A STUDY OF PSEUDOARTHROSIS OF THE BOVINE METACARPOPHALANGEAL JOINTS

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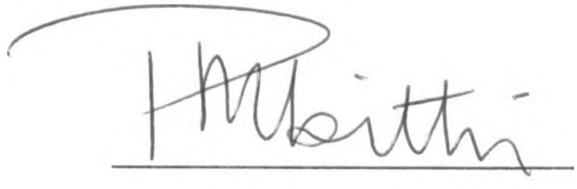
DECLARATION

This thesis is my original work and has not been presented for a degree in any other university.



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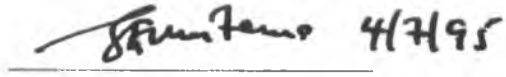

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DEDICATION

To The Late Professor Stanley Mbaka Mbiuki

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ABSTRACT

Experimental surgical curettage of the left lateral metacarpophalangeal (LLMCP) joints of calves was performed in an attempt to develop and describe a suitable surgical and post-operative management protocol for creating pseudoarthrosis of the curetted joints, in order to obtain clinical and radiological data with respect to function of curetted joints, to determine the macroscopic and microscopic features of and the repair tissue resurfacing the articular cartilage defects and to evaluate the ability of dexamethasone and phenylbutazone to modulate body temperature, pain and limping after joint surgery in calves.

Six to twelve months old male Friesian calves weighing 50-70kg were obtained from established farms. On acquisition, physical clinical and radiographic examination was done on each calf. Only calves free from disease, blood parasites, gastrointestinal parasites, gait or conformational defect and with clinically and radiologically normal metacarpophalangeal joints were included in the study.

Thirty of the disease free calves were randomly divided into three (I,II & III) groups of ten. Under general anaesthesia and standard surgical conditions

left-lateral metacarpophalangeal arthrotomy and curettage were performed on group I and group II. Only arthrotomy incisions without curettage (sham operations) was performed on group III calves. The operated joints were then partially immobilized by application of a plaster of Paris cast and the operated limbs immediately after surgery but before recovery from general anaesthesia.

One hour after recovery from general anaesthesia each calf in group I was given phenylbutazone intramuscularly at the dosage rate of 4.4mg/kg; while each group II calf was given 0.2mg/kg dexamethazone intramuscularly. Group III calves were given 0.5ml of isotonic solution (Water for Injection, Infusion, Kenya Ltd., Nairobi) intramuscularly. These treatments were repeated on the third and the seventh day after surgery and plaster of Paris casts were removed on the 21st post-operative day.

Post-operative recordings of the degree of limping and rectal temperatures were taken in the mornings of day 1 to 7 days 10, 14, 21 and from then on weekly until the 135 post-operative day. Weekly recordings of pain and joint mobility were taken starting from the 21st post-operative day up to the 135th post-operative day. The degree of limping of each calf was assessed by the surgeon and marked on a 5mm visual anolog scale (VAS) running from 'no

limping' (0mm) to limping 'cannot be worse' (5mm). The surgeon assessed the intensity of pain felt by the calves by exerting digital pressure on the operated joints. The pain estimate was marked on a VAS running from 'no pain' (0mm) to 'pain cannot be worse' (5mm). Joint healing was assessed by evaluation of radiographs of the operated joints taken 3, 6, 9, and 15 weeks after surgery. The healing was evaluated on the basis of "radiographic union" and graded against a semi- quantitative scale from 0 to 4:-

0 - No evidence of union. A radioluscent line where the joint space originally was (intercondylar space).

1 - Callus bridging the intercondylar space is partially ossified.

2 - Intercondylar space is filled with ossified tissue whose radio-opacity does not match the remaining cortex.

3 - Most of the osseous tissue in the intercondyler space has the same radio-opacity as the rest of the cortex.

4 - Intercondylar space is undecernible as it is completely filled with radio-opaque bone.

Joint mobility was assessed by subjectively evaluating the angles of flexion through palpation and visual examination of operated joints and scored

as a percentage of the normal angle of flexion of the contra-lateral joint.

Rectal temperatures were recorded in degrees celcius (°C) for each calf using a mercury thermometer.

All the calves were euthanatized on the 135th post operative day. The operated joints were then cut out and dissected open for macroscopic examination. The repair tissue resurfacing the articular cartilage defects was harvested, fixed in 5% formalin embedded in paraffin wax and standard histological sections prepared and stained with Hematoxylin and Eosin (H/E) stain. The cellular composition of the repair tissue was assessed by viewing the sections under a light microscope and assigning one of three categories:-

1. Fibrous tissue containing predominantly spindle shaped fibroblasts.
2. Incomplete differentiated mesenchymal tissue composed of cells beginning to differentiate towards chondrocytes.
3. "Hyline-like" articular cartilage containing chondrocytes in lacunae.

Data collected were analysed and assessed for normality and the t-test used for comparing means.

Blood samples collected from all the calves on the 14 and 2 days before surgery, on the day of

surgery and on the 1st, 3rd, 5th, 7th, 9th, 11th and the 13th post-operative days. Serum from the blood samples collected was analysed for gamma-glutamyltranspeptidase.

The arthrotomy and surgical curettage of the metacarpophalangeal joints in the thirty calves was well tolerated and did not impair the general well being of the calves. When the calves recovered from anaesthesia associated with initial surgery they walked well having only minor gait changes. The calves remained bright and alert and had a good appetite.

Temperatures above the pre-operative cut-off of 38.7°C were recorded on the days of surgery and cast removal in all calves. However in the two groups the temperatures went down within 24hrs of surgery or cast removal. Calves treated with dexamethasone had a mean peak temperature reading of 39°C and 39.1°C on the first and the second post-operative days respectively. From then on there was a sharp decline in temperature readings by the third day after surgery until day 21 when there was another peak of 39.7°C. Temperature readings for calves treated with phenylbutazone followed a similar trend to that recorded for the calves treated with dexamethasone. The mean peak reading on the first day of surgery was 40.0°C whereas the peak on day 21 was 39.4°C. The

temperature readings of sham operated calves described similar trends to those recorded for calves treated with dexamethazone and those treated with phenylbutazone. The mean peak reading on the first day of surgery was 39.9°C whereas the peak on day 21 was 39.7°C.

In the three groups there was a sharp decrease to pre-operative levels in the temperature readings after the 21st post-operative day. There was no significant difference in the ability of dexamethazone and phenylbutazone to reduce rectal temperatures in these calves ($p<0.05$).

Peak recordings for limping were recorded on the first day after surgery but there was a steady decrease until the 21st post-operative day when there was another peak recording.

On the first day after surgery the mean peak recording for the phenylbutazone treated calves was 4.1 compared with 3.5 and 2.2 for the dexamethasone treated and sham operated calves respectively. On the 21st day after surgery the mean peak recordings were 3.4, 3.1 and 2.0 for the phenylbutazone treated, dexamethasone treated and sham operated calves respectively. The mean recordings for all the calves diminished steadily after cast removal 21 days after surgery and reached zero by day 48 in dexamethasone treated calves, day 68 in pneylbutazone treated

calves and day 35 in sham operated calves

There was moderate pain on palpation of the operated joints of group 1 and group II calves on the 21st post-operative day (day of cast removal). There was however a steady reduction in this parameter such that "no pain" was assessed on palpation of the joints by day 70 in the phenylbutazone treated group and the dexamethasone treated group. A pain estimate of 1 was recorded on day 21 for group 3 calves. Similar to group I and II the pain diminished steadily and an estimate of '0' (no pain) was recorded on day 35. Overall there was no significant difference in the reduction of pain between the two treatment groups ($p<0.5$) but there was a general tendancy for dexamethasone to be more potent than phenylbutazone.

The lowest mean scores for joint mobility were assessed on the 21st day after surgery. The mean mobility on this day (21st post-operative day) was assessed at 90% for the dexamethasone treated group, at 76% for the phenylbutazone treated and 90% for the sham opereated calves. There was tremendous individual variation and a progressive increase in the joint mobility in all the calves to a maximum possible mobility of 100% on the 49 post-operative day for the dexamethasone treated calves. The mean maximum mobility for the phenylbutazone treated

calves was 92% and was reached 77 days after the curettage. The maximum joint mobility of 100% was reached on the 49 post operative day for the sham operated calves.

Three weeks after curettage there was marked soft tissue swelling at the site of surgery in all treatment groups. The joints of group I and II calves had a widened radioluscent area where the joint space originally was (intercondylar space) while there was no other detectable change in the operated joints of group III calves. Six weeks post-operatively, the intercondylar spaces of the joints of group I and II calves were further widened but remained radioluscent. At nine weeks, some joints showed wide radioluscent intercondylar spaces while in other joints the widened intercondylar spaces had a barely detectable radiodensity.

Fifteen weeks after surgery some of the intercondylar spaces in group 1 and II had greater radiodensity than seen at nine weeks, but this radiodensity did not match that of the surrounding cortex. In other joints the intercondylar spaces were still radioluscent at fifteen weeks after joint curettage. There was no significant difference in the scores recorded for the joint healing between the phenylbutazone treated and dexamethasone treated calves. Soft tissue swelling was present at the

surgical sites of all the operated joints. There was no evidence of union and a radioluscent line was apparent in the intercondylar spaces of sham operated joints upto 15 weeks after surgery.

When the joints were opened 135 days after surgery there was fibrous tissue reaction involving the subcutaneous tissue and the joint capsule at the surgical site of the calves in the three groups. The articular cartilage of sham operated (group III) joints was pink, entire and glistening and the joints contained straw-coloured, viscous and stickly synovial fluid.

Contrastingly, there was no articular cartilage in any of the curetted joints (groups I and II) except near the proximal sessamoid bones, laterally and medially. In each joint the distal end of the third metacarpal bone and the proximal end of the first phalanx were covered by a dark brown repair tissue with thick fibrous bands joining the central parts of the distal end of the third metacarpal bone and the opposing surface on the proximal end of the first phalanx. A synovial membrane like tissue joined these fibrous bands to the joint capsule. The synovial-like fluid of the curetted joints was similar to that of sham operated joints but blood tinged. The interosseous ligament between the left medial and the left lateral metacarpophalangeal

joints was very tough and thicker than that of the opposite limb of the same calves. No adhesions or repair tissue were detected in the sham operated joints.

Histologically the repair tissue in curetted joints (groups I and II) was mainly made up of predominantly spindle shaped fibroblasts. No significant difference was detected between the scores recorded for joints of the calves treated with phenylbutazone and those treated with dexamethasone. The trabecular pattern of the subchondral bone beneath the repair tissue was disrupted and a few osteoclast-like cells were seen near the areas of bone destruction. The synovium and articular cartilage adjacent to the repair tissue were inflammed and hypertrophied. There was an increase in the number of vascular channels in the subchondral bone.

No obvious changes were detected in the histology of the articular cartilage of sham operated joints. In each section, the articular cartilage surface was smooth and formed the four layers typical of cartilage. The superficial layer was composed of flattened chondrocytes which were parallel to the articular surface; deeper, the cartilage cells were round and arranged in columns at right angles to the surface; adjacent to the subchondral bone, columns of

chondrocytes were evident. There was a dark line crossing from one side to the other indicating the junction of calcified and non-calcified intercellular substance (tide-mark). Deep to the tide-mark, cartilage was replaced by bone with well developed haversian systems. Examination of the growth plates revealed four distinct zones. A zone of moderately-sized, irregularly-arranged cartilage cells lay immediately below the epiphysis. Deeper, there was a zone of thin, wedge-shaped chondrocytes, stacked together in columns at right angles to the axis of the bone below which was another zone of rounded cells which were also in columns. Adjacent to the diaphysis, a thin, flat layer of rounded cells merged directly into the bone.

The mean pre-operative values for serum gamma-glutamyltranspeptidase (Y-GT) were 30.2 I.U. for the dexamethazone treated, 29.9 I.U. for the phenylbutazone treated and 30.9 for the sham operated calves. The post-operative Y-GT values were 30.1 I.U., 29.4 I.U. and 30.5 I.U. for the dexamethazone treated, phenylbutazone treated and the sham operated calves respectively. There was no significant difference between the pre-operative and post-operative levels of serum Y-GT in all the three groups ($p<0.05$).

Based on the results of this study the following conclusions were made:-

1. A surgical procedure and post-operative management protocol for recreating curetted bovine metacarpophalangeal joints (surgical pseudoarthrosis) has been developed and described.
2. The protocol for surgical pseudoarthrosis developed in this study could be usefully adopted for the surgical management of bovine arthritides when curettage is indicated.
3. The surgical removal of the articular cartilage and subchondral bone of the bovine metacarpophalangeal joints (curettage) with subsequent three weeks partial immobilization of the operated joints is well tolerated and does not impair the general well being of the animals.
4. Curetted and partially immobilized bovine metacarpophalangeal (MCP) joints remain functional with joint mobility of more than 92% being maintained upto the 135th post-operative day.
5. Deep articular cartilage defects created by curettage of the bovine MCP joints heal by metaplasia of the connective tissue and 135 days old defects of partially immobilized joints are

resurfaced by fibrous tissue which unites the distal metacarpal condyles to the proximal first phalangeal condyles of the curetted joints.

However, further studies are warranted to determine whether or not the repair tissue remains static or modulates to other forms of tissue later in the repair process.

6. Both dexamethazone and phenylbutazone are effective in reducing pain, limping and body temperature subsequent to radical joint surgery in cattle with a tendency for dexamethazone to be more potent than phenylbutazone.

7. Serum gamma-glutamyltranspeptidase may not be a good indicator of inflammation in young calves aged 6-12 months.

CHAPTER ONE

INTRODUCTION

Lameness is of appreciable economic importance to the cattle industry. Economic losses in lame cattle arise from reduced weight gains, lower carcass values, diminished milk production and/or reduced breeding function.

Although lameness can result from many other causes, several studies indicate that septic arthritis is the commonest cause of foot lameness in cattle (Greenough, et.al., 1988; Weaver, 1990; Mbithi, et.al., 1991). In the past calves with septic arthritis were treated medically using antibiotics and occasionally joint lavage was performed. The success rate in these procedures was suboptimal and in many instances surgical intervention was warranted (Ferguson, 1985). Currently surgical curettage of the bovine metacarpophalangeal joint is the most successful procedure for treating septic arthritis of the joint (Greenough et. al., 1988, Ferguson et.al., 1991). The procedure aims at arthrodesing the joint and thus rendering it functionless. Earlier reports indicated that the curettage yielded good results with return to milk production, weight gain and efficient breeding function. However, later follow-up on some limited number of calves whose

metacarpophalangeal joints had been conventionally arthrodesed revealed that the arthrodeses broke down and the joints became moveable and painless suggesting the formation of pseudoarthrosis. (Ferguson, et.al., 1991, Mbithi, et.al., 1991). Pseudoarthrosis is a condition characterized by the formation of a cleft between layers of connective tissue covering bone ends (Salter, 1983) Connective tissue cells at the periphery of the cleft differentiate into synoviocytes which secrete synovial fluid whereas the adjacent connective tissue forms a joint capsule-like structure (Harrelson, 1977).

Traditionally, pseudoarthrosis has a pathological connotation and is a common complication of fracture healing in long bones of humans and animals (Jubb, et.al., 1985). The condition is recognized as a common complication of posterior spinal fusion for the treatment of human Scoliosis (Fernadez, 1986). Congenital pseudoarthrosis of the distal tibia and ulna in human beings is difficult to treat and develops subsequent to pathological fractures at birth (Salter, 1983).

However, in certain instances, pseudoarthrosis is desirable and hence not considered a pathological entity. Surgical curettage of septic bovine metacarpophalangeal joints creates a functional

pseudoarthrosis (Ferguson, 1986; Ferguson et.al., 1991). Resection of the femoral head and neck in dogs and cats is done to induce a pseudoarthrosis. In human beings excision arthroplasty is a salvage procedure that gives a painless hip with reasonable amount of movement (Ferguson, 1980, Vassuer, 1983).

Although radiography and surgical exploration have been used to identify pseudoarthrosis (Adams, 1976, Harrelson, 1977), the biological basis of wound healing after surgical curettage of joints has not been exhaustively studied.

Anti-inflammatory drugs are used in veterinary medicine for the treatment of painful inflammatory conditions of domestic animals (Flower, et.al., 1980). The drugs are classified as steroidal anti-inflammatory drugs (SAID) and non-steroidal anti-inflammatory drugs (NSAID).

Phenylbutazone has been the most commonly used non-steroidal anti-inflammatory drug in veterinary medicine. The drug produces its effects by inhibition of the cyclo-oxygenase enzyme system responsible for the synthesis of prostanoids and consequently suppressing the development of cardinal signs of inflammation (Flower, et.al., 1980; Pugh, 1982). Phenylbutazone has been used in horses and dogs for many years and the pharmacokinetic and clinical studies in these species have been reported (Sullivan

and Snow, 1982, Maitho, 1991; Mbugua, 1987). The information available for other species cannot be extrapolated for cattle due to well documented species differences in the distribution and the elimination of this drug, although these factors influence the ability to determine peri-operative clinical phenomena. Phenylbutazone is widely used in some countries for treating arthritis, laminitis and other inflammatory conditions in cattle but there are few published clinical reports on the ability of the drug to modulate peri-operative clinical events in the bovine species (Eberhadson, et.al., 1979; Decker, et.al., 1980).

Dexamethasone is a glucocorticoid, SAID; which is commonly used in cattle practice for the management of primary Ketosis, orthopaedic conditions, stress, allergic and skin conditions. Glucocorticoids are the most powerful anti-inflammatory drugs. The drugs reduce edema and pain and lower body temperature. Their effects are due to blocking of the arachdonic acid cascade at different points thus blocking the formation of inflammatory mediators. However, glucocorticoids have a potential to impair wound healing and the defence mechanisms against infection. Consequently, there is widespread controversy towards their use post-operatively (Blackwell et al., 1980; Gloert, 1981; Hynes and

Murad 1985).

There is need to determine the biological basis of joint wound healing in the formation of the bovine metacarpophalangeal pseudoarthrosis with a view to developing a surgical procedure and post operative management protocol for 'surgical creation' of bovine fetlock pseudoarthrosis, when indicated. Since radical joint surgery often requires the use of analgesics/anti-inflammatory drugs peri-operatively, studies on anti-inflammatory drugs will enable determination of their suitability as analgesics/anti-inflammatory agents for radical surgery in cattle.

Consequently, the objectives of the present study were undertaken to investigate the following parameters.

1. To develop and describe a surgical procedure and post-operative management protocol for recreating curetted bovine metacarpophalangeal joints.
2. To obtain clinical data with respect to function in calves with curetted articular cartilage of the fetlock joint.
3. To evaluate the composition of the reparative tissue in healing deep articular cartilage defects in the calf.

4. To evaluate the efficacy of phenylbutazone and dexamethasone to reduce body temperature, pain and limping after fetlock joint curettage in calves.

CHAPTER TWO

2. LITERATURE REVIEW

2.1 Synovial Joints

Normal synovial joints are made up of bone ends. The bone ends are covered by articular cartilage and are hinged by a joint capsule and bridging ligaments with a cavity in between. The capsule is lined internally with synovial membrane which produces synovial fluid. The outer part of the capsule is composed of dense fibrous tissue. Within the joint cavity there may be fibrocartilaginous discs called menisci. In the joint cavity there is the viscous synovial fluid (Wilkins 1981). The synovial membrane is made up of between one and three layers of flat stellate cells whose cytoplasmic processes overlap and intertwine with one another forming a smooth surface. Externally the synovial tissues may be fibrous, areolar or fatty and vary in density and thickness. The cellular components of these tissues are fibroblasts, histiocyte, mast cells and adipose cells. Distributed in the fibrous tissue are blood vessels, lymphatic and nerve fibers. The blood supply is derived from the afferent artery of the epiphysis and drains to the efferent vein (Horky, 1984; Jalani and Ghadially, 1986).

2.2 Articular Cartilage

Articular Cartilages are unique connective tissue structures which serve as the principal working components of synovial joints. The cartilage covers the bone ends that form the joint and is responsible for the frictionless movement of the articulating surfaces on each other and the resiliency of the osteo-articular segment (Mankin, 1981). The Mammalian articular cartilage is firmly attached to the underlying subchondral cortical bone and measures less than 5mm in thickness but with a considerable variation depending on the species, the joint and the site within the joint (Meachim, 1971).

