JAMES M. CASEY, D.V.M., M.S.

EQUINE VETERINARY SERVICES

MARYLAND, VIRGINIA, PENNSYLVANIA, DELAWARE,
FLORIDA, GEORGIA, NEW JERSEY, KENTUCKY, &
ST. KITTS, WEST INDIES

Presenting:

EQUINE JOINT DISEASE

EQUINE JOINT DISEASE

- Traumatic joint disease is the leading cause of lameness in horses.

EQUINE JOINT DISEASE

- Joint Disease can happen to any horse at any time.

EQUINE JOINT DISEASE

- Joint Disease may be cause by one incident.

EQUINE JOINT DISEASE

- Although it is most likely to appear after repeated episodes of stress and trauma to the joints.

EQUINE JOINT DISEASE

Smarty Jones' failed attempt to win the Belmont Stakes, his only defeat. He never raced again.

- Often results in poor performance, downtime, and economic loss.

EQUINE JOINT DISEASE

- The effects of traumatic and degenerative joint disease can be devastating.

EQUINE JOINT DISEASE

- Joint Disease is not restricted to top athletic horses.
- All horses can suffer from Joint Disease

EQUINE JOINT DISEASE

- More than 1/2 of all equine lameness is due to non-septic joint disease and injury
- Causes significant economic loss due to:
  - cost of therapy
  - loss of performance ability
  - loss time in training
  - premature end of career

LOSS OF PERFORMANCE DUE TO JOINT DISEASE IN THROUGHBRED RACE HORSES

- If a horse can run a mile in 1:40.00 or 100 seconds over a fast track, his relative value would be about $20,000.
- If this same horse were to lose 1% of his performance or run a mile in 1:41.00 or 101 seconds over a fast track, his value would likely drop to about $10,000.
- If this same horse were to improve 1% in his performance or run a mile in 1:39.00 or 99 seconds, his value would likely increase to $40,000.

EQUINE JOINT DISEASE

- ANATOMY AND PHYSIOLOGY OF NORMAL JOINTS
- BASIC SCIENCE OF INFLAMMATION
- FACTORS PREDISPOSING TO JOINT INJURY
- PATHOLOGY OF JOINT DISEASE
- DIAGNOSIS OF JOINT DISEASE

PLANNING AHEAD

- Incorporate preventive veterinary medicine into both your short and long range goals.
- Be proactive, not reactive.

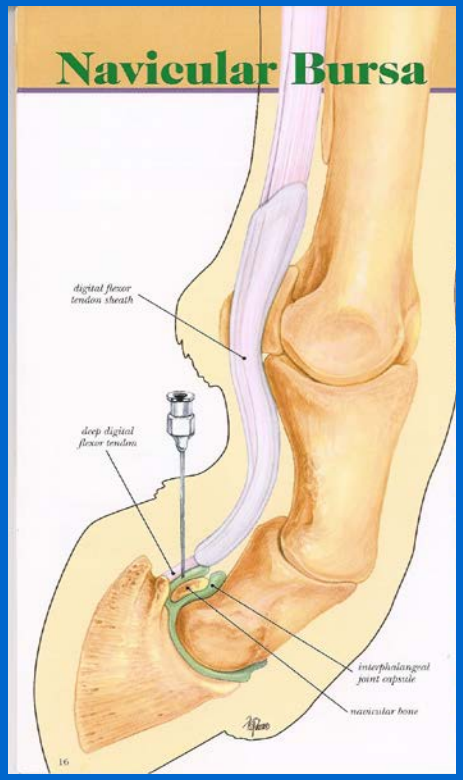
EQUINE JOINT DISEASE

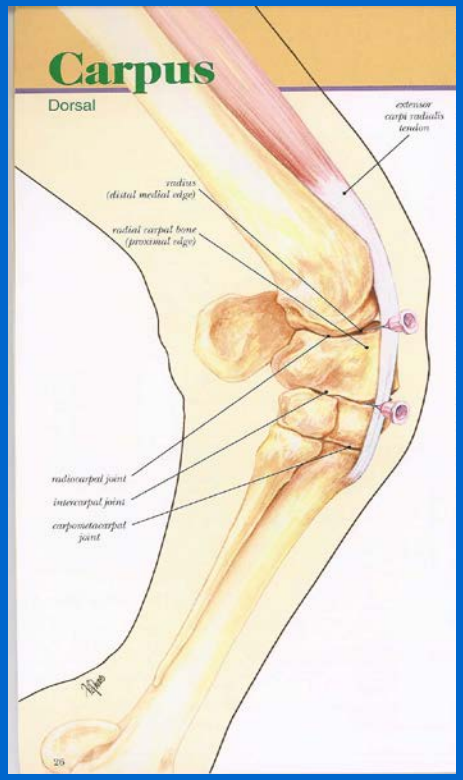
- Preventive measures are also needed to extend the usefulness and productivity of your horse.

EQUINE JOINT DISEASE

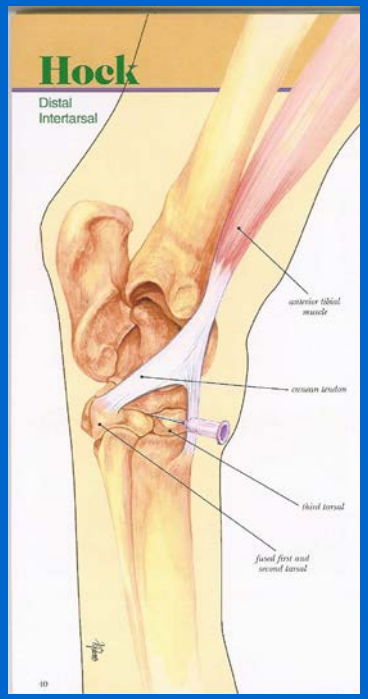
- Therapies for joint disease
  - Rest
  - Surgery
  - Physical therapies
  - Corticosteroids
  - NSAIDs and other anti-inflammatory drugs
  - Hyaluronate (HA)
  - PSGAG (Adequan)
  - IRAP / ORTHOKINE (IL – 1 Antagonist)

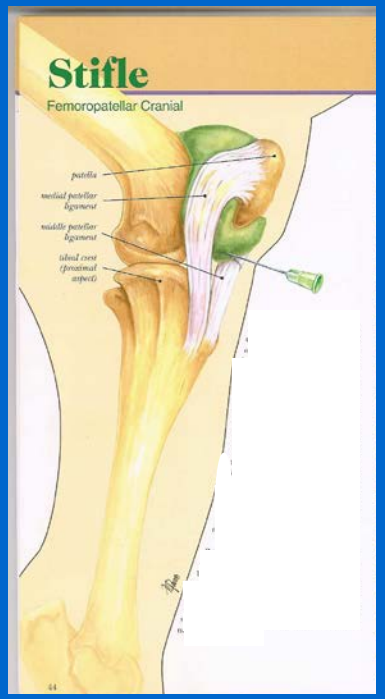
INTRAARTICULAR TREATMENT



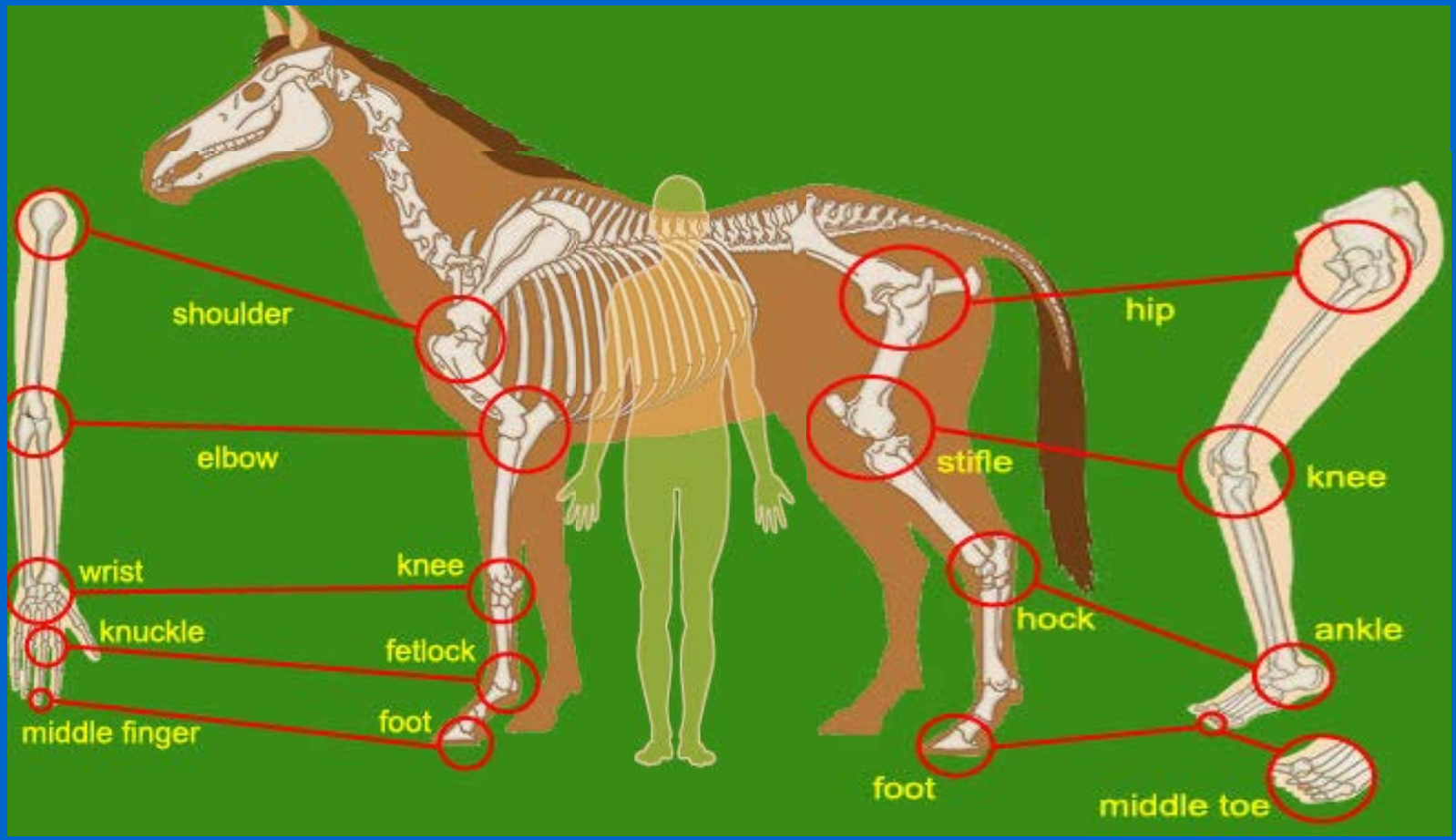


INTRAARTICULAR TREATMENT

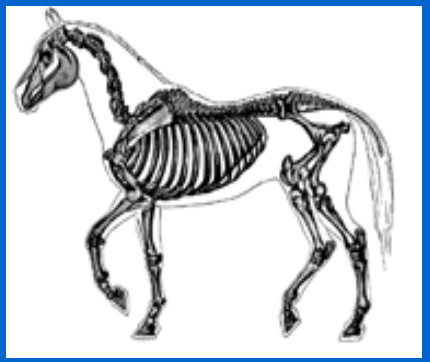


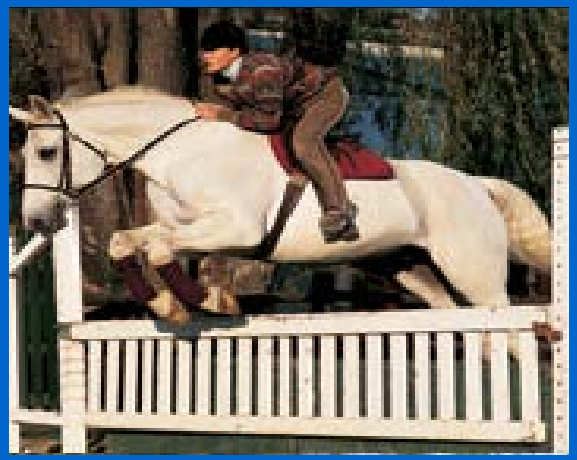


COMPARATIVE ANATOMY



ANATOMY AND PHYSIOLOGY OF NORMAL JOINTS





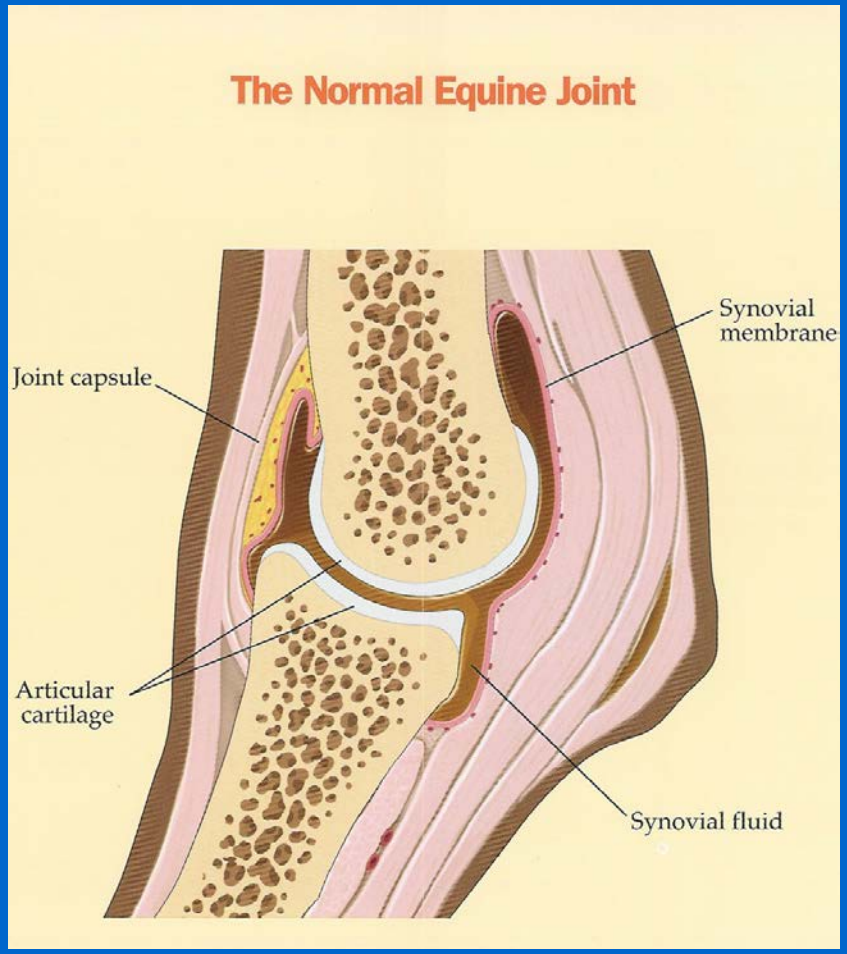
JOINT

- A joint is defined as a structure which joins two or more bones to form a single anatomic entity

- Types of joints
  - fibrous (suture joints in skull)
  - cartilaginous (joins ribs to sternum)
  - synovial (joins 2 or more bones to form a moveable articulation)

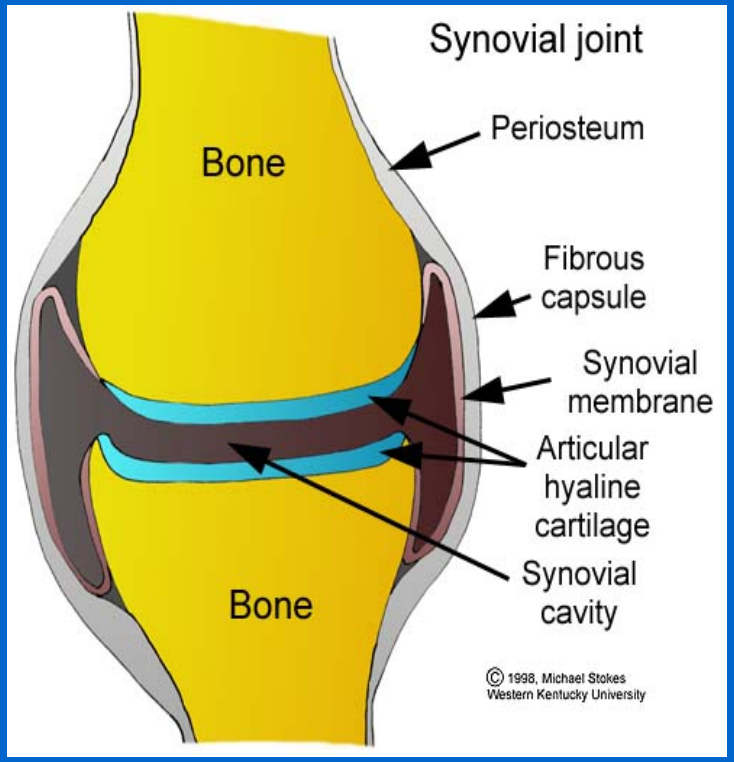
JOINT COMPONENTS

- EXTERNAL SUPPORTIVE STRUCTURE
- JOINT CAPSULE
- SYNOVIAL FLUID
- ARTICULAR CARTILAGE
- SUBCHONDRAL BONE



SYNOVIAL MEMBRANE

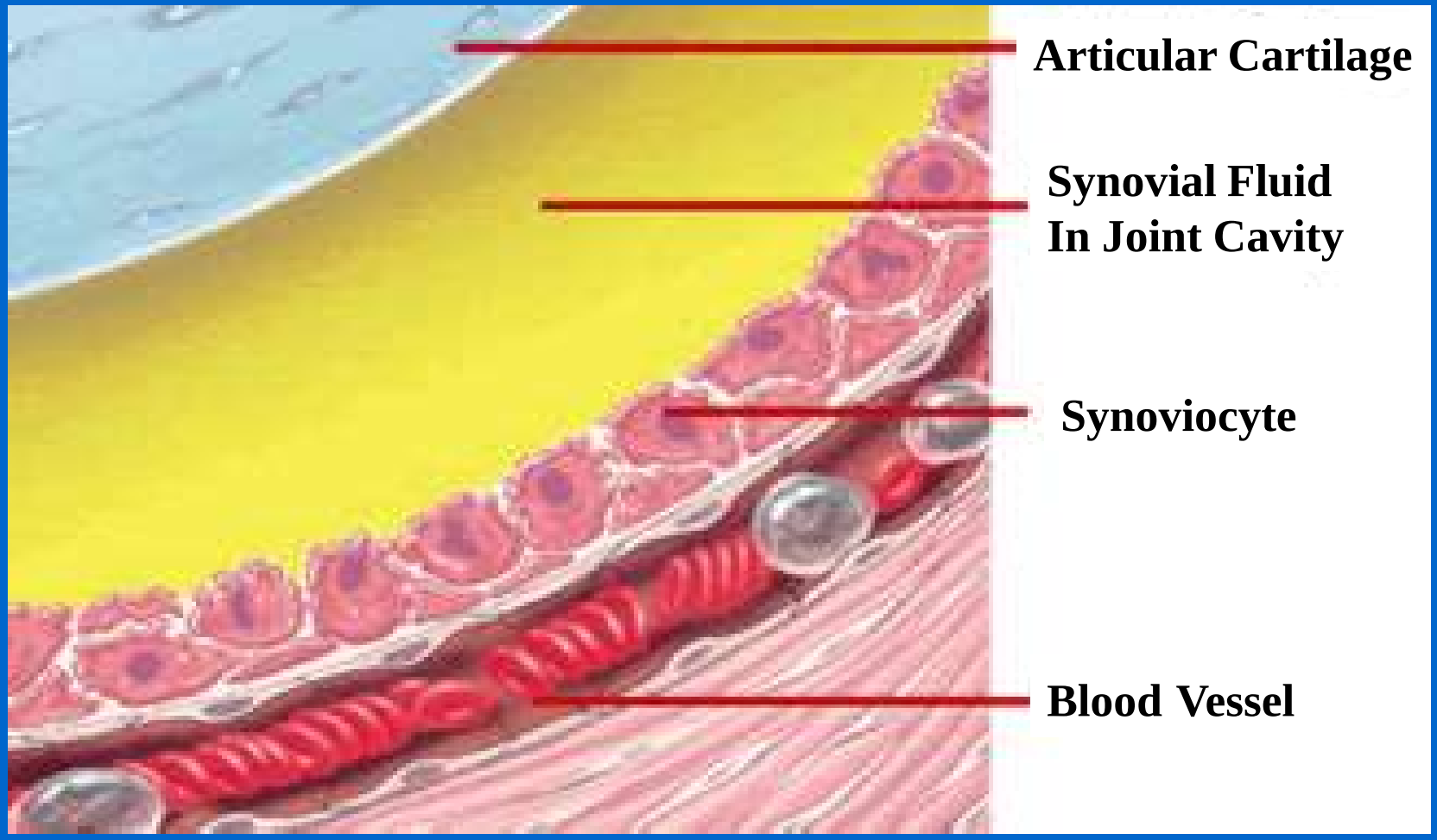
- Very important to the health of normal joint
- Loose layers of cells on the inner portion of the joint capsule (permeable)



SYNOVIAL MEMBRANE

- Lies in very close contact with blood vessels in the joint capsule
- Filters plasma from blood vessels to form synovial fluid
- Synthesizes hyaluronic acid

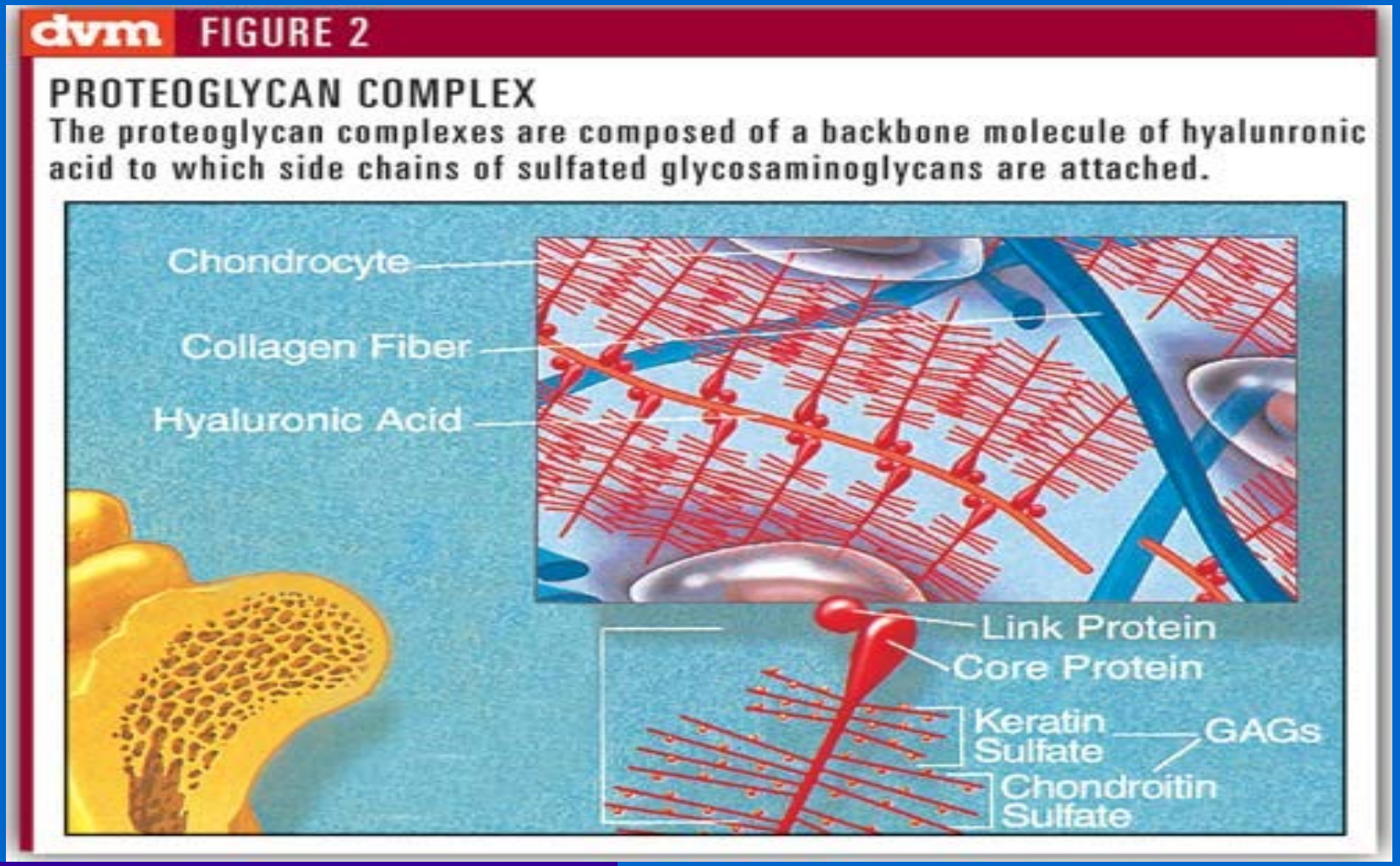
SYNOVIAL MEMBRANE



Hyaluronic Acid

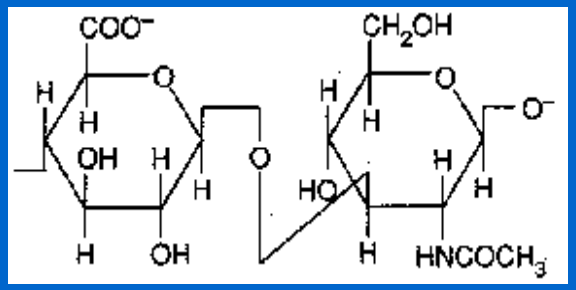
- A giant molecule with molecular mass between 10^5 to 10^7.
- Most abundant in embryonic tissues and in specialized connective tissues such as synovial fluid where it acts as a lubricant, or the vitreous where its function is to provide a clear plastic gel
- Composed of D-glucoronic acid linked to N-acetyl-glucosamine by a β-(1 →3) linkage, the latter in turn linked to the next glucoronic acid by a β-(1 →4) linkage.

