Fragments are resorbed within a total period of two months. Fibroblast
surface cells forming the pseudocapsule and phagocytic cells of the synovium
reduce the macroscopic fragment to numerous smaller particles. Grossly
recognizable signs of fragments, if apparent at all, appear as pale plaques on
synovial surfaces. Microscopically, they are composed of connective tissue and
fibroblast cells.

Synovitis, both localized and general, results from synovial exposure to
osteoochondral debris. Synoviocyte phagocytosis of debris results in induction
and release of degradative enzymes and cytokines capable of inducing secondary
cartilage damage. In this study, synovitis was apparent, and stimulated a
significant inflammatory response at two months. It appeared to promote
chondrocyte degenerative change adjacent to defects created from direct
abrasion by loose fragments.
Continuous low grade synovitis, secondary to fragment induction, compromised cartilage function through chemical mediators, resulting in accentuation of existing cartilage damage when exercise was initiated. Radiographic changes represent manifestations of chronic synovitis and cartilage damage, and were detected in five of six joints at six months.

Potential for osteochondral fragments to induce articular damage has been demonstrated. From a clinical standpoint, recognition of the high incidence of debris remaining within joints after arthroscopic surgery prompted an immediate utilization of methods to reduce incidence and degree of this problem.

Improved individual arthroscopic expertise plays a critical role in reduction of residual debris. Controlled curettage and immediate removal of created fragments under direct arthroscopic visualization reduce joint debris.

Substantial evidence attesting to the inferior nature of repair tissue in full thickness cartilage defects has resulted in a strong tendency not to convert partial thickness defects in anticipation of better repair. As a result, there is reduction of potential debris within the joint.

Use of large bore infusion cannulas as egress ports allows lavage with large volumes of balanced electrolyte solution. Free fragments will be washed from the joint. Routinely, two liters of solution are flushed through the middle carpal joint at the end of a surgical procedure.

In larger joints, use of mechanical burring devices in conjunction with a vacuum or suction system will greatly reduce the incidence of debrided
fragments locating in preferred cul de sacs of the joint capsule. Manipulation of the leg during lavage, as well as repeated distension and collapse of the joint capsule enhances fragment recovery from the joint.

Recommendations can be made regarding those joints in which fragments remain after a procedure. Knowing the potential effects of debris, if the fragments are of considerable size and number, a second procedure to remove loose bodies may be indicated. Presence of fragments detracts from the quality of surgery, and may also extend the recovery period. Care and planning are necessary to find and remove loose bodies. In these cases, lateral recumbency may allow for specific gravitational placement of the fragments. For fragments located palmarly, a surgical approach has been described (McIlwraith, 1990). Intraoperative radiographs may assist in locating any elusive loose bodies.

If a second procedure to remove retained fragments is not elected, it would be prudent to consider certain changes in postoperative management based on the findings of this study. Animals should not be allowed exercise for at least two months so as to minimize potential for direct cartilage injury. Radiographic evaluation should be performed at one and two months to assess attachment and subsequent resorption of fragments. Once fragments are resorbed, patients could be allowed paddock or pasture turnout and increasing exercise levels commensurate with the original injury. Cartilage fragment analysis may be helpful to determine if deeper articular changes are occurring during the recovery period. Resumption of training should be based on synovial samples demonstrating normal or reducing number and depth of cartilage
fragments.

In small joints, especially those with some degree of inflammatory change, majority of fresh osteochondral fragments will resorbed by synovium. Ability to function as a loose body, and perhaps enlarge appears rare. Methods to reduce incidence of loose bodies must be aggressively adopted. If free debris is recognized, removal is indicated. If not removed, appropriate measures must be taken to prevent potential pathology resulting from its presence.
REFERENCES


Boniface RT, Cain PR, Evans CH. Articular responses to purified cartilage proteoglycans. Arthr and Rheum 1988;31:258-266.


Evans CH, Mears DC, Mazzocchi RA. Chemical and physical components in the release of neutral proteases from macrophages provoked by cartilaginous wear particles. Trans Orthop Res 1980a;3:341-348.


Schneider RK. Incidence and location of fractures within the carpus. Proceedings, American Association of Equine Practitioners 1979;25:145-146.


APPENDIX
SYNOVIAL MEMBRANE ANALYSIS

HORSE NUMBER: _______________________
SIDE (Left or Right): ________________

<table>
<thead>
<tr>
<th>SYNOVIAL PALMAR</th>
<th>SYNOVIAL DORSAL VILLOUS (SDV)</th>
<th>SYNOVIAL DORSAL NONVILLOUS (SDN)</th>
</tr>
</thead>
</table>

1. SYNOVIAL CELL AND VILLOUS HYPERPLASIA

2. DEPTH OF INFLAMMATION

3. DEGREE OF INFLAMMATION

4. CHARACTER OF INFLAMMATORY REACTION
   - Mononuclears
   - PMNs

5. OTHER FINDINGS (Fibrosis, Granulation, Subintimal Edema, Intimal Hyperplasia, Fibrin Deposition, etc.)

SCALE: 0 = Normal 1 = Mild 2 = Moderate 3 = Severe
OSTEOCHONDRAL EVALUATION

NORSE NUMBER: __________________________

SIDE (Left or Right): ______________________

CARPAL BONE AREA: ________________________
(Radial, Intermediate, Third Radial Facet, Third Intermediate Facet)

1. ARTICULAR CARTILAGE MORPHOLOGY
(Scores: 0 = normal, 1 = surface frayed, 2 = horizontal fibrillation,
3 = vertical fibrillation, 4 = cartilage erosion)

2. MATRIX STAINING (Safranin 0)
(Scores: 0 = no matrix staining, 1 = slight, 2 = moderate, 3 = normal)
   a. Superficial
   b. Intermediate
   c. Deep

3. DEGENERATIVE ARTICULAR CHANGES (H & E)
(Scores: 0 = normal, 1 = minor loss of chondrocyte nuclear staining,
2 = eosinophilic chondrocyte nuclei and empty lacunae, 3 = empty lacunae
and disorganized matrix, 4 = all chondrocytes necrotic, loss and/or
collapse of matrix)

4. COMMENTS:
   Integrity of Tidemark (+ or -)
   Subchondral Sclerosis (+ or -)
   Chondrocyte Changes
   (Chondrone formation, hyper/hypocellularity)
FRAGMENT ANALYSIS

NORSE NUMBER: ______________________
SIDE: ______________________

1. TETRACYCLINE LABEL (+ or -) - 20 micron

2. SIZE OF FRAGMENT (Radius/Circumference)

3. DISTRIBUTION OF CARTILAGE AND BONE
   (Ratio and relative location)

4. CELLULAR INFILTRATION

5. MORPHOLOGY OF ATTACHMENT

6. SURFACE OF ATTACHMENT/ORIENTATION

7. MORPHOLOGY OF TISSUES
   (Cartilage and bone)