Grossly, articular cartilage are dense white, tending to become somewhat yellow in advanced age. They are superhydrated but feel semi-solid, indentable with compression and return to original form when compression is released (Meachim, 1971). Articular cartilage are avascular, aneurotic and alymphatic & depend on a double diffusion system for nutrition. The nutrients must first pass across the synovial membrane into the synovial fluid and then through the dense matrix of the cartilage to reach the chondrocytes (Mankin, 1974). The bearing surfaces of articular cartilage depend on capsular, synovial, subchondral bone and muscular nerve endings for proprioception and appreciation of pain. The

cartilage, thus exists in relative isolation from the remainder of the body's tissues depending only on changes in the chemical composition in the synovial fluid and variations in joint pressure to receive signals that regulate metabolism (Mankin, 1974).

Vast extracellular matrix exists in articular cartilage and interspersed within the matrix are cells which are arranged in zones. The tangential zone is composed of elongated cells which are parallel to the surface; the transitional zone consists of rounded cells which are randomly distributed; the radial zone has cells which are lined up in short, irregular columns while the calcified zone is separated from the radial zone by a wavy, irregular, bluish (Hematoxylin and Eosin Stain) line called the tidemark. On its deep surface, the tidemark merges with the end plate of the underlying bone (Green, et.al., 1970). The underlying bone shows mature Haversian systems and differs from the cortical bone in other sites by the orientation of the osteons which lie parallel to the joint rather than along the axis of the bone. The subchondral bone and the marrow beneath it are richly supplied with vascular elements. The tidemark and the calcified zone mark the limits of avascular cartilage which is not nourished in contradiction to the highly vascular bone lying beneath it (Mc Kibben and Holdsworth,

1966).

The biochemical properties of articular cartilage differs markedly from other tissues. The cartilage has a high concentration of proteoglycan molecule consisting of a protein and glycopolysacharides. The water content reaches up to 80%. This water is freely exchangeable with synovial fluid and appears to be bound in the form of proteoglycan - collagen gel. The water movement provides the cartilage with its resiliency and a boundary lubricating system for the almost frictionless motion characteristic of synovial joints (Jaffe, et.al., 1974; Lane and Weiss, 1975).

The most abundant organic constituent of articular cartilage is collagen, accounting for over 50% of the dry weight (Lane and Weiss, 1975; Weiss, et.al., 1968). The collagen of articular cartilage is of a different genetic species from that of skin or bone (type I) and is classified as type II. (Miller, 1973; Mitchel and Shepard, 1980). The remainder of organic solids consists of proteoglycans, calcium salts, lipids and lysozyme (Rosenberg, et.al., 1975. Bonner, 1975, Kuettner, et.al., 1989)

2.3 Bovine Metacarpophalangeal (Fetlock) Joint

There are two fetlock joints to each bovine digit. The palmar parts of the two joint capsules

communicate. There is a network of ligaments which join the large metacarpal bone to the proximal phalanges (Greenough, et.al., 1981, Weaver, 1990). A strong proximal inter digital ligament consisting of short intercrossing fibers unites the middles of the interdigital surfaces of the proximal phalangeal digits and prevents undue divergence of the phalanges. The interdigital phalangosessamoidan ligaments connect with the proximal end of the opposite proximal phalanx while the intersessamoidan ligament connects all four sessamoids (Greenough, et.al., 1981; Weaver, 1990). For each digit, there are two short, strong bands which extend from the distal margins of the proximal ends of the proximal phalanges. The deep distal sessamoidan ligaments are distinctly strong and cruciate. The interosseous tendon, also called the suspensory ligament is markedly muscular and in the young animal it consists largely of muscular tissue. At the distal third of the metacarpus, the suspensory ligament divides into three branches which give rise to five subdivisions either by bifurcation of the lateral or medial branches or trifurcation of the middle branch. The two lateral and the two medial bands end on the proximal sessamoid bones and the distal end of the large metacarpal bone. The middle band passes through the groove between the two divisions of the distal

end of the metacarpus and divides into two branches which join the proper fibers to the interdigital collateral ligaments and to the central sessamoids. The interosseous muscle detaches a band which unites more distally with the superficial digital flexor tendons and thus enclosing the deep digital flexor tendon (Greenough, et.al., 1981; Weaver, 1990). The bovine metacarpophalangeal joint is extremely mobile and the joint capsule is capacious with a large pouch on the planter aspect between the bone and the interosseous ligament. Between the interosseous and the flexor tendons are the proximal limits of the two digital synovial sheaths which rarely communicate with each other. Distally each synovial sheath envelops the superficial and deep digital flexor tendons almost to the distal joint capsule and distal sessamoid bursa with neither of which it communicates (Greenough, et.al., 1981; Greenough et.al; 1988; Weaver 1990).

2.4 I N F L A M M A T I O N

2.4.1 General Introduction

Inflammation is a vascular and cellular response designed to defend the body against foreign substances and to dispose of dead and dying tissues in preparation for the repair process (Peacock and Van Winkle, 1984). An inflammatory reaction with

release of intracellular materials into the extracellular compartment of injured tissue can be caused by physical or chemical injury or by infection. Furthermore every surgical procedure results in an inflammatory reaction. In clinical terms inflammation is signaled by redness, heat, swelling, pain and loss of function of the affected tissue. At cellular and humoral level intricate events occur in a 37 - Step pathway Scheme for a model inflammation (Vinegar, et.al., 1982, Peacock and Van Winkle 1984).

2.4.2 Acute Inflammation.

Acute inflammation is basically a non-specific and stereotyped reaction which may be initiated by various injurious agents (Ryan and Majno, 1977). Immediately after injury leukocytes at the site appear to become sticky and adhere to the endothelium especially the venules. Initially, there is vasoconstriction, but in five to ten minutes there is also vasodilation accompanied by leakage of plasma into the extracellular space. The endothelial cells in the venules appear to shrink and gaps appear between them. Leukocytic cells, mainly polymorphonuclear leukocytes migrate out of the vessels into the interstitium by diapedesis. They exhibit a positive but random motion in the direction

of the injury (Flower, et.al., 1975; Peacock and Van Winkle, 1984). In the early stages of inflammation the cellular exudate is composed of polymorphonuclear leukocytes whereas later the mononuclear phagocyte series predominate.

Injured tissues liberate vasoactive compounds which cause vasodilation and increased blood flow. The inflammatory agent and or the inflammatory reaction stimulate sensory nerve endings by an antidromic reflex, provoke dilation of arterioles as well as venules (Furness and Marshall,1974). Blood flow through the bed is controlled by nervous influence in larger vessels. The precapillaries regulate the rate of flow in response to circulating catecholamines (Furness and Marshall, 1974). Lipid soluble molecules diffuse through the endothelial cytoplasm and the lipid insoluble molecules move out of the vasculature during inflammation by endothelial vesicles or by crossing the tight endothelial junctions and then through the basement membrane (Bohm, 1976).

Endogenous mediators of inflammation are derived from the injured host as opposed to exogenous mediators which originate either from plasma or the tissues and they are interrelated (Ryan and Majno 1977). Plasma factors that mediate inflammation include the kinin system, the complement system and

the clotting system. The kinin system starts by the activation of Hageman's factor XII which can then follow three pathways:-

1. Triggering of the clotting cascade by activating clotting factor XI.
2. Triggering of the fibrinolytic cascade by activating plasminogen proactivator producing plasminogen activator which converts plasminogen to plasmin.
3. Stimulation of prekallikrein activator activity. Prekallikrein activator converts prekallikrein to Kallikrein which converts kininogen to bradykinin, a powerful vasodilator and pain stimulator in the presence of other chemicals like prostamin E.

Other by-products of Hageman's factor activity which are biologically active in the inflammatory process are C3, C5, C6, and C7 complement fragments (Ryan and Majno, 1977).

2.4.3 Chronic Inflammation

Chronic inflammation exists when wounds become contaminated or when they contain foreign bodies that cannot be removed during the acute inflammatory process. The monocyte is the predominant cell in chronic inflammation. These cells differentiate into phagocytic macrophages and undergo local

proliferation (Jones and Hamm, 1977). When leukocytes die, they undergo autolysis and should the accumulation be rapid and emigration from the area fail they breakdown and form an abscess. The discharge of enzymes from dead cells may damage more tissue and intensify inflammation (Jones and Horn, 1977; Peacock and Van Winkle, 1984). If the leukocytes die without autolysis, a coagulative necrosis involves them and the surrounding tissue producing caseation as in a tubercle (Peacock and Van Winkle, 1984). Mesenchymal cells attracted to the wound site by chemotaxis differentiate into fibroblasts which lay down collagen around the lesion. Eventually fibroblasts enclose the lesion in a dense capsule. A similar process occurs when there is a foreign body in the tissues and the cellular changes persist as long as the foreign body is present in the tissues (Peacock and Van Winkle, 1984).

2.5 SEPTIC ARTHRITIS AND MANAGEMENT OF ARTHRITIDES

2.5.1 Septic Arthritides

Septic arthritis can be either primary as a result of a penetrating object inoculating bacteria directly into or very close to the joint or secondary following hematogenous spread from an infectious focus elsewhere in the body (Bailey, 1985). Primary

septic arthritis is more commonly associated with adult animals and usually affects only one joint while secondary arthritis more commonly affects multiple joints in young animals (Bailey, 1985). In adult cattle secondary septic arthritis is reported to be associated with chronic reticuloperitonitis, septic metritis, abscesses and interdigital phlegmonmatitis (Van Pelt, 1978, Bailey 1985; Greenough and Johnson, 1988).

The bovine fetlock joint is predisposed to primary septic arthritis through ascending infection with tenosynovitis, puncture wounds, pyemia hematogenous spread and tuberculosis. In this joint secondary arthritis results from bacteria infecting wounds of the dorsolateral and or dorsomedial aspects of the joint (Greenough et.al., 1988).

The pathophysiology of joint destruction due to infection is complex. Bacteria circulating in the blood stream gain access to the joint either via the blood vessels to the metaphysis or epiphysis or via the blood supply to the synovial membrane. As blood passes through the metaphyseal vessels, it flows in a network of venous sinusoids in which the rate of flow is greatly reduced. This provides the circulating bacteria with an ideal opportunity to establish themselves and develop a site of infection (Bailey, 1985). Once an infection site has been

established the infecting bacteria can spread into the joint either through the infected bone or through the sorrounding soft tissue (Firth, 1983). When infection becomes established in the joint an intense inflammatory response is elicited in the synovial membrane and the joint capsule. The permeability of the membrane is altered and this results in changes in the composition of synovial fluid. The protein levels of the fluid change and fibrin clots develop. There is a marked influx of polymorphonuclear cells in response to the infective agents and a resultant appearance of lysosomal and other enzymes (Alexander, 1980). These enzymes cause degeneration of the articular cartilage. Further cartilage damage occurs due to lack of nutrition of the chondrocytes caused by alteration of the synovial fluid and fibrin deposition on the cartilage. This degeneration of cartilage elicits more intense synovitis thereby perpetuating the process. If this cycle is not halted, the end result is damage to the articular end plate which also leads to permanent impairment of the joint function (Alexander, 1980; Firth, 1983).

2.5.2 Management of Arthritides

A number of fundamental principles should be honored in order to apply a rational management of septic joints. Joint infection that is earlier than

72 hours is effectively treated by use of parenteral antibiotics (Firth, 1983). After 72 hours articular cartilage damage is initiated and there is increased periarticular fibrosis and pus formation in the joint cavity. At this level treatment requires the dislodging of the clots and pus from the joint cavity using suitable fluid (joint lavage). At the same time administration of broad spectrum parenteral and/or intra articular antibiosis is necessary. Joint lavage is an important part of the treatment of septic arthritis and serves also to remove bacteria and leukocytic lysosomal enzymes which are responsible for cartilage damage (Firth 1983). Optimally a buffed polyenic sterile solution that is essentially non-irritant in the joint should be used. This minimized further inflammation of the synovium (Bailey, 1985). Conservative methods of joint lavage involve the use of 14 - or 16 gauge needles or catheters that are introduced into the joint space using aseptic technique under adequate restraint (Weaver, 1990). Large volumes of the lavage fluid are put into the joint and removed. The process is repeated until the fluid coming out of the joint is clean and does not contain any pus, fibrin clots or tissue debris. Two methods of lavaging joints are available; distention lavage and through lavage. Distention lavage refers to the introductions of a needle or catheter in the

most dependent portion of the joint; lavage solution is infused under sufficient pressure to distend the synovial membrane. This is followed by aspiration and removal of inflammatory debris from the joint. The process is repeated several times until the aspirated fluid is clear. The procedure should be repeated on a daily basis and thus indwelling silastic catheters are put into the joint and sutured to the skin to facilitate repeated lavages that are required (Bailey, 1985).

In case of through and through lavage two needles are introduced into opposite sites of the joint to serve as inflow and outward tracts. Large quantities of lavage solution are used and allowed to circulate freely in the joint (Greenough et.al., (1988).

The organization of the exudate and development of fibrin clots occurs as soon as seven days after joint infection in rabbits (Daniel et.al; 1976) and the same is suspected to occur in cattle and horses (Bailey, 1985). Once the exudate has organized the only effective way to remove the clots and clear the joint is by arthrotomy and joint curettage. Arthrotomy also provides an opportunity for careful debridement of soft tissue, excision of hypertrophied synovium and the removal of hypertrophied cartilage and bone (Bailey, 1985).

When the anatomy and function of the joint permit, total curettage of the articular cartilage and immobilization resulting in arthrodesis have been successfully applied as a method of treatment (Verschooten, et.al., 1974; Weavers, 1990). Surgical pseudoarthrosis has also been suggested as a salvage procedure for alleviating pain and lameness in humans, dogs and cats. In human beings, excision arthroplasty is a salvage procedure that gives a painless hip with reasonable amount of movement (Adams 1976). Resection and removal of the femoral head and neck in cats and dogs is done to induce a functional pseudoarthrosis (Vassuer, 1983). Studies on pseudoarthrosis on clinical cases in cattle has revealed that fetlock pseudoarthrosis is an effective salvage procedure for lame calves especially those having fetlock septic arthritides (Ferguson, et.al., 1990). However there appears to be need for further studies in cattle to develop dependable management protocol and understand the biological basis of wound healing.

The severe inflammatory process in septic joints is both painful and self perpetuating. Prostaglandin synthesis plays an integral role in this process. Therefore administration of steroidal anti-inflammatory drugs may be indicated but it is necessary to remember the prolonged half-lives some

of these drugs have in cattle (Lees, 1991). A recommended dosage for phenylbutazone consists of administering a loading dose of 9mg/kg body weight orally and maintenance doses of 4.5mg/kg orally at 48 hour intervals (Eberhardson, et.al., 1979). Clinically administration of dexamethasone to cattle at the dosage rate of 4.4mg/kg given every other day relieves most of the post-operative inflammatory signs (Ferguson, 1985.). Maitho (1987) used 4.4mg/kg, of phenylbutazone and reported good success rates in adult cattle.

There is controversy regarding the recommendations related to immobilization of infected joints. Complete immobilization is thought to enhance the development of adhesions and fibrosis which results in a limited range of motion (Leitch, 1979). From a clinical point of view, some movement may be desirable, but the use of support bandages in the acute phase seems to make the animals more comfortable (Bailey, 1985).

2.6 PROPHYLAXIS AND THERAPY OF INFLAMMATION.

Several methods have been developed to alleviate the unwanted effects of inflammation. These include the application of cold packs to affected areas, compression bandages, and use of anti-inflammatory

drugs (Allgower and Parren, 1976; Peacock and Van Winkle, 1984).

2.6.1 Anti- inflammatory drugs

Anti-inflammatory drugs are those drugs that reduce edema, and pain and lower elevated body temperature. The drugs are classified as steroidal or non-steroidal. Steroidal anti-inflammatory drugs (SAID) include both the natural and synthetic glucocorticoids. The non-steroidal anti-inflammatory drugs (NSAID) are weak organic acids with similar anti-inflammatory properties. The mode of action of both groups includes the blocking of arachdonic acid cascade at different points thus blocking the formation of inflammatory mediators.

2.6.2 Steroidal anti-inflammatory drugs (SAID)

Steroidal anti-inflammatory drugs (SAID) are glucocorticoids. The drugs suppress the development of the cardinal signs of inflammation. Microscopically they inhibit edema, fibrin deposition, capillary dilatation and migration of leukocytes. They further stabilize lysosomal membranes, inhibit capillary proliferation, fibroblastic proliferation, deposition of collagen and cicatrization. Glucocorticoids inhibit inflammation whether the physical, chemical,

infectious or immunological. Their anti-inflammatory effect is palliative only while the underlying cause of the disease remains. The anti-inflammatory effect of glucocorticoids may be due to inhibition of eicosanoid synthesis (Flower, 1981). The glucocorticoids interact with specific membrane receptors, and after transcriptional and translational events lead to the formation of macrocortin which inhibits phospholipase A_2 (Blackwell, et.al., 1980, Flower, 1981). The availability of arachdonic acid is thus restricted and the formation of both cyclooxygenase and lipooxygenase products is reduced. Macrocortin may exist in a preformed store within some cells and glucocorticoids induce first its release (1-2 hours) then its resynthesis (3-4 hours). Cortisol is a natural hormone from the adrenal cortex. Synthetic glucocorticoids have been introduced into therapeutics on the basis of having anti-inflammatory potency greater than cortisol without having a corresponding tendency to retain sodium and partly also because of their longer duration of action.

2.6.3 Non-Steroidal Anti-inflammatory drugs. (NSAIDS)

The prototype of NSAID is aspirin. Thus all

NSAID are usually referred to as aspirin - like or acetylsalicylic acid - like (ASA-like) drugs. Many modes of action of NSAID have been described by Nickander, et.al; 1979. These are:-

a) inhibition of the biosynthesis of mucopolysacharides.

b) antagonist effects on mediators of inflammation other than prostaglandins.

c) inhibition of chemotaxis of cells implicated in the inflammatory process.

d) inhibition of lysosomal membrane labilization.

e) sulfhydryl - disulfide stabilization.

f) uncoupling of oxidative phosphorylation.

g) fibrinolytic activity.

h) inhibition of collagenase production.

A main mechanism of action of NSAID is the inhibition of eicosanoids synthesis. The drugs inhibit the conversion of arachdonic acid to the unstable endoperoxide intermediate, PGG_2 which is catalyzed by cyclooxygenase (Flower, et.al., 1985).

2.7 TISSUE REPAIR

2.7.1 Healing of Articular Cartilage Defects

The response of articular cartilage to injury depends on whether or not the injury violates the junction of the calcified zone and the under-lying

bony end plate (Convery, 1972).

The response to injuries confined to the substance of cartilage is devoid of an inflammatory component because the tissue is avascular (Calandruccio the Gilmer, 1962; Campel, 1969; Salter, et.al., 1980). The reaction is independent of the depth or extent of the lesion and evokes only a short-lived metabolic and enzymatic response which fails to provide sufficient number of cells or matrix to repair even the minimum defect. (Convery, 1972; Simmonds et.al., 1981). These lesions remain as defects even for a year and although their long term effect is still unknown it is speculated that the lesions do not produce clinical chondromalacia and or osteoarthritic degenerative processes (Simmonds, et.al., 1981, Mitchel and Shepard, 1980; Fischer, et.al., 1986).

The response of articular cartilage to deep lesions (injuries that cross the tide - mark) is similar to that of other vascularized tissues because the lesions violate the vasculature of the underlying bony end plate (Simmonds, et.al., 1981; Bailey, 1960). The deep cartilage defect almost immediately fill with blood. The hematoma that forms becomes organized into a fibrin clot in which are trapped red blood cells, white blood cells and other undifferentiated cells from the marrow and

endothelial linings (Salter, et.al., 1980, Mitchel and Shepard, 1980; Furukawa, et.al., 1980). The cells within the hematoma modulate into fibroblasts and capillaries grow from the vascular bed into the fibrin clot making it a vascular fibroblastic tissue (Albretcht, 1983, Kubo, 1983). This tissue undergoes progressive fibrosis which makes it become less vascular and more sclerotic (Wolff, et.al., 1992; Coults, et.al., 1982). At the same time active new bone growth occurs and extends towards the joint. The bone formation stops at the margin of the old cartilage-bone junction leaving the fibrous tissue to unite the wound edges. Meanwhile the fibrous tissue undergoes progressive hyalinization and subsequently becomes chondrified to produce a fibrocartilaginous mass. The fibrocartilaginous mass welds the wound edges and remains fused to the underlying bone (Fisher et.al., 1986; Kim, et.al., 1991).