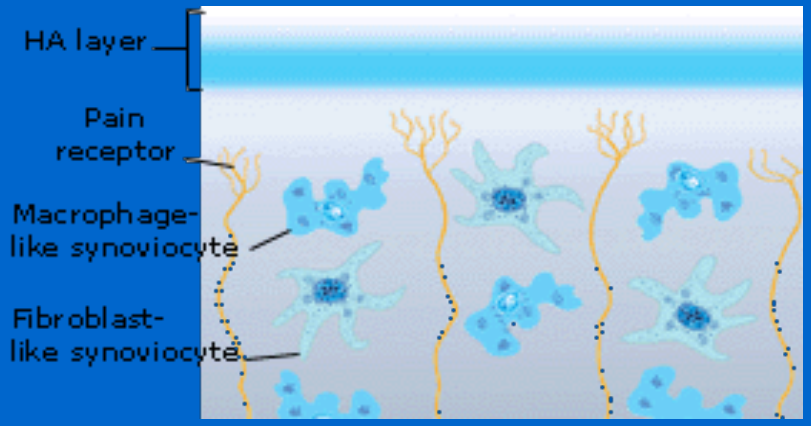
HYALURONIC ACID



HYALURONIC ACID

- Long chain non-sulfated glycosaminoglycan
- Folds into very thick reticulum in the synovial fluid
- Acts as a barrier to cells and larger molecules and prevents them from entering synovial cavity
- Boundary lubricant of the joint capsule and synovial membrane

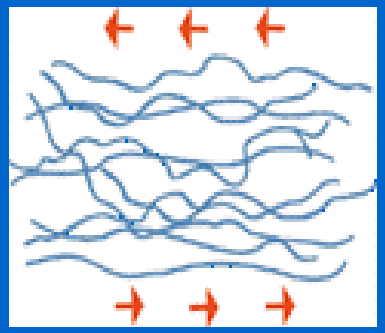


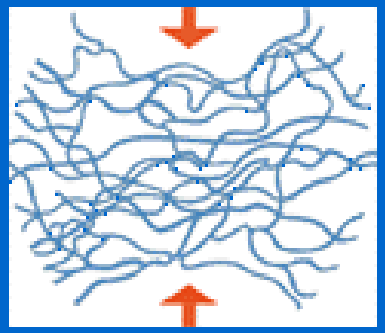


HYALURONIC ACID

Gradual Stress

Lubrication



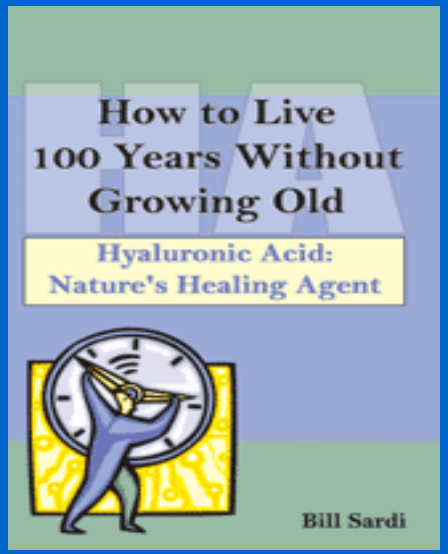


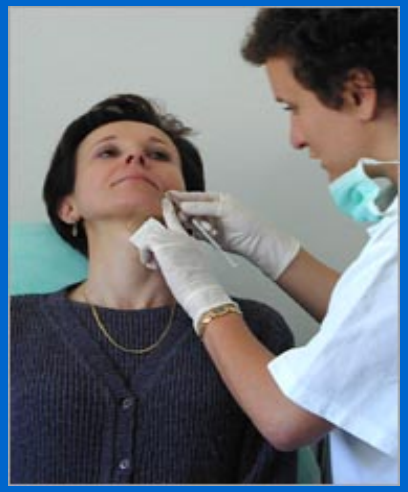
Intense Stress

Shock Absorption

HYALURONIC ACID USE IN MAN

HYALURONIC ACID
(Suplasyn®, Orthovisc®, Synvisc®)
INJECTION

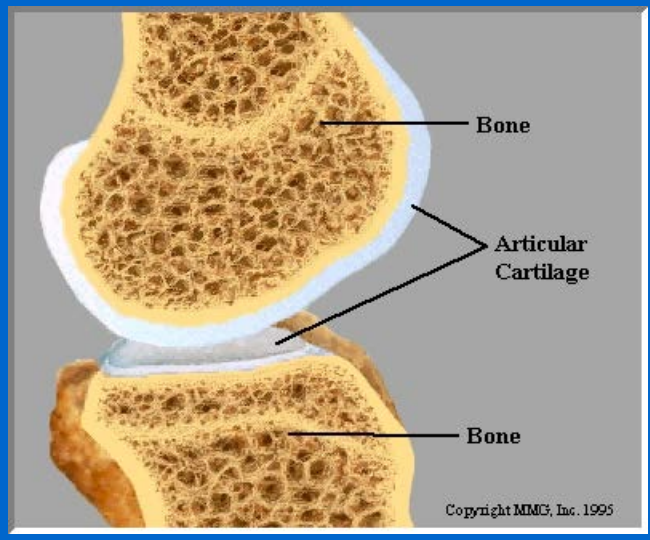




NOTHING BEATS YOUTH

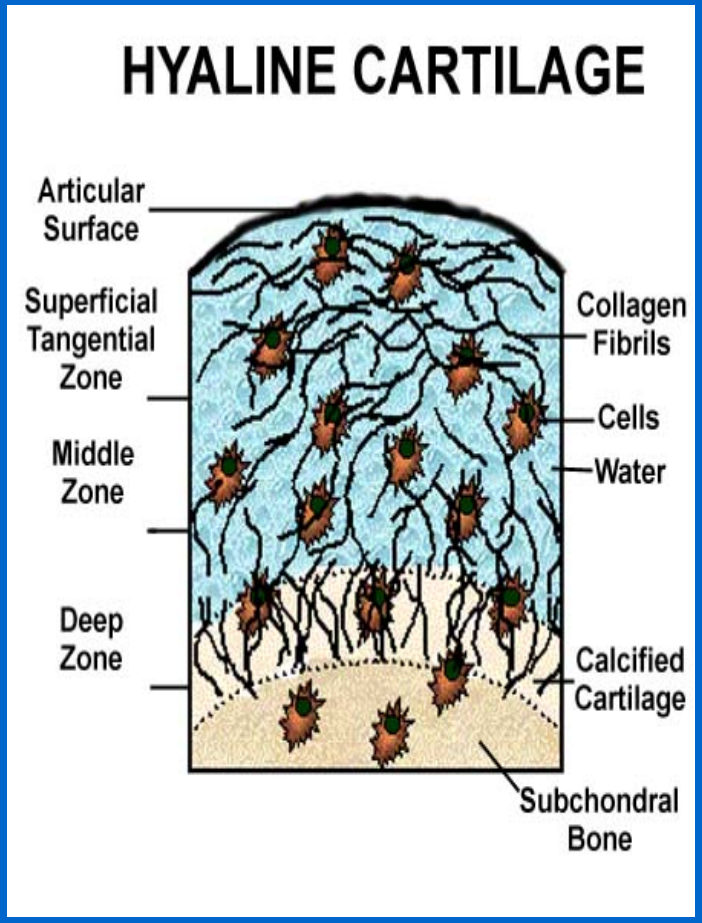
ARTICULAR CARTILAGE

- Glistening white substance which covers the ends of bones within joint
- Allows for compliance to forces acting on the joint
- Health of articular cartilage is the limiting factor on the amount of work a joint can perform



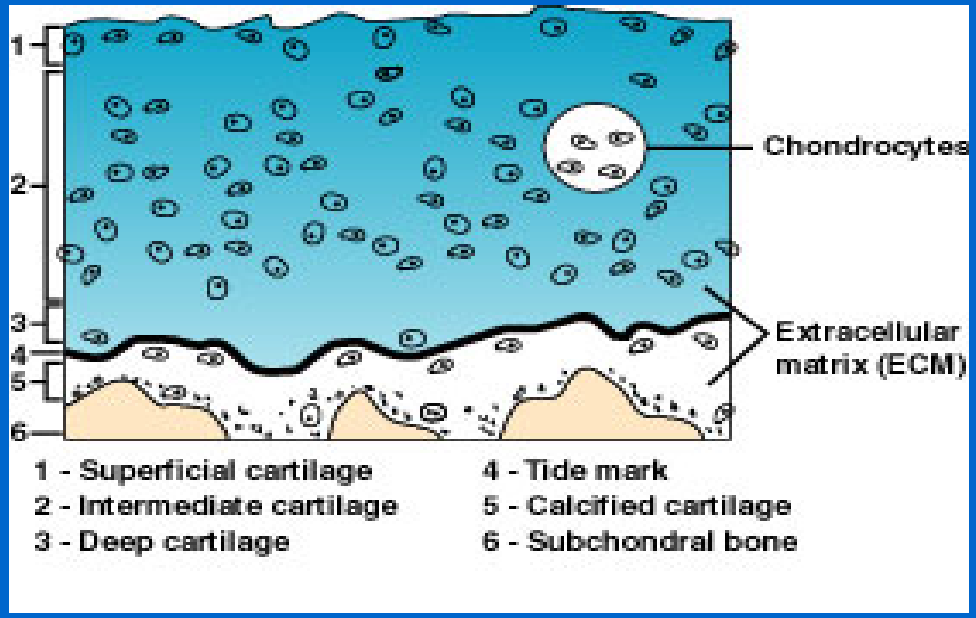
COMPONENTS OF ARTICULAR CARTILAGE

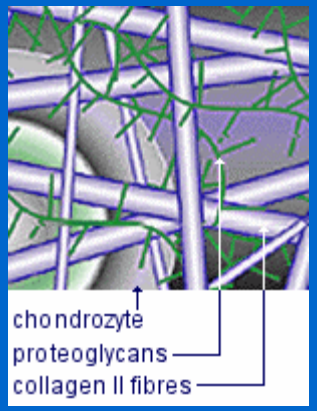
- Extra cellular Matrix
  - Proteoglycan complexes
  - Collagen fibers
- Chondrocytes
- Water
- Cartilage contains no blood vessels and no sensory nerves



EXTRA CELLULAR MATRIX

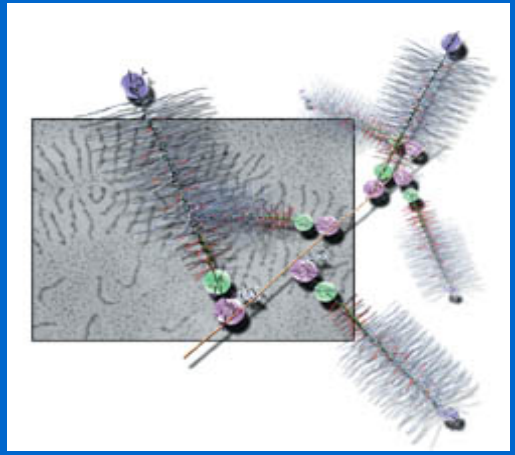
- Components synthesized and broken down by chondrocytes
- Proteoglycan complexes
- Collagen Fibers
- Hyaluronic acid

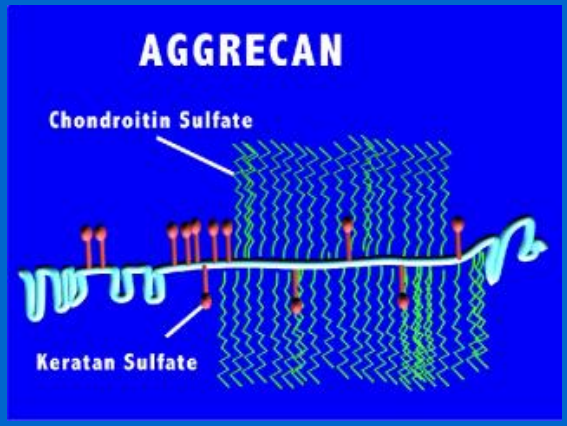




PROTEOGLYCAN COMPLEXES

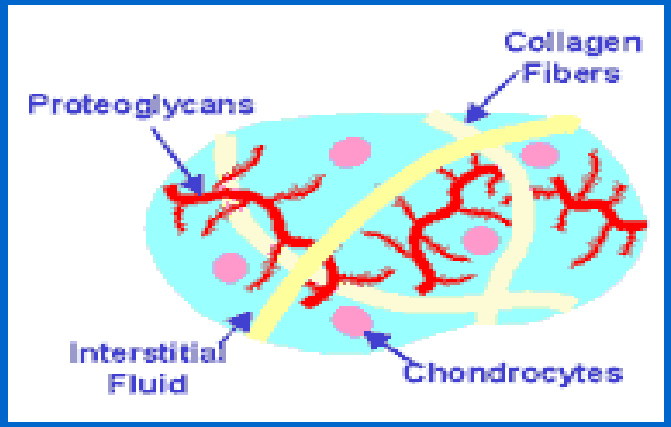
- Linked to a strand of HA by link protein
- Protein core
- Side chains of GAGs (keratin and chondroitin sulfates)
- Adjacent sulfate groups have negative charges which repel and cause the complex to stand out like a bottle brush and trap water

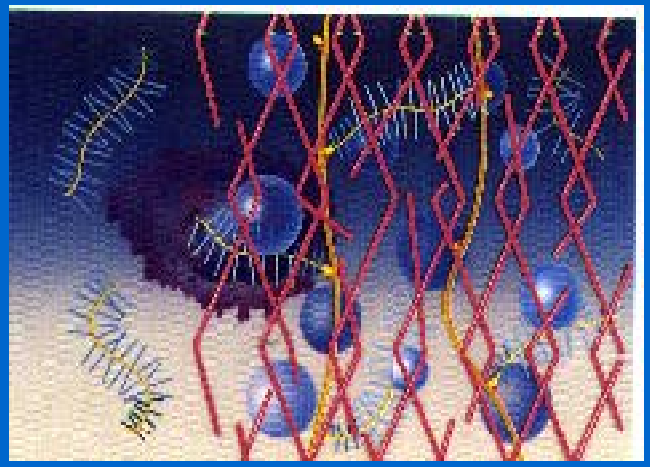




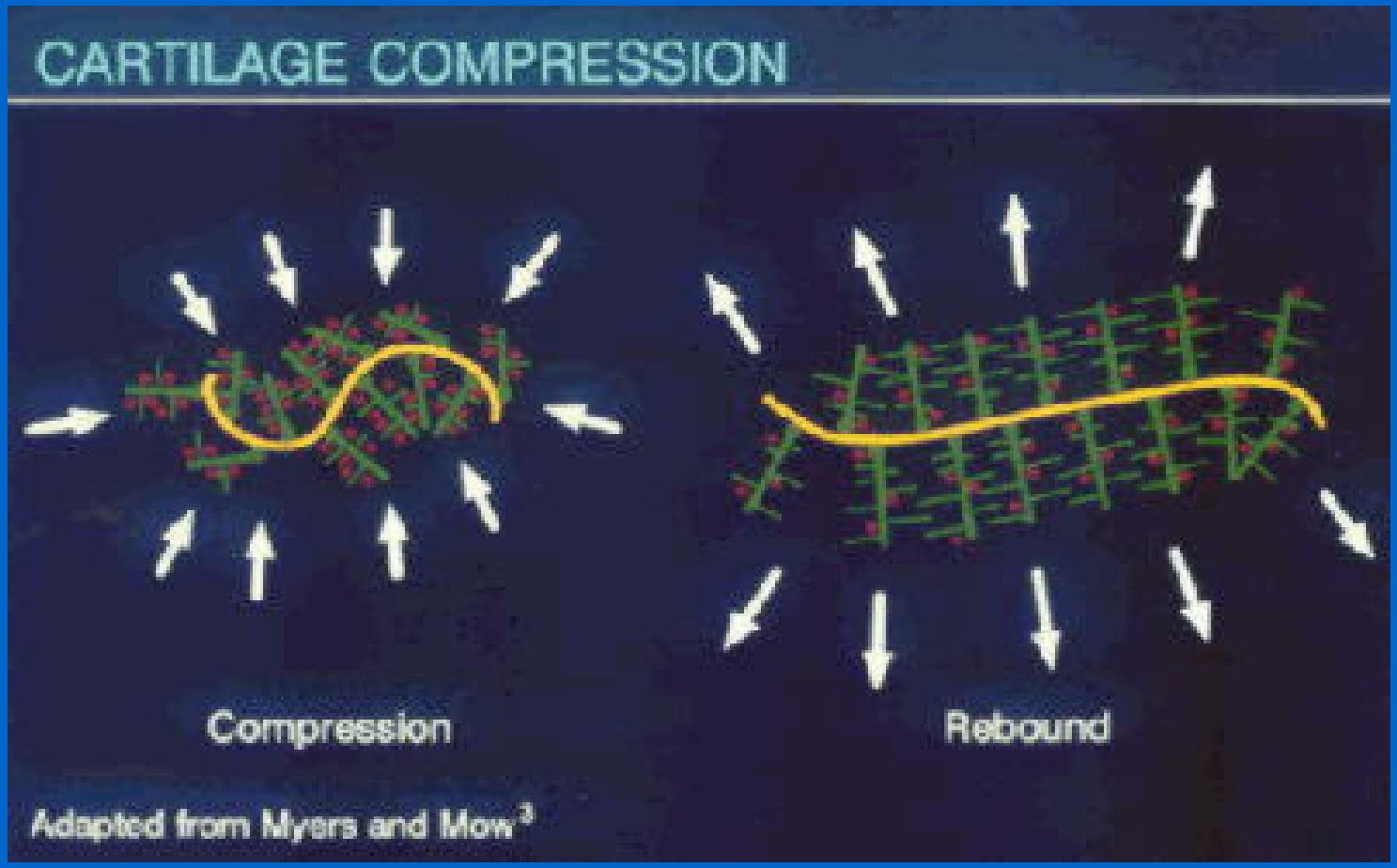
CARTILAGE COMPLIANCE

- When force is placed on the cartilage water is forced out of the bottle brush configuration as the complexes are squeezed together
- As force is removed, the adjacent negative charges repel and the bottle brush returns
- As the complexes spread water is drawn back into the complexes (resumes shape)

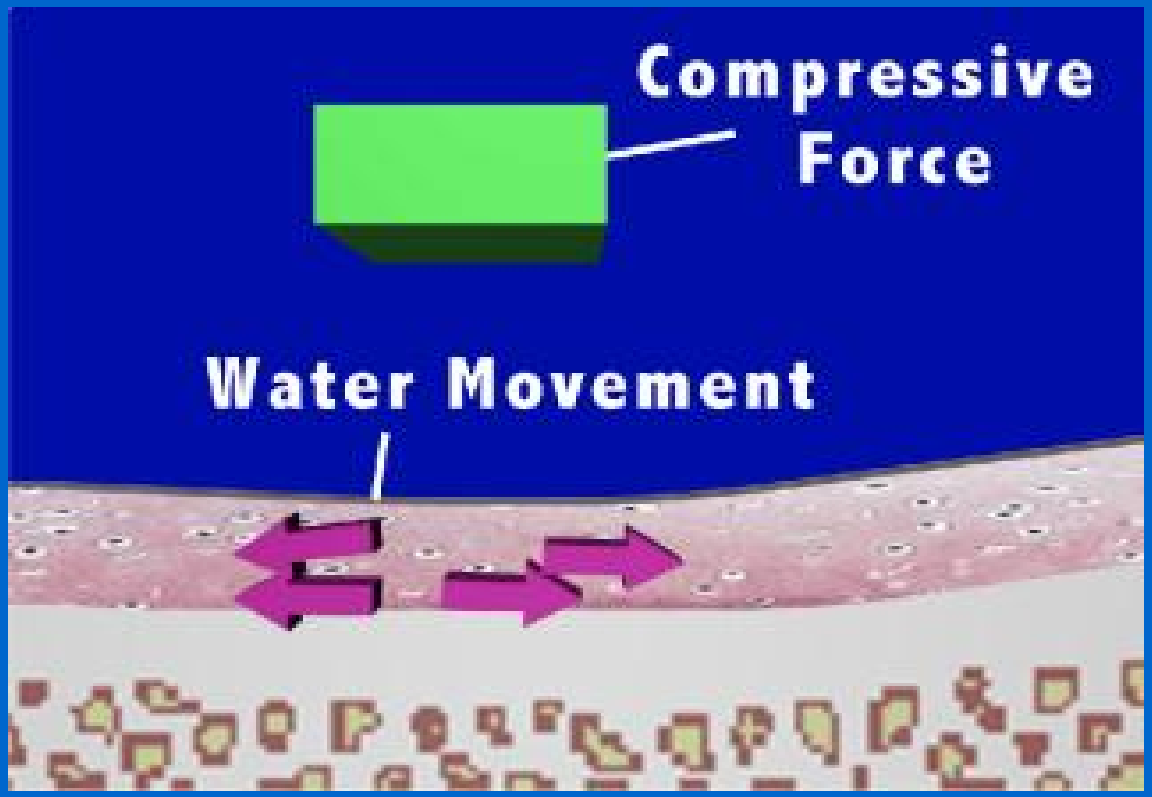




CARTILAGE COMPLIANCE

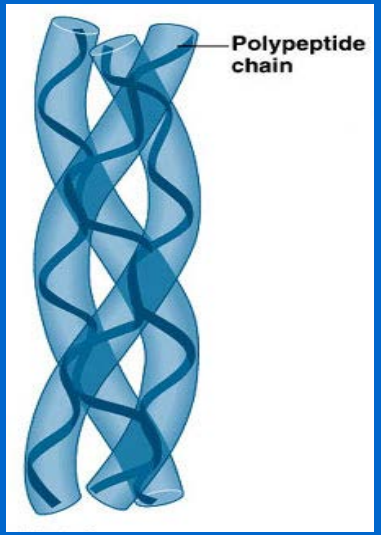


CARTILAGE COMPLIANCE

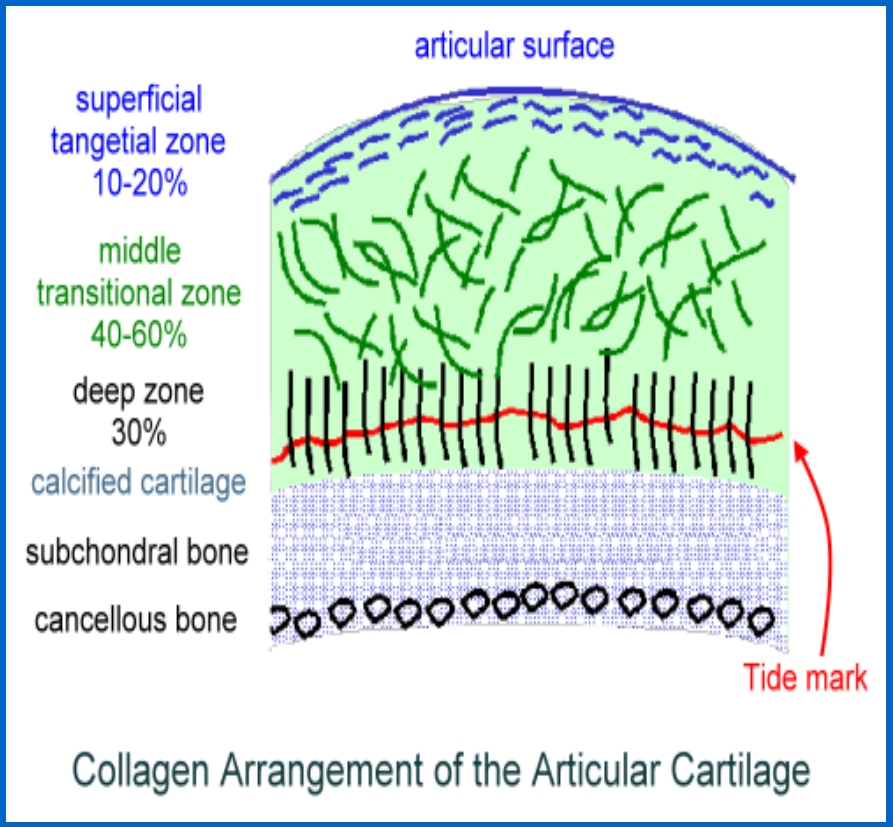


COLLAGEN FIBERS

- Amino acid chains form the skeletal framework of the cartilage
- Very tough fibrils give the cartilage its compressive stiffness and allow for the absorption and distribution of shearing forces
- Most simply a “coil spring” arrangement



Collagen Fibers

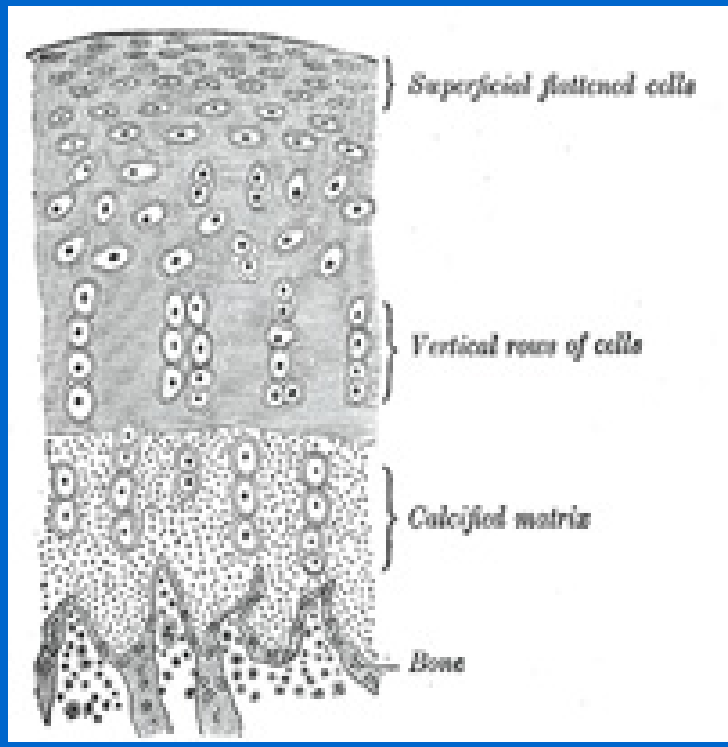


Collagen Arrangement of the Articular Cartilage

- Orientation of collagen fibers in the cartilage matrix allow for the initial resistance to shock, the distribution of shock evenly throughout the matrix and transmit the shock into the subchondral bone

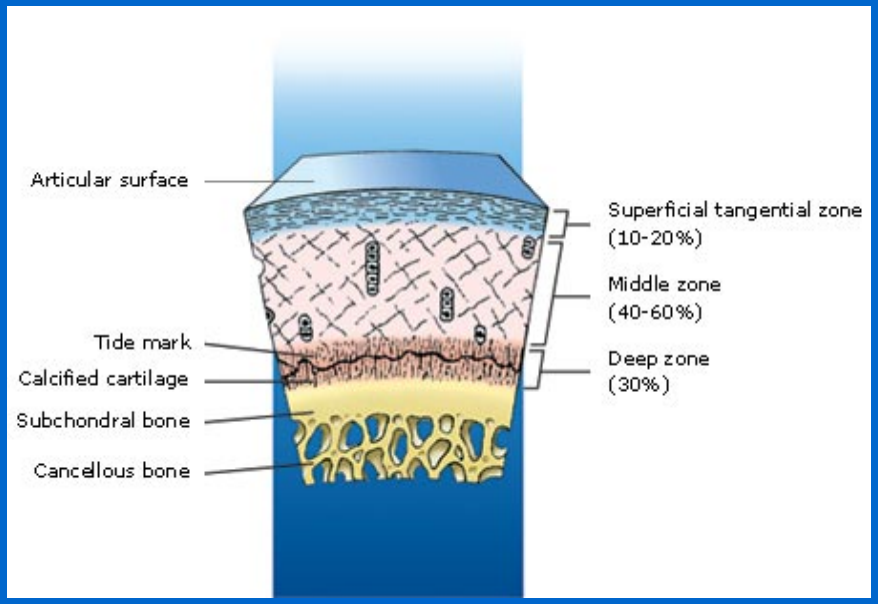
ARTICULAR CARTILAGE

- The matrix is normally in a “balance” between synthesis of new matrix components, repair of damaged matrix, and degradation and replacement of worn out components
- This “balance” means there is no real net loss of articular cartilage components



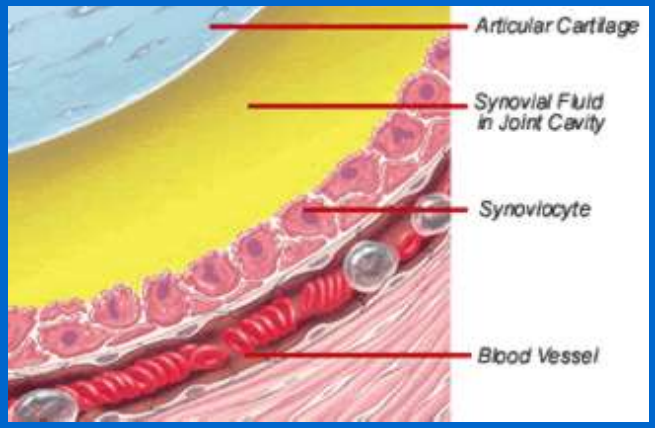
SUBCHONDRAL BONE

- Defined as the bone beneath the cartilage surface and within the joint capsule
- Very important for 2 reasons
  - blood vessels which supply nutrients to the cartilage and help carry out waste products
  - **it is the structure which ultimately absorbs the shock of forces acting on the cartilage**



JOINT LUBRICATION

- SYNOVIAL MEMBRANE AND JOINT CAPSULE IS LUBRICATED BY HYALURONIC ACID IN THE SYNOVIAL FLUID



- CARTILAGE IS LUBRICATED BY:
  - "SQUEEZE FILM LUBRICATION"
  - GLYCOPROTEIN LUBRICANTS
  - SYNOVIAL H.A.

SHOCK ABSORPTION

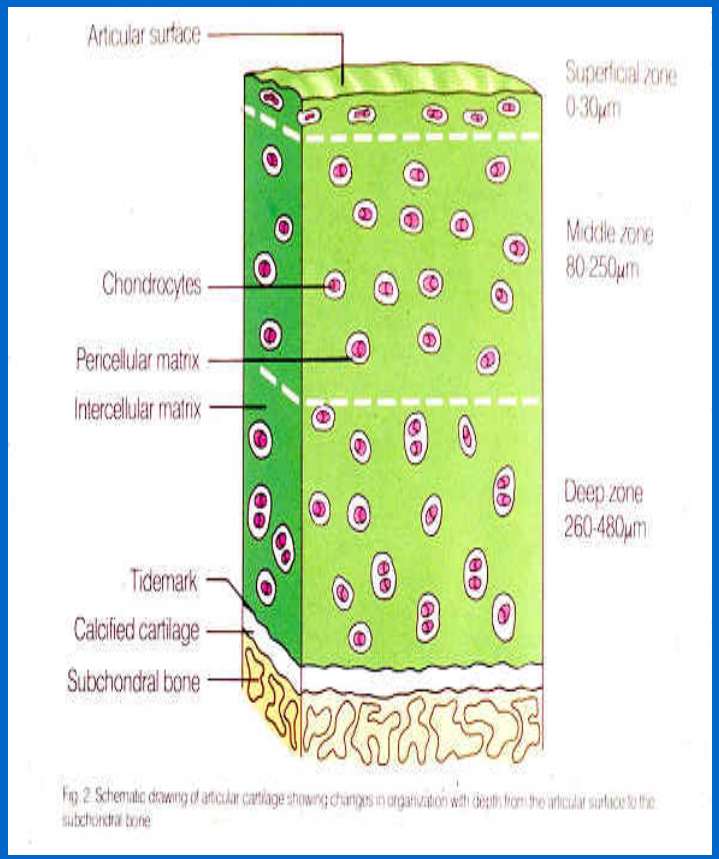
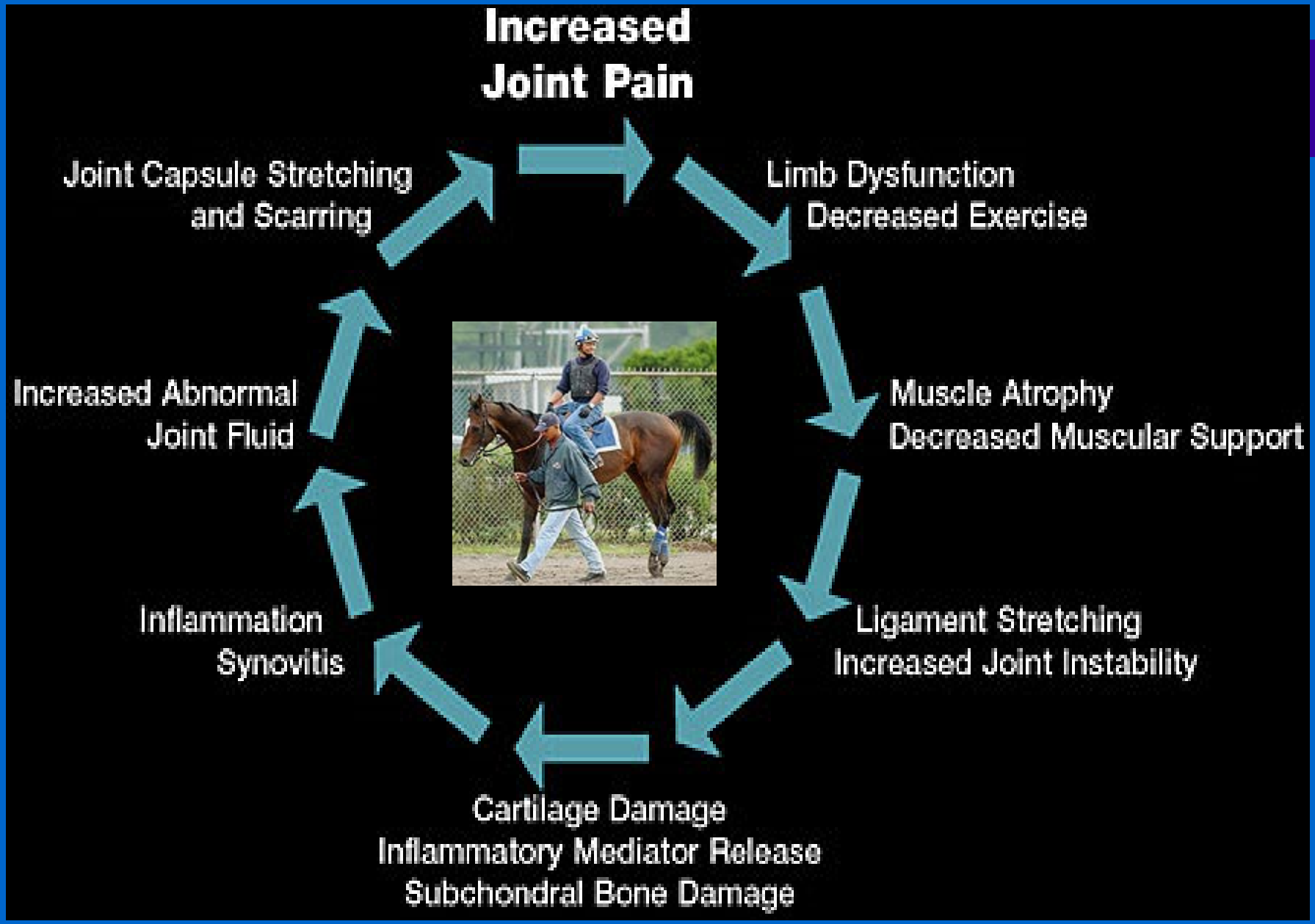


Fig. 2. Schematic drawing of articular cartilage showing changes in organization with depth from the articular surface to the subchondral bone

- Many have the mistaken belief that cartilage absorbs shock; cartilage transmits shock evenly from the surface to the subchondral bone
- **<u>Subchondral bone is the ultimate shock absorber for the joint</u>**

JOINT DISEASE

- In order to understand how to treat joint disease it is essential that one learn:
  - normal joint anatomy and function
  - what factors predispose to joint injury
  - what is the pathologic process that leads to degenerative joint disease
  - how can these pathologic processes be interrupted

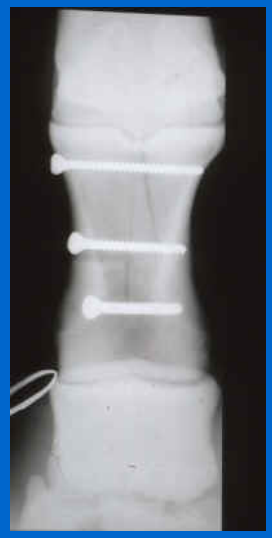

Increased
Joint Pain
Limb Dysfunction
Decreased Exercise
Muscle Atrophy
Decreased Muscular Support
Ligament Stretching
Increased Joint Instability
Cartilage Damage
Inflammatory Mediator Release
Subchondral Bone Damage
Inflammation
Synovitis
Increased Abnormal
Joint Fluid
Joint Capsule Stretching
and Scarring

PREDISPOSING FACTORS FOR JOINT DISEASE

- Equitable distribution of forces on the joint. Inequitable distribution of forces leads to abnormal forces acting on the joint
  - poor conformation
  - incorrect shoeing
  - angular limb deformities

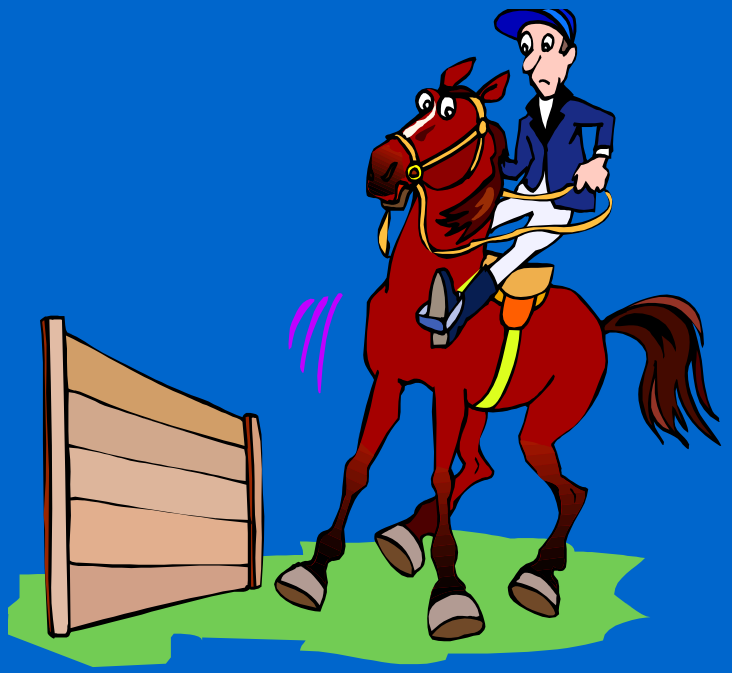
PREDISPOSING FACTORS FOR JOINT DISEASE

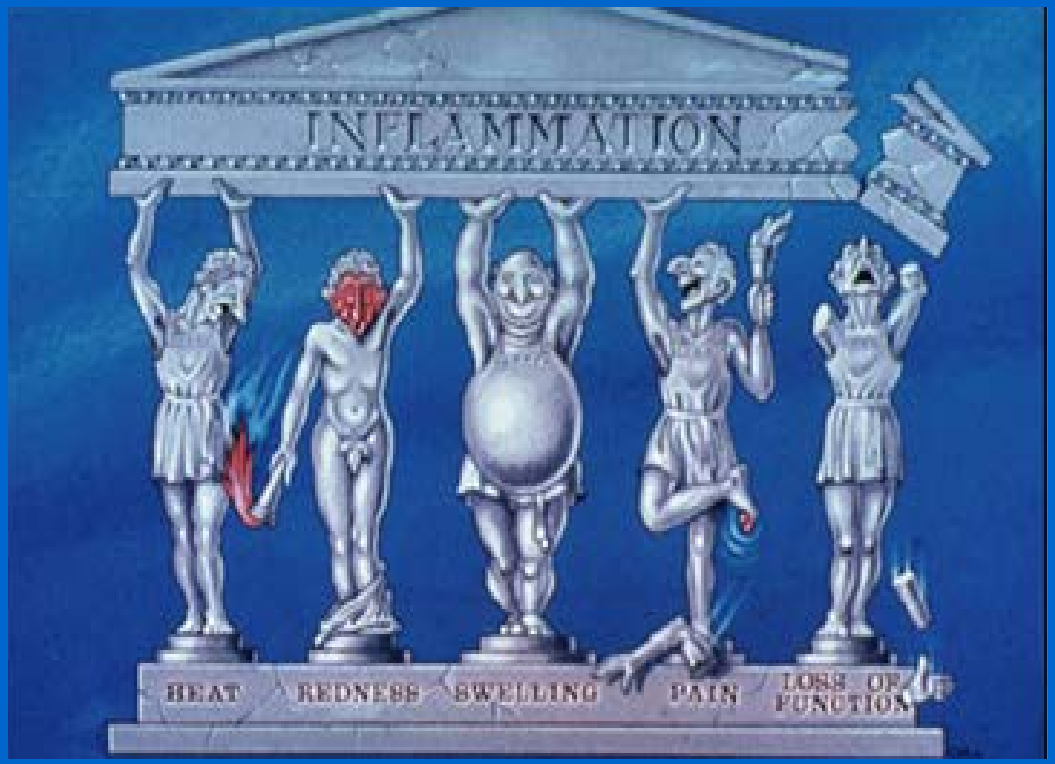
Elements Necessary for normal joint function:



- Mechanical stability is required to prevent physiologically abnormal forces from acting on the joint
- Factors which lead to joint instability include:
  - intraarticular fractures
  - tendon, ligament, or severe skin injuries

JOINT INJURIES ARE OFTEN CAUSED DIRECTLY BY HUMAN INTERVENTION: POOR BREEDING, FEEDING, TRAINING, SHOEING AND MANAGEMENT



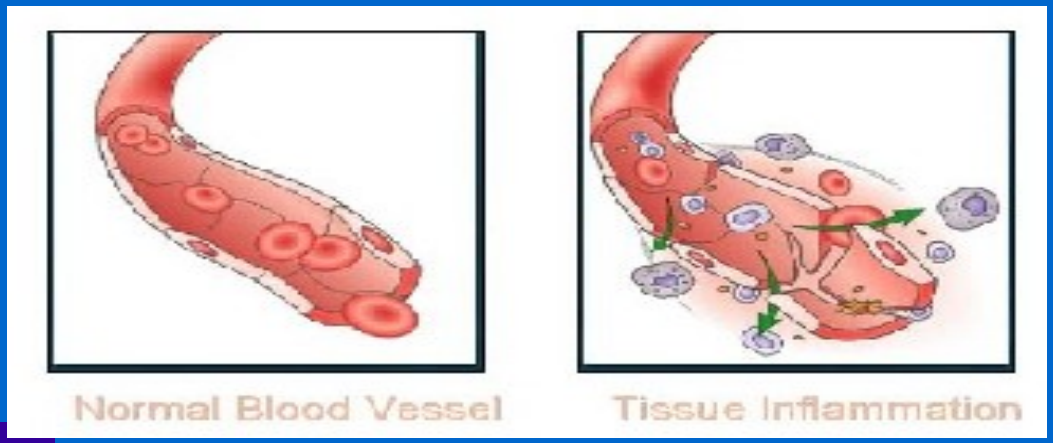

INFLAMMATION
HEAT
REDNESS
SWELLING
PAIN
LOSS OF FUNCTION

INFLAMMATION

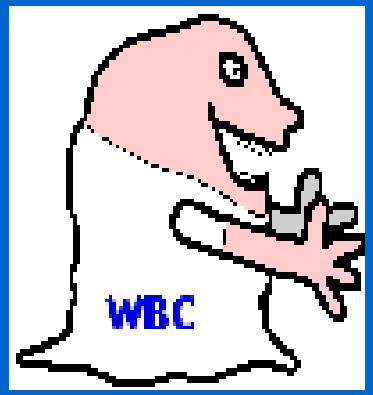
- Inflammation is the process by which the body identifies, isolates, destroys and removes an inflammogen (microbe, damaged tissue, foreign substance)
- Inflammation is a normal body function which leads to repair and wound healing
- Inflammation can go out of control if the stimulus is strong enough

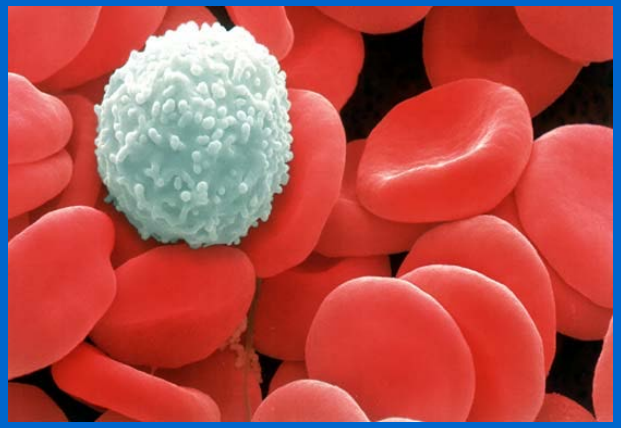
INFLAMMATION

- Begins with vasodilation (increased blood flow; heat and redness) and increased permeability of blood vessels (leaking fluid; swelling)
- Action of enzymes on cell membrane lead to formation of prostaglandins (pain potentiation)



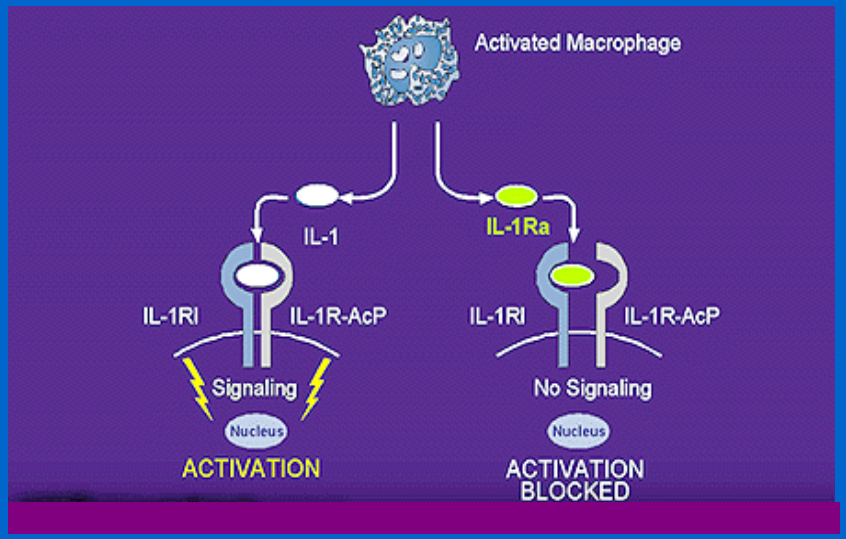
INFLAMATION

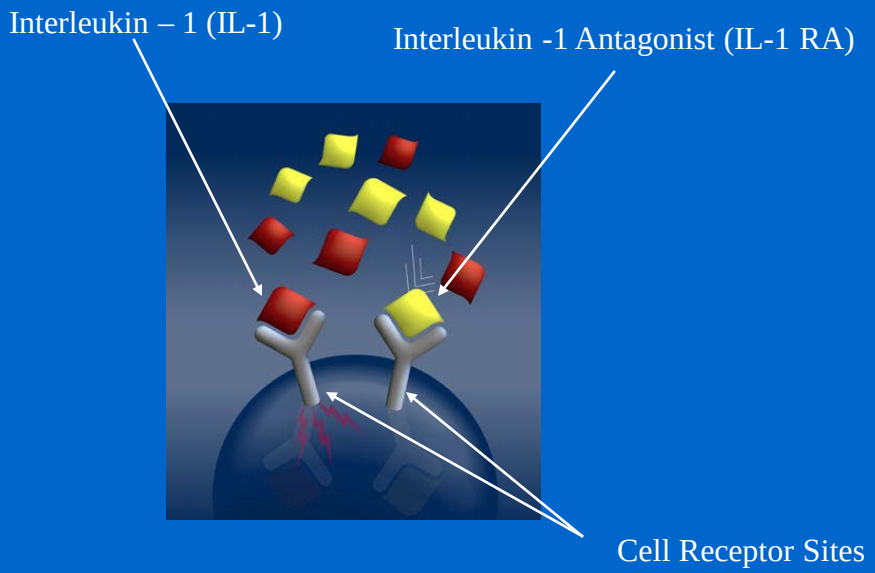




- White Blood Cells are an integral part of the inflammatory process.

INFLAMMATION

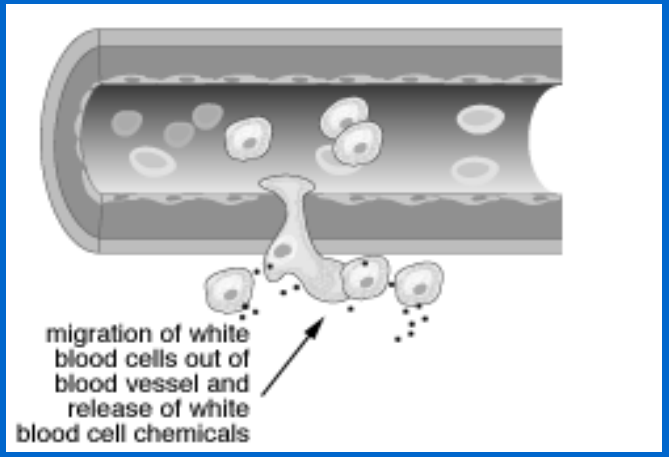




- Interleukin – 1 is the central inflammatory mediator released from a white blood cell.
- Interleukin – 1 binds to joint receptor cell sites and drives the inflammatory process via activation of tissue necrosis factor (TNF).

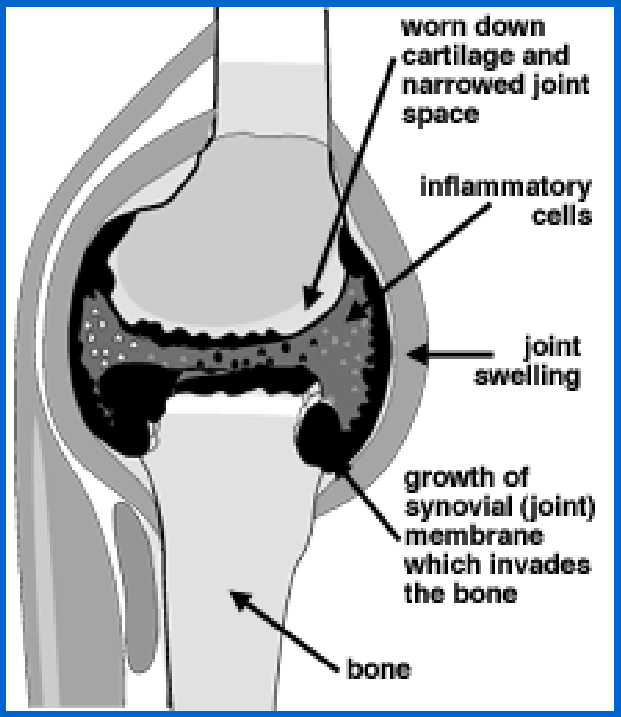
INFLAMMATION

- Chemotaxis occurs and cells are drawn to area to kill microbes, engulf dead microbes and tissue and digest all extraneous matter
- As these cells perform their function and die they accumulate in tissue (pus)
- Growth factors act on tissue to support repair and wound healing.

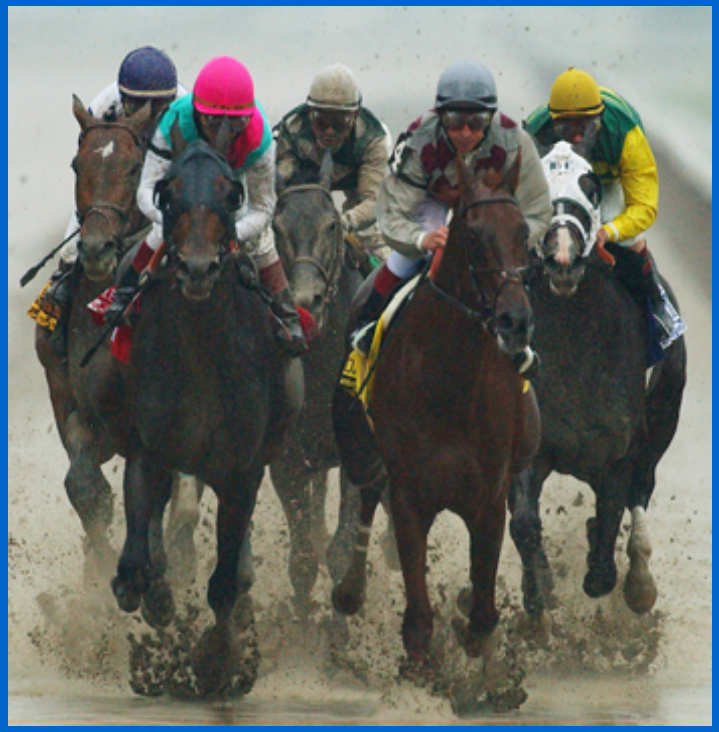


CARDINAL SIGNS OF INFLAMMATION

- HEAT
- PAIN
- SWELLING
- REDNESS
- LOSS OF FUNCTION



CONTRIBUTING FACTORS OF JOINT INJURY



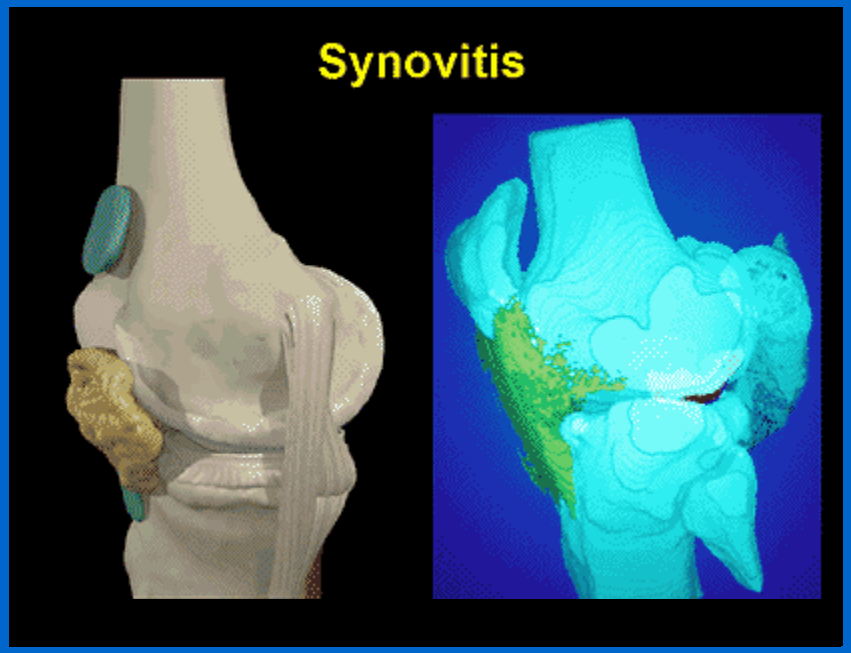
- Injuries increase when racing on muddy tracks.