Mitchel and Shepard, (1980) described the fate of the newly formed fibrocartilage in rabbits. They demonstrated that within one year the cartilaginous nature of this repair tissue was less obvious and appeared more fibrous. The surface layers were more typical of fibrocartilage than hyaline while the site of the defect remained clearly visible as a slightly discolored, roughened pit or linear groove on the otherwise quite normal surface of the adjacent

hyaline cartilage. Similar observations were made (French, et.al., (1989) and Trotter et.al., (1989) in horses.

Factors of clinical importance that have been shown to enhance the healing of deep articular cartilage defects are continuous passive motion and application of electrical fields (Salter; 1980; Trotter, 1980). Coring defects in the articular cartilage were made through the underlying bone on the distal femur of rabbits and the animals then treated in three ways; by cage ambulation; by plaster immobilization and by continuous passive motion. After four weeks, the cartilage defects were assessed histologically and histochemically. The assessment revealed that the reparative tissue in animals subjected to continuous passive motion more closely approximated hyaline cartilage (Salter, 1980). In another experiment deep articular cartilage defects which were treated by application of electrical field were observed to produce repair tissue superior to that of defects that were not similarly treated (Trotter, et.al., 1980). Thus cartilaginous tissue is capable of responding to modifications in chemical and physical potential for repair. There is definitely tremendous opportunity in methods that can be evolved to improve the current treatment of articular cartilage defects.

2.7.2. Bone healing

The mechanical consequences of a fracture are movement in the fracture zone and disturbance of the transmission of forces along the bone. These consequences are subsequently counteracted by healing of the fracture which restores normal transmission of forces and eliminates movement (Peacock and Van Winkle, 1984). A good blood supply, accurate positioning of the fragments, adequate immobilization and early ambulation are necessary for optimal bone healing (Dingwal, 1974).

Following trauma the reaction of the periosteum, endosteum and intracortical haversian system is characterized by infiltration of fibroblastic or fibrocartilargic tissue as well as capillaries in the gaps around the fragment ends. Any movement in the defect delays healing by disturbing and destroying newly formed cells and capillary beds. The thickness of the new tissue, the callus cuff, is in proportion to the fragment movement (Prieur and Somner Smith, 1984). The differentiation of the stem cell is related to its environment. Stress (compression) plus high oxygen tension results in osteoid or bone formation; tension plus high oxygen tension results in the formation of fibrous tissue; and stress associated with low oxygen tension results in cartilage formation (Dingwal 1974). Fibroblastic

cells that differentiate in the well vascularized area near the bone become osteoblasts forming bony trabeculae. Cells further away from the vascularized area differentiate in an avascular environment, become chondroblasts and form cartilage (Dingwal, 1974). The tissue that forms between the fractural parts and the medullary cavity is called internal callus. External callus develops around the bone ends. Thickening of the callus increases the transverse lever arms and thus diminishes the extent of fracture movement. When external callus and trabeculae of the internal callus bridge the site, the fracture is united. The rigidity of the callus is improved by the transformation of the initial interfragmentary callus to rigid fibrocartilage, followed by ossification and consequent fracture stabilization. When the fracture site is bridged by trabecular bone, it is said to have healed. Once the fracture is stabilized, a remodelling and substitution of the bony (woven bone) callus with lamellar bone and Haversian systems is possible (Prieur and Somner-Smith, 1984). Healing in the afore mentioned manner is called spontaneous healing.

Fracture healing in the presence of internal fixation of varying rigidity follows the same pattern as does spontaneous healing, but may be reduced to a single step if the fracture is sufficiently stable

(Perren, 1981). In stable motionless areas, haversian canals cross the discontinuity from fragment to fragment (contact healing) thus restoring the original structure of the bone in a one step procedure. Where a gap exists, lamellar bone filling is seen in the gap oriented at right angles with the original bone structure, a phenomenon known as gap healing. The gap is protected from strain by nearby contact areas, a situation found in plated fractures. The bone cortex next to the plate heals by contact healing whereas the cortex furthest from the plate heals by gap healing (Rittman and Perren, 1974, Peacock an Van Winkle, 1984).

The healing of an infected fracture is characterized by cloudy callus, resorption at the fragment ends, sequestration and patchy bone resorption. If compression is maintained in a rigid internal fixation system, primary bone healing will prevail inspite of the infection (Dingwal, 1974; Rittman and Perren, 1974; Prieur and Somner Smith, 1984).

2.7.3 Secondary Wounding and Pseudoarthroses.

Secondary wounding in bone is usually the result of delayed manipulation of an improperly reduced fracture. It is similar to making a secondary wound in soft tissues and also does not delay fracture

healing during the cellular proliferative stage. Secondary manipulation after the primary cellular stage (7 - 10 days) significantly delays and may even prevent normal healing (Peacock and Van Winkle, 1984). Secondary manipulation, either intentional or unintentional, because of poor immobilization produces the mechanical stimulation for the formation of a joint surface. Thus fractures which normally heal without cartilage formation can be induced to form large amounts of cartilage and actually proceed to pseudoarthrosis if the fracture is manipulated after the cellular proliferation stage of healing (Peacock and Van Winkle, 1984). Furthermore it has been suggested that "improper" joint immobilization or early removal of casts is an integral part of surgical pseudoarthrosis (Ferguson, 1985). Pseudoarthrosis occurs in stages. The simplest form of pseudoarthrosis is a fibrous union between two bone ends. An extension of this is a stage at which either fibrous or hyaline cartilage develops within the uniting fibrous tissue. In the next and highest stage of refinement of pseudoarthrosis, clefts form in the cartilaginous tissue and a synovial like tissue lines the 'new' joint. This final form of pseudoarthrosis may be termed nearthrosis. (Jubb, et.al., 1985).

2.8 METHODS USED TO EVALUATE INFLAMMATION AND THE HEALING PROCESS

2.8.1 Hyperpyrexia

In animal models, local or systemic pyrexia (fever) have been obtained by administration of brewer's yeast or bacterial pyrogens. Measurement of skin temperature may be accomplished by contact thermometers, infrared radiometers or by infrared thermography. There is no widely accepted standard experiment which utilizes the increase of temperature of an inflammed site for assessment of anti-inflammatory activity (Arrigoni - Martelli, 1979). In veterinary clinical practice routine assessment of systemic temperature is determined by recording rectal temperature using mercury thermometers. Local pyrexia is subjectively evaluated by digital palpation of the inflammed site.

2.8.2 Pain

In experimental models, pain is caused by local application of brewer's yeast, intraperitoneal injection of 2-phenyl -1-4-benzoquinone or acetic acid in rodents or by surgical procedures in human beings and other animals. The degree of pain is determined by applying a force of increasing magnitude. The force at which the animal begins to struggle or vocalize is assumed to represent the pain

threshold and serves as the end point (Arrigoni - Martelli, 1979). In other studies the number of stretches were used to determine the degree of pain in rats as the number of stretches of the abdomen were found to increase with pain intensity (Muzue, 1983). The most successful efforts to quantify pain in humans are those accepting the patient's own report (Arrigoni - Martelli, 1979). In veterinary surgery the assessment of pain is usually subjective and descriptions of the degree of pain such as severe, moderate, mild etc are routinely applied. Visual analog scales (VAS) were utilized to evaluate post - operative pain in dogs. The surgeon estimated the pain felt by the animal by exerting digital pressure on the surgical site. The pain estimated was marked on a VAS that ran from 'no pain' (0,mm) to 'pain cannot be worse' (100 mm) (Mbugua, 1987).

2.8.3 Limping

Limping is an abnormality in the gait of an individual which is commonly caused by pain. Limb surgery is often associated with post-operative limping. The degree of limping or lameness is routinely assessed as either severe (swinging leg or 'carrying leg') moderate or mild. To quantify lameness associated with post-operative pain visual analog scales (VAS) are utilized. The surgeon

assesses the degree of limping on the VAS running from 'no limping' (0mm) to 'limping cannot be worse' (100mm). (Mbugua 1987).

2.8.4 Joint Mobility

Synovial joint have definite angles of flexion and extension. These angles usually decrease when the joints are arthritic. Decrease in the range of motion of a joint is consequently used to assess joint function(Ferguson, 1985). In clinical situations the range of movement of diseased joints is compared with that of a non-diseased contralateral limp. When more objective data is required the angle of distention or flexion of the diseased joint is measured using a pair of calipers and a protractor and then expressed as a percentage of the normal (Ferguson; 1985; Ferguson, et.al., 1990).

2.8.5 Radiographic evaluation of joint healing

Radiographic evaluation of healing joints is often necessary especially if the joints have been bandaged with plaster. In such cases, it is important to determine what is happening in the soft tissue under the cast and in the joint. In cattle, immobilized joints should be radiographically evaluated every 1-2 weeks. Anteroposterior and lateral views should be taken in order to expose

every aspect of the joint (Farrow, 1985). Evaluation of the joint healing using the radiographs may be based on several parameters; radiographic union of the bone ends, degree of callus formation, evidence of infection and/or presence of foreign body reaction (Mbugua, 1987). Although these details are designed to evaluate bone healing the criteria fits for curetted joints where all the articular cartilage has been removed from the bone ends simulating a fracture situation (Ferguson 1990). Radiographic union of bones can be graded against a semi quantitative scale from 0 to xxxx according to the following criteria (Mbugua, 1987):-

0 - No evidence of union. A radiolucent line is found where the joint space originally was.

x - Callus bridging the joint space is partially ossified.

xx - Joint space is filled with ossified tissue whose radio-opacity does not match the remaining cortex.

xxx - Most of the osseous tissue in the joint space has the same radio-opacity as the rest of the cortex.

xxxx - That space is undecernible as it is completely filled with radio -opaque bone.

2.8.6 Nature of the reparative tissue in healing deep articular cartilage defects

Several reports describe the assessment of the nature of the reparative tissue in healing articular cartilage defects (Salter, et.al., 1980; French and Barber, 1989; Simmonds et.al., 1981). The repair tissue is harvested at post mortem or through arthroscopy techniques and fixed in formalin for routine Hematoxylene and Eosin (H/E) and/or Safranin - 'O' staining (French, and Barber, 1989, Ferguson et.al., 1990) H/E stained sections are examined for the cellular composition of the repair tissue. Categories of repair tissue may be described and assigned (French, et. al., 1989);-

1. Fibrous tissue containing predominantly spindle shaped fibroblasts.
2. Incompletely differentiated mesenchymal tissue composed of cells beginning to differentiate into fibroblasts.
3. "Hyaline - like" articular cartilage containing chondrocytes in lacunae.

Safranin -'O'- stained sections are used to evaluate the degree of chondrification of the repair tissue. The stain is taken up by glycosaminoglycan depicting the concentration of cartilage cells in the repair tissue. Cartilage is therefore quantified by

assigning a grade 1-to 4 of the safranin-'O'- stained sections:-

1. - No stain uptake
2. - Light staining minimal uptake
3. - Moderate staining
4. - Normal dark staining.

2.8.7 Biochemical markers of Inflammation

Assessment of cyclooxygenase inhibition has been the standard biochemical technique of evaluation of anti-inflammatory drugs (Ferreira and Vane, 1979). Singh, et.al.. (1986) described gamma-glutamyltranspeptidase (y-GT) as a biochemical marker of inflammation. The enzyme plays an important role in the turn-over of glutathione and in protein synthesis, hence its value for assessment of anti-inflammatory drugs. The in-vivo increase in y-GT activity was prevented from occurring in proportion to the anti-inflammatory potencies of test drugs given oraly in rats. The authors used whole homogenates (10%w/v) of edematous, granulomatous and inflammed skeletal tissues of rats. However Mitema, (1989) suggested that serum y-GT activity could also be of use in evaluating anti-inflammatory drugs. Boelsterli and Zbinden (1980) described the determination of y-GT activity. 50 ml samples of the biological probes were incubated at 37° for 15-30 min

with 450 ml of buffer substrate solution (100mM Tris-HCl, pH.7.6; 75mM glycylglycine; 10mM $MgCl_2$, 4mM Y-glutamyl -p-nitroanilide. H_2O). The reaction was terminated with 1.5ml of 10% acetic acid. The tubes were cooled in ice, centrifuged and read at 405nm in a spectrophotometer against a blank. Protein was determined using bovine serum albumin as a standard (Lowry et.al; 1951).

The normal values for Y-GT in the bovine range from 0-27 I.U (Kraft et. al; 1983).

2.9 REQUIREMENTS FOR ORTHOPAEDIC SURGERY

2.9.1 Aseptic Technique

Every effort should be made to ensure that the basic minimum requirements for asepsis are met in every orthopaedic surgery. The operating room should be dust free and should have facilities for general anaesthesia. Aseptic techniques cannot be practiced when the animal occasionaly moves. There should be minimal movement in the operating room and adequate lighting made available. The animal should be adequately padded and drapped (Jennings, 1984).

The skin should be clipped immediately prior to surgery. Povidone-iodine scrub with a 70% isopropyl alcohol rinse is an accepted technique for skin preparation in orthopaedic surgery. Surgeons should wear sterile rubber gloves, long-sleeved operating

gown, a nose and mouth mask and a cap (Jennings, 1984). In addition to sterile drapping of the operative site, the entire patient should be drapped to contain dust from the animals's body.

2.9.2 Use of Tourniquets

Tourniquets are commonly used in orthopedic surgery on horses and cattle. Tourniquets are used in combination with an Esmarch's bandage on horses whereas tourniquets are used alone in cattle (Jennings, 1984). The aim of a tourniquet is to provide a bloodless field to the distal limb. The tourniquet is usually applied above the carpal or tarsal joint. For surgeries involving the fetlock joint and below the tourniquet can be placed over the proximal metacarpal or metatarsal region (Ferguson, 1980). Surgery can progress quickly with a tourniquet on because of the bloodless field, the surgeon does not spend time interrupting the surgery to wipe capillary ooze from the tissues. The vessels that require coagulation with electrocautery or ligation with suture material are readily visible, even in a bloodless field (Ferguson, 1980; Jennings, 1984). The small bleeding vessels that miss the attention of surgeon while the limb is under tourniquet are taken care of by a firm pressure bandage applied over the surgical site at completion

of the surgery before the tourniquet is released (Jennings, 1984).

2.9.3 External Coaptation

External coaptation is an essential part of large animal orthopedic surgery and is often indicated for fractures, tendon and other soft tissue injuries and as adjunct to internal fixation and joint curettage (Ferguson, 1982, Jennings, 1984). Several methods of external coaptation for large animals have been described by Jennings (1984). The methods include the use of slings and splints, application of plaster or resin casts and application of Robert Jone's bandages (Jennings, 1984).

2.9.3.1 Plaster casts

2.9.3.1.1 Usage

Application of plaster casts is the most commonly used method of external coaptation in large animals. In cattle plaster casts are commonly indicated for fractures, arthrodeses subsequent to joint curettage and for management of contracted tendons (Ferguson, 1982).

2.9.3.1.2 Principles of application

One of the foundamental rules in the treatment of any fracture with casts is the immobilization of

the joint above and below the fracture line. The cast should not end in the middle of a long bone as the fulcrum effect will produce severe rubbing sores and unwarranted forces on the diaphysis of the bone. The cast should always enclose the entire foot because if it is left exposed the axial force of weight bearing is transmitted up the leg leading to instability in the fracture. An exposed foot also results in unwanted rubbing sores especially on the coronary band (Ferguson, 1980, Jennings, 1984).

Similar principles are applied for joint immobilization as for fracture fixation (Ferguson, 1986). However, in this case the joint being immobilized is treated as the fracture line. If joint fusion (arthrodesis) is not desired the joint above the diseased joint may be partially immobilized inorder to reduce pain and joint degeneration while maintaining joint function. Casts applied to enclose the hoof and reach two inches above the carpal joint partially immobilize the fetlock joints of young calves (Ferguson, 1980, Ferguson et al., 1986, Mbithi, et al., 1991).

2.9.3.1.3 **Convalescent care of cattle with cast**

- An animal with a cast on its limb should be under constant veterinary supervision. Cattle with casts are usually kept in the farm for economic

reasons but ideally they should be hospitalized. Animals with casts should be kept in a clean, dry and well bedded stall. Such animals should not be turned out when they can be bothered by other members of the herd or flock. The casts should be closely monitored and inspected for cracks, excessive wear and excessive or abnormal discharge. A crack can quickly spread around the cast resulting in lack of immobilization and development of rubbing sores (Jennings, 1984, Tulleners, 1986). Broken casts should be changed immediately. The casts should be felt for excessive warmth and swelling above them which may indicate complications under the cast and warrant a cast change. The best way to judge how well the patient is tolerating the cast is to watch its ability to use the cast (Jennings, 1984). Sometimes an animal with a cast may lick or bite at the cast indicating pain/pruritis in the cast part of the limb and warranting a cast change. This phenomenon is also accompanied by a rise in the body temperature, pulse and respiratory rates (Ferguson, 1980). Animals on drugs such as phenylbutazone should be watched more closely as the effects of such drugs may mask problems under the cast (Jennings, 1984).

2.9.3.1.4 Cast Removal

Once the cast has served its useful purpose, it is removed (Ferguson, 1984). The duration the cast is left on depends on the indication for its application (Jennings, 1984). For young calves with fractures the casts are left for 3-5 weeks while for adults the casts are left for 6-8 weeks (Jennings, 1984). Casts used for immobilization of curetted fetlock joints in calves are usually left for 3 weeks (Jennings, 1984, Ferguson, 1984, Ferguson, 1986).

CHAPTER THREE

3. MATERIALS AND METHODS

3.1 Location

This work was conducted at the Department of Clinical Studies, University of Nairobi; at Kabete. Kabete lies approximately 1°16S and 36°44E at an altitude of 1932 meters above sea level.

3.2 Experimental Animals

Six to twelve month old male Fresian calves weighing between 50kg-70kg were used. The calves were obtained from established farms and four calves were housed in one unit stall made of concrete walls and floor and corrugated asbestos sheeting roofs. The Stalls were of uniform area measuring 3 x 3.75 meters of floor space and a height of three meters from the ground. Each stall had at least one open window measuring 0.6 x 0.85 meters located above a half door for adequate ventilation. The calves were provided with water, hay (Rhodes grass), maize bran and mineral salt (Maclic - Twiga Chemicals, Nairobi), ad.libitum.

On acquisition, physical examination was done on each calf. Whole and clotted blood samples was also taken from each calf. From the blood samples the complete blood count (CBC), the blood urea nitrogen (BUN), total protein (TP) albumin, globulin and

alkaline phosphatase (AP) were determined. Blood slides from each calf were examined for blood parasites; East coast fever (ECF) piroplasms, babesia, anaplasma bodies and trypanosomes. All calves were dewormed using albendazole (Valbazen^{R}, Kenya Swiss.Co. Ltd Nairobi, Kenya) administered orally at the dosage rate of 10mg/kg body weight. Fecal samples were taken 48 hours after deworming, examined for helminths and the albendazole treatment repeated for each positive case.

Anteroposterior (AP) and lateral (L) view radiographs were taken at the left metacarpophalangeal joint of each calf. From the radiographs, the bone contours, cartilage surfaces, joint spaces and continuity of surrounding soft tissue were evaluated. Only calves free from disease, blood parasites, gastrointestinal parasites and gait or conformational defect and with normal metacarpophalangeal joints were included in the study.

3.3 Experimental design

Thirty calves were randomly divided into three groups of ten. Group one calves were operated to induce pseudoarthrosis of the left lateral metacarpophalangeal joint and were treated with phenylbutazone (Mac's pharmaceutical, Nairobi, Kenya)

post-operatively. Group two calves were operated similar to group one calves but were treated with dexamethasone (Dexafort^{R} intervet International, BV Boxmeer, Holland) post-operatively. Group three calves were 'sham' operated and given a placebo post-operatively.

3.4 Joint curettage

The left lateral metacarpophalangeal joints of five calves were operated on in the mornings of six days.

3.4.1 Preparation for surgery

Feed and water were withheld twelve hours before surgery. All the calves were prepared for aseptic surgery by clipping hair on the left fore-limb from approximately 5 cm above the carpal joint to enclose the hoof.