CONTRIBUTING FACTORS OF JOINT INJURY

Soft or yielding turf

Slippery footing

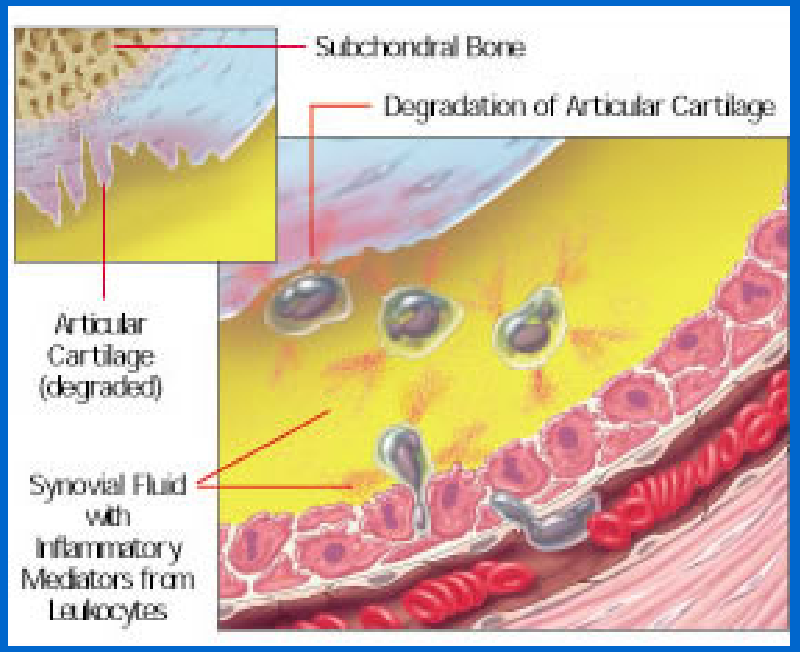
JOINT INJURY



- In the horse joint disease most commonly begins as traumatic synovitis secondary to use trauma.
- Local blood vessels in the synovial membrane dilate and the walls become more permeable allowing cells and large molecules to escape into the synovial fluid.

JOINT INJURY

- As WBCs enter the synovial fluid they undergo a respiratory burst releasing toxic oxygen radicals and enzymes.
- These inflammogens break down the HA and destroy the lubricant and barrier function.
- Inflamed synovial cells also begin to produce enzymes.



JOINT INJURY

- Cells and enzymes now gain access to the articular cartilage
- Damage to cartilage matrix includes breakdown of proteoglycan complexes and collagen fibers
- In response the chondrocytes begin to produce enzymes to try to clean up the damage (further breakdown)

JOINT INJURY

- An increase in water content in the matrix leads to poor compliance and interference with exchange of nutrients and waste products

- These factors increase stress on chondrocytes (lack of nutrition) and on subchondral bone (poor cartilage compliance.

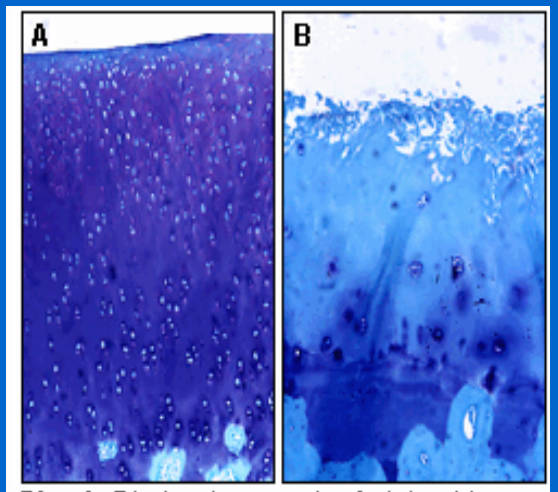
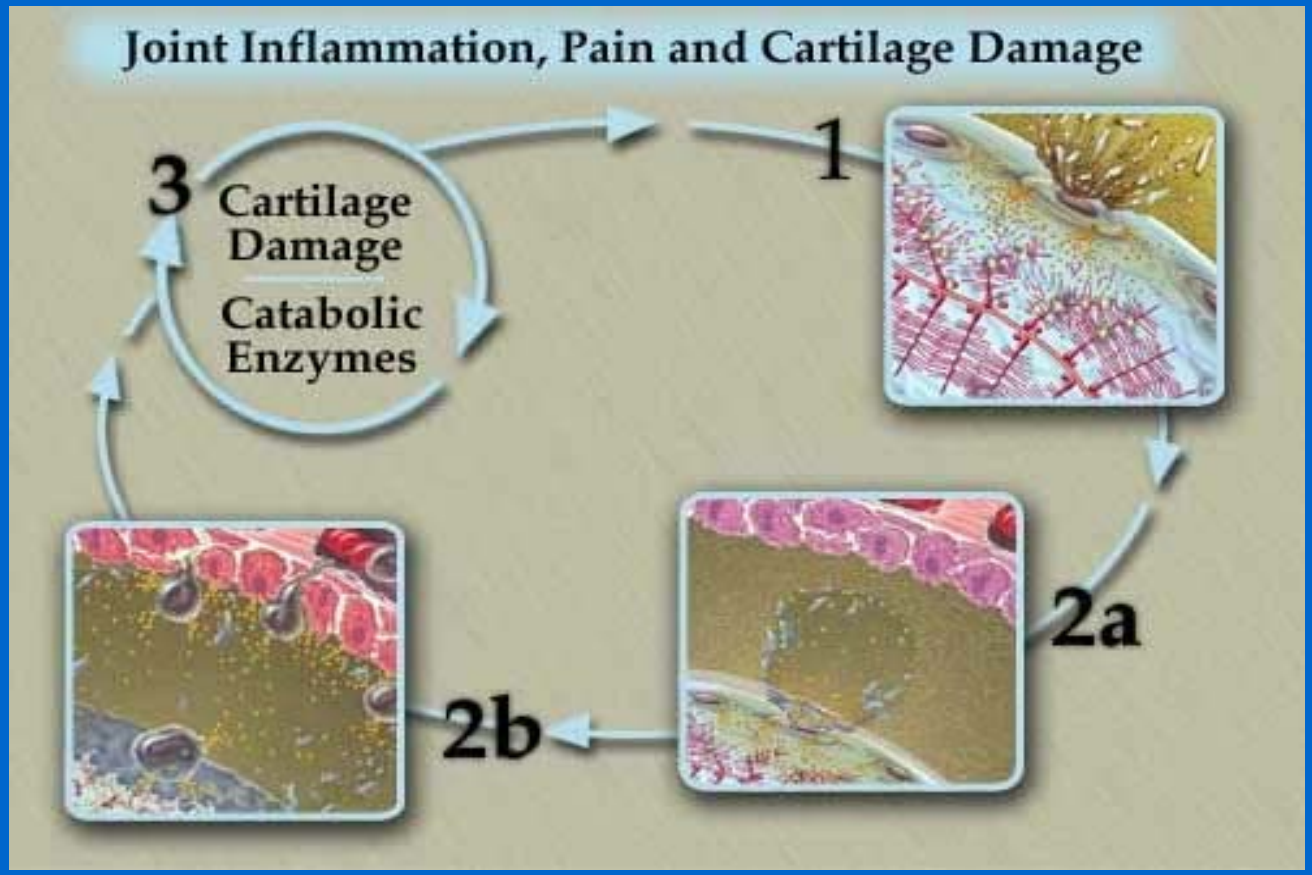
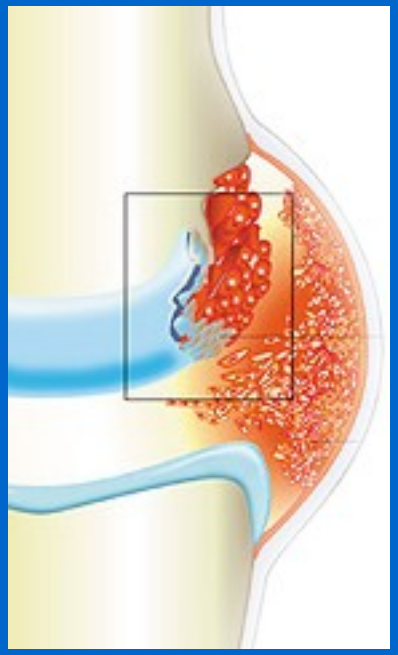


Fig. 4. Photomicrograph of alcian blue-stained sections of femoral condylar articular cartilage from (a) normal joints and (b) osteoarthritic joints. Note the surface fibrillation, loss of staining for proteoglycans and chondrocyte nesting (chondrons) in osteoarthritic cartilage. *Magnification: x 100.*

JOINT INJURY CARTILAGE DAMAGE



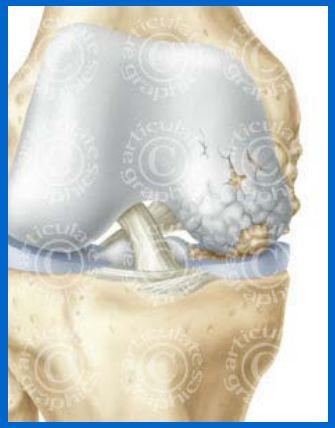


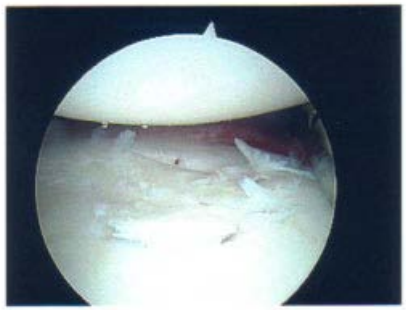
JOINT INJURY

- The surface of the cartilage begins to fray releasing fragments of cartilage and matrix components into synovial fluid
- This particulate matter in the synovial fluid leads to increase synovial inflammation
- Deep clefts form in the cartilage and can progress to full thickness erosions

JOINT INJURY

- Chondrocytes respond by dividing and clumping into groups called clones
- Due to overwhelming damage and impaired metabolism, the chondrocytes cannot replace matrix as fast as it is loss
- This net loss of cartilage matrix components is the hallmark of degenerative joint disease or osteoarthritis





Arthroscopic Image

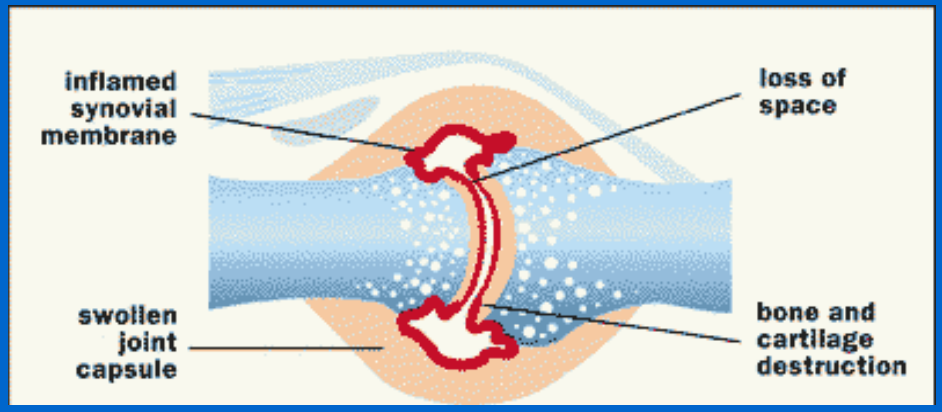
JOINT INJURY

- Due to increased forces acting on subchondral bone micro fractures occur beneath the cartilage surface
- In response the bone will repair resulting in the formation of osteophytes and by subchondral bone sclerosis

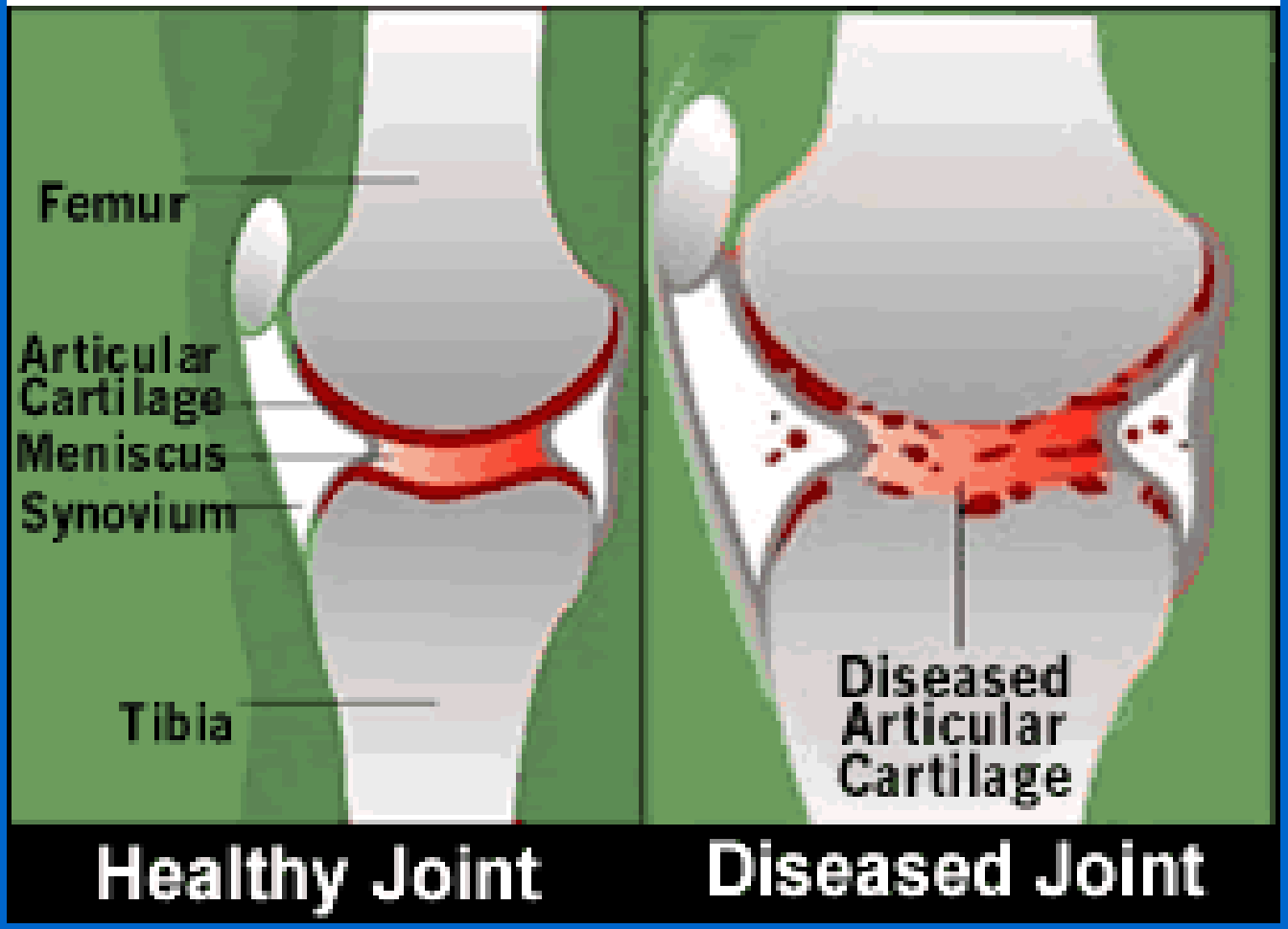
Arthroscopic Image

JOINT INJURY

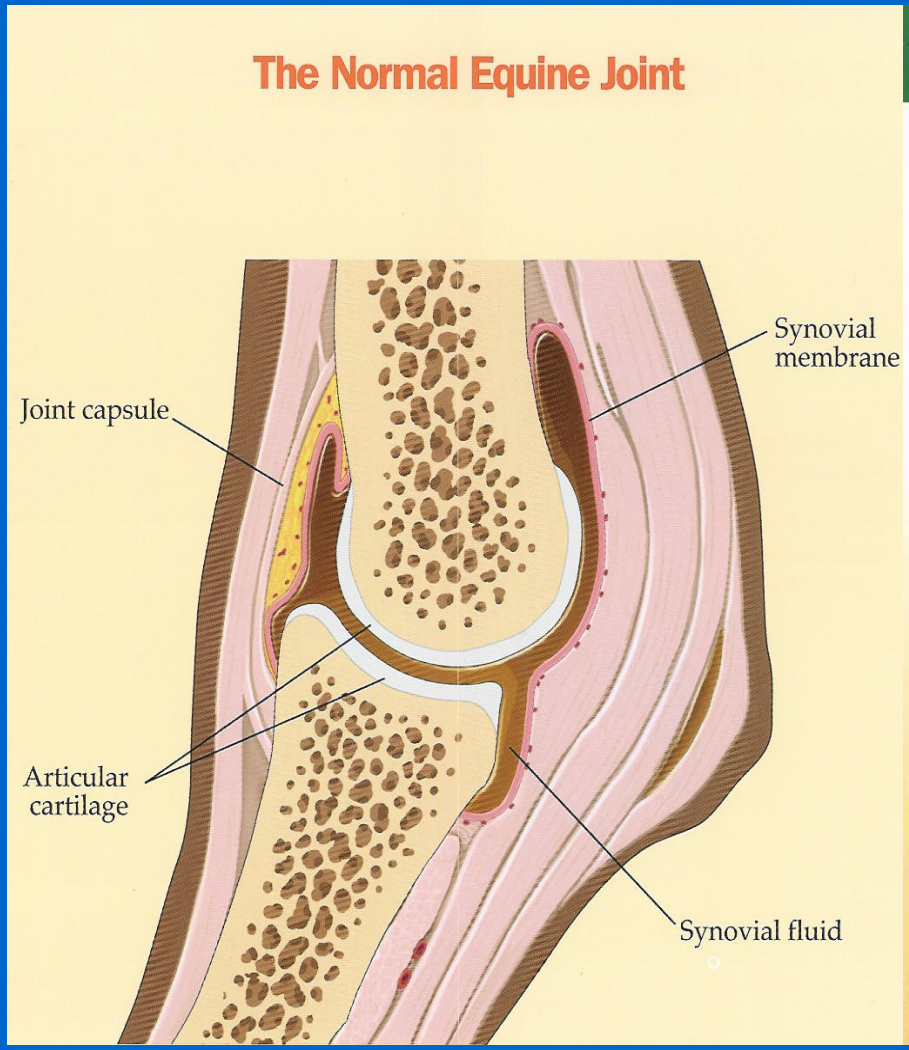
- This damaged bone cannot absorb shock normally and may fragment forming osteochondral bone “chips.”

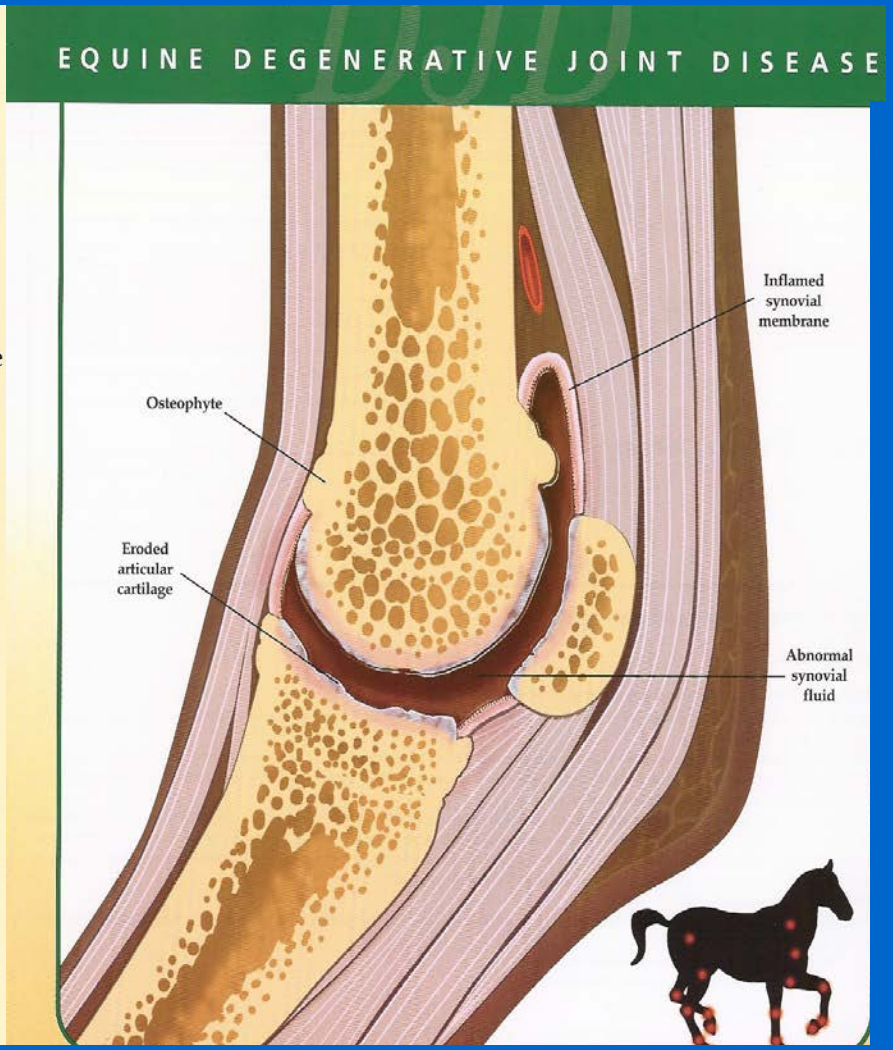


The Effect of Osteoarthritis



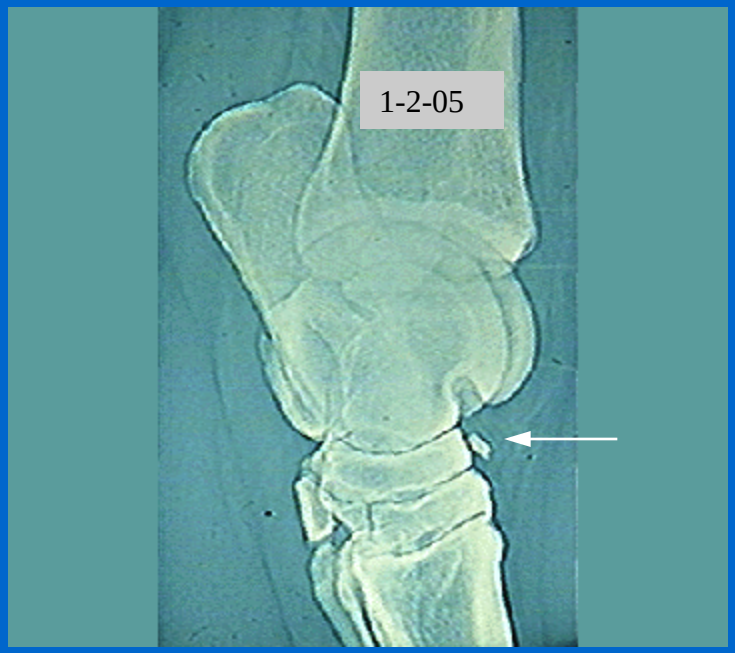
NORMAL VS. ABNORMAL JOINT





JOINT INJURY

- Pain in degenerative joints occurs primarily from 2 sources:
- Damaged subchondral bone (sclerosis, osteochondral chips, osteophytes)



Xeroradiographic Image

Chip Fracture in Hock

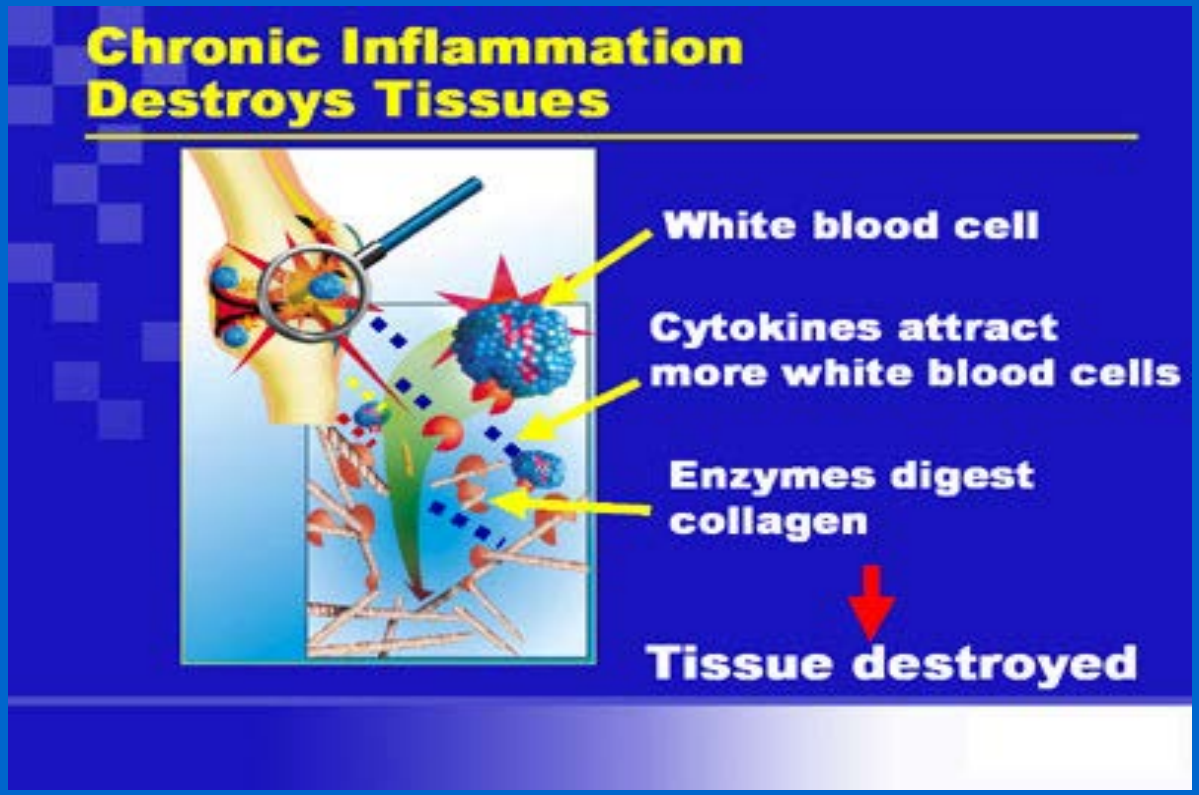
JOINT INJURY

Pain also comes from:

- Joint capsule: pressure of fluid distention
- Joint capsule may become thickened reducing joint mobility and > pain