3.4.2 Premedication and anaesthesia

Each calf was premedicated just before surgery. Xylazine Hydrochloride (Rompun^{R}, Bayer, E.A) given intravenously and atropine sulphate (veterinary drug Co Ltd. York U.K.) given subcutaneously at the dosage rate of 0.2 and 0.1 mg/kg body weight respectively were used for premedication. General anaesthesia was then induced and maintained using Halothane

(Fluothane^{R}, ICI, Cheshire, U.K) - oxygen mixture in a semi-closed system.

A tourniquet was applied proximal to the elbow of the experimental limb and the animal draped for aseptic surgery (Figure 1).

3.4.3 The surgical procedure

A 50 mm long incision was made through the skin, subcutaneous tissue, retinacula and the joint capsule of the left lateral metacarpophalangeal joint (LLMCPJ) at right angles to the axis of the limb (Figure 2). Joint curettage was performed in all twenty calves of group one and two. In these calves bone curettes were used to remove all the articular cartilage from the distal third metacarpal and proximal first phalangeal condyles of the joint (Figure 3). The curetted joints were lavaged with 100 ml of isotonic solution (Water for Injection, Infusion, Kenya Ltd. Nairobi) to remove all the cartilage chips (Figure 4). No curettage was performed in group three calves but the joints were lavaged with 100 ml of isotonic solution immediately after the arthrotomy incisions. Operated joints of the calves in the three groups were closed in the same manner. The joint capsule and the subcutaneous tissue were closed in one layer using number one polydioxinone (Dexon^{R}, Ethicon Ltd. U.S.A) suture

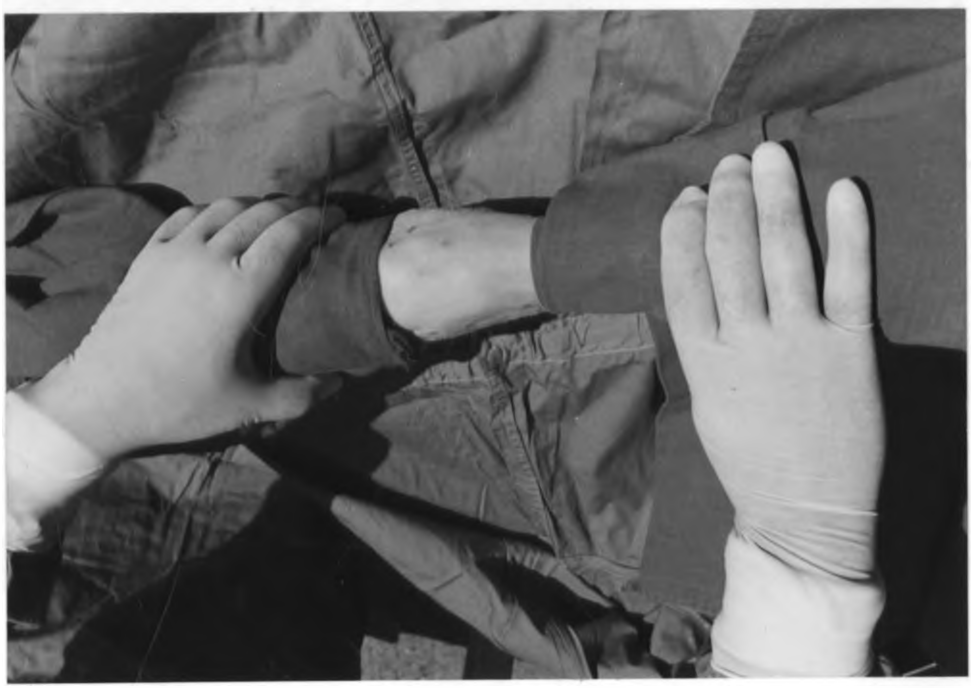


Figure 1: The surgical procedure: Surgical site prepared and ready for operation.

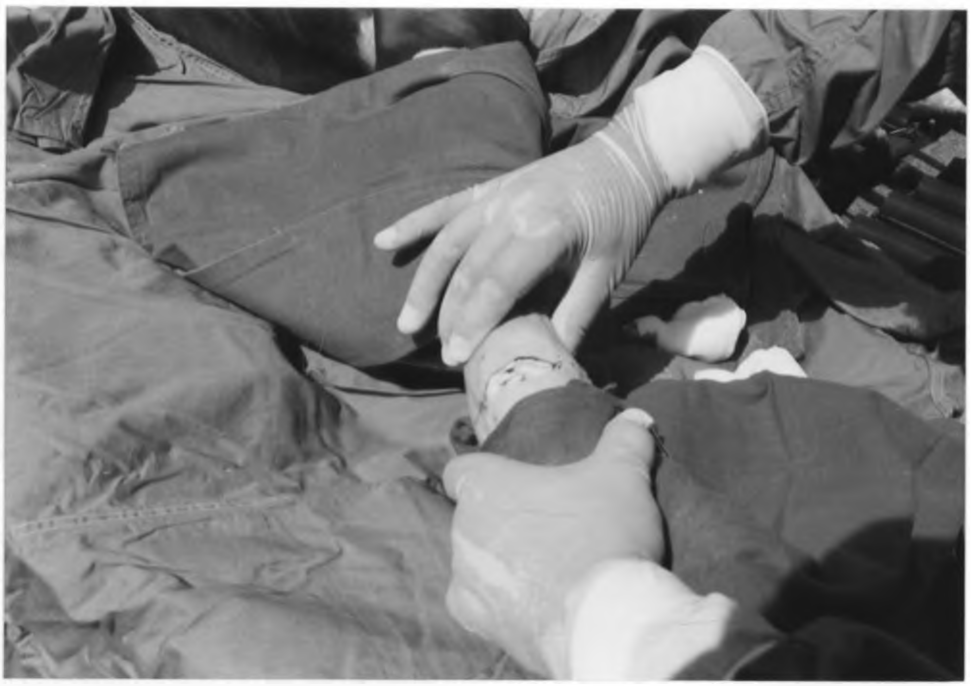


Figure 2: The surgical procedure: Incision made through the skin, subcutaneous tissue, retinacula and the joint capsule to expose the articular cartilage.

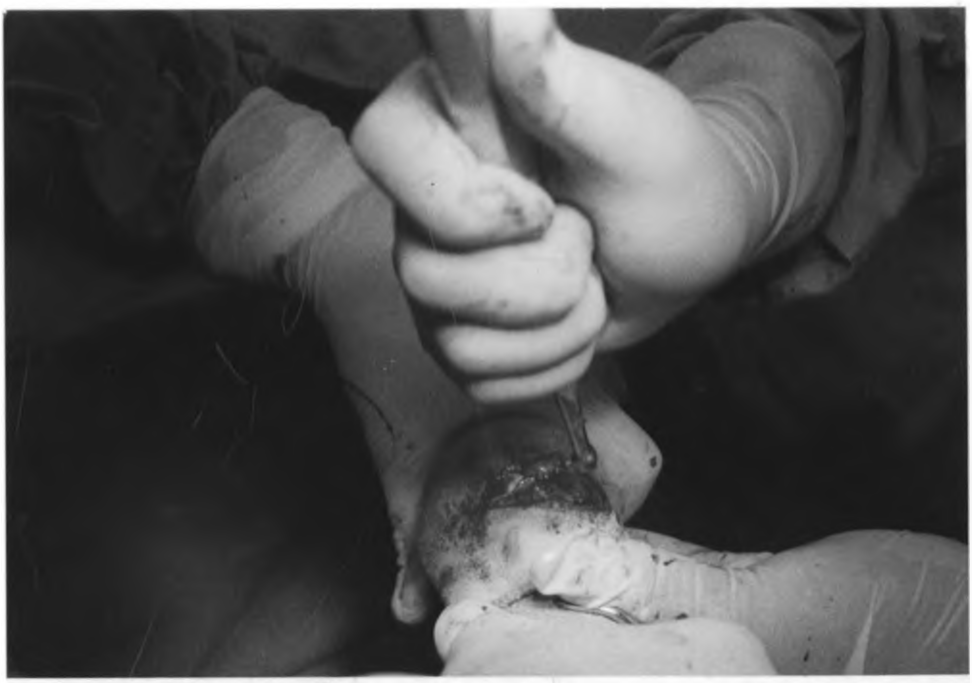


Figure 3: The surgical procedure: Curettage of the articular cartilage and subchondral bone with a bone curette.

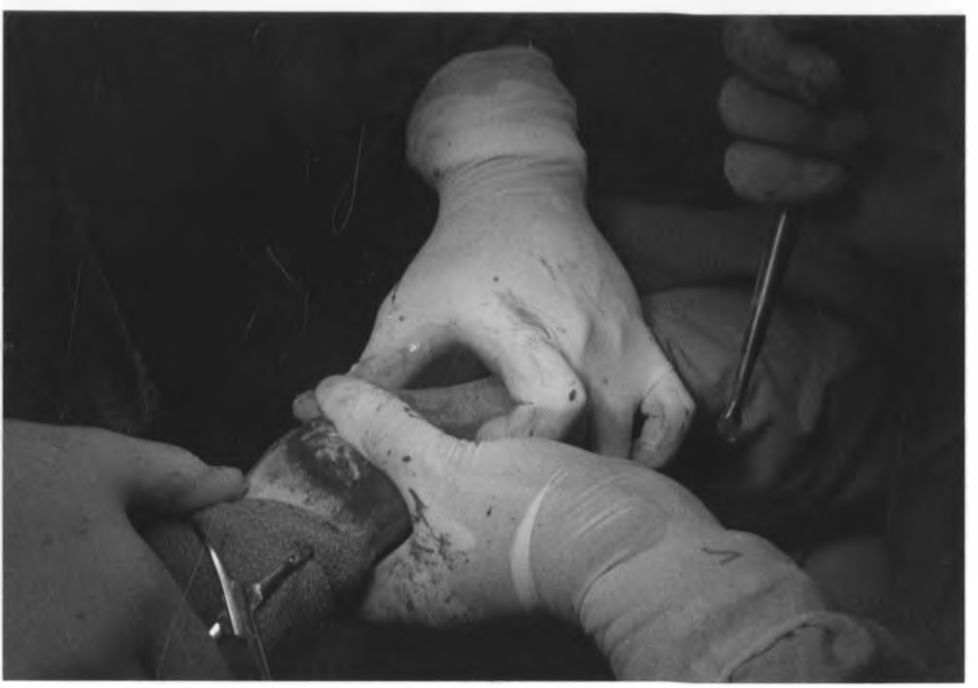


Figure 4: The surgical procedure: Curetted joint after lavage with saline to remove the cartilage chips.

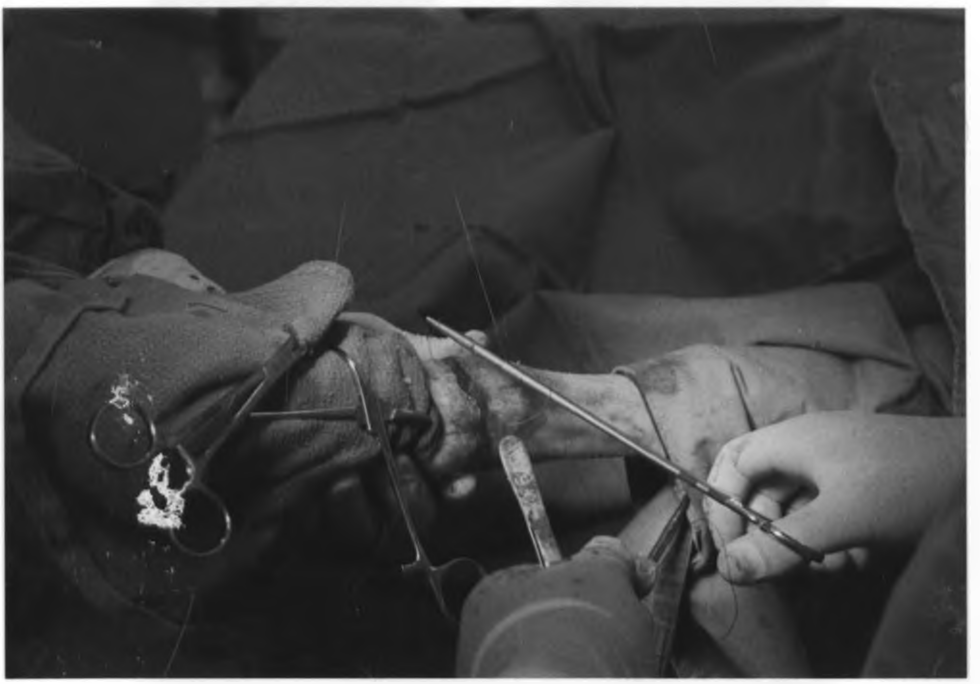


Figure 5: The surgical procedure: Closure of the joint capsule and subcutaneous tissue.

Figure 6: The surgical procedure: Skin sutures are placed to complete the procedure.

material in a simple continuous pattern (Figure 5) while the skin was closed with number one nylon sutures in simple interlocking pattern (Figure 6). The surgical incision was covered with a non-adhesive pad (Helmplast^{R}, HELM Pharmaceutical, GMBH, Germany). supported by a light gauge bandage. The tourniquet was removed and anaesthetic discontinued.

3.4.4 Partial immobilization of operated joints

All the operated joints were partially immobilized immediately after surgery and while the calves were recovering from anaesthesia.

A double layer of stockinette (Helmplast^{R}, Helm Pharmaceutical, GMBH, Germany) was placed over the limb to include the foot up to the distal radius. Plaster of Paris cast was then applied starting 5 cm above the carpal joint and reaching the hoof to only partially immobilize the operated metacarpophalangeal joint. To construct the cast plaster of Paris casting bandages (Helm^{R}, Helm Pharmaceutical GMBH, Germany) was soaked in hot water for about five seconds and excess water removed by gentle squeezing of bandage. The casting bandage was applied in a spiral overlapping fashion starting at the metacarpophalangeal joint and spreading proximally and then distally overlapping the previous turn by one-half to two thirds. Additional rolls were added

and the proximal end of the stockinette reflected before application of the last roll of casting bandage over the surface. The constructed casts were allowed to dry and set for 30 minutes while the calves recovered from anaesthesia in an adjacent room. Five rolls of the same type and size of casting bandage were used in each calf and all casts were constructed in the same manner.

3.4.5 Treatment

Drugs were administered intramuscularly using the gluteal muscles immediately the calves recovered from anaesthesia and were able to walk to their stalls. All group one calves were given dexamethasone (Dexafort^{R}, Intervet International, B.V. Boxmeer, Holland) and all group two calves were given phenylbutazone (Mac's Pharmaceutical, Nairobi, Kenya) at dosage rates of 0.2 and 4.4 mg/kg body weight respectively. Group three calves were injected with placebo, 0.5 ml isotonic solution (Water for Injection, Infusion, Kenya Ltd, Nairobi). The treatments were repeated on the third and the seventh day after surgery.

3.5 ASSESSMENTS

Post-operative recordings of the degree of limping and rectal temperatures were taken in the

mornings of 1 to 7 days and on day 10, 14, and 21 and from then on weekly until the 135th post-operative day. Weekly recordings of pain and joint mobility were taken starting from the 21st post-operative day up to the 135th post-operative day.

3.5.1 Limping

The surgeon assessed the degree of limping of each calf on a 5 mm Visual Analog Scale (VAS) running from no limping (0 mm) to limping cannot be worse (5 mm).

3.5.2 Temperature

Rectal temperatures were recorded in degrees Celsius for each calf using a mercury thermometer.

3.5.3 Joint mobility

The angles of flexion of operated joints were subjectively evaluated through palpation and visual examination and scored as percentage of the normal angle of flexion of the same joint in the unoperated contralateral limb starting at 21 days after surgery and on the day of cast removal.

3.5.4 Pain

The surgeon assessed the pain felt by the calves by exerting digital pressure on the operated joints.

The pain estimate was marked on a VAS running from 'no pain' (0 mm) to 'pain cannot be worse' (5mm).

3.5.5 Joint healing

Radiographs of the operated joints were taken 3, 6, 9 and 15 weeks after each operation. Anteroposterior and lateral views of these radiographs were evaluated on the basis of "radiographic union". This parameter was graded against a semi-quantitative scale from 0 to 4:-

0 - No evidence of union. A radiolucent line where the joint space originally was (intercondylar space).

1 - Callus bridging the intercondylar space is partially ossified.

2 - Intercondylar space is filled with ossified tissue whose radio-opacity does not match the remaining cortex.

3 - Most of the osseous tissue in the intercondylar space has the same radio-opacity as the rest of the cortex.

4 - Intercondylar space is undecernible as it is completely filled with radio-opaque bone.

3.5.6 Nature of the reparative tissue in healing articular cartilage defects.

On the 135th post-operative day the calves were euthanatized and immediately after death, the operated limb was disarticulated at the carpus. The metacarpophalangeal joints of each operated limb were opened, examined visually and photographed (Figure 4). The third metacarpal and the first phalangeal condyles were then cut out with a band saw and immersed in 10% formalin solution.

Serial sagittal section (30mm) were cut out of each condyle using a Gillings Hamco Thin Sectioning device (Hamco Meachines, Inc; Rochester, New York). The thin sections were then decalcified in 10% Formic acid solution. Decalcified sections from the following sites were selected and prepared routinely for histological examination.

i) The mid-sagittal ridge on the distal third metacarpal condyle and the opposing site on the proximal first phalangeal condyle.

ii) A section from approximately 30mm lateral to the mid-sagittal ridge and another section from the opposing location on the proximal first phalanx.

iii) One section from approximately 30mm medial to the mid-sagittal ridge and another

section from the opposing site on the proximal first phalanx.

Using a protocol established by Salter et. al., (1980), Hematoxylin and Eosin stained sections from the above sites were analyzed and categorized according to the nature of the predominant reparative tissue in each joint, then placed in one of three categories:-

1. Fibrous tissue containing predominantly spindle shaped fibroblasts.
2. Incompletely differentiated mesenchymal tissue composed of cells beginning to differentiate towards chondrocytes.
3. "Hyaline-like" articular cartilage containing chondrocytes in lacunae.

3.5.7 Evaluation of serum Y-glutamyltranspeptidase (Y-GT) activity.

Blood samples were drawn for analysis of Y-GT in the plasma. Pre-operatively, the samples were taken 14 days before surgery, 2 days before surgery and on the day of surgery just before the calves were premedicated for induction of general anaesthesia. Post-operatively, blood samples were drawn every

other day upto the 13th post-operative day (i.e. days, 1,3,5,7, ... 13). The blood samples were centrifuged to harvest serum which was kept in a refrigerator at 4°C. Y-GT activity was determined within the day of sample collection. For this purpose a biochemical analyzer was prepared according to the manufacturers instructions and the serum samples fed in. The serum Y-GT activity in international units were produced in a print-out.

3.6 STATISTICAL ANALYSES

Data collected were analysed and assessed for normality according to Lehmann and D'abrera (1975). The t-test was used for comparing the means (PC-SAS Statistical Package, SAS Institute 1990)

CHAPTER FOUR

RESULTS

4.1 General

The arthrotomy and surgical curettage of the metacarpophalangeal joints in the thirty calves was well tolerated and did not impair the general well being of the calves. When the calves recovered from anaesthesia associated with initial surgery they walked well having only minor gait changes. The calves remained bright and alert and had a good appetite.

4.2 Fever

Pre-operative and post-operative rectal temperature for the three treatments are shown in Table 1, Figure 7 and Appendix 1,2 and 3. Temperatures above the pre-operative cut-off of 38.7°C were recorded on the days of surgery and cast removal in all calves. However in all groups the temperatures went down within 24hrs of surgery or cast removal. Calves treated with dexamethasone had a mean peak temperature reading of 39°C. From then on there was a sharp decline in temperature readings by the third day after surgery until day 21 when there was another peak of 39.7°C. Temperature readings for calves treated with phenylbutazone followed a similar trend to that recorded for the

Table 1: Post - operative rectal temperature in °C after curettage of fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone(P) or mg/kg dexamethasone(D) calves or sham operations and injection with placebo (S) in calves.

	Post-operative days					
	Day -1			Day 1		
	D	P	S	D	P	S
Mean	38.5	38.3	39.9	39.5	40.0	39.9
Std.Dev.	0.1	0.2	0.32	0.6	0.4	0.18
Std.Error	0.05	0.08	0.10	0.2	0.1	0.05
Range	38.2 38.8	38.0 38.7	39.0 40.2	38.5 40.5	39.5 41.0	39.5 40.0
	Day 2			Day 3		
	D	P	S	D	P	S
Mean	39.0	39.0	39.4	38.5	38.3	38.9
Std.Dev.	0.4	0.3	0.47	0.3	0.1	0.28
Std.Error	0.1	0.1	0.15	0.09	0.06	0.09
Range	38.1 39.7	38.6 39.5	38.8 40.0	38.0 38.9	38.0 38.6	38.4 39.5
	Day 4			Day 5		
	D	P	S	D	P	S
Mean	38.5	38.4	38.5	38.4	38.5	38.3
Std.Dev.	0.2	0.2	0.21	0.1	0.1	0.25
Std.Error	0.08	0.07	0.06	0.06	0.05	0.08
Range	38.1 38.8	38.0 38.7	38.2 38.9	38.2 38.7	38.2 38.8	38.0 38.7

Table 1 (Contd.): Post-operative rectal temperature in ℃ after curettage of fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P), 2 mg/kg dexamethasone(D) or sham operations and injection with placebo (S) in calves.

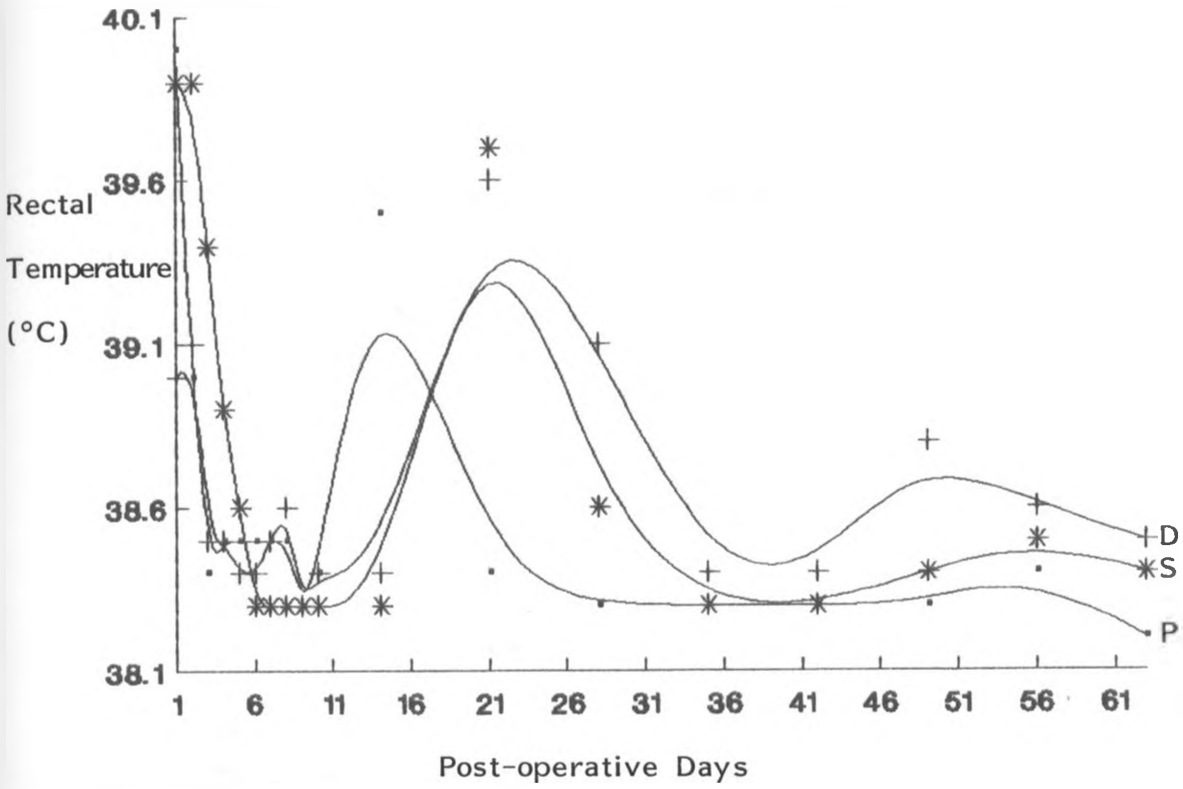
	Post-operative Days					
	Day 6			Day 7		
	D	P	S	D	P	S
Mean	38.3	38.4	38.3	38.4	38.5	38.3
Std.Dev.	0.2	0.2	0.17	0.3	0.1	0.20
Std.Error	0.07	0.09	0.05	0.1	0.05	0.06
Range	38.0 38.8	38.0 38.8	38.0 38.5	38.0 39.0	38.2 38.8	38.6 38.6
	Day 9			Day 11		
	D	P	S	D	P	S
Mean	38.5	38.4	38.3	38.3	38.4	38.3
Std.Dev.	0.1	0.3	0.13	0.2	0.5	0.19
Std.Error	0.06	0.09	0.04	0.09	0.18	0.06
Range	38.2 38.8	38.0 38.9	38.1 38.4	38.0 38.9	38.0 39.6	38.0 38.8
	Day 14			Day 21		
	D	P	S	D	P	S
Mean	38.4	38.3	38.3	38.5	39.5	39.6
Std.Dev.	0.2	0.2	0.21	0.2	0.3	0.62
Std.Error	0.08	0.07	0.06	0.09	0.10	0.19
Range	38.0 38.8	38.1 38.9	38.0 38.6	38.2 39.0	39.0 40.0	38.1 40.0

Table 1(Contd.): Post-operative rectal temperature in ℃ after curettage of fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P), 0.2 mg/kg dexamethasone (D) or sham operations and injection with placebo (S) in calves.

	Post-operative Days					
	Day 28			Day 35		
	D	P	S	D	P	S
Mean	39.6	38.5	38.3	39.1	38.3	38.3
Std.Dev.	0.5	0.2	0.18	0.4	0.2	0.20
Std.Error	0.1	0.08	0.05	0.1	0.07	0.06
Range	38.8 40.5	38.1 38.9	38.2 38.8	38.6 39.8	38.6 38.7	38.0 38.7
	Day 42			Day 49		
	D	P	S	D	P	S
Mean	38.4	38.2	38.3	38.3	38.3	38.4
Std.Dev.	0.2	0.2	0.19	0.2	0.1	0.22
Std.Error	0.08	0.08	0.06	0.07	0.05	0.07
Range	38.0 38.8	38.0 38.6	38.0 38.6	38.0 38.7	38.0 38.6	38.0 38.7
	Day 56			Day 63		
	D	P	S	D	P	S
Mean	38.8	38.3	38.5	38.5	37.6	38.4
Std.Dev.	0.2	0.1	0.18	0.2	0.05	0.09
Std.Error	0.06	0.05	0.06	0.07	0.80	0.03
Range	38.4 39.1	38.0 38.6	38.1 38.7	38.0 38.6	37.6 38.8	38.2 38.5

Figure 7

Mean rectal temperature (°C) after curettage of fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P) or 0.2 mg/kg dexamethasone (D) against sham operations and injection with placebo (S) in calves.



calves treated with dexamethasone. The mean peak reading on the first day of surgery was 40.0°C whereas the peak on day 21 was 39.4°C. The temperature readings of sham operated calves described similar trends to those recorded for calves treated with dexamethazone and those treated with phenylbutazone. The mean peak reading on the first day of surgery was 39.9°C whereas the peak on day 21 was 39.7°C.

In the three groups there was a sharp decrease to pre-operative levels in the temperature readings after the 21st post-operative day. There was no significant difference in the ability of dexamethazone and phenylbutazone to reduce rectal temperatures in these calves ($p<0.05$).

4.3 Limping

The mean post-operative recordings for limping are shown in Table 2, Figure 8 and Appendix 4,5 and 6. Peak levels were recorded on the first day after surgery but there was a steady decrease until the 21st post-operative day when there was another peak recording.

On the first day after surgery the mean peak recording for the phenylbutazone treated calves was 4.1 compared with 3.5 and 2.2 for the dexamethasone treated and sham operated calves respectively. On

Table 2: Post-operative limping in mm, assessed by a VAS after curettage of the fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P), 0.2 mg/kg/ dexamethasone (D) or sham operations and injection with placebo (S) in calves.

	Post-operative Days					
	Day 1			Day 2		
	D	P	S	D	P	S
Mean	3.2	4.1	2.0	3.0	3.7	1.0
Std.Dev.	0.4	0.7	0	0.5	0.6	0
Std.Error	0.1	0.2	0	0.1	0.2	0
Range	3-4	3-5	2-2	2-4	3-4	1-1
	Day 3			Day 4		
	D	P	S	D	P	S
Mean	1.8	3.1	1.0	1.4	2.4	1.0
Std.Dev.	0.6	0.7	0	0.5	0.6	0
Std.Error	0.2	0.2	0	0.1	0.2	0
Range	1-3	2-4	1-1	1-2	1-3	1-1
	Day 5			Day 6		
	D	P	S	D	P	S
Mean	1.0	2.0	1.0	1.1	1.8	1.0
Std.Dev.	0	0.5	0	0.4	0.6	0
Std.Error	0	0.1	0	0.1	0.2	0
Range	1-1	1-3	1-1	1-2	1-3	1-1

Table 2(Contd.): Post - operative limping in mm, assessed by a VAS after curettage of the fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P), 0.2 mg/kg dexamethasone (D) or sham operations and injection with placebo (S) in calves.

	Post-operative Days					
	Day 7			Day 10		
	D	P	S	D	P	S
Mean	1.2	1.8	1.0	1.2	1.6	1.0
Std.Dev.	0.4	0.6	0	0.4	0.5	0
Std.Error	0.1	0.2	0	0.1	0.2	0
Range	1-2	1-3	1-1	1-2	1-2	1-1
	Day 14			Day 21		
	D	P	S	D	P	S
Mean	1.0	1.4	1.0	3.1	3.4	2.0
Std.Dev.	0	0.5	0	0.3	0.5	0
Std.Error	0	0.2	0	0.1	0.2	0
Range	1-1	1-2	1-1	3-4	3-4	2-2
	Day 28			Day 35		
	D	P	S	D	P	S
Mean	2.2	2.1	1.0	1.2	1.5	0
Std.Dev.	0.4	0.3	0	0.4	0.5	0
Std.Error	0.1	0.1	0	0.1	0.2	0
Range	2-3	2-3	1-1	1-2	1-2	0

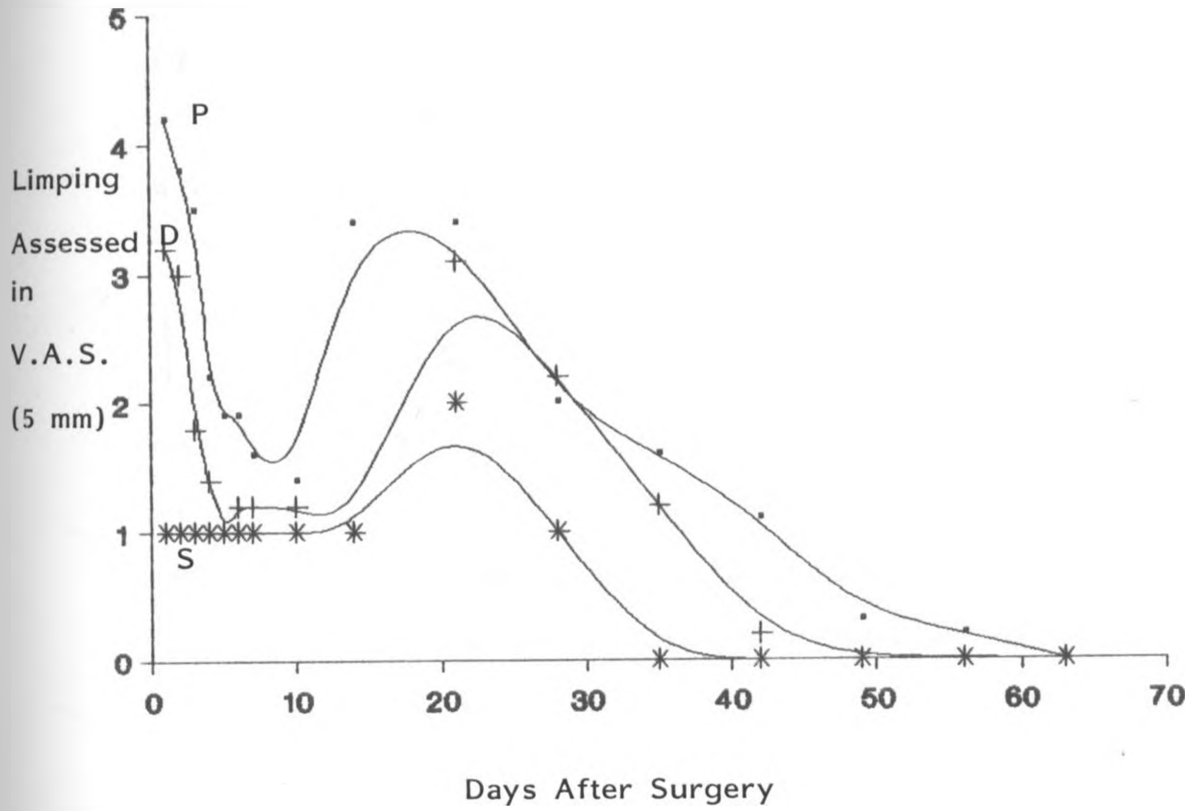
Table 2(Contd.): Post - operative limping in mm, assessed by a VAS after curettage of the fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P), 0.2 mg/kg dexamethasone (D) or sham operations and injection with placebo (S) in calves.

	Post-operative Days					
	Day 42			Day 49		
	D	P	S	D	P	S
Mean	0.2	1.1	0	0	0.3	0
Std.Dev.	0.4	0.6	0	0	0.5	0
Std.Error	0.1	0.2	0	0	0.2	0
Range	0-1	0-2	0	0	0-1	0

	Day 56		
	D	P	S
Mean	0	0.2	0
Std.Dev.	0	0.4	0
Std.Error	0	0.1	0
Range	0	0-1	0

Figure 8

Mean limping in mm, assessed by VAS, after curettage of fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P) or 0.2 mg/kg dexmethasone (D) against sham operations and injection with placebo (S) in calves.



the 21st day after surgery the mean peak recordings were 3.4, 3.1 and 2.0 for the phenylbutazone treated, dexamethasone treated and sham operated calves respectively. The mean recordings for all the calves diminished steadily after cast removal 21 days after surgery and reached zero by day 48 in dexamethasone treated calves, day 68 in phenylbutazone treated calves and day 35 in sham operated calves

4.4 Pain

The scores for post operative pain for the three treatment groups are shown in Table 3, Figure 9 and Appendix 7 and 8. There was moderate pain on palpation of the operated joints of group 1 and group II calves on the 21st post-operative day (day of cast removal). There was however a steady reduction in this parameter such that "no pain" was assessed on palpation of the joints by day 70 in the phenylbutazone treated group and the dexamethasone treated group. A pain estimate of 1 was recorded on day 21 for group 3 calves. Similar to group I and II the pain diminished steadily and an estimate of '0' (no pain) was recorded on day 35. Overall there was no significant difference in the reduction of pain between the two treatment groups ($p<0.5$) but there was a general tendancy for dexamethazone to be more potent than phenylbutazone.

Table 3: Post-operative pain in mm, assessed by VAS after curettage of the fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P), 0.2mg/kg dexamethasone (D) or sham operations and injection with placebo (S) in calves.

	Post-operative Days					
	Day 21			Day 28		
	D	P	S	D	P	S
Mean	3.6	3.8	1.0	2.6	3.3	1.0
Std.Dev.	0.5	0.6	0	0.5	0.5	0
Std.Error	0.1	0.2	0	0.2	0.2	0
Range	3-4	2-4	1-1	2-3	3-4	1-1

	Day 35			Day 42		
	D	P	S	D	P	S
Mean	2.0	2.2	0	1.3	1.5	0
Std.Dev.	0.5	0.4	0	0.5	0.7	0
Std.Error	0.1	0.1	0	0.1	0.2	0
Range	1-3	2-3	0	1-2	1-3	0

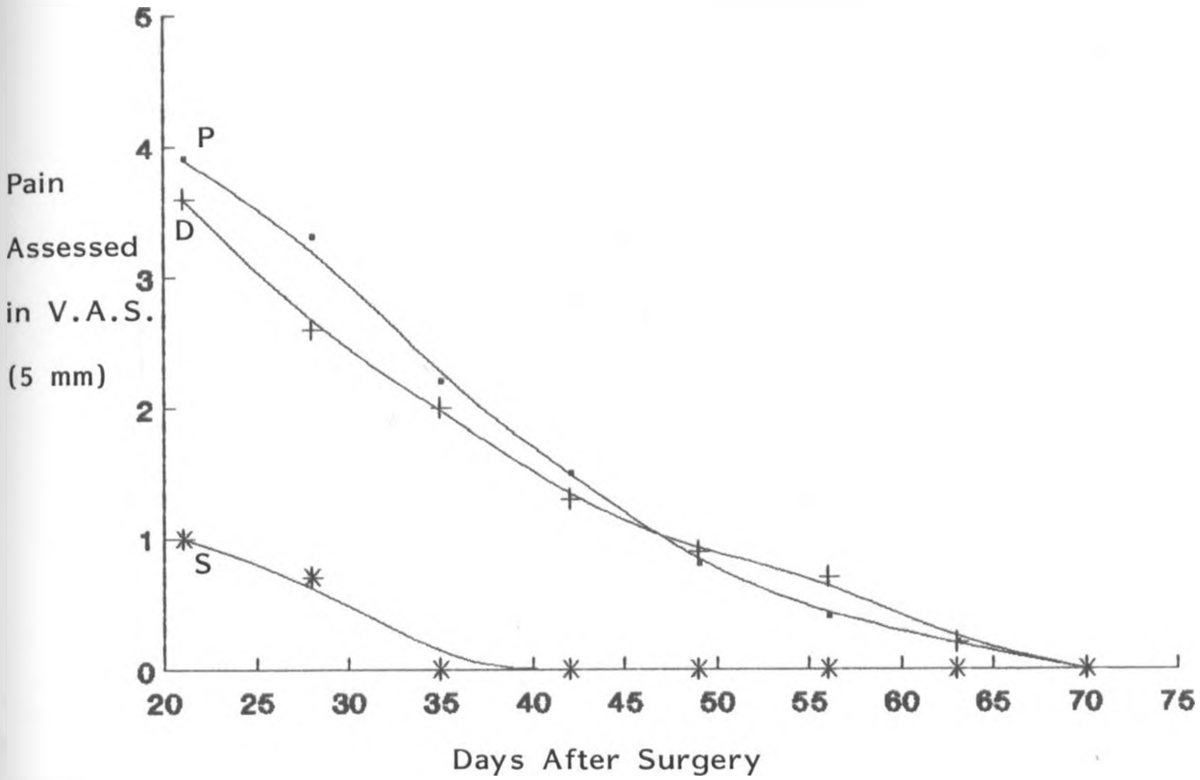
Table 3 (Contd.): Post-operative pain in mm, assessed by VAS after curettage of the fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P), 0.2mg/kg dexamethasone (D) or sham operations and injection with placebo (S) in calves.

	Post-operative Days					
	Day 49			Day 56		
	D	P	S	D	P	S
Mean	0.9	0.8	0	0.7	0.4	0
Std.Dev.	0.3	0.7	0	0.4	0.5	0
Std.Error	0.1	0.2	0	0.1	0.1	0
Range	0-1	0-2	0	0-1	0-1	0

	Day 63		
	D	P	S
Mean	0.2	0.1	0
Std.Dev.	0.4	0.3	0
Std.Error	0.1	0.1	0
Range	0-1	0-1	0

Figure 9

Mean pain in mm, assessed by VAS after curettage of fetlock joints and 3, three days apart i.m. injections in 4.4 mg/kg phenylbutazone (P) or 0.2 mg/kg dexamethasone (D) against sham operations and injection with placebo (S) in calves.



4.5 Joint Mobility

Joint mobility scores for the calves in the three treatment groups are presented in Table 4, Figure 10 and Appendix 9, 10 and 11. The lowest mean scores for this parameter were assessed on the 21st day after surgery. The mean mobility on this day (21st post-operative day) was assessed at 90% for the dexamethazone treated group, at 76% for the phenylbutazone treated and 90% for the sham operated calves. There was tremendous individual variation and a progressive increase in the joint mobility in all the calves to a maximum possible mobility of 100% on the 49 post-operative day for the dexamethazone treated calves. The mean maximum mobility for the phenylbutazone treated calves was 92% and was reached 77 days after the curettage. The maximum joint mobility of 100% was reached on 49 post operative day for the sham operated calves.