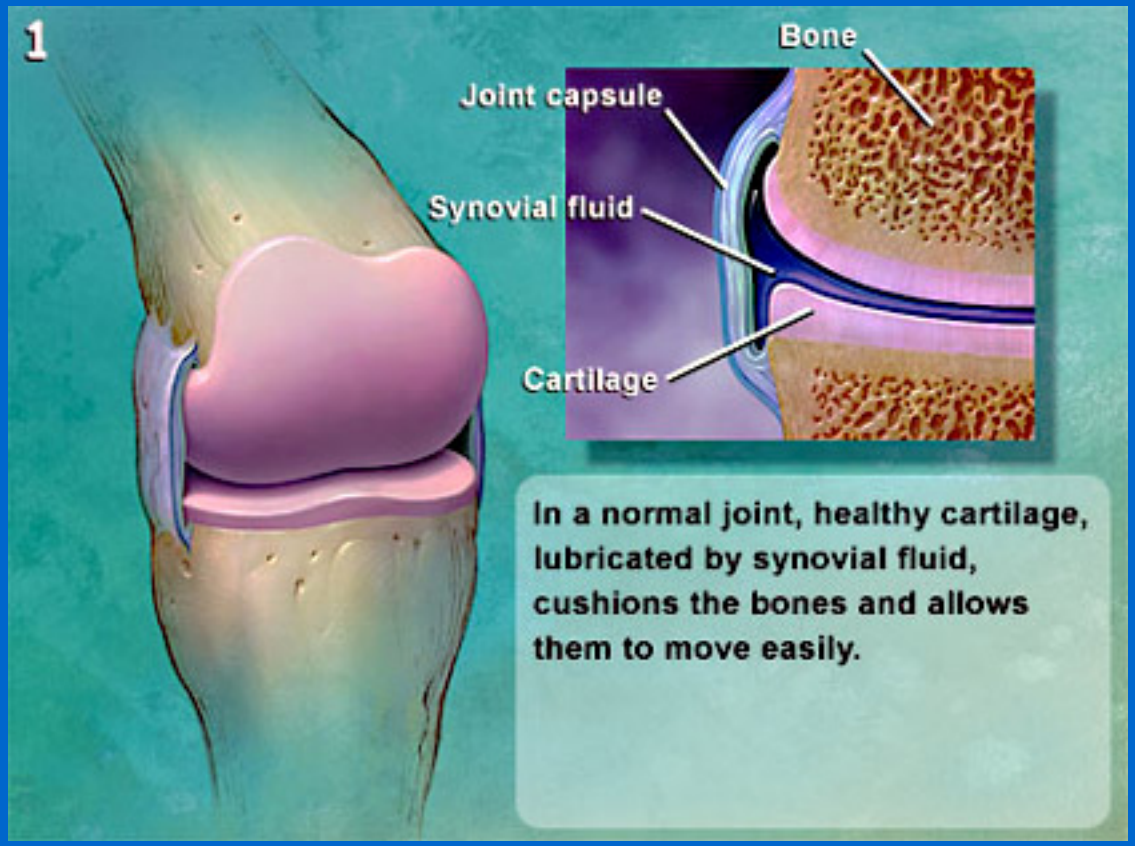
Capsulitis

DEGENERATIVE JOINT DISEASE BECOMES A "VICIOUS CYCLE" WHERE PATHOLOGY ONE PLACE FEEDS OTHER PATHOLOGY

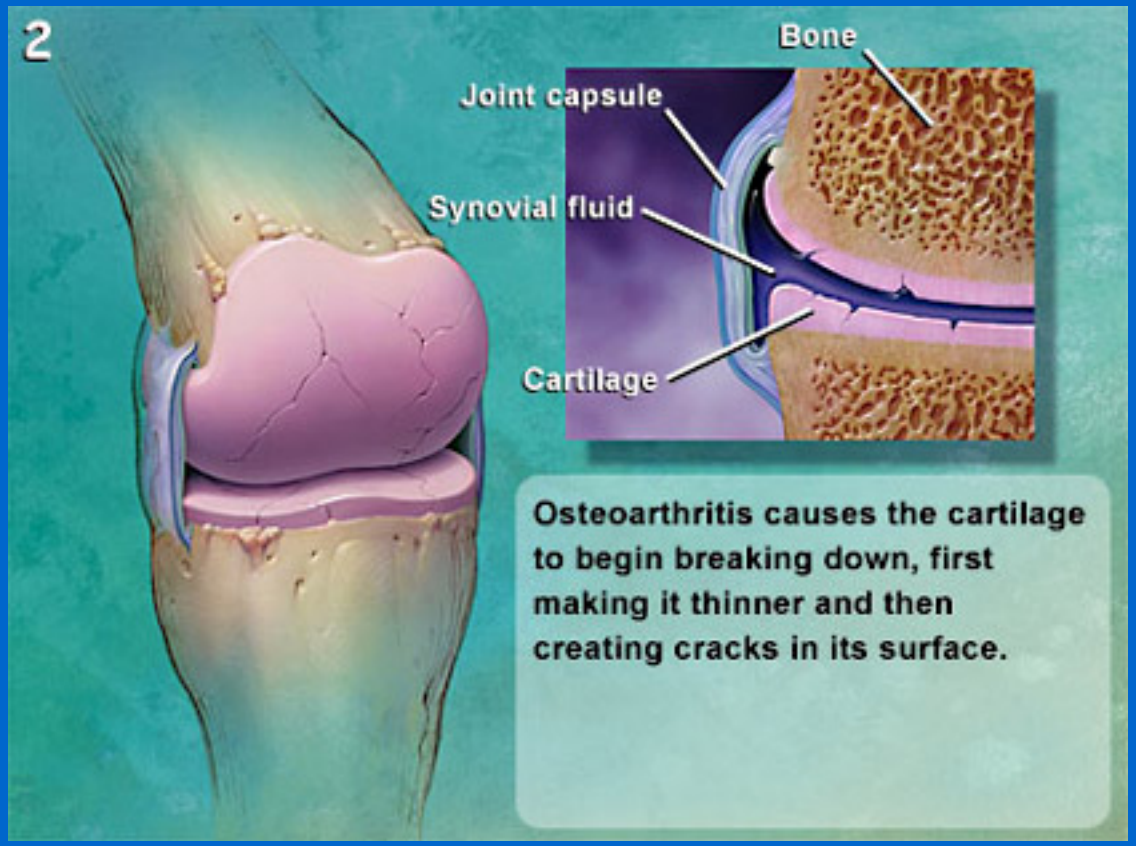


UNLESS THIS CYCLE IS INTERRUPTED PRIOR TO FULL THICKNESS CARTILAGE LOSS OR SUBCHONDRAL SCLEROSIS; PERMANENT DAMAGE OCCURS

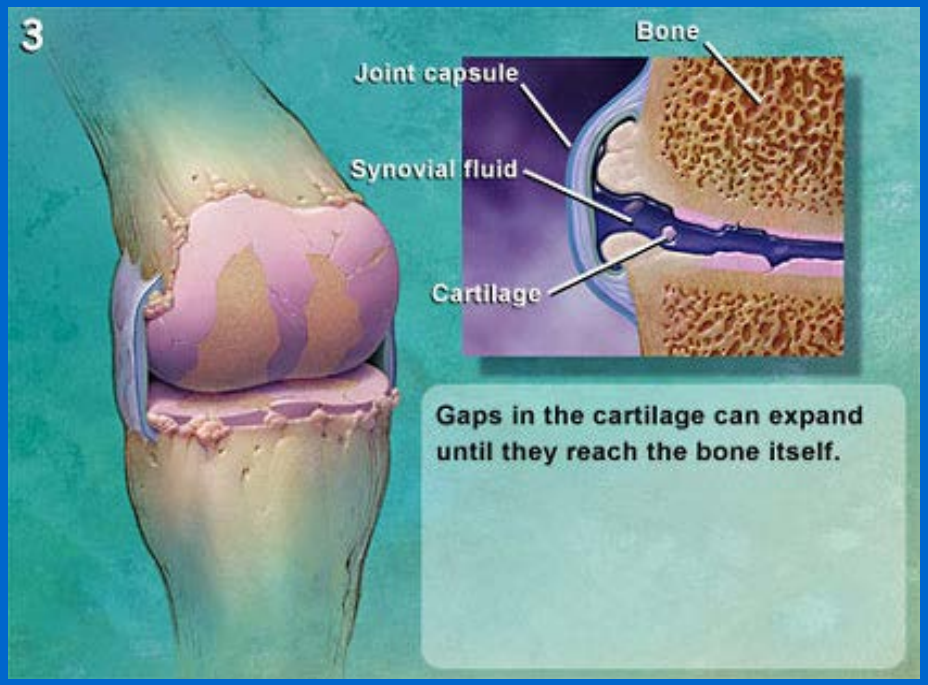
OSTEOARTHRITIS



OSTEOARTHRITIS



OSTEOARTHRITIS



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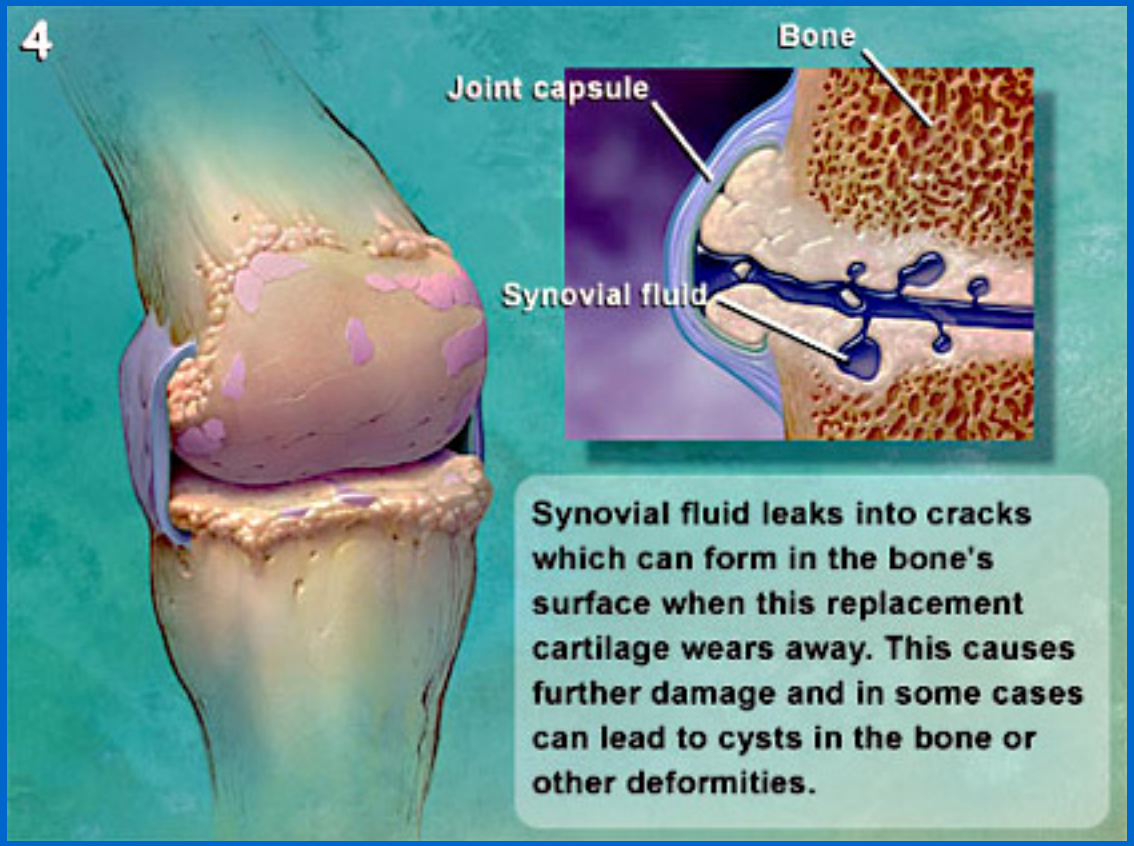

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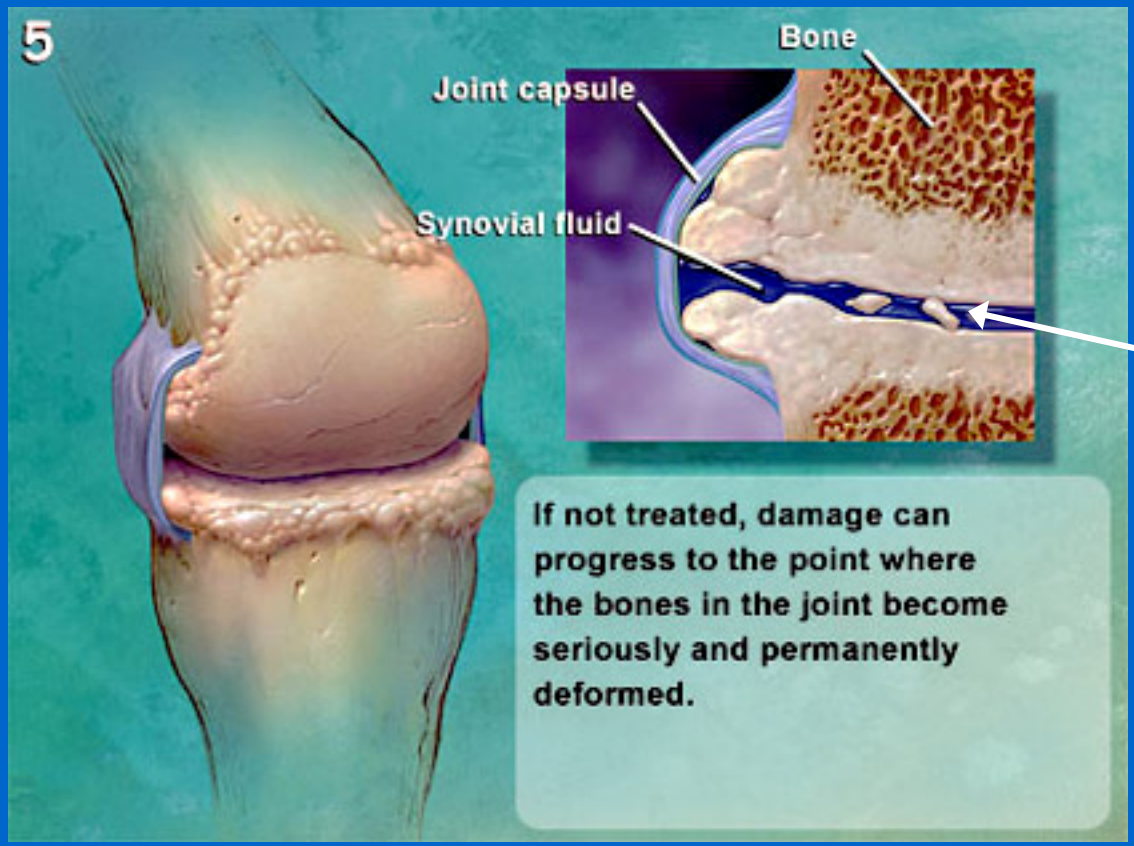
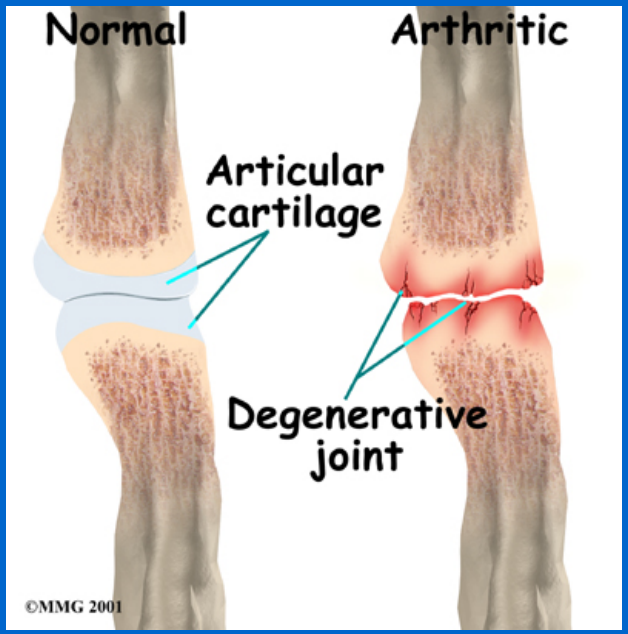


Bone Chips

CARTILAGE LOSS

- When full thickness loss of cartilage occurs, this is permanent
- Hyaline cartilage is replaced with less resilient fibrocartilage
- No drug treatment can lead to replacement of lost cartilage (including Adequan)
- Repair of cartilage before full thickness loss should be the goal of treatment



DIAGNOSIS OF JOINT DISEASE

- Lameness exam: watch horse in motion, flexion tests
- Physical exam: swelling, heat, pain on flexion, pain on palpation

DIAGNOSIS OF JOINT DISEASE

- Radiography: remember radiographic changes occur late in the pathogenesis. Cartilage damage cannot be seen readily on X-rays.
- Cartilage damage can be assessed to some degree with Xeroradiography.
- Diagnostic blocks.

Radiograph showing chip fracture in the ankle

DIAGONISTIC (Riding Exam)

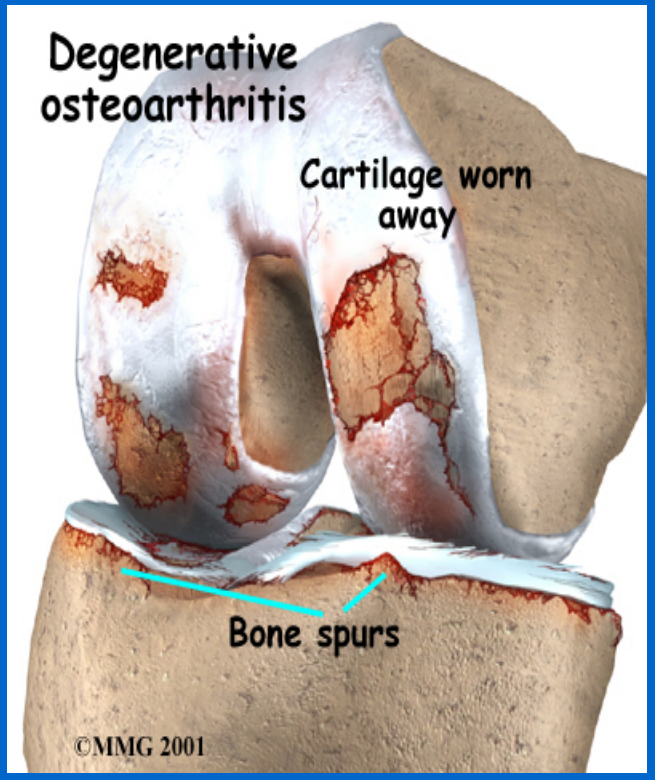
DIAGANOSIS (Riding Exam)

- Slight roughness or changes in gait.
- Subtle indications when changing leads.
- Differences in the way the horse picks up the bit.

Diagnostic Riding Exam

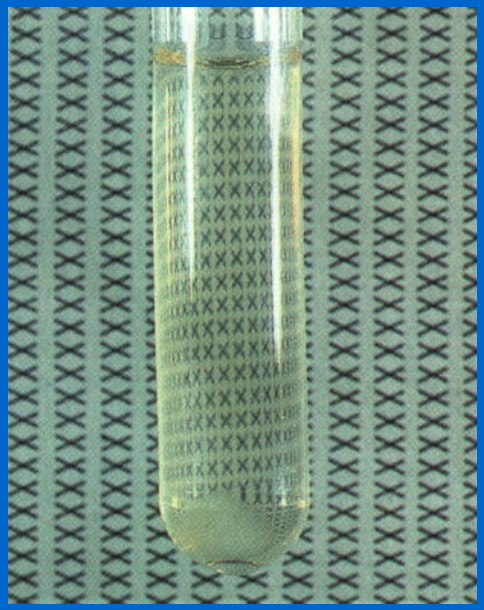
- Difference in the aggressiveness of how a horse trains

DIAGNOSIS OF JOINT DISEASE



DIAGNOSIS OF JOINT DISEASES

- Synovial fluid analysis
  - appearance and consistency
  - protein
  - WBC count
  - HA content
  - other biomarkers?



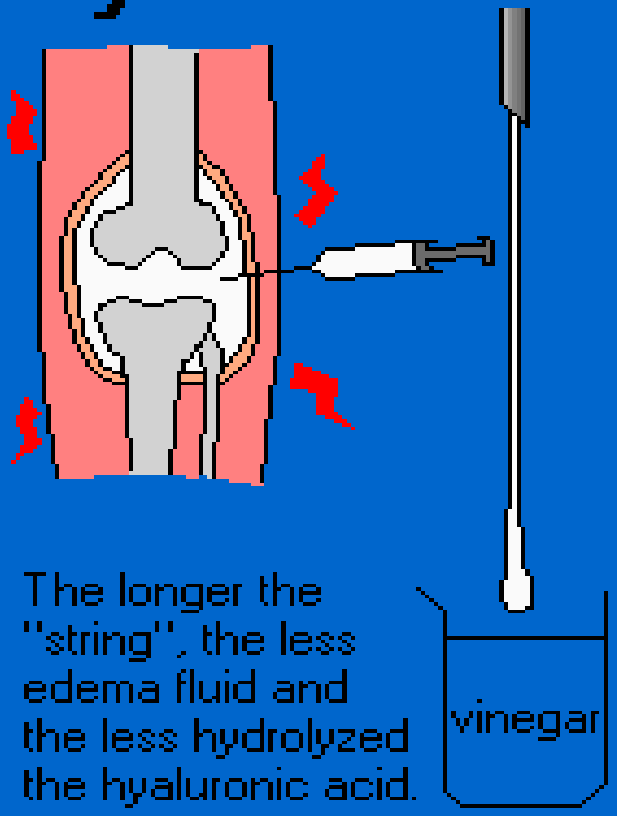
Synovial Fluid

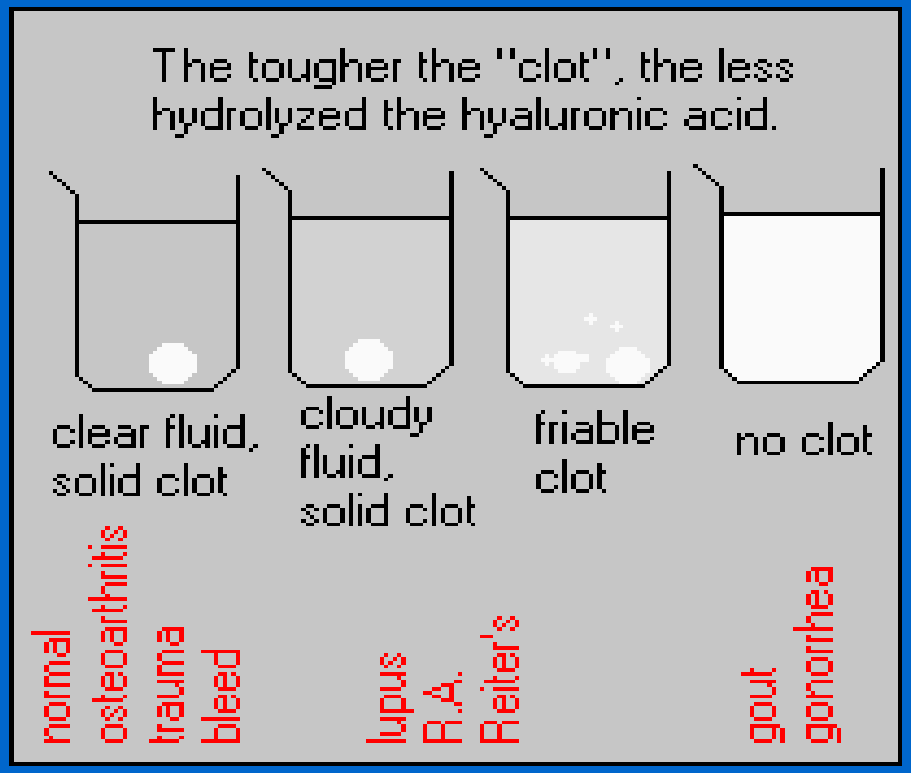
Needle is aseptically inserted into joint and fluid is withdrawn.

Visual qualitative analysis of the Synovial Fluid is an excellent indication of the health of an equine joint.

HA CONCENTRATION IN JOINT FLUID

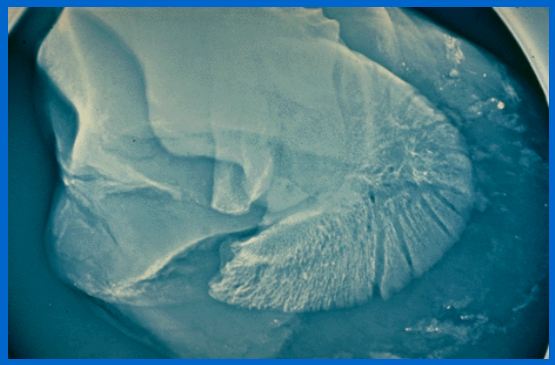
Synovial Fluid



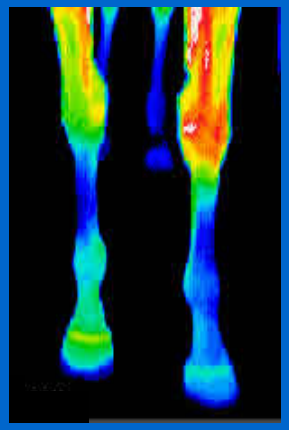


DIAGNOSIS OF JOINT DISEASE

- Other diagnostic imaging techniques:
  - Infrared Thermography
  - Magnetic Resonance Imaging (MRI)
  - Ultrasonography
  - Computed Tomography
  - Xeroradiography
  - Digital Radiography



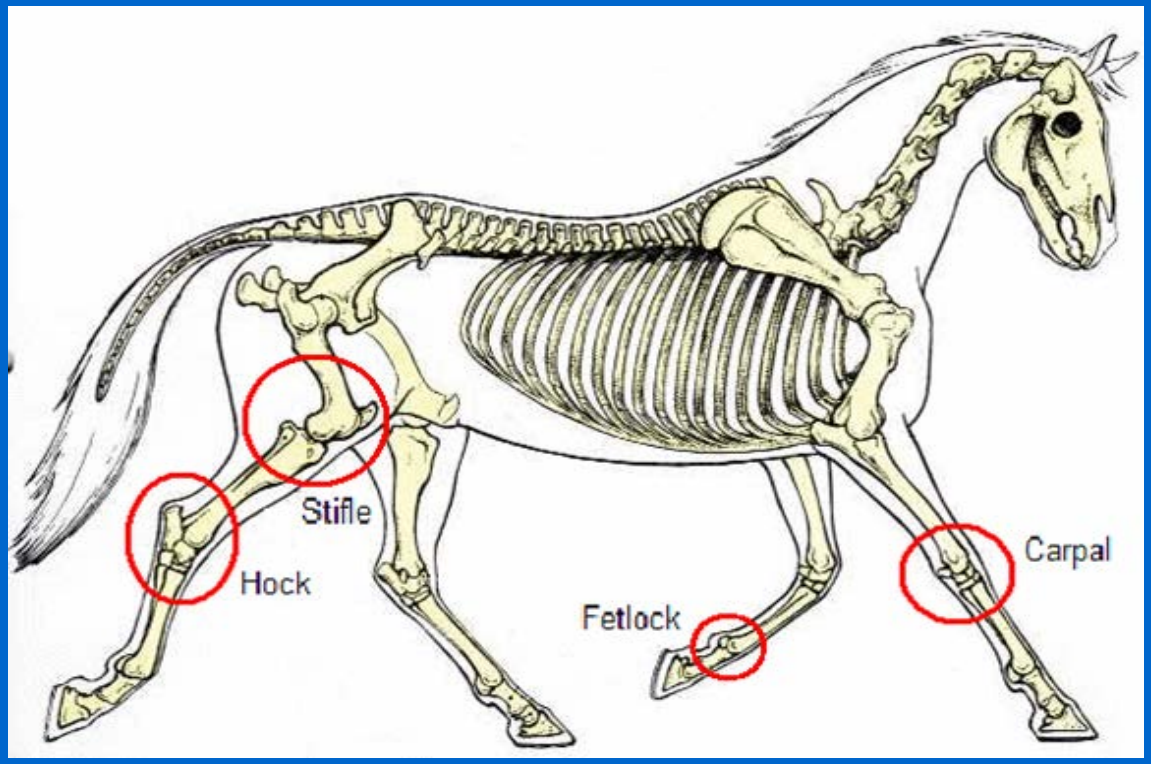
Xeroradiograph



Thermal Image

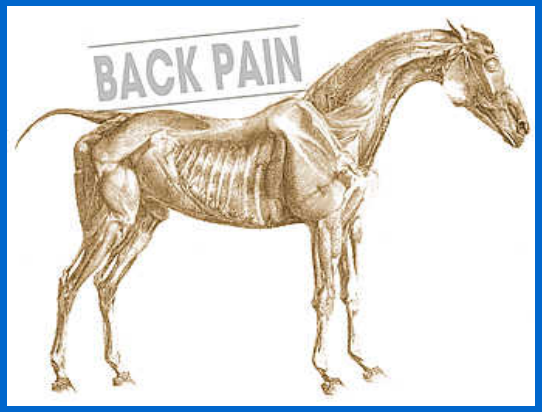
Digital X-Ray

DIAGNOSIS OF JOINT DISEASE

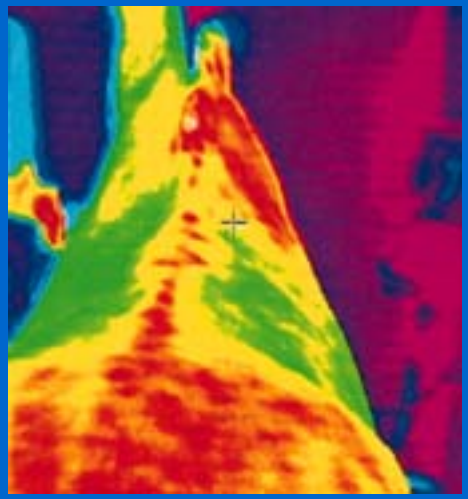


- Look at the entire horse during an examination
- In many cases more than one joint is effected

DIAGNOSIS OF JOINT DISEASE



- Problems in the lower limbs of horses can, due to disruption of normal body physiology / kinesiology / biomechanics, result in pain elsewhere.