4.6 Joint healing

The assessments of joint healing after 3, 6, 9 and 15 weeks of surgery are presented in Table 5 and Appendix 12 and 13. Three weeks after curettage there was marked soft tissue swelling at the site of surgery in all treatment groups. The joints of group I and II had a widened radiolucent area where the joint space originally was (intercondylar space)

Table 4 : Joint mobility (per cent) after curettage of the fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P), 0.2 mg/kg Dexamethasone (D) or sham operations and injection with placebo (S) in calves.

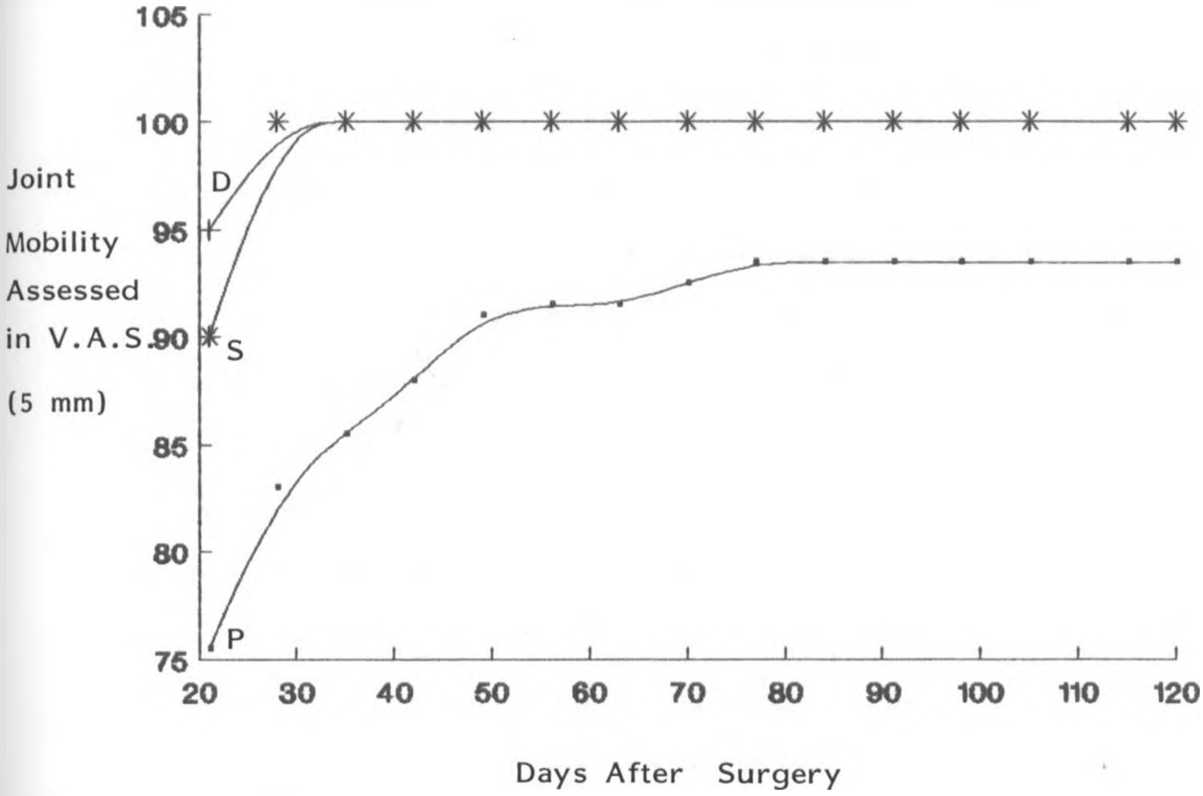
	Post-operative Days					
	Day 21			Day 28		
	D	P	S	D	P	S
Mean	95	75	90	100	83	99
Std.Dev.	5.2	20.2	0	0	18.7	3.1
Std.Error	1.6	6.3	0	0	5.9	1.0
Range	90-100	40-100	0	100-100	50-100	90-100
	Day 35			Day 42		
	D	P	S	D	P	S
Mean	100	85	99.5	100	88	99.5
Std.Dev.	0	19.2	1.5	0	18.1	1.5
Std.Error	0	6.0	0.5	0	5.7	0.5
Range	100-100	50-100	95-100	100-100	50-100	95-100
	Day 49			Day 56		
	D	P	S	D	P	S
Mean	100	91	100	100	91	100
Std.Dev.	0	18.0	0	0	17.3	0
Std.Error	0	5.7	0	0	5.4	0
Range	100-100	50-100	0-100	100-100	50-100	0-100

Table 4 (Contd.): Joint mobility (per cent) after curettage of the fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P), 0.2 mg/kg Dexamethasone (D) or sham operations and injection with placebo (S) in calves.

	Post-operative Days					
	Day 63			Day 70		
	D	P	S	D	P	S
Mean	100	91	100	100	92	100
Std.Dev.	0	17.3	0	0	16.2	0
Std.Error	0	5.4	0	0	5.1	0
Range	100-100	50-100	0-100	100-100	50-100	0-100
	Day 77			Day 84		
	D	P	S	D	P	S
Mean	100	93	100	100	93	100
Std.Dev.	0	15.6	0	0	15.6	0
Std.Error	0	4.9	0	0	4.9	0
Range	100-100	50-100	0-100	100-100	50-100	0-100
	Day 91			Day 98		
	D	P	S	D	P	S
Mean	100	93	100	100	93	100
Std.Dev.	0	0.6	0	0	15.6	0
Std.Error	0	4.9	0	0	4.9	0
Range	100-100	50-100	0-100	100-100	50-100	100-100

Figure 10

Mean values for joint mobility after curettage of fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P) or 0.2 mg/kg dexamethasone (D) against sham operations and injection with placebo (S) in calves.



while there was no other detectable change in the operated joints of group III calves (Figure 11). Six weeks post-operatively, the intercondylar spaces of the joints of group I and II calves were further widened but remained radiolucent; at nine weeks, some joints showed wide radiolucent intercondylar spaces while in other joints the widened intercondylar spaces had a barely detectable radiodensity.

Fifteen weeks after surgery some of the intercondylar spaces in group 1 and II had greater radiodensity than seen at nine weeks, but this radiodensity did not match that of the surrounding cortex (Figure 12). In other joints the intercondylar spaces were still radiolucent at fifteen weeks after joint curettage. There was no significant difference in the scores recorded for the joint healing between the phenylbutazone treated and dexamethasone treated calves. Soft tissue swelling was present at the surgical sites of all the operated joints. There was no evidence of union and a redioluscent line was apparent in the intercondylar spaces of sham operated joints upto 15 weeks after surgery.

4.7 Gross appearance of opened joints.

When the joints were opened 135 days after surgery there was fibrous tissue reaction involving the subcutaneous tissue and the joint capsule at the

Table 5: Scores for radiographic healing of fetlock joints after curettage and 3, three days apart i.m. injections of 0.2mg/kg dexamethasone (D), 4.4 mg/kg phenylbutazone (P) or sham operations and injection with placebo (S) in calves.

	Post Operative Period					
	Week 3			Week 6		
	D	P	S	D	P	S
Mean	1.2	1.2	0	1.1	1.4	0
Std. Dev.	0.4	0.6	0	0.3	0.5	0
Std. Error	0.1	0.2	0	0.1	0.1	0
Range	1-2	0-2	0	1-2	1-2	0

	Week 9			Week 15		
	D	P	S	D	P	S
Mean	2.1	2.2	0	2.2	2.4	0
Std. Dev.	0.5	0.6	0	0.6	0.5	0
Std. Error	0.1	0.2	0	0.2	0.1	0
Range	1-3	1-3	0	1-3	2-3	0

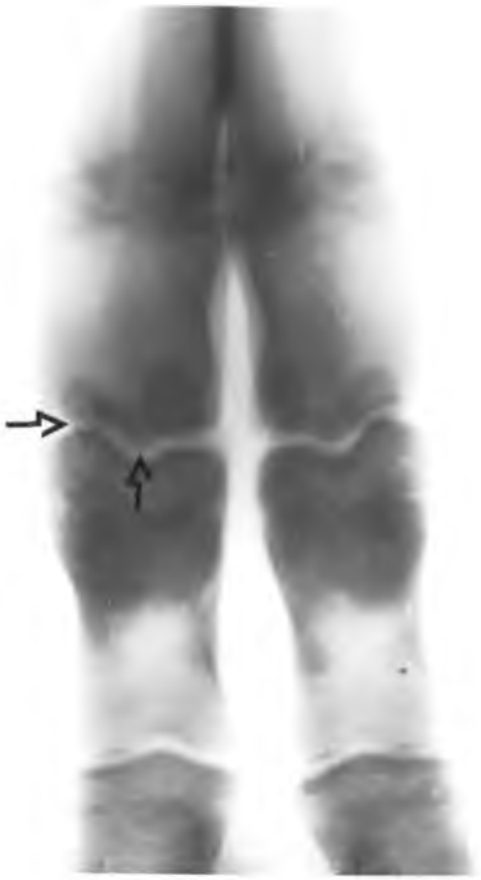


Figure 11: Radiographic assessment of joint healing. Widened radioluscent intercondylar spaces of curetted joints 21 days after surgery (arrow).

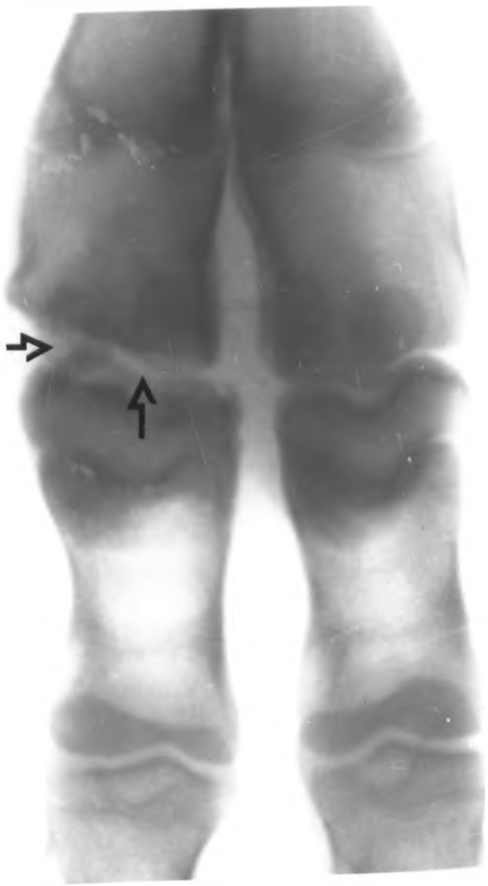


Figure 12: Radiographic assessment of healing: Widened intercondylar spaces curetted joints 15 weeks after surgery showing increased radiodensity (arrow).

surgical site of the calves in the three groups. The articular cartilage of sham operated (group III) joints was pink, entire and glistening and the joints contained straw-coloured, viscous and stickly synovial fluid (Figure 13).

Contrastingly, there was no articular cartilage in any of the curetted joints (groups I and II) except near the proximal sessamoid bones, laterally and medially. In each joint the distal end of the third metacarpal bone and the proximal end of the first phalanx were covered by a dark brown repair tissue with thick fibrous bands joining the central parts of the distal end of the third metacarpal bone and the opposing surface on the proximal end of the first phalanx (Figure 14). A synovial membrane like tissue joined these fibrous bands to the joint capsule. The synovial-like fluid of the curetted joints was similar to that of sham operated joints but blood tinged. The interosseous ligament between the left medial and the left lateral metacarpophalangeal joints was very tough and thicker than that of the opposite limb of the same calves. No adhesions or repair tissue were detected in the sham operated joints.

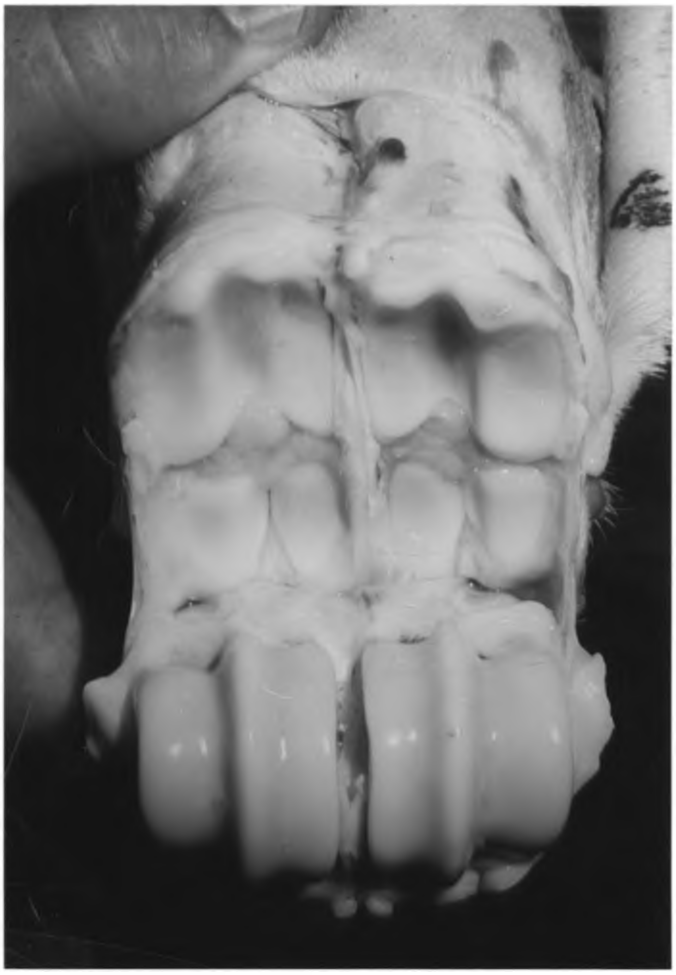


Figure 13: Gross appearance of opened joints: Opened sham operated joints showing pink, entire and glistening articular cartilage.

Figure 14: Gross appearance of opened joints: Opened curetted joint showing the dark brown repair tissue.

4.8 Histology of repair tissue

The scores for the histological assessment of the repair tissue in curetted joints are given in Table 6, Figure 15 and 16, and Appendix 8. There was marked variation between sections of any one joint and between individual joints/calves. The repair tissue in curretted joints (groups I and II) was mainly made up of predominantly spindle shaped fibroblasts (Figure 16). No significant difference was detected between the scores recorded for joints of the calves treated with phenylbutazone and those treated with dexamethasone. The trabecular pattern of the subchondral bone beneath the repair tissue was disrupted and a few osteoclast-like cells were seen near the areas of bone destruction. The synovium and articular cartilage adjacent to the repair tissue were inflammed and hypertrophied. There was an increase in the number of vascular channels in the subchondral bone.

No obvious changes were detected in the histology of the articular cartilage of sham operated joints. In each section, the articular cartilage surface was smooth and formed the four layers typical of cartilage. The superficial layer was composed of flattened chondrocytes which were parallel to the articular surface; deeper, the cartilage cells were round and arranged in columns at right angles to the

Table 6: Mean Scores for nature of reparative tissue 135 days after curettage of fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P) or 0.2 mg/kg dexamethasone (D)in calves.

Calf Number	Nature of reparative tissues	
	P	D
1	2	2.3
2	1.5	1.8
3	1.2	1.6
4	1.2	1
5	1.5	1.7
6	2.3	1.3
7	1	1.3
8	1.5	2
9	1.5	1.3
10	1	1.5
N = 10	1.47	1.58

Key:

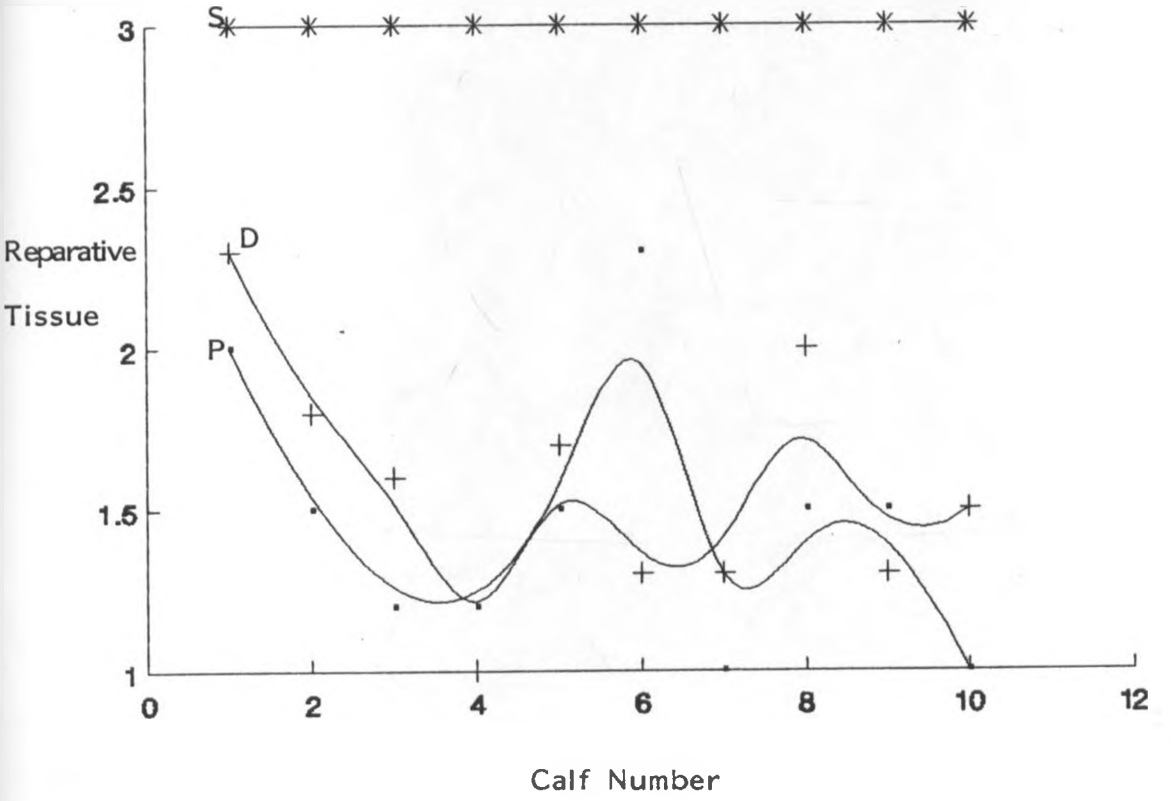
1 = Fibrous tissue containing predominantly spindle shaped fibroblasts.

2 = In completely differentiated mesynchymal tissue composed of cells beginning to differentiate towards chondroblasts.

3 = "Hyaline-like" articular cartilage containing chondrocytes in lacunae.

Figure 15

Mean scores for nature of reparative tissue 135 days after curettage of fetlock joints and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P) or 0.2 mg/kg dexamethasone (D) against sham operations and injection with placebo (S) in calves.



Key:

1 = Fibrous tissue containing predominantly spindle shaped fibroblasts.
2 = In-completely differentiated mesynchymal tissue composed of cells beginning to differentiate towards chondroblasts.
3 = "Hyaline-like" articular cartilage containing chondrocytes in lacunae.