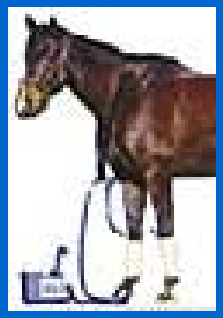
Thermography of a horse's back

TREATMENT OF JOINT DISEASES

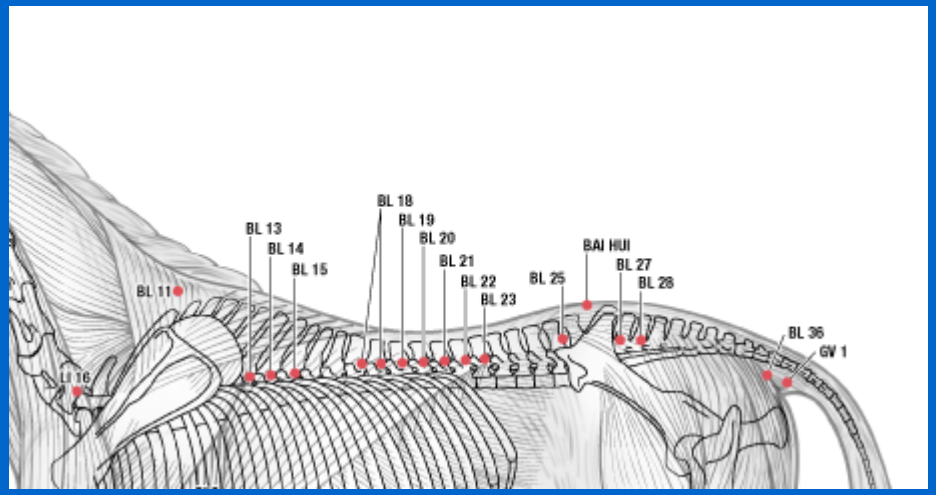
- REST: benefits are obvious; relieves use trauma and allows time for inflammation to subside and damage to heal
  - by itself, rest is usually inadequate to repair extensive damage
  - rest is often not a economically feasible option for competitive horses
  - often a part of overall approach to therapy

TREATMENT OF JOINT DISEASE

- Physical therapies: all of value in overall approach
  - cold hydrotherapy: for acute inflammation
  - heat: for chronic inflammation (> blood flow)
  - support wraps
  - liniments, braces, tighteners, vesicants
  - poultices



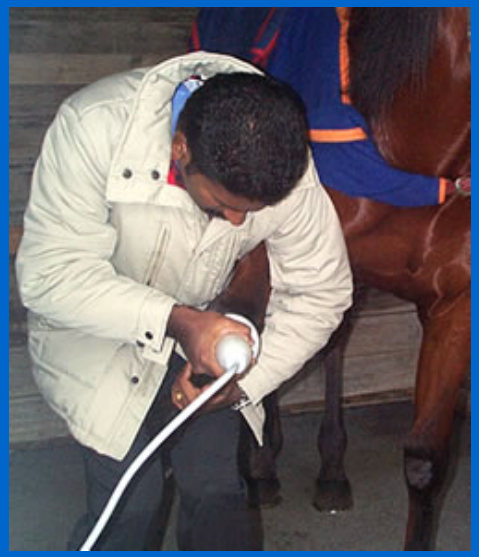
TREATMENT OF JOINT DISEASE



Acupuncture

UNPROVEN PHYSICAL THERAPIES

- These modalities are used but the true value has not been fully established by extensive research
  - ultrasonography
  - sound wave therapy
  - magnetic blankets and boots
  - laser therapy

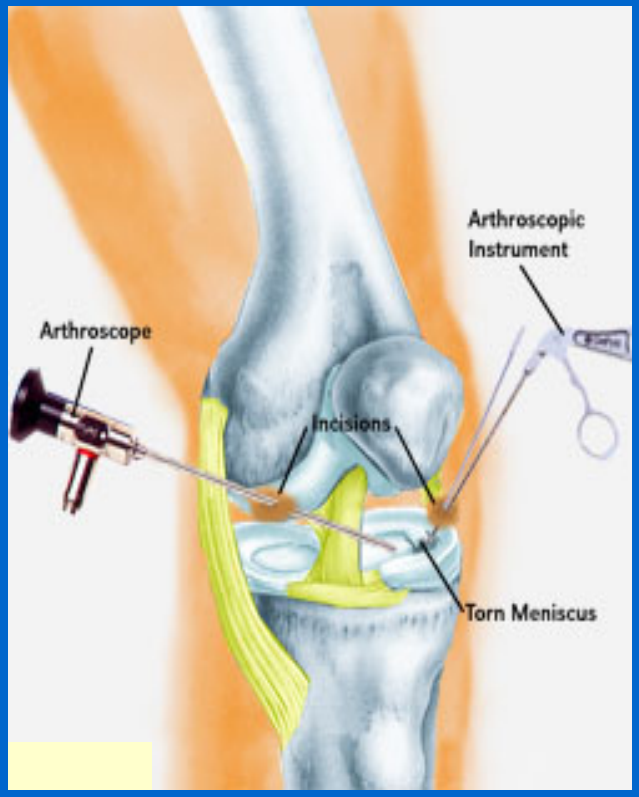


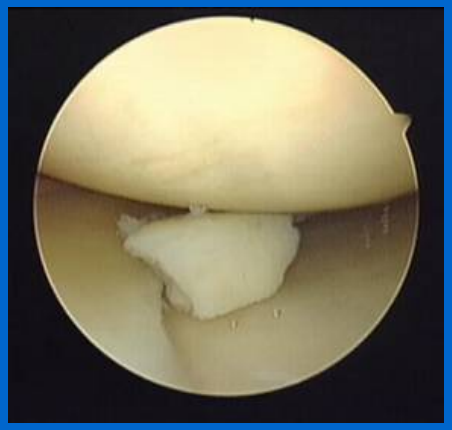
SURGERY

- Arthroscopy has improved results by decreasing trauma and scarring
- Of great value when indicated
  - remove osteochondral fragments
  - stabilize intraarticular fractures
  - remove disease cartilage and synovial membrane

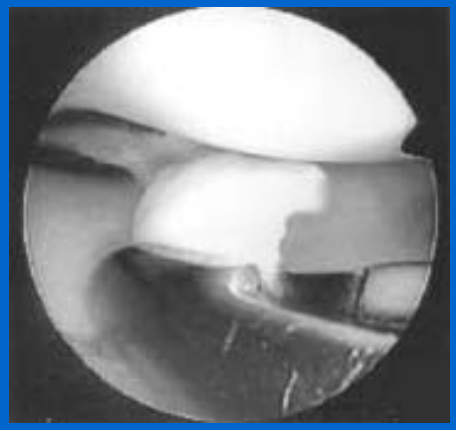
SURGERY

Arthroscopic Surgery is performed thru small incisions.





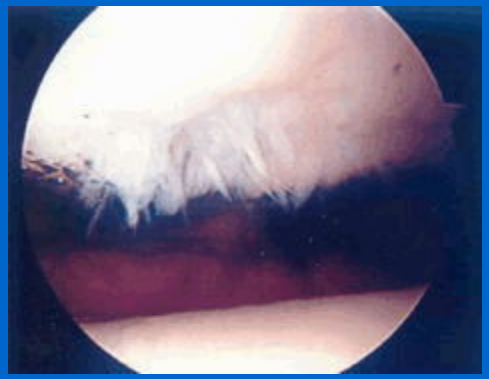
Bone Chip Fracture



Bone Chip Removal

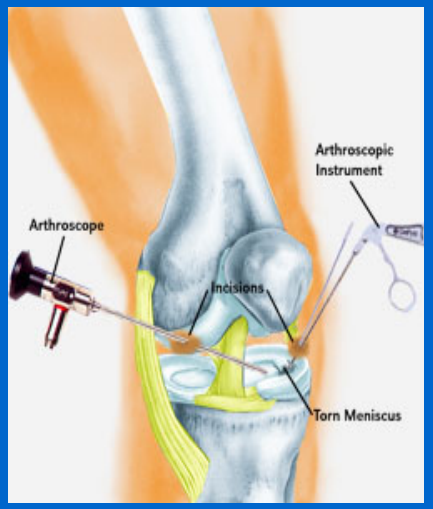
SURGERY

Arthroscopic Surgery



Before

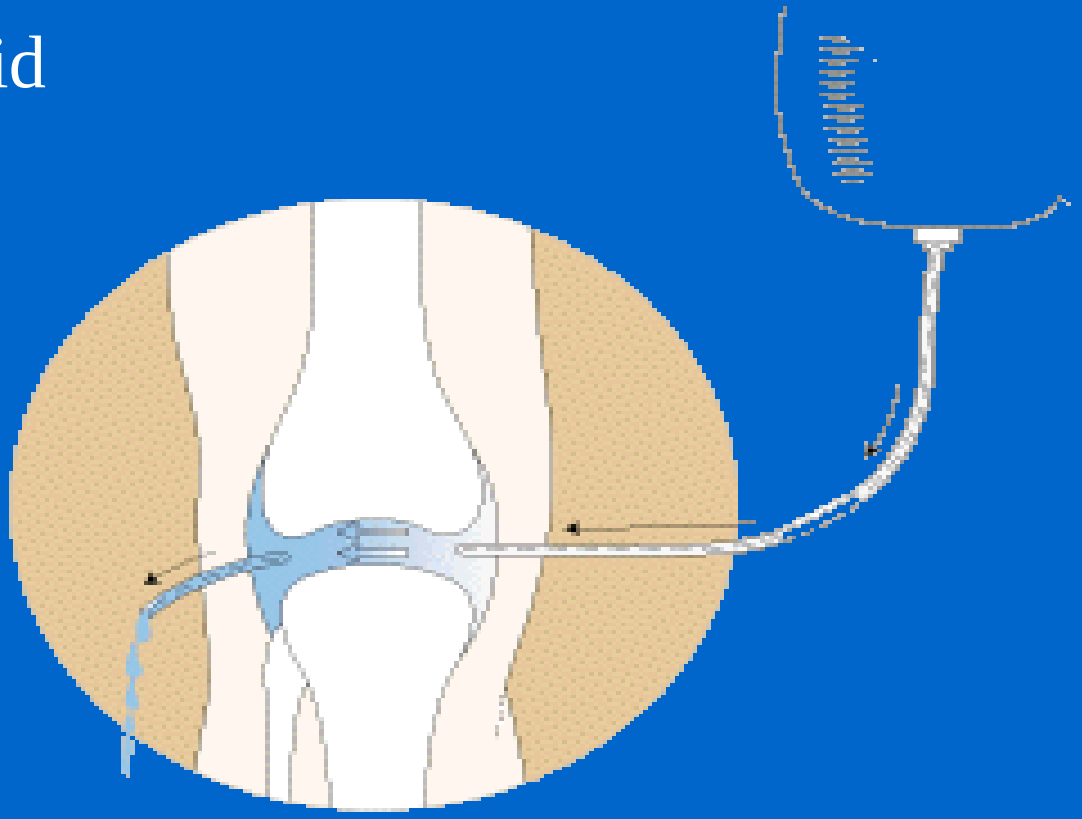
After



Using the Arthroscope and other instrumentation, diseased synovial membrane is removed.

JOINT LAVAGE

- Joint lavage to remove debris and diseased Synovial Fluid



The choice is yours. Treat the disease or treat only the pain and inflammation.

- **Adequan® i.m.** (POLYSULFATED GLYCOSAMINOGLYCAN) stimulates cartilage repair processes, while at the same time, relieves pain and inflammation.
- **Steroids** – "While corticosteroids are popular in veterinary use because they block the horse's immune response and have a short-term anti-inflammatory response, they may also retard the healing process and they have no effect on dealing with whatever caused the inflammation in the first place."[1]

Syndrome	Adequan® i.m.	NSAIDs	Steroids	Oral GAGs	Hyaluronic Acid
Mild synovitis	Yes	Temporary pain relief	Yes		Yes
Moderate synovitis	Yes	Temporary pain relief	Yes		Yes
Severe synovitis	Not initially	Yes	Yes		Not initially
Cartilage Damage	Yes	Temporary pain relief	May be a detriment		Little direct benefit
Mild DJD	Long term benefits possible	Temporary pain relief	Occasional use may be a benefit		Relief may be temporary
Severe DJD	Stabilizes DJD process	Temporary pain relief	May worsen DJD		Relief may be temporary

- **Oral GAGs** – In a randomized, blinded, controlled study using an adjuvant-induced degenerative joint (DJD) model in horses, no anti-inflammatory or chondroprotective effect could be demonstrated when oral GAGs were used to treat equine DJD.[2]
- **Hyaluronic Acid** – In a replicated, randomized, blinded trial using a chemically-induced equine carpitis model, Adequan® i.m. and intravenous sodium hyaluronate (HAIV) were administered at recommended dosage rates and evaluated. When compared to intravenous treatments, Adequan® i.m. demonstrated more rapid and significantly better recovery in lameness score, carpal flexion and stride length.[3]

MEDICAL THERAPY

CORTICOSTEROIDS

- Corticosteroids are big guns in our arsenal to reduce inflammation from traumatic joint disease and osteoarthritis.

MEDICAL THERAPY

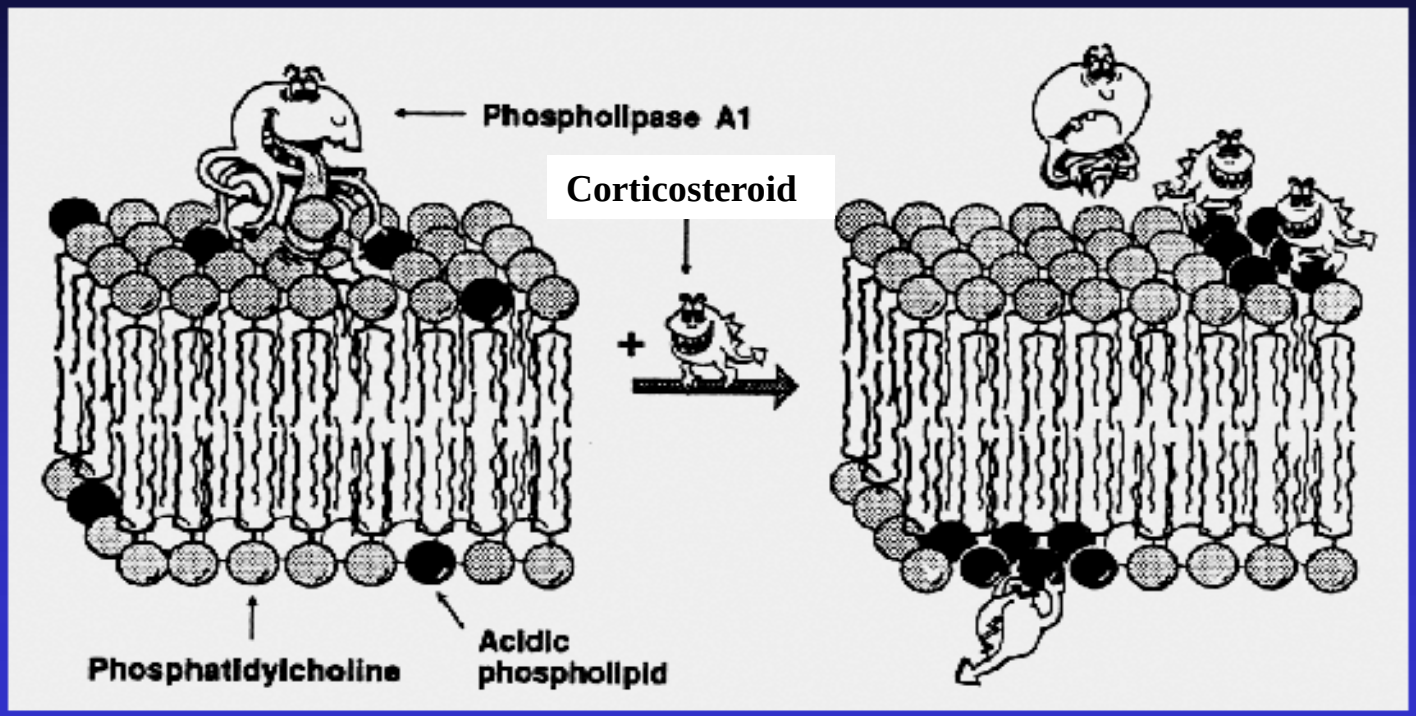
CORTICOSTEROIDS

- Powerful anti-inflammatory drugs which act by inhibiting phospholipase
- Lead to rapid decrease in the inflammatory response
- Primarily used as an intraarticular injection
- Very valuable drugs when used judiciously
- Often used with other drugs and treatments

MEDICAL THERAPY

CORTICOSTEROID MEMBRANE STABILIZATION

Corticosteroid-phospholipid interactions leading to inhibition of lysosomal phospholipase activity



MEDICAL THERAPY

TYPES OF INJECTABLE CORTICOSTEROIDS

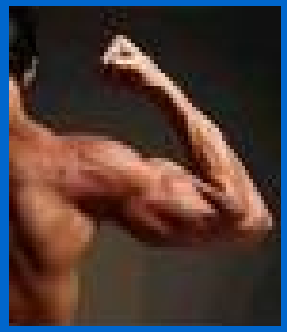
- Doses for all intraarticular corticosteroids are empirical
- Very Long Acting
  - Methylprednisolone acetate (Depo-Medrol)
- Intermediate to Long Acting
  - Triamcinolone (Vetalog / Kenalog)
- Short & Long Acting Properties
  - Betamethasone (Celestone)

MEDICAL THERAPY

CORTICOSTEROIDS STRENGTH COMPARED TO HYDROCORTISONE

TYPES OF INJECTABLE CORTICOSTEROIDS

- Methylprednisolone acetate (Depo-Medrol)
  - very long acting steroid
  - 30 times stronger than Hydrocortisone



- Triamcinolone (Vetalog / Kenalog)
  - intermediate to long acting steroid
  - 50 times stronger than Hydrocortisone

- Betamethasone (Celestone)
  - both short and long acting properties
  - 50 times stronger than Hydrocortisone

MEDICAL THERAPY

CORTICOSTEROIDS

- Potential side effects
  - delay in healing
  - decreased resistance to infection
  - reduction in PG content in cartilage
  - probably only important in misuse of steroids
  - probably more important with long acting drug

- Methylprednisolone acetate (Depo Medrol) at doses of 100 mg or greater per separate joint injection in at least 1 or more studies have shown these effects.

MEDICAL THERAPY

- Methylprednisolone Acetate (Depo Medrol) was **not** shown to have regressive effects on equine cartilage at doses of less than 100 mg per joint injection.
- Triamcinolone Acetonide (Vetalog) may even protect cartilage in the horse.
- Betamethasone was shown to have no detrimental effects even with repeated injections.
- Studies indicate judicious use of intraarticular steroids does more good than harm.

MEDICAL THERAPY

CORTICOSTEROIDS COMBINATIONS

- Methylprednisolone Acetate (Depo Medrol) is used for its very long acting effects but at a dose less than 100 mg per joint injection.

- Combined with either:
  - Triamcinolone Acetonide (Vetalog) for its more potent effects than Depo Medrol, cartilage protection ability, and intermediate to long acting effects.

Or

- Betamethasone (Sodium Phosphate and Acetate) for its relatively higher potency than Depo Medrol, both short and long acting properties, and lack of detrimental effects with repeated injections.

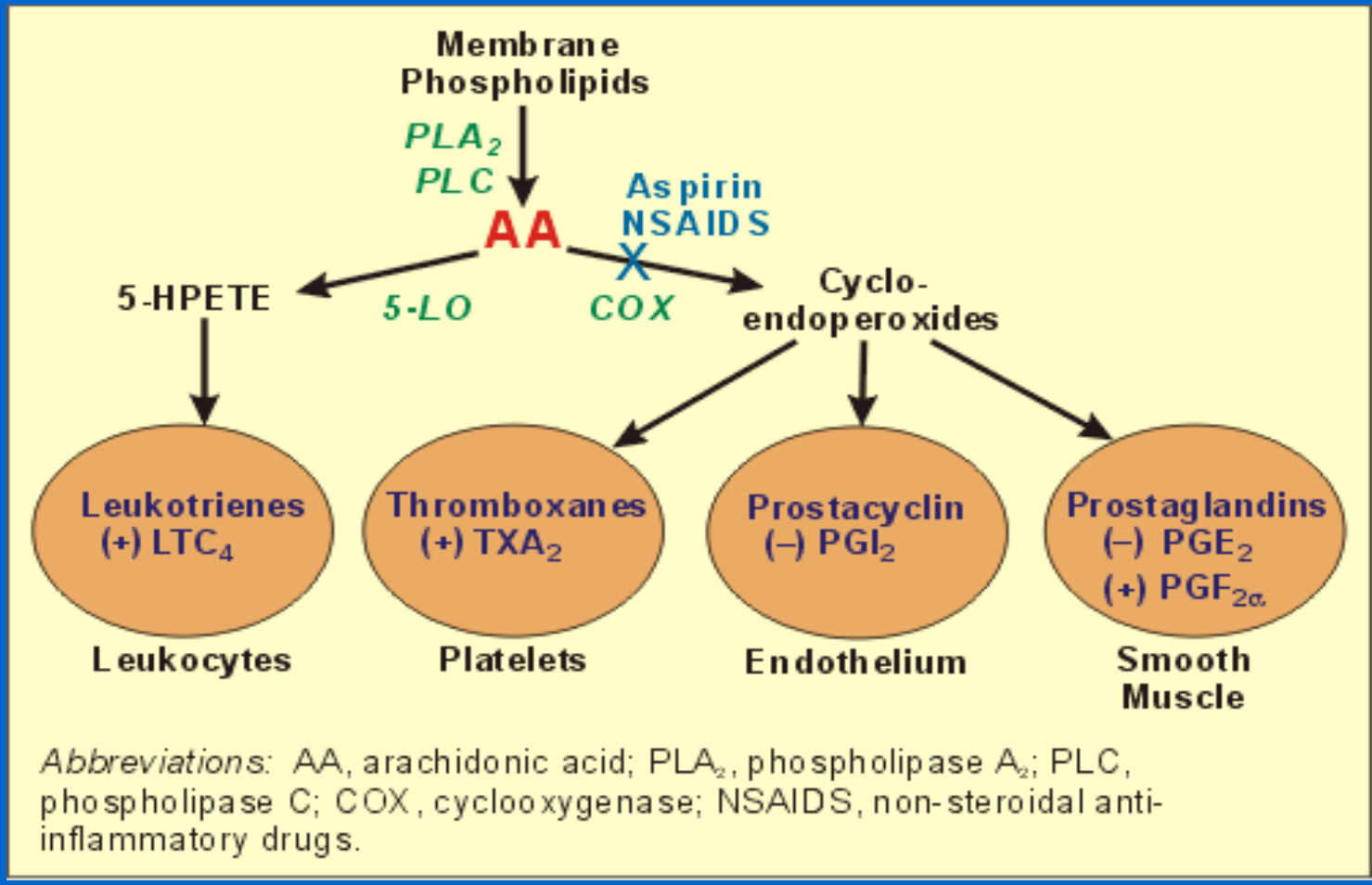
MEDICAL THERAPY

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

- Act primarily by inhibition of cyclooxygenase pathways reducing prostaglandin production
  - COX-1 inhibitors include all drugs currently approved for equine use
  - COX-2 inhibitors include newer human and canine drugs. Was believed to have less side effects, however recent reports have led some of these to be taken off the market in human medicine.

MEDICAL THERAPY

MECHANISM OF ACTION OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS



Abbreviations: AA, arachidonic acid; PLA_2, phospholipase A_2; PLC, phospholipase C; COX, cyclooxygenase; NSAIDS, non-steroidal anti-inflammatory drugs.

MEDICAL THERAPY

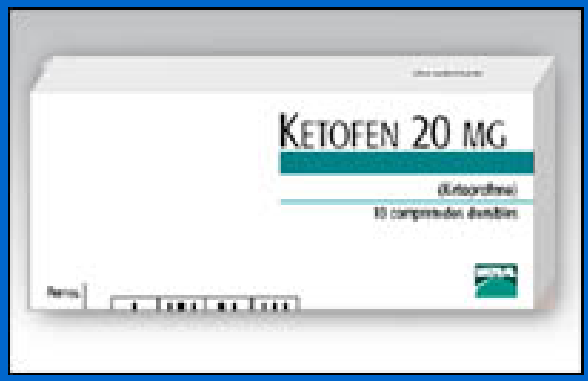
NSAIDs

- Very important drugs for the short term relief of pain and inflammation
- Usually administered daily for short periods of time
- Often part of an overall approach to joint disease therapy
- Rapid, potent, easily administered, relatively safe

MEDICAL THERAPY

NSAIDS

- Several available for horses
  - Phenylbutazone: inexpensive, effective
  - Flunixin (Banamime) good for visceral pain
  - Aspirin: inexpensive
  - Ketaprofen (Ketofen)
  - Meclofenamic acid
  - Naproxen
  - Surpass



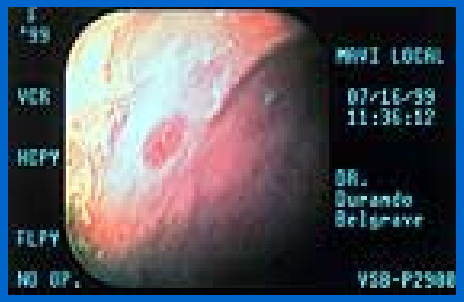
MEDICAL THERAPY

Topical Anti-Inflammatory Cream
for Use in Horses

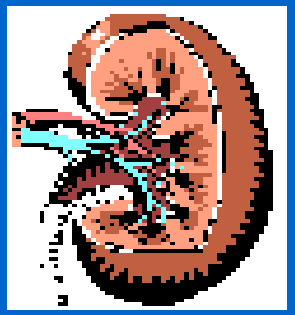
MEDICAL THERAPY

NSAIDS

- Potential side effects: most common in young foals and with chronic use
  - blood coagulopathies
  - gastrointestinal ulcers
  - oral ulcers
  - renal damage
  - decrease in proteoglycan synthesis



Stomach Ulcers



Kidney Damage

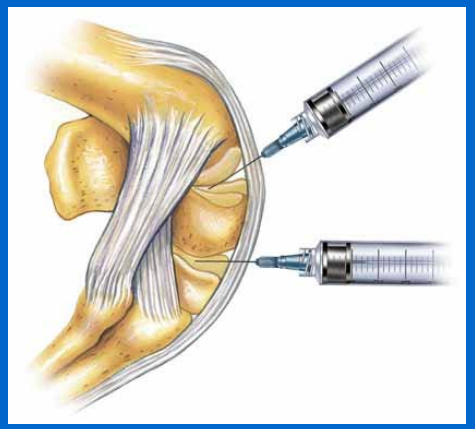
MEDICAL THERAPY

SODIUM HYALURONATE (HA)

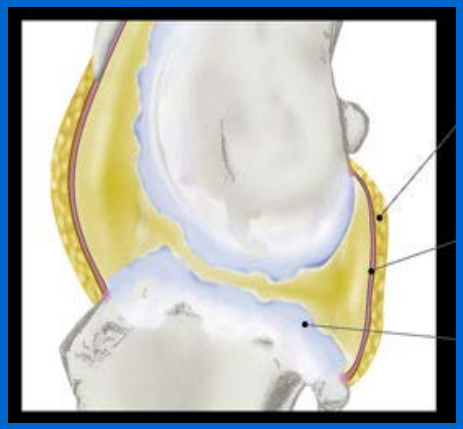
- Sodium salt of naturally occurring non-sulfated GAG
- Anti-inflammatory
  - inhibits PGE2
  - inhibits toxic oxygen radicals
  - inhibits cell migration
  - increases soft tissue lubrication

MEDICAL THERAPY

SODIUM HYALURONATE (HA)



- Helps restore the function of HA lost due to inflammation
  - improves boundary lubrication
  - increases endogenous HA production by metabolic effects on synoviocytes
  - beneficial effects on synovial fluid last much longer than the drug's presence in SF



MEDICAL THERAPY

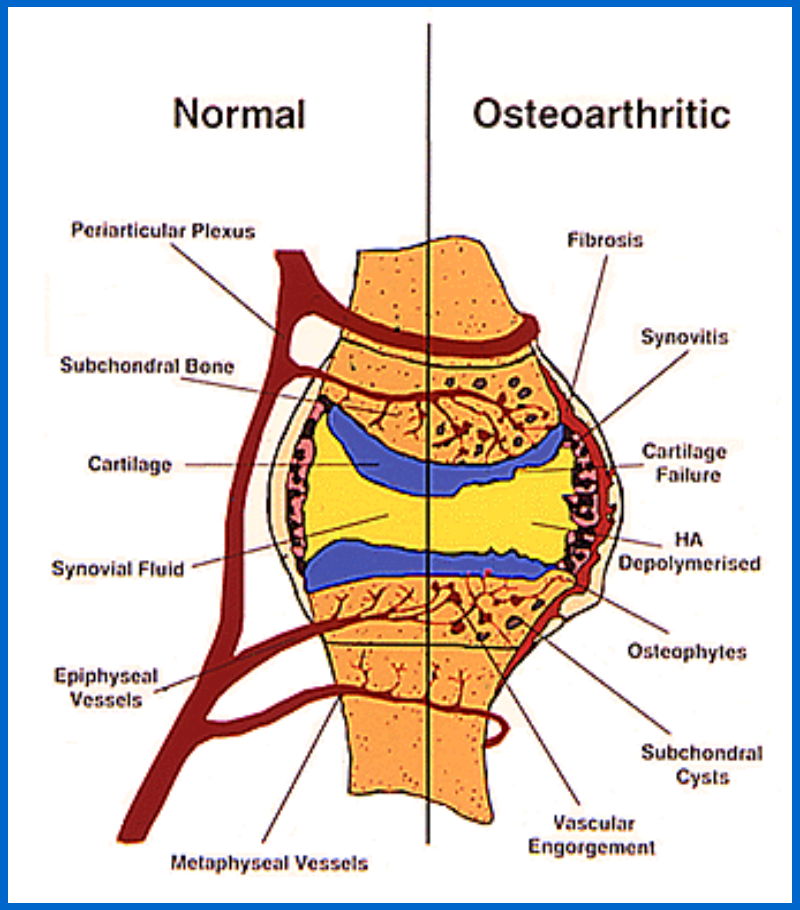
SODIUM HYALURONATE (HA)

- No evidence of any incorporation into cartilage matrix
- No evidence of direct benefits to damaged articular cartilage
- Some indirect benefits possible due to improved environment in SF (i.e.; improved chondrocyte nutrition)

MEDICAL THERAPY

SODIUM HYALURONATE (HA)

- Indications: for the treatment of mild to moderate synovitis
- Rapid clinical benefits seen after IA injection; duration dependent on MW?



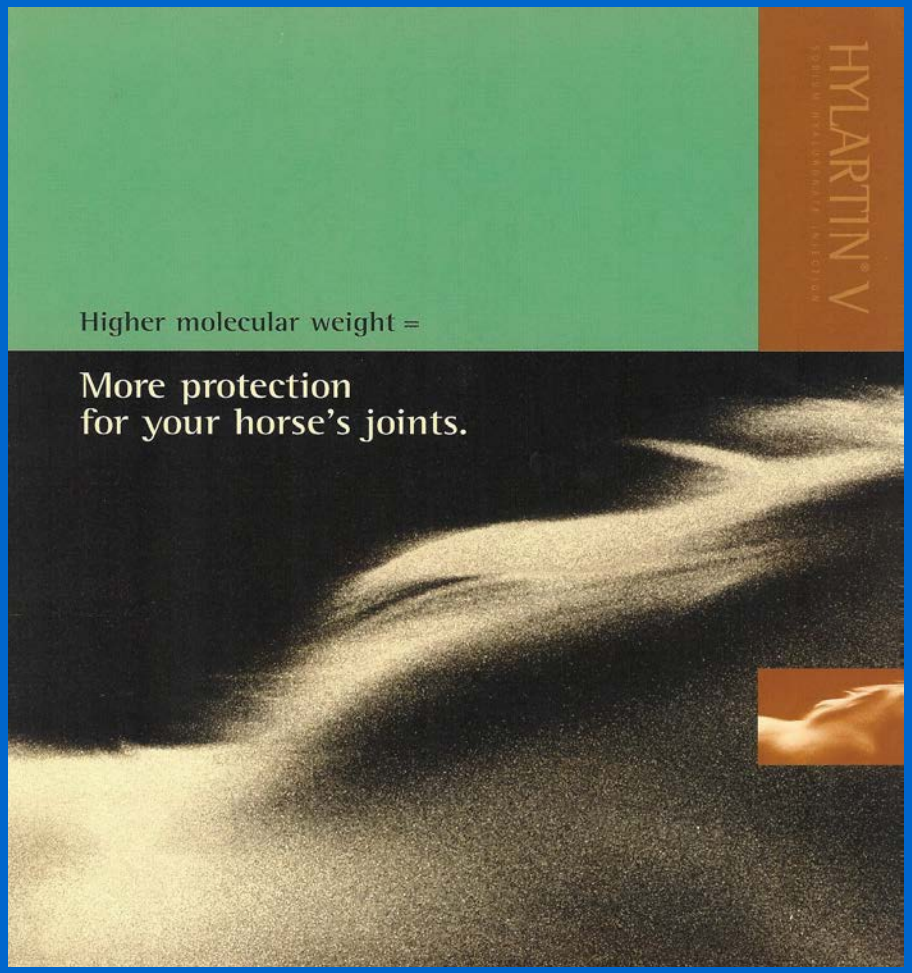
MEDICAL THERAPY

SYSTEMIC HYALURONATE (HA)

- Also available as an IV injection (Legend)
  - lesser clinical effect and shorter duration than IA
  - safe and easy to administer

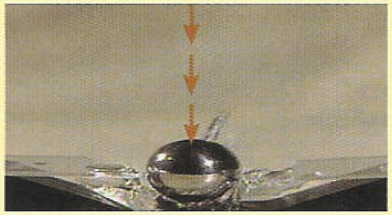
MEDICAL THERAPY

SODIUM HYALURONATE (HA)



- Available Products
  - Hylartin-V: high molecular wt
  - Hyvisc: moderate molecular wt
  - Legend IA: low molecular wt
  - Legend IV
  - Map-5: not approved for equine use

Injected directly into the inflamed joint, HYLARTIN V replaces the natural hyaluronate that provides an important lubricant for these tissues. It also stimulates the natural production of hyaluronate as a long-term benefit.



Actual video clips

Figure 1:
A glass slide coated with a low-molecular-weight hyaluronate formulation. With a molecular weight of as little as 500,000 daltons, this joint treatment can't protect the slide from the force of the ball bearing.

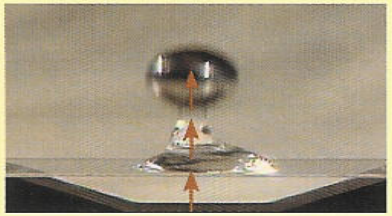


Figure 2:
A slide coated with HYLARTIN V. With a molecular weight of 3,000,000 daltons, HYLARTIN V deflects the force of the ball bearing, preventing the glass slide from breaking.

Most sodium hyaluronate equine joint treatments have comparatively low molecular weight, well below the optimum range for effective treatment. HYLARTIN V, up to *six times heavier* than low-weight competitors, has a molecular weight high enough to provide adequate healing.

Superior elasticity.

High molecular weight gives HYLARTIN V superior elasticity. Upon high velocity impact, the flexible network of long intertwined molecules of the HYLARTIN V product compresses, absorbing the trauma of impact. The molecules then spring back to their previous shape, ready to help absorb the next shock.

The high molecular weight of HYLARTIN V provides positive results by serving as a barrier to protect the tissue within the joint cavity. Low-molecular-weight sodium hyaluronate has no filter effect at all, or it is considerably reduced because its short molecular chains cannot form filters of entangled molecules of the same high efficiency as high-molecular-weight sodium hyaluronate.

Get straight to the problem.

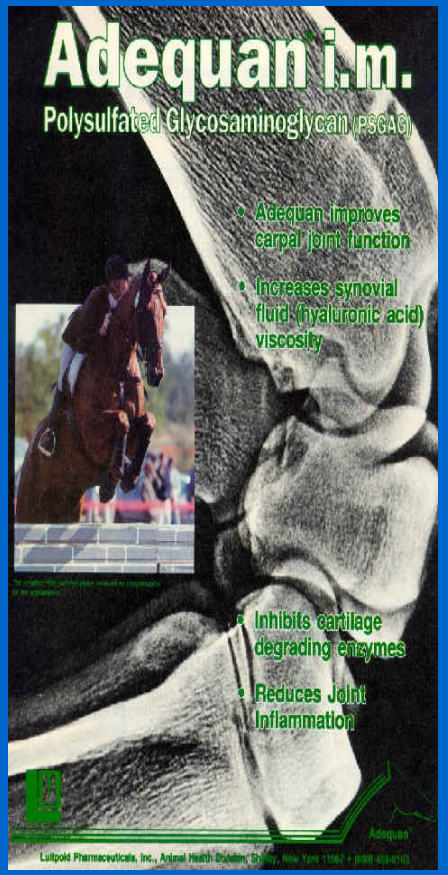
Weaker low-molecular-weight treatments require repeated applications – but easy-to-use HYLARTIN V gets straight to the problem with just one intra-articular treatment, healing most lameness after just one administration.

Hylartin V is a product of Pfizer Animal Health

MEDICAL THERAPY

PSGAG

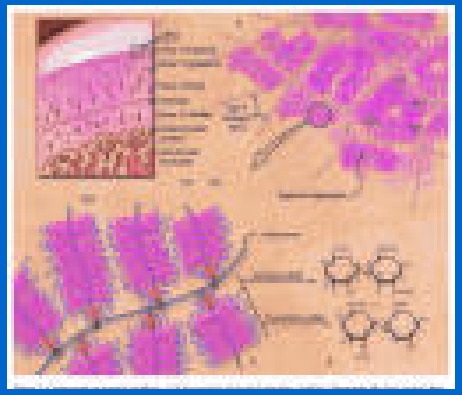
- Polysulfated glycosaminoglycan (3-4 sulfate groups per disaccharide group)
- Made by extracting chondroitin sulfate from bovine tracheal tissue and semi-synthetically adding sulfate
- Human use first described in 1959
- Horse and dog use first described in 1966



MEDICAL THERAPY

PSGAG

- Low molecular weight allows the molecule to pass readily through the synovial membrane
- PSGAG is taken up into cartilage by diffusion
- Drug is then deposited into the cartilage matrix although the exact binding site is not known

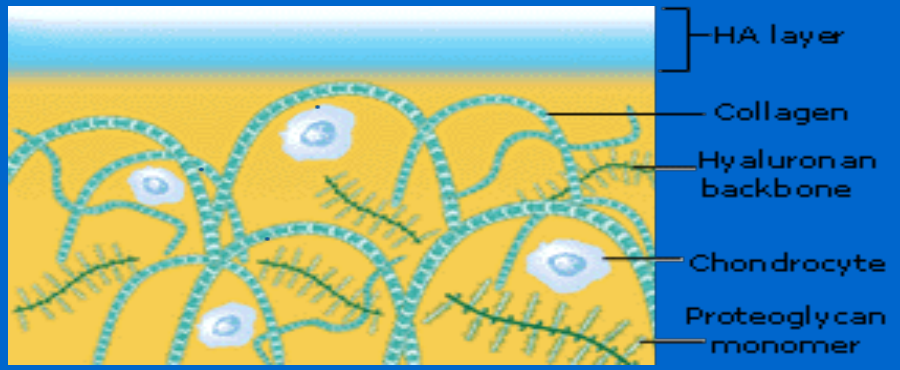


Proteoglycan Complexes in the Cartilage Matrix

MEDICAL THERAPY

PSGAG

- Biochemical effects in diseased joints include incorporation into articular cartilage matrix
  - may be used as a substrate for cartilage repair
  - may improve the biochemical properties of damaged matrix
  - may act as a substrate for enzyme action thus protecting cartilage matrix



MEDICAL THERAPY

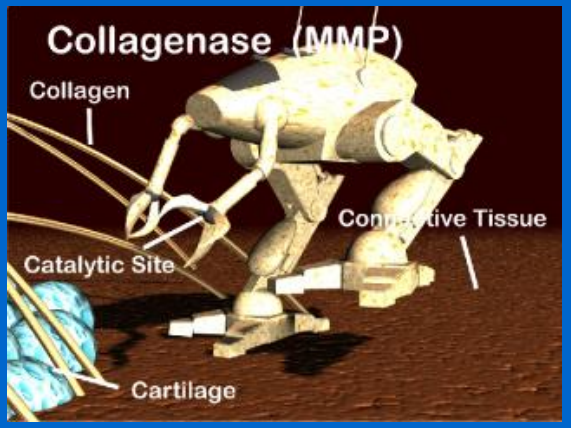
PSGAG

- Inhibits enzymes that degrade synovial fluid and cartilage matrix components
  - potent inhibitor of many major enzymes at very low drug concentrations
  - inhibition may be competitive, electrostatic, or involve inhibition of enzyme activation
  - inhibition of many enzymes has been shown in vitro and in vivo at concentrations readily achievable in joint tissues

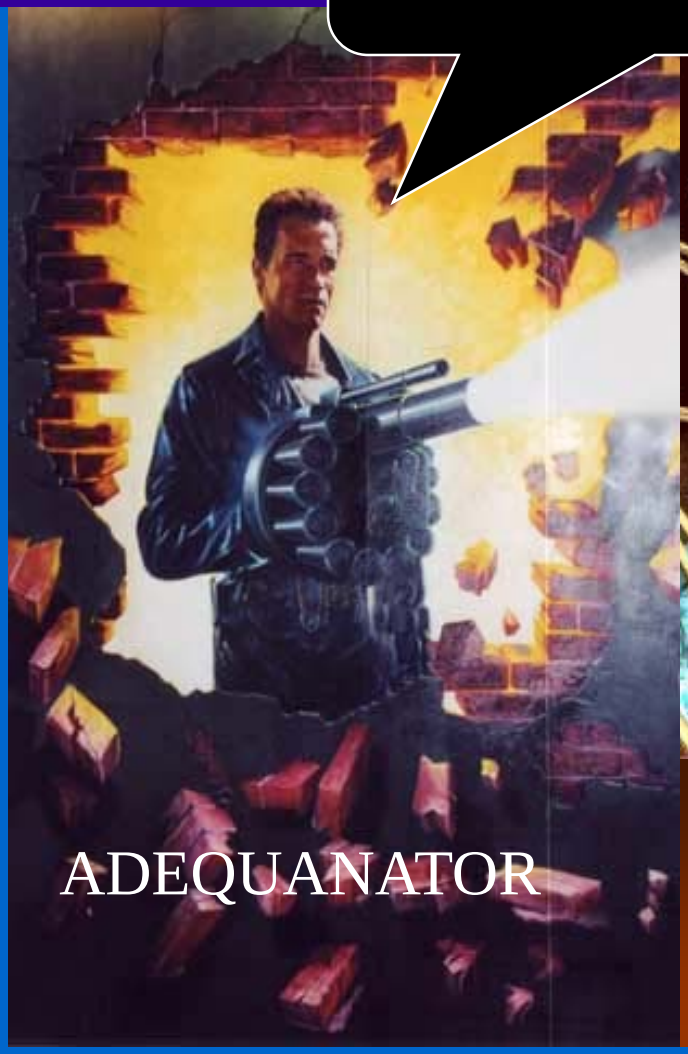
MEDICAL THERAPY

ENZYMES INHIBITED BY PSGAG

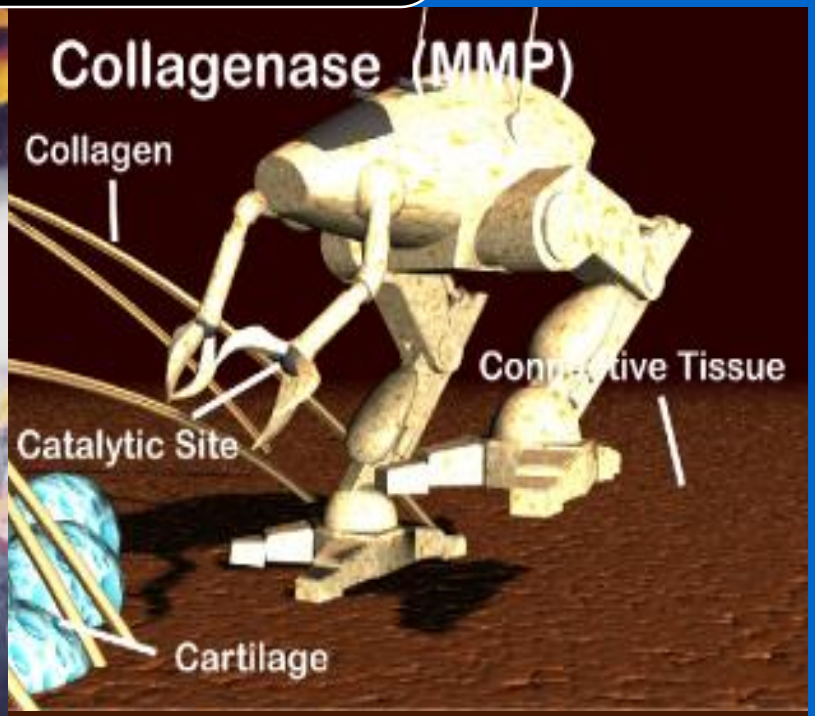
- Stromelysin (neutral metalloprotease) very potent degrader of PG complexes
- Elastase degrades a wide range of connective tissues including collagen and proteoglycans
- Hyaluronidases degrade HA
- PSGAG thus inhibits loss of proteoglycan, collagen and HA by enzyme action



HASTA LA VISTA, BABY!



ADEQUANATOR



EVIL CARTILAGINOUS ENZYME

MEDICAL THERAPY

PSGAG

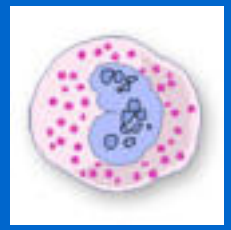
- PSGAG has been shown to have numerous anabolic effects on diseased joint tissue
  - stimulates proteoglycan synthesis (confirmed in equine cell cultures)
  - stimulates collagen synthesis (confirmed in equine cell cultures)
  - stimulates synthesis of HA by synoviocytes (has been shown in vivo in horses)

MEDICAL THERAPY

PSGAG

Adequan® i.m.
(POLYSULFATED GLYCOSAMINOGLYCAN)

- PSGAG has been shown to possess anti-inflammatory effects by several mechanisms:
  - inhibits synthesis of prostaglandin E2
  - PSGAG decreases production of toxic oxygen radicals by neutrophils (white blood cell)
  - inhibits the complement cascade
  - inhibits blood coagulation



White Blood Cell

MEDICAL THERAPY

PSGAG

The ideal drug for the treatment of osteoarthritis should:

- Inhibit cartilage matrix degeneration
- Stimulate production of cartilage matrix components
- Improve synovial lubrication
- Decrease inflammation
- Relieve pain

MEDICAL THERAPY

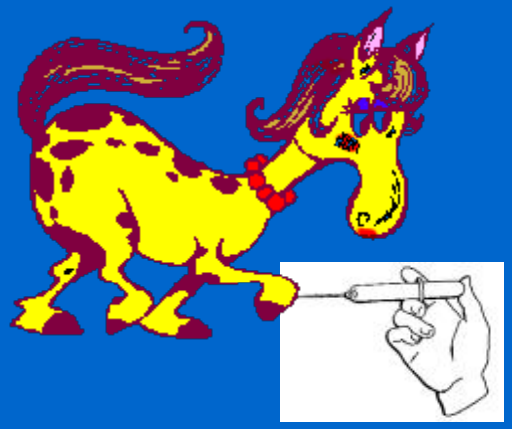
PSGAG

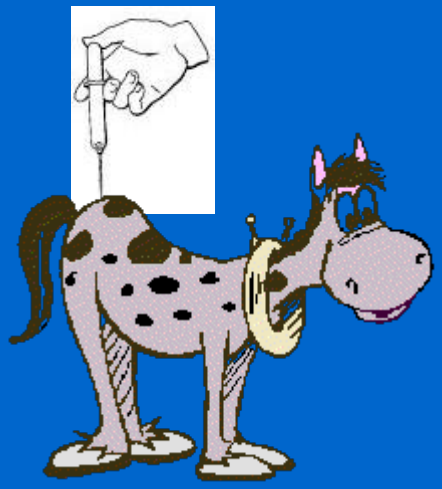
- PSGAG treatment results in a reduction of the net loss of cartilage matrix and synovial fluid components
- Chondroprotective drugs which can reduce this net loss in laboratory tests or in vivo
- DMOADs are drugs which prevent or reverse the morphologic changes of DJD in vivo

Adequan® i.m.
(POLYSULFATED GLYCOSAMINOGLYCAN)

RX WORKS

MEDICAL THERAPY





PSGAG

- Adequan IA was approved by FDA for horses in 1984
  - 250 mg once a week for up to 5 weeks
- Adequan IM was approved by FDA for horses in 1990
  - 500 mg every 4 days for 7 injections

MEDICAL THERAPY

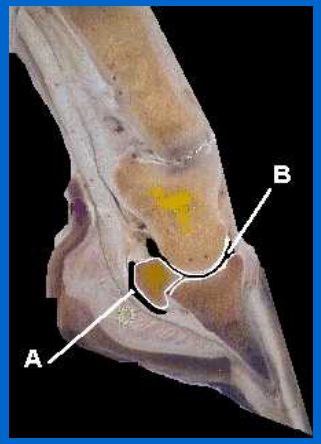
ADEQUAN AS A PREVENTIVE

- Adequan is often given as a preventive:
  - to yearlings as a preventive for clinical signs due to Developmental Orthopedic Diseases (OCD, epiphysitis)
  - to horses in intense training to prevent or lessen the effects of joint injuries
  - to performance horses pre-performance to prevent joint injuries and enhance performance

MEDICAL THERAPY

ADEQUAN: OTHER EQUINE USES

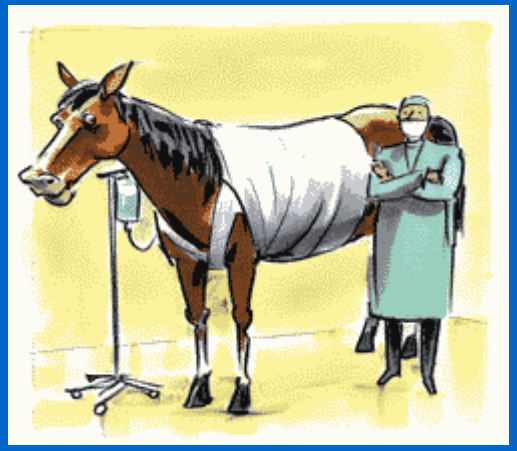
- Navicular Disease: similar to DJD in many respects
- Bursitis: seems to work very well for biciptal bursitis in performance horses
- Tendonitis: experimental and clinical data support the use of PSGAG
- Corneal ulcers: cornea is an avascular connective tissue



MEDICAL THERAPY

COMBINATIONS WITH OTHER DRUGS

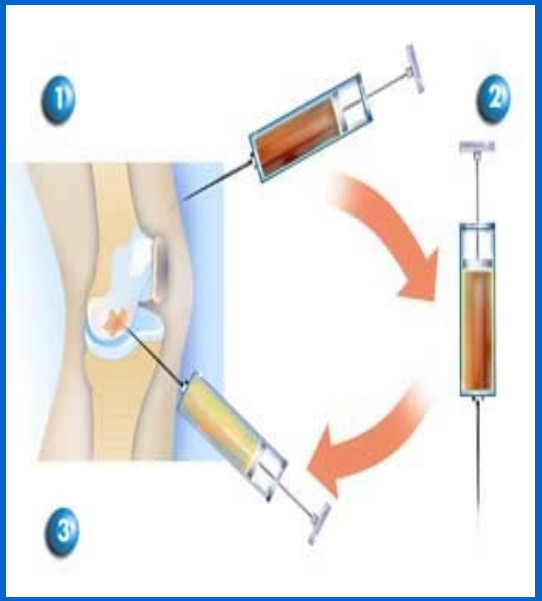
- Adequan IA is often combined with other drugs (these drugs should not be mixed in the same syringe):
  - Amikacin
  - corticosteroids
  - HA
  - systemic NSAIDs



NON PHARMALOGICAL TREATMENT

IRAP / ORTHOKINE

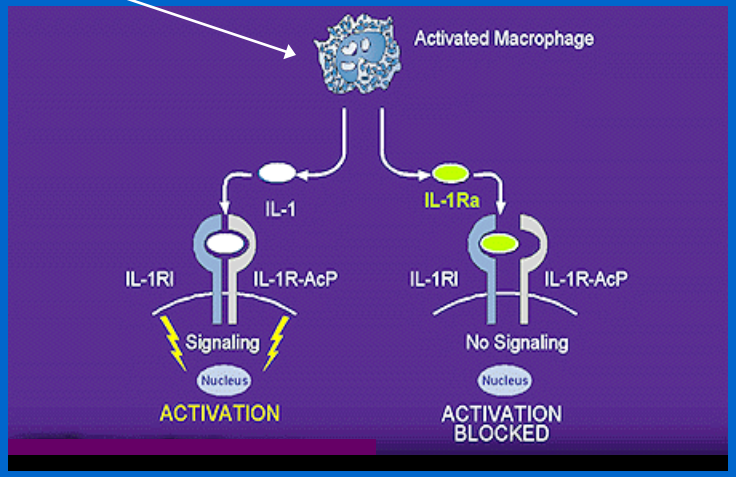
- Interleukin -1 Receptor Antagonist (IL-1 RA).
- Processed from the horse's own blood.
- Delivered back via interarticular injection to the same horse's affected joints.
- Natural Regenerative Therapy.