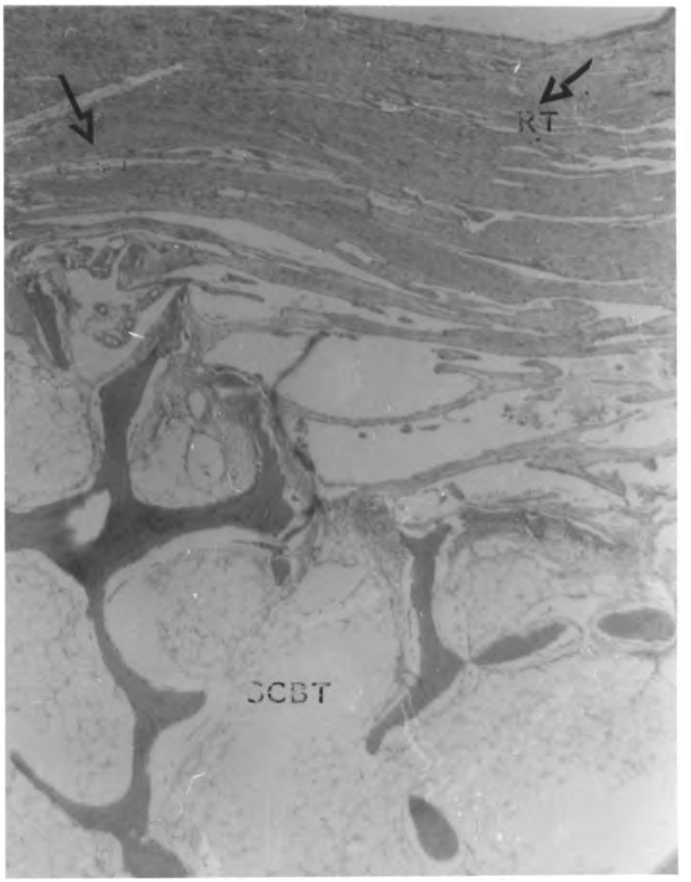


Figure 16: Histology of repair tissue: Light photomicrograph of the repair tissue resurfacing curetted joints (Mag. x10).

RT = Repair Tissue
SCBT = Subchondral Bone Trabeculae

surface; adjacent to the subchondral bone, columns of condrocytes were evident. There was a dark line crossing from one side to the other indicating the junction of calcified and non-calcified intercellular substance (tide-mark). Deep to the tide-mark, cartilage was replaced by bone with well developed haversian systems. Examination of the growth plates revealed four distinct zones. A zone of moderately-sized, irregularly-arranged cartilage cells lay immediately below the epiphysics. Deeper, there was a zone of thin, wedge-shaped chondrocytes, stacked together in columns at right angles to the axis of the bone below which was another zone of rounded cells which were also in columns. Adjacent to the diaphysis, a thin, flat layer of rounded cells merged directly into the bone.

4.9 Serum Gamma-glutamyl-transpeptidase

The results of analysis for serum gamma-glutamyl-transpeptidase for the phenylbutazone treated and the dexamethazone treated calves are presented in Table 7 Figure 17 and Appendix 14. There was marked variation between the groups and also between individuals in the same groups. No significant difference was found between pre-operative and post-operative values in the three groups ($p<0.05$).

Table 7: Serum Gamma Glutamyl transpeptidase values before and after fetlock joint curettage and 3, three days apart i.m. injections of 0.2 mg/kg dexamethasone (D) or 4.4 mg/kg phenylbutazone (P) in calves.

	Peri-operative Days					
	Day -14		Day -2		Day 0	
	D	P	D	P	D	P
Mean	30.5	28.1	29.9	30.4	29.3	32.3
Std.Dev.	3.17	2.08	3.38	4.8	2.45	4.41
Std.Error	1.00	0.69	1.06	1.61	0.77	1.47
Range	26-36	24-31	25-36	25-40	26-34	27-41

	Day 1		Day 3		Day 5	
	D	P	D	P	D	P
Mean	28.7	30.1	30.7	31.9	29.5	30.4
Std.Dev.	1.63	3.25	4.87	4.2	4.35	3.60
Std.Error	0.51	1.08	1.54	1.41	1.37	1.20
Range	26-31	26-35	25-38	27-38	25-37	25-36

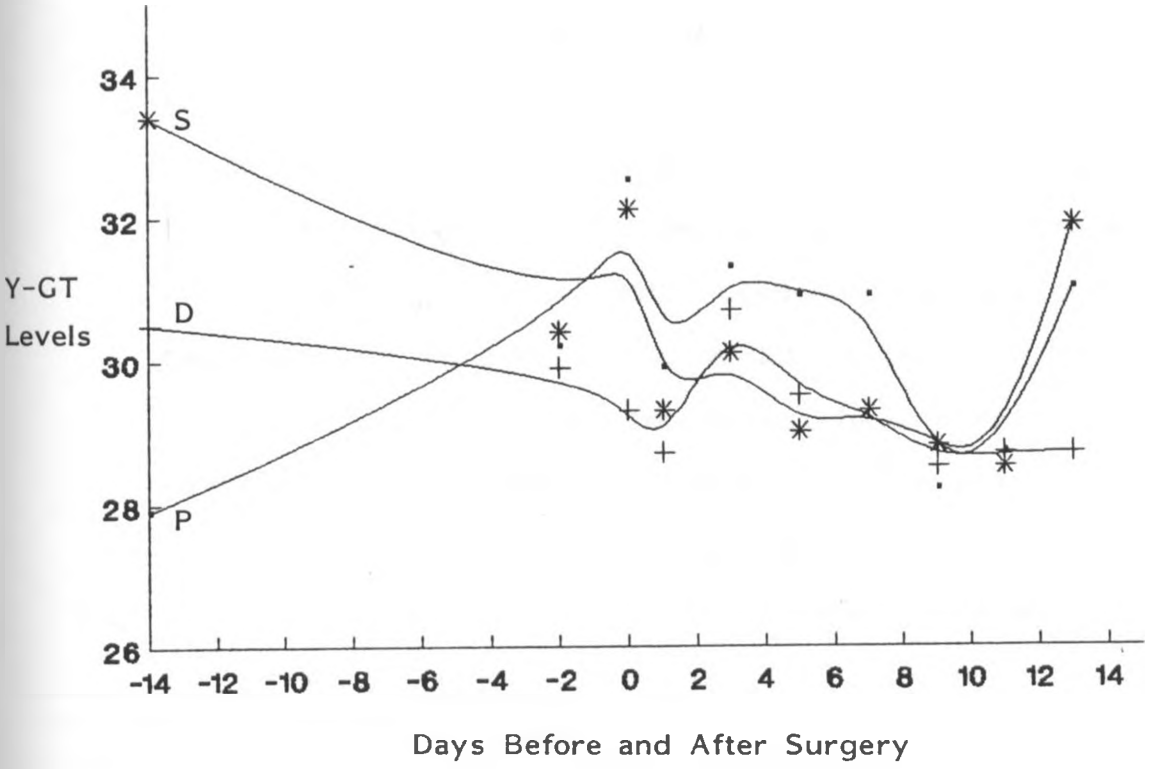
Table 7(Contd.): Serum Gamma Glutamyl transpeptidase values before and after fetlock joint curettage and 3, three days apart i.m. injections of 0.2 mg/kg dexamethasone (D) or 4.4 mg/kg phenylbutazone (P) in calves.

	Post Operative Days			
	Day 7		Day 9	
	D	P	D	P
Mean	29.3	29.77	28.5	28.0
Std. Dev.	2.90	3.07	2.50	1.87
Std. Error	0.91	1.02	0.79	0.62
Range	24-33	26-37	26-33	25-31

	Day 11		Day 13	
	D	P	D	P
Mean	28.5	28.6	28.7	30.4
Std. Dev.	1.90	1.50	2.49	4.15
Std. Error	0.60	0.50	0.78	1.38
Range	26-31	26-30	24-33	26-40

Figure 17

Mean serum Y-Gt levels (I.U) before and after fetlock joint curettage and 3, three days apart i.m. injections of 4.4 mg/kg phenylbutazone (P) against 0.2 mg/kg dexamethasone (D) against sham operations and injection with placebo (S) in calves.



CHAPTER FIVE

DISCUSSION

The general clinical observations demonstrate that the removal of the articular cartilage and subchondral bone of the left lateral metacarpophalangeal joints of calves is well tolerated and does not impair the general well-being of the animals.

The most clinically obvious abnormality during the first 21 days after surgery was lameness (assessed as limping). The initial peak limping in the three groups was induced by the surgical trauma on the periarticular soft tissues and articular cartilage and subchondral bone during the curettage. The steady decrease in limping may have been due to several factors. Partial immobilization may reduce pain stimuli from the surgical site and consequently reduce the degree of limping. A cast bears most of the weight leaving less pressure on the immobilized part of a limb. Furthermore even in cases of painful limb fractures casting relieves pain and enables the animal to use the limb. After the response subsided the production of pain mediators at the joint reduced with a resultant decrease in limping. Thirdly the apparent reduction in the degree of limping assessed may reflect the pain relief obtained with the use of phenylbutazone and/or dexamethasone. The mere

presence of a cast on a limb changes the gait of the animal. It was therefore not possible to register a 0mm value for limping during the period the limbs were cast even in the control calves that were subjected to less surgical trauma than the calves in groups I and II whose joints were curetted.

Although all the athrotomy wounds were clinically healed when the casts were removed on the 21st post-operative day, there was marked limping after the cast removal. This increase in limping may have been a reflection of pain elicited at the joint by re-injury of the incompletely healed articular cartilage and subchondral bone caused by the removal of the cast leaving the joints with greater range of motion. That the pain assessed for the sham operated joints was less than that of the curetted joints suggests that increased joint movement induced pain in a degree directly proportional to the amount of surgical trauma inflicted in the joints.

The high and positive corellation between pain and limping assessed and body temperature recorded was predictable. Pain due to initial injury and again due to increased joint mobility on the day of cast removal was inflammatory. Mediators of inflammation were most likely the cause of pain at the joint and elevated body temperature. Limping being only an outward sign of pain in the joint

obviously corellated positively with the pain felt by the calves.

In veterinary practice radical joint surgery elicits very severe pain, limping and fever. The operated animals appear sick and are unable to bear any weight on the operated limbs or even feed properly unless anti-inflammatory drugs are used. The apparent general well-being of the calves in this study demonstrated the ability of phenylbutazone and dexamethasone to reduce pain and body temperature. Although the results showed a general similarity in the ability of the two drugs to reduce pain, limping and body temperature, there was a tendency for dexamethasone to be more potent than phenylbutazone at the dosage rates and treatment regimen applied in this study. This observation agrees with results of similar studies in dogs (Mbugua, 1987). Limping, pain and temperature were assessed as normal for the sham operated calves. This finding indicates that joint surgery that causes trauma on the soft tissues and not the articular cartilage and subchondral bone may not require the post-operative administration of either phenylbutazone or dexamethasone.

The reduction in joint mobility of curetted joints recorded on the day the casts were removed may have been due to formation of intracapsular adhesions and deposition of repair tissue. Increase in joint

mobility might then have been achieved progressively as the adhesions were broken by the pressure imposed on the joints on ambulation. This suggestion is supported by the finding in this study that all the curetted joints, except where there was fusion, achieved the maximum joint mobility of 100%. The results generally indicate that the partial immobilization of the joint induced the formation of functional joints compared with 'fused' non-functional joints produced by conventional methods of arthrodesis as described previously Ferguson et. al., (1990) who reported the formation of pseudoarthroses several months after conventional arthrodeses. These 'false' joints were formed not by design but because of a break in the arthrodeses. The very early and limited reduction in the range of motion of some sham operated joints was probably due to the presence of a transudate which resorbed quickly allowing the joints to attain the maximum range of motion.

The results of the radiographic assessment of joint healing and those of joint mobility were strongly supported by the gross and histological findings. Except in two cases of the curetted joints where there was some bony fusion on the lateral aspect, the repair tissue in the curetted joints was composed mainly of fibroblasts and collagen fulfilling the classical description of secondary

wounding in healing bone by Peacock and Van Winkle (1984). The authors observed that fractures that heal without cartilage formation can be induced to form large amounts of cartilage and eventually proceed to pseudoarthrosis if the fracture is manipulated after the cellular proliferative stage of healing. The results agree with those of other studies involving surgically produced lesions in experimental animals which indicate that the articular cartilage defects extending to the subchondral bone healed by the growth of granulation tissue into the defects with transformation into fibrocartilage. The authors also reported variation in the rate of healing of full-thickness articular cartilage defects but a period of up to eight months was usually required for hyaline cartilage to become the predominant repair tissue in rabbits, dogs and horses (French, and Barber; 1989, Trotter, et. al; 1989).

It is conceivable that providing more time for healing in the present study, the fibrous repair tissue would probably have undergone further differentiation into fibrocartilage or even hyaline cartilage and eventually establish close to normal fibrocartilaginous articulating surfaces.

The immediate post-operative peri-articular soft tissue swelling was radiographically similar in the

three groups of calves, indicating that arthrotomy induced equal inflammatory response in the soft tissues of all operated joints which was expected because the surgical trauma was standard for all the calves. The widening of the area between the distal end of the third metacarpal bone and the proximal first phalanx of curetted joints was initially due to the removal of articular cartilage and subchondral bone. The soft tissue density of this area likely represented the hematoma and inflammatory exudate that filled the area subsequent to surgery and seems to agree with results of other studies on the healing of deep articular cartilage and subchondral bone defects which showed that the defects are filled with a hematoma and inflammatory exudate soon after they are created (Mitchel and Shephard, 1980). Progressive osteolysis of the distal third metacarpal bone and the proximal first phalanx, in response to trauma of surgery and subsequent joint instability caused greater widening of the area occupied by the reparative tissue. The organization of the initial hematoma and deposition of the reparative tissue gave the intercondylar space a detectable radiodensity.

In this study the areas of articular cartilage adjacent to the sessamoid bones were inaccessible by a number four curette through the 55mm long arthrotomy incisions. In clinical cases, better

accessibility to all the articular cartilage surfaces can be achieved by using smaller curettes and making larger arthrotomy incision.

In some joints, there was some fusion at the lateral aspects which reduced the joint mobility. The reason behind this observation is not entirely clear. However, it was evident that there was more of the subchondral bone in the fused areas compared with other areas filled with repair tissue where the subchondral bone had undergone some lysis. It is suggested that there may not have been sufficient removal of subchondral bone in these fusion areas. Given a clinical situation where some particular areas of the cartilage and subchondral bone have to be removed, say because they are infected, larger incisions should be made and various sizes of curettes utilized so that the various suspected "niches" are properly curetted.

With regard to the effects of dexamethasone and phenylbutazone on wound healing, it has been suggested on the basis of clinical observations in humans. (Pfeifer, 1967), in dogs, (Mbugua, 1987), and in cattle (Mbithi, et. al., 1994) that phenylbutazone and dexamethasone do not disturb the healing of bone injuries when given for a short-term peri-operatively. Actually phenylbutazone was reported to accelerate the repair of damaged muscle fibres

(Morger, 1967). In this study it was not possible to detect either the beneficial effects of phenylbutazone on wound healing nor the deleterious effects of dexamethasone on these processes. In the first instance all the arthrotomy incisions were clinically healed on the 21st post-operative day when the casts were removed. Secondly the delay in "fracture" healing was mostly attributed to the 'improper' immobilization of the operated joints rather than on the drugs. These results agree with those of Allgower and Perren, S., 1967, Mbugua, 1987 and Mbithi et. al., 1994, who concluded that short-term treatment with these drugs has no effect on wound healing. It might be that the period of drug administration was too short to reveal the effects on healing and the cessation of the treatment soon after surgery allowed normal healing to occur.

The results of the present study indicate no difference in the pre-operative and post-operative levels of Y-GT for both the phenylbutazone treated and the dexamethasone treated calves. It is possible that the expected invivo increase in Y-GT activity due to the inflammation in the curetted joints was prevented from occurring by the anti-inflammatory effects of dexamethasone and phenylbutazone. This observation agrees with that of Singh, et al (1986) who found that inflammation induced increase in Y-GT

activity in rats was prevented from occurring in proportion to the anti-inflammatory potencies of some test drugs.

That there was no difference in the pre-operative and post-operative Y-GT levels in the sham operated calves seems to indicate that the sham operations did not induce sufficient inflammation to significantly alter the serum Y-GT levels. Further, from a clinician point of view, this observation may suggest that anti-inflammatory drugs are not indicated for simple joint surgery (arthrotomy with curettage) in the bovine. This observation is supported by the fact that in this study the clinical parameters (temperature, limping and pain) remained at relatively safe and acceptable levels.

The tremendous individual variation in Y-GT levels in this study presents some difficulties in interpreting the results. This is compounded by the fact that the pre-operative values were significantly higher than those previously recorded for cattle. Further studies are therefore warranted inorder to elucidate the suitability of Y-GT activity in calf serum as a model for studying inflammatory responses in the bovine species.

Based on the results of this study the following conclusions were arrived at:-

1. A surgical procedure and post-operative management protocol for recreating curetted bovine metacarpophalangeal joints (surgical pseudoarthrosis) has been developed and described.
2. The protocol for surgical pseudoarthrosis developed in this study could be usefully adopted for the surgical management of bovine arthritides when curettage is indicated.
3. The surgical removal of the articular cartilage and subchondral bone of the bovine metacarpophalangeal joints (curettage) with subsequent three weeks partial immobilization of the operated joints is well tolerated and does not impair the general well being of the animals.
4. Curetted and partially immobilized bovine metacarpophalangeal (MCP) joints remain functional with joint mobility of more than 92% being maintained upto the 135th post-operative day.
5. Deep articular cartilage defects created by curettage of the bovine MCP joints heal by metaplasia of the connective tissue and 135 days old defects of partially immobilized joints are

resurfaced by fibrous tissue which unites the distal metacarpal condyles to the proximal first phalangeal condyles of the curetted joints.

However, further studies are warranted to determine whether or not the repair tissue remains static or modulates to other forms of tissue later in the repair process.

6. Both dexamethasone and phenylbutazone are effective in reducing pain, limping and body temperature subsequent to radical joint surgery in cattle with a tendency for dexamethasone to be more potent than phenylbutazone.
7. Serum gamma-glutamyltranspeptidase may not be a good indicator of inflammation in young calves aged 6-12 months.

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A P P E N D I C E S

Appendix 1

Individual and mean readings of rectal temperature (℃) preoperative and after radical joint surgery and 3, three days apart 1M injections of 4.4mg/kg phenylbutazone in 10 calves.

		Post-operative Days							
Calf No.	Pre-operative Day	1	2	3	4	5	6	7	9
1	38.7	39.6	39.1	38.5	38.7	38.4	38.8	38.5	38.3
2	38.7	39.5	38.8	38.4	38.7	38.6	38.3	38.4	38.2
3	38.0	39.9	38.9	38.2	38.6	38.6	38.1	38.4	38.9
4	38.1	40.1	38.7	38.4	38.3	38.8	38.6	38.7	38.8
5	38.3	40.0	38.6	38.0	38.2	38.6	38.8	38.7	38.7
6	38.0	41.0	39.0	38.6	38.4	38.5	38.7	38.5	38.8
7	38.0	40.1	39.5	38.4	38.0	38.6	38.7	38.8	38.3
8	38.2	39.8	38.8	38.2	38.6	38.2	38.5	38.5	38.2
9	38.5	40.0	39.5	38.5	38.5	38.3	38.2	38.2	38.0
10	38.2	40.2	39.5	38.6	38.6	38.6	38.0	38.3	38.6
Mean	38.3	40.0	39.0	38.4	38.5	38.5	38.5	38.5	38.5

	Post-operative Days									
Calf No.	10	14	21	28	35	42	49	56	63	70
1	38.8	38.2	39.8	38.3	38.4	38.1	38.6	38.2	38.1	38.5
2	39.6	38.4	39.6	38.7	38.2	38.0	38.4	38.3	38.3	38.0
3	39.4	38.9	39.4	38.8	38.0	38.6	38.2	38.4	38.2	38.3
4	38.2	38.3	40.0	38.6	38.7	38.4	38.3	38.6	38.3	38.1
5	38.0	38.3	39.4	38.9	38.6	38.0	38.4	38.0	30.4	38.0
6	38.2	38.4	39.6	38.1	38.6	38.1	38.2	38.1	38.6	38.2
7	38.3	38.5	39.3	38.8	38.3	38.6	38.3	38.3	38.5	38.0
8	38.1	38.5	39.1	38.7	38.2	38.5	38.0	38.2	38.7	38.3
9	38.0	38.1	39.0	38.2	38.1	38.0	38.2	38.5	38.6	38.4
10	38.0	38.2	40.0	38.7	38.6	38.4	38.5	38.4	38.5	38.3
Mean	38.3	38.4	39.5	38.4	38.3	38.3	38.3	38.3	38.4	38.2

Appendix 2

Individual and mean readings of rectal temperature (℃) preoperative and after radical joint surgery and 3, three days apart 1M injections of 0.2 mg dexamethasone in 10 calves.