IRAP / ORTHOKINE INTERLEUKIN -1 RECEPTOR ANTAGONIST (IL-1 RA)

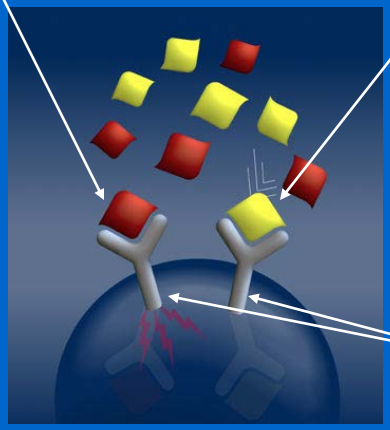
NON PHARMALOGICAL TREATMENT

White Blood Cell



Interleukin – 1 (IL-1)

Interleukin -1 Antagonist (IL-1 RA)



Cell Receptor Sites

Chondrocyte (Cartilage Cell)

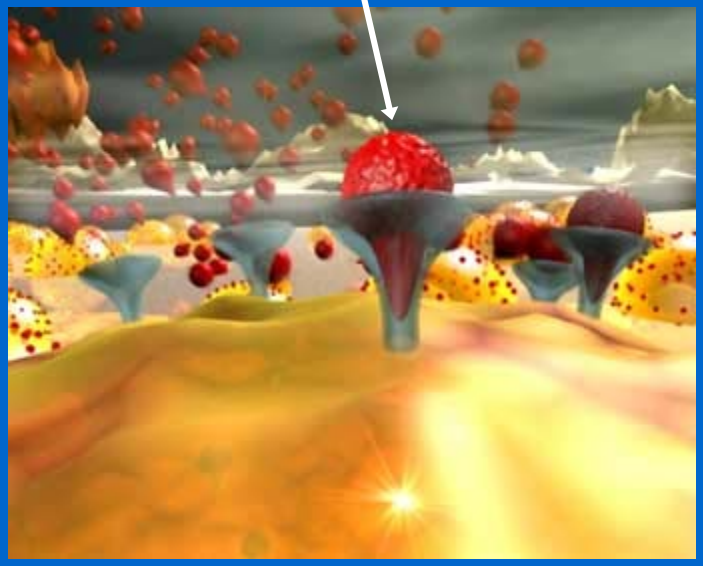
- Interleukin -1 (IL-1) the chief inflammatory mediator that bonds to cell receptor sites and drives the inflammatory process with production of tissue necrosis factor (TNF).
- IRAP / Orthokine which is Interleukin -1 Receptor Antagonist (IL -1 RA) competes for the same bonding sites as Interleukin -1.
- Therefore, Interleukin-1 Receptor Antagonist (Il-1 RA) blocks the inflammatory driven process of Interleukin-1 (IL-1)

NON PHARMALOGICAL TREATMENT

- In cases of osteoarthritis, there is not sufficient IL-1 RA produced to block the destructive effects of increased IL-1.

- Results in:
  - inflammation
  - joint pain
  - cartilage destruction

Interleukin -1 (IL-1) (Red Sphere) bonding to receptor site and driving the inflammatory process



IRAP / ORTHOKINE

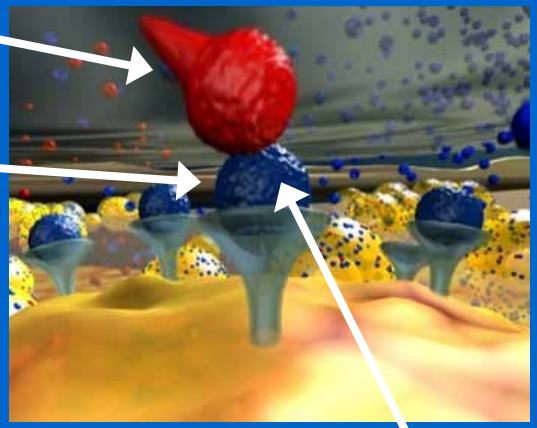
NON PHARMALOGICAL TREATMENT

- Harvested blood is incubated for 24 hours in the processing system to increase anti-inflammatory and regenerative properties.
- Interleukin -1 receptor antagonist (IL-1 RA) rich material is then injected into the affected joints to block the inflammatory process.

IRAP / ORTHOKINE

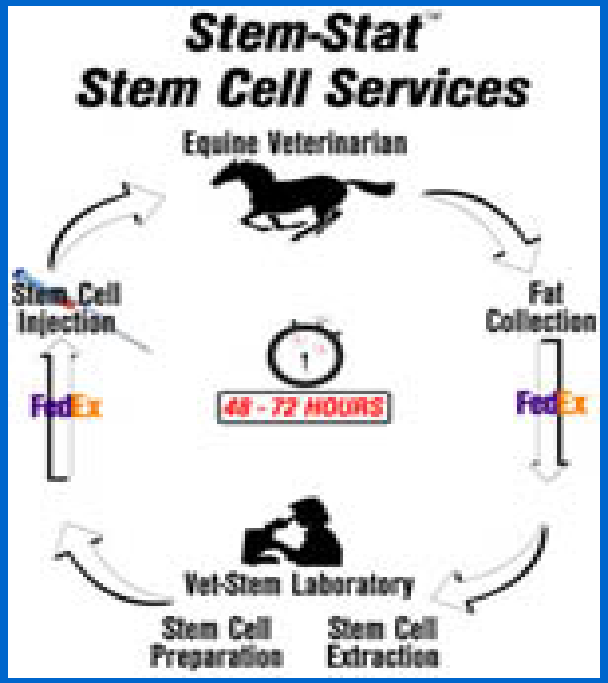
NON PHARMALOGICAL TREATMENT

- Interleukin-1-Receptor Antagonist (blue spheres) has occupied the receptors. IL-1 is kept away and the inflammation process is blocked.



- This is a Non Pharmalogical process.
- We use the horse's own natural resources to heal itself.
- No drugs are used.

ADJUNCT AND REGENERATIVE THERAPY



Fat is collected from the horse. Stem cells are extracted from the fat material, prepared, and reinjected into soft tissue injuries (ligaments and tendons).

ADJUNCT AND REGENERATIVE THERAPY

Hyperbaric Oxygen Therapy

Pressurized Oxygen Treatment

- Promotes Healing of Bones, Tendons, and Ligaments
- Excellent for Treating Respiratory Infections
- Many other applications

THERAPIES NOT APPROVED FOR USE IN THE U.S . HOWEVER AVAILABLE THROUGH SPECIAL PERMIT

CEVA Pharmaceutical

Tildren

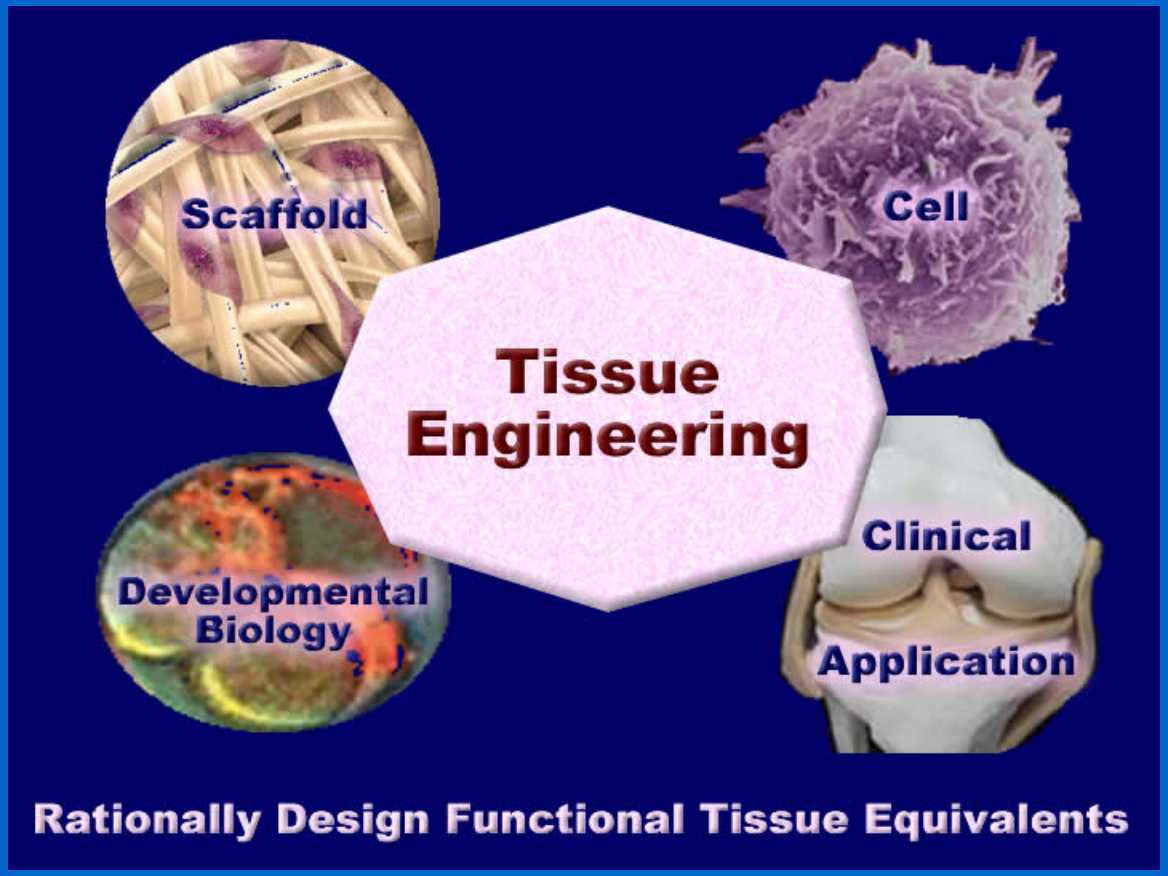
- Tiludronic acid is an active ingredient whose main pharmacological property is the inhibition of bone re-absorption.

- Has been an effective treatment for Navicular Syndrome

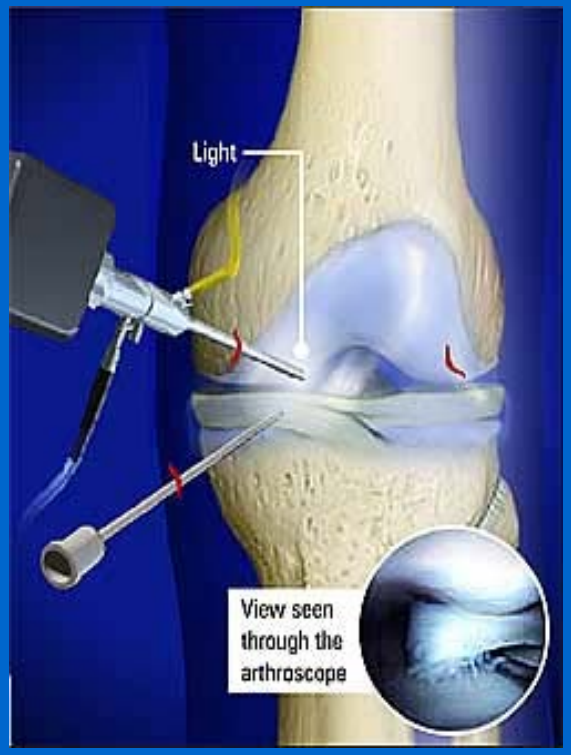
Equigen

Equine Growth Hormone

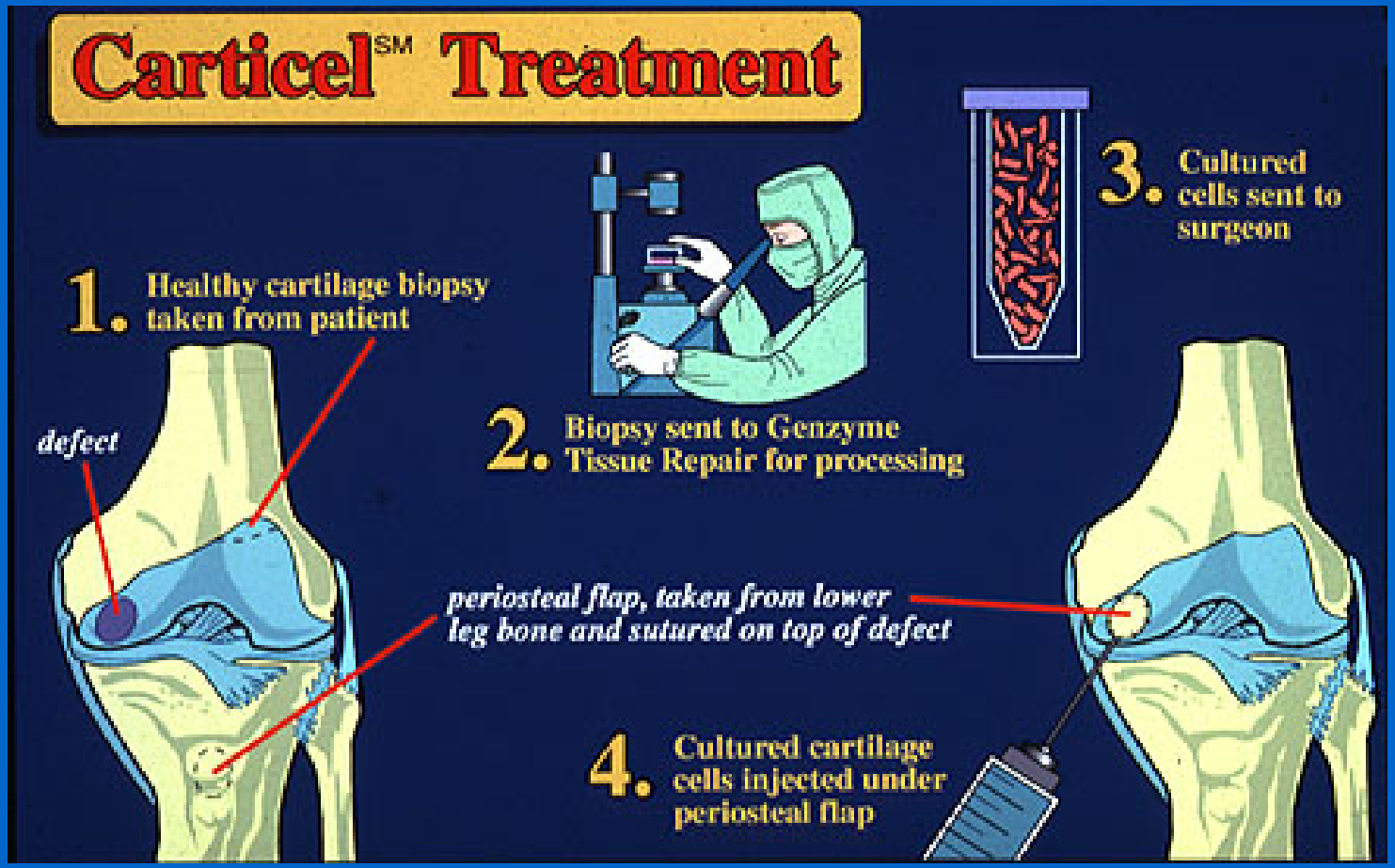
JOINT TREATMENT OF THE FUTURE



JOINT TREATMENT IN THE FUTURE

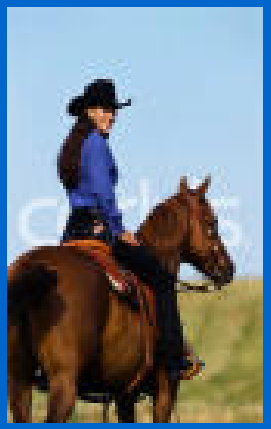


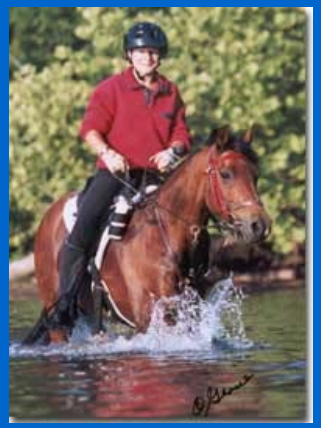
JOINT TREATMENT IN THE FUTURE



TREATING DEGENERATIVE JOINT DISEASE

- There is no set regimen. The need for follow up treatment is dependent on:
  - severity of the joint disease
  - joints involved
  - use of the horse
  - intensity of training and competition





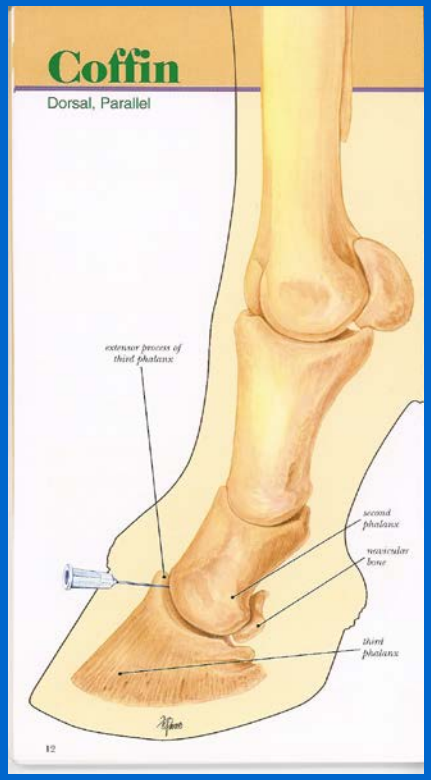
Dr. Casey's Medical Treatment for Joint Disease

Joint Aspiration and Injection Procedure:

- Cleansing and Preparation with Surgical Scrub etc.
- Joint Aspiration and Synovial Fluid Evaluation
- Injection/Infusion with Depo Medrol (low motion joints)
- Injection/Infusion with Vetalog and Betamethasone (most joints)
- Injection/Infusion with Adequan I.A.
- Injection/Infusion with Hylartin V
- Injection/Infusion with Amikacin
- Apply Gauze dressing and Sof-Kling Bandage

INTERARTICULAR JOINT INJECTIONS

INTERARTICULAR JOINT INJECTIONS



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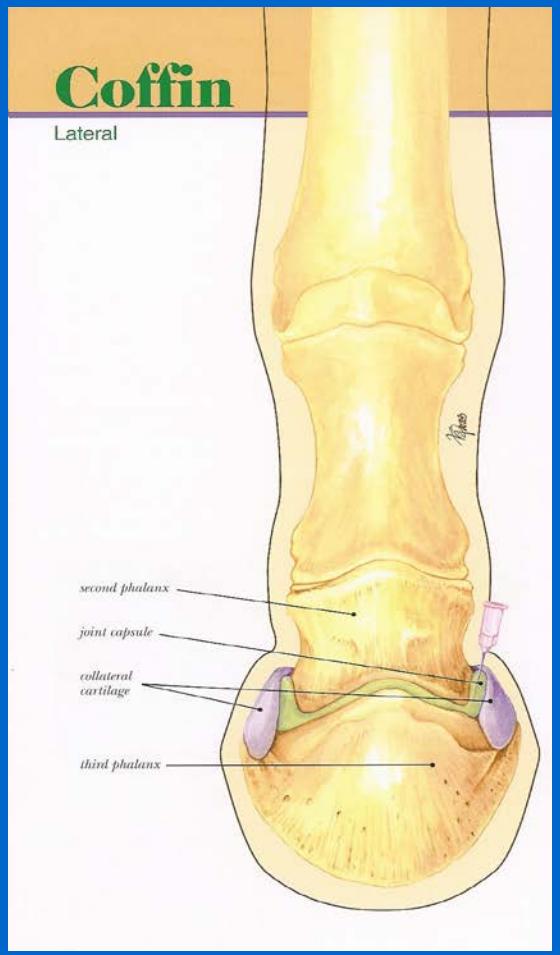

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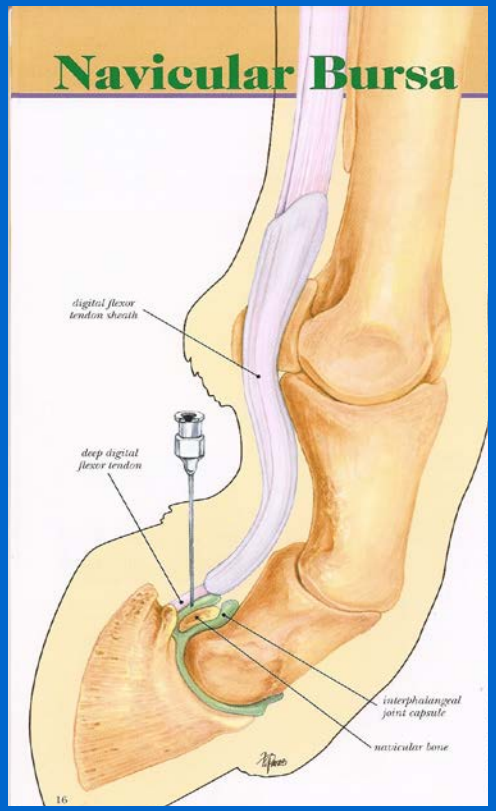
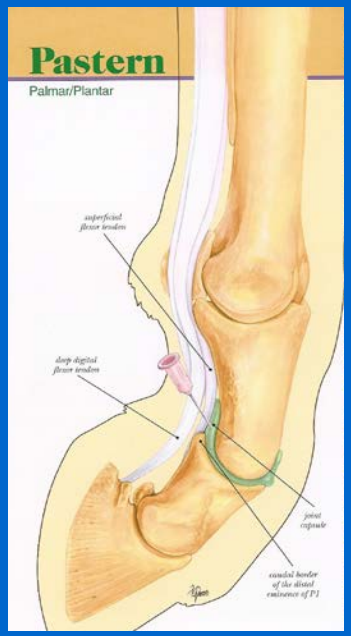
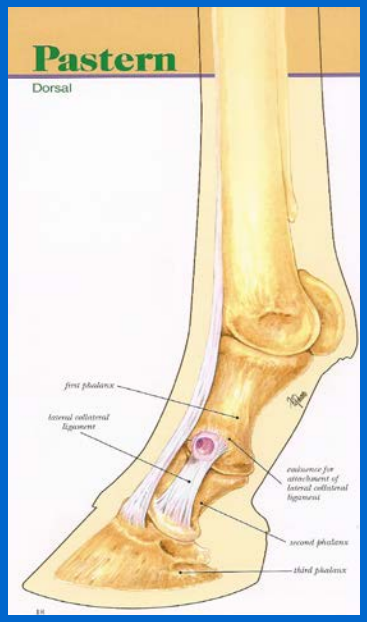


NAVICULAR BURSA THERAPY WITH DIRECT INJECTIONS OF PSGAG, HA, STEROIDS

SHOCK WAVE THERAPY FOR NAVICULAR DISEASE

INTERARTICULAR JOINT INJECTIONS





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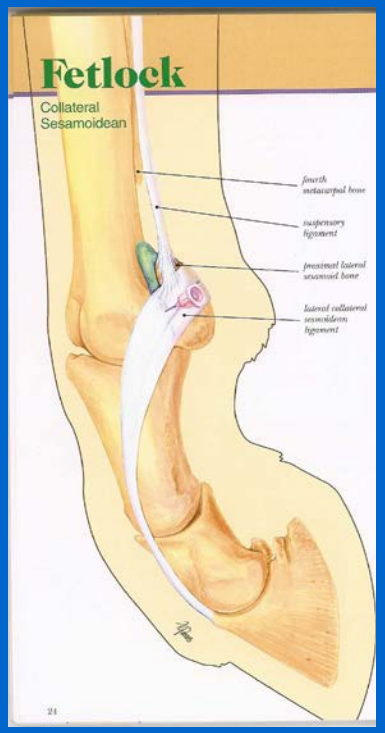

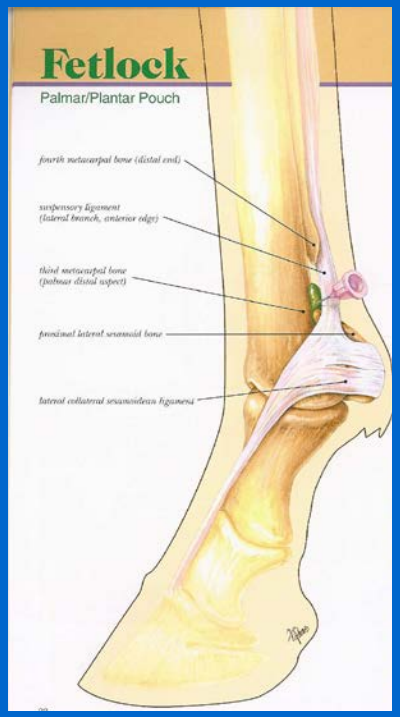

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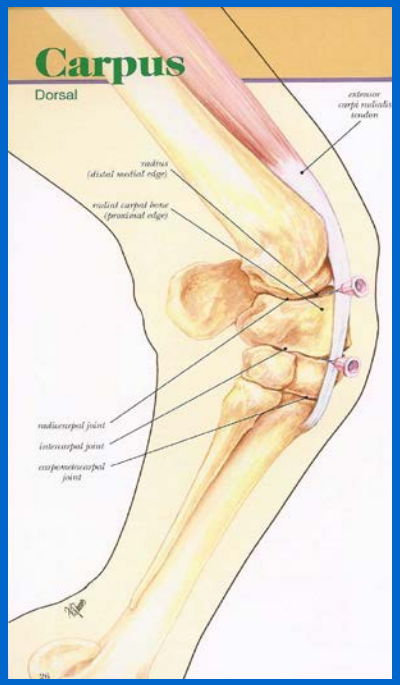