		Post-operative Days							
Calf No.	Pre-operative Day	1	2	3	4	5	6	7	8
1	38.7	38.5	38.1	38.0	38.5	38.5	38.5	38.0	38.4
2	38.4	39.6	39.4	38.8	38.6	38.2	38.4	38.6	38.7
3	38.5	39.9	39.5	38.7	38.7	38.2	38.4	38.0	38.8
4	38.6	38.9	39.0	38.5	38.1	38.4	38.0	38.2	38.6
5	38.5	38.9	39.0	38.4	38.6	38.7	38.1	38.6	38.8
6	38.8	39.5	38.5	38.6	38.6	38.2	38.2	38.3	38.5
7	38.5	38.9	38.9	38.7	38.7	38.5	38.8	38.5	38.2
8	38.5	40.1	39.5	38.4	38.8	38.6	38.5	38.6	38.4
9	38.2	40.0	39.7	38.0	38.1	38.7	38.6	38.8	38.6
10	38.4	40.5	39.0	38.9	38.8	38.4	38.3	39.0	38.4
Mean	38.5	39	39.1	38.5	38.5	38.4	38.4	38.5	38.6

	Post-operative Days									
Calf No.	9	10	14	21	35	42	49	56	63	70
1	38.6	38.4	38.2	39.4	38.9	38.7	38.5	38.4	38.5	38.6
2	38.2	38.4	38.5	39.5	38.8	38.6	38.5	38.6	38.8	38.8
3	38.0	38.3	39.0	38.9	39.0	38.4	38.7	38.8	38.7	38.5
4	38.5	38.0	38.6	39.5	39.0	38.2	38.5	39.0	38.6	38.6
5	38.4	38.6	38.5	40.2	39.5	38.5	38.2	39.1	38.4	38.3
6	38.9	38.6	38.2	40.0	39.8	38.8	38.5	38.7	38.7	38.5
7	38.3	38.4	38.3	39.8	38.7	38.3	38.0	38.8	38.8	38.2
8	38.2	38.8	38.7	39.5	38.6	38.0	38.1	38.5	38.0	38.6
9	38.7	38.5	39.0	38.8	38.8	38.6	38.0	38.8	38.5	38.6
10	38.1	38.0	38.7	40.5	39.6	38.7	38.5	38.8	38.6	38.4
Mean	38.3	38.4	38.4	39.6	39.1	38.4	38.4	38.8	38.6	38.5

Appendix 3

Individual and mean readings of rectal temperature (°C) pre-operative and after sham operations on the metacarpophalangeal joints in 10 calves.

Calf No.	Pre-operative Day	Post-operative Days							
		1	2	3	4	5	6	7	8
1	38.4	39.9	39.8	39.2	39.0	38.8	38.4	38.3	38.4
2	38.0	40.1	10.0	39.0	39.0	38.6	38.1	38.1	38.0
3	38.2	40.0	40.0	39.1	38.9	38.2	38.0	38.0	38.2
4	38.6	39.9	40.0	38.9	38.6	38.4	38.4	38.5	38.6
5	38.4	40.2	39.8	38.8	38.4	38.4	38.7	38.3	38.4
6	38.5	40.0	39.6	40.0	38.8	38.9	38.6	38.4	38.4
7	38.0	40.0	40.0	39.8	39.0	38.5	38.5	38.1	38.0
8	38.4	39.8	40.0	39.9	39.0	38.4	38.1	38.2	38.3
9	38.3	39.0	40.0	40.0	39.5	38.5	38.2	38.4	38.3
10	38.5	39.9	39.5	39.3	39.0	38.7	38.0	38.5	38.6
Mean	38.3	39.9	39.9	39.4	38.9	38.6	38.3	38.3	38.3

Calf No.	Post-operative Days									
	9	10	14	21	35	42	49	56	63	70
1	38.4	38.4	38.3	39.6	38.7	38.4	38.4	38.6	38.4	38.2
2	38.1	38.1	38.1	38.1	38.5	38.3	38.1	38.0	38.2	38.3
3	38.1	38.1	38.4	40.0	38.7	38.2	38.1	38.7	38.1	38.4
4	38.4	38.2	38.0	39.8	38.8	38.0	38.2	38.5	38.6	38.4
5	38.2	38.4	38.6	39.9	38.7	38.4	38.4	38.4	38.5	38.3
6	38.4	38.6	38.1	40.0	38.6	38.2	38.6	38.6	38.4	38.4
7	38.1	38.0	38.0	40.0	38.4	38.7	38.5	38.7	38.6	38.4
8	38.3	38.4	38.4	39.1	38.4	38.5	38.4	38.4	38.6	38.4
9	38.2	38.3	38.2	39.1	38.2	38.2	38.0	38.3	38.7	38.2
10	38.4	38.5	38.5	40.0	38.5	38.5	38.3	38.2	38.5	38.5
Mean	38.3	38.3	38.3	39.7	38.6	38.3	38.3	38.4	38.5	38.4

Appendix 4

Individual and mean values for post-operative limping in mm measured by VAS after radical joint surgery and 3, three days apart IM injections of 4.4 mg/kg phenylbutazone in 10 calves.

Calf No.	Post-operative days											
	1	2	3	4	5	6	7	10	14	21	28	35
1	5	4	4	3	2	2	2	2	1	3	2	2
2	4	4	4	2	2	2	2	2	2	4	2	1
3	5	3	3	2	2	2	2	1	2	3	2	2
4	4	4	3	3	3	2	2	2	1	4	2	2
5	4	4	3	3	3	3	3	2	2	4	2	1
6	4	4	3	3	2	2	2	2	2	4	2	1
7	5	4	4	3	2	2	2	1	1	3	2	2
8	4	4	3	2	2	1	1	2	1	3	2	1
9	3	3	2	1	1	1	1	1	1	3	3	2
10	3	3	2	2	2	1	1	1	1	3	2	1
Mean	4.2	3.8	3.5	2.2	1.9	1.9	1.6	1.4	3.4	3.4	2	1.6

Calf No.	Post operative days											
	42	49	56	63	70	77	84	91	98	105	112	120
1	1	1	0	0	0	0	0	0	0	0	0	0
2	1	0	0	0	0	0	0	0	0	0	0	0
3	2	1	1	0	0	0	0	0	0	0	0	0
4	2	0	0	0	0	0	0	0	0	0	0	0
5	1	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	1	1	1	0	0	0	0	0	0	0	0	0
8	1	0	0	0	0	0	0	0	0	0	0	0
9	1	0	0	0	0	0	0	0	0	0	0	0
10	1	0	0	0	0	0	0	0	0	0	0	0
Mean	1.1	0.3	0.2	0	0	0	0	0	0	0	0	0

0-minimum; 5 - maximum.

Appendix 5

Individual and mean values for post-operative limping in mm measured by VAS after radical joint surgery and 3, three days apart IM injections of 0.2 mg/kg dexamethasone in 10 calves.

Calf No.	Post-operative Days											
	1	2	3	4	5	6	7	10	14	21	28	35
1	3	2	1	1	1	1	2	2	1	4	2	1
2	4	3	2	2	1	1	1	1	1	3	2	1
3	3	3	2	2	1	1	2	1	1	3	3	2
4	3	4	3	2	1	2	1	1	1	3	2	1
5	3	3	2	2	1	1	1	1	1	3	2	1
6	4	3	1	1	1	1	1	1	1	3	2	1
7	3	3	1	1	1	2	1	2	1	3	2	1
8	3	3	2	1	1	1	1	1	1	3	3	2
9	3	3	2	1	1	1	1	1	1	3	2	1
10	3	3	2	1	1	1	1	1	1	3	2	1
Mean	3.2	3	1.8	1.4	1	1.2	1.2	1.2	1	3.1	2.2	1.2

Calf No.	Post-Operative Days										
	42	49	56	70	77	84	91	98	105	112	120
1	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0
3	1	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0
9	1	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0
Mean	0.2	0	0	0	0	0	0	0	0	0	0

0-minimum; 5 - maximum.

Appendix 6

Individuals and mean values for post-operative limping in mm measured by VAS after sham operations on the metacarpal joints of ten calves.

Calf No.	Post Operative Days											
	1	2	3	4	5	6	7	10	14	21	28	35
1	2	1	1	1	1	1	1	1	1	2	1	0
2	2	1	1	1	1	1	1	1	1	2	1	0
3	2	1	1	1	1	1	1	1	1	2	1	0
4	2	1	1	1	1	1	1	1	1	2	1	0
5	2	1	1	1	1	1	1	1	1	2	1	0
6	2	1	1	1	1	1	1	1	1	2	1	0
7	2	1	1	1	1	1	1	1	1	2	1	0
8	2	1	1	1	1	1	1	1	1	2	1	0
9	2	1	1	1	1	1	1	1	1	2	1	0
10	1	1	1	1	1	1	1	1	1	2	1	0
Mean	2.2	1	1	1	1	1	1	1	1	2	1	0

0 - minimum; 5 - maximum

Calf No.	Days Post Operatively									
	42	49	56	63	70	84	91	105	112	120
1	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0
Mean	0	0	0	0	0	0	0	0	0	0

0 - minimum; 5 - maximum

Appendix 7

Individual and mean values for post-operative pain assessed by a VAS in calves and 3, three days apart 1M injections of 4.4mg Phenylbutazone or 0.2 mg/kg dexamethasone and following radical joint surgery.

Phenylbutazone

Calf No.	Day 21	Day 28	Day 35	Day 42	Day 49	Day 56	Day 63	Day 70
1	4	3	3	2	1	1	0	0
2	2	3	2	1	0	0	0	0
3	4	3	2	1	0	0	0	0
4	4	4	2	1	0	0	0	0
5	4	4	2	1	0	0	0	0
6	4	3	2	2	2	1	0	0
7	4	3	2	1	1	1	0	0
8	4	4	3	3	2	0	0	0
9	4	3	2	2	1	1	1	0
10	4	3	2	1	1	0	0	0
Mean	3.9	3.3	2.2	1.5	0.8	0.4	0.2	0

Dexamethasone

Calf No.	Day 21	Day 28	Day 35	Day 42	Day 49	Day 56	Day 63	Day 70
1	3	2	2	2	1	1	0	0
2	3	2	2	1	1	0	0	0
3	3	2	1	1	1	1	0	0
4	4	3	3	2	1	1	0	0
5	4	3	2	1	1	1	0	0
6	4	3	2	2	1	1	1	0
7	4	3	2	1	1	1	0	0
8	3	2	2	1	0	1	1	0
9	4	3	2	1	1	0	0	0
10	4	3	2	1	1	0	0	0
Mean	3.6	2.6	2.0	1.3	0.9	0.7	0.2	0

0 - minimum, 5 - maximum

Appendix 8

Individual and mean values for post-operative pain measured by VAS after sham operations on the metacarpophalangeal joint of 10 calves.

Calf No.	Post-operative Days							
	21	28	35	42	49	56	63	70
1	1	1	0	0	0	0	0	0
2	1	0	0	0	0	0	0	0
3	1	1	0	0	0	0	0	0
4	1	0	0	0	0	0	0	0
5	1	0	0	0	0	0	0	0
6	1	1	0	0	0	0	0	0
7	1	1	0	0	0	0	0	0
8	1	1	0	0	0	0	0	0
9	1	1	0	0	0	0	0	0
10	1	1	0	0	0	0	0	0
Mean	1	0.7	0	0	0	0	0	0

Appendix 9

Individual values for joint mobility after radical joint surgery and 3,three days apart 1M injectioons of4.4 mg/Kg bwt phenylbutazone in 10 calves.

Calf No.	Post Operative Days							
	1	21	28	35	42	49	56	63
1	100	75	80	80	90	95	95	95
2	100	60	55	55	60	65	70	70
3	100	40	50	50	50	50	50	50
4	100	80	100	100	100	100	100	100
5	100	85	90	100	100	100	100	100
6	100	90	100	100	100	100	100	100
7	100	75	80	80	90	100	100	100
8	100	100	100	100	100	100	100	100
9	100	100	100	100	100	100	100	100
10	100	50	75	90	90	100	100	100
Mean	100	75.5	83	85.5	88	91	91.5	91.5

Calf No.	Post Operative Days							
	70	77	84	91	98	105	115	120
1	95	95	95	95	95	95	95	95
2	80	90	90	90	90	90	90	90
3	50	50	50	50	50	50	50	50
4	100	100	100	100	100	100	100	100
5	100	100	100	100	100	100	100	100
6	100	100	100	100	100	100	100	100
7	100	100	100	100	100	100	100	100
8	100	100	100	100	100	100	100	100
9	100	100	100	100	100	100	100	100
10	100	100	100	100	100	100	100	100
Mean	92.5	93.5	93.5	93.55	93.5	93.5	93.5	93.5

0-minimum; 100 - maximum.

Appendix 10

Individual values for joint mobility after radical joint surgery and 3, three days apart 1M injections of 0.2mg/Kg dexamethasone in calves.

Calf No.	Post Operative Days							
	1	21	28	35	42	49	56	63
1	100	90	100	100	100	100	100	100
2	100	100	100	100	100	100	100	100
3	100	100	100	100	100	100	100	100
4	100	90	100	100	100	100	100	100
5	100	100	100	100	100	100	100	100
6	100	90	100	100	100	100	100	100
7	100	90	100	100	100	100	100	100
8	100	100	100	100	100	100	100	100
9	100	100	100	100	100	100	100	100
10	100	90	100	100	100	100	100	100
Mean	100	95	100	100	100	100	100	100

Calf No.	Post Operative Days							
	70	77	84	91	98	105	115	120
1	100	100	100	100	100	100	100	100
2	100	100	100	100	100	100	100	100
3	100	100	100	100	100	100	100	100
4	100	100	100	100	100	100	100	100
5	100	100	100	100	100	100	100	100
6	100	100	100	100	100	100	100	100
7	100	100	100	100	100	100	100	100
8	100	100	100	100	100	100	100	100
9	100	100	100	100	100	100	100	100
10	100	100	100	100	100	100	100	100
Mean	100	100	100	100	100	100	100	100

Appendix 11

Individual and mean values for post-operative joint mobility (percent) in sham operated metacarpophalangeal joints in 10 calves.

Calf No.	Post Operative Days							
	1	21	28	35	42	49	56	63
1	100	90	100	100	100	100	100	100
2	100	90	100	100	100	100	100	100
3	100	90	100	100	100	100	100	100
4	100	90	90	95	95	100	100	100
5	100	90	100	100	100	100	100	100
6	100	90	100	100	100	100	100	100
7	100	90	100	100	100	100	100	100
8	100	90	100	100	100	100	100	100
9	100	90	100	100	100	100	100	100
10	100	90	100	100	100	100	100	100
Mean	100	90	99	99.5	99.5	100	100	100

0 - minimum, 100 - maximum

Calf No.	Post-operative Days							
	70	77	84	91	98	105	115	120
1	100	100	100	100	100	100	100	100
2	100	100	100	100	100	100	100	100
3	100	100	100	100	100	100	100	100
4	100	100	100	100	100	100	100	100
5	100	100	100	100	100	100	100	100
6	100	100	100	100	100	100	100	100
7	100	100	100	100	100	100	100	100
8	100	100	100	100	100	100	100	100
9	100	100	100	100	100	100	100	100
10	100	100	100	100	100	100	100	100

0 - minimum; 100 - maximum

Appendix 12

Radiographic evaluation of fetlock joint healing subsequent to radical curettage and three, 3-days apart i.m. injections of 4.4mg/kg phenylbutazone(P), or 0.2 mg/kg dexamethasone in calves against 'sham' operated joints (S) in calves.

Key:

0 - No evidence of union. A radioluscent line where the joint space origionally was. (intercodylar space).

1 - No evidence of Union. A widened intercondylar space.

2 - Intercondylar space is filled with tissue with some detectable radiodensity which does not match that of the cortex.

3 - Callus bridging the intercondylar space is ossified.

4 - The intercondylar space is undescernible as it is completely filled with radio-opaque bone.

N/A - Radiographic error. Film not properly processed; Reading inconclusive.

Appendix 13

Radiographic assessment of joint healing subsequent to radical metacarpophalangeal joint curettage and 3, three days apart intramuscular injections of 4.4 mg/kg phenylbutazone (P) or 0.2mg/kg dexamethasone (D) against 'sham' operated joints (S) in calves 3 and 6 weeks after surgery.

Calf No.	Week 3	P	D	S
1		2	1	0
2		1	1	0
3		2	1	0
4		1	2	0
5		1	1	N/A
6		1	1	0
7		1	2	N/A
8		N/A	1	0
9		2	1	0
10		1	1	N/A

Calf No.	Week 6	P	D	S
1		2	1	0
2		2	1	0
3		2	1	0
4		1	2	0
5		2	1	0
6		1	1	0
7		1	1	0
8		1	1	0
9		1	1	0
10		1	1	0
n = 10		1.4	1.1	0

Appendix 14

Radiographic assessment of the healing subsequent to radical metacarpophalangeal joint curettage and 3, three days apart intramuscular injection of 4.4mg/kg phenylbutazone (P) or dexamethasone (D) against 'sham' operated joints (S) in calves 9 and 15 weeks after surgery.

Calf No.	Week 9	P	D	S
1		3	1	0
2		3	1	0
3		2	2	0
4		3	3	0
5		2	2	0
6		2	2	0
7		2	3	0
8		1	2	0
9		2	2	0
10		2	2	0
		2.4	2.3	0

Calf No	Week 15	P	D	S
1		3	2	0
2		3	3	0
3		3	1	0
4		2	3	0
5		2	2	0
6		2	3	0
7		2	2	0
8		3	2	0
9		2	2	0
10		2	2	0
		2.4	2.3	0

Appendix 15

Individual calf serum Y-GT levels before and after joint surgery and 3, three days apart IM injections of 4.4mg/kg phenylbutazone.

Calf No.	DAYS BEFORE AND AFTER SURGERY AND TREATMENT									
	-14	-2	0	1	3	5	7	9	11	13
1	31	30	31	30	38	25	28	29	30	28
2	30	25	41	33	29	29	29	26	26	40
3	30	27	35	27	31	35	37	28	28	30
4	27	25	33	27	27	29	30	27	28	26
5	27	31	30	28	32	30	31	26	30	30
6	28	32	36	33	27	36	28	26	30	27
8	28	29	30	26	30	27	29	31	27	29
9	24	40	27	35	35	30	26	30	28	33
10	28	35	28	32	38	33	30	29	30	31
Mean	27.9	30.2	32.5	29.9	31.3	30.9	30.9	28.2	28.7	31.0

Appendix 16

Individual calf serum Y-GT levels before and after joint surgery and 3, three days apart IM injections of 0.2mg/kg dexamethasone.

CALF Nos.	DAYS BEFORE AND AFTER SURGERY AND TREATMENT									
	-4	-2	0	1	3	5	7	9	11	13
1	30	27	34	30	27	27	31	28	26	30
2	27	27	28	29	26	30	25	27	26	28
3	33	33	28	31	29	37	24	28	30	30
4	29	29	30	30	33	36	33	26	29	33
5	33	33	30	27	35	28	30	33	29	30
6	28	28	26	28	33	26	30	27	31	30
7	26	25	29	27	36	26	29	27	30	24
8	36	36	26	26	25	27	32	33	28	28
9	30	31	31	29	25	33	31	27	26	26
10	33	30	31	30	38	25	28	29	30	28
Mean	30.5	29.9	29.3	28.7	30.7	29.5	29.3	28.5	28.7	28.7

Appendix 17

Individual calf serum Y-GT before and after sham operations and treatment with placebo in calves.

Calf No.	Days before and after Sugery									
	-14	-2	0	1	3	5	7	9	1	13
1	30	33	30	31	29	27	30	27	29	37
2	30	30	40	30	30	26	26	26	27	30
3	33	33	44	29	32	35	23	31	27	31
4	29	30	35	28	33	26	34	27	28	27
5	30	31	30	30	27	29	31	34	28	27
6	30	30	27	27	28	28	29	31	30	33
7	32	23	36	37	30	28	29	28	30	26
8	31	28	24	30	31	27	30	29	28	31
9	29	33	30	31	30	29	33	27	27	38
10	29	33	35	30	30	29	28	28	31	35
Mean	33.4	30.4	32.1	29.3	30.1	29.0	29.3	28.8	28.9	31.9

ADDENDUM

1. Page i, third paragraph ..... submitted in fulfilment for .....

2. Page 133 between reference JARLOV, N. ..... and JILANI, M. .....

JENNINGS, P.B. JR. 1984. Functional anatomy and physiology of diarthrodial joints. In The Practice of Large Animal Surgery. Jennings P.B. (ed.) W.B. Saunders Philadelphia P.A. pp. 687-715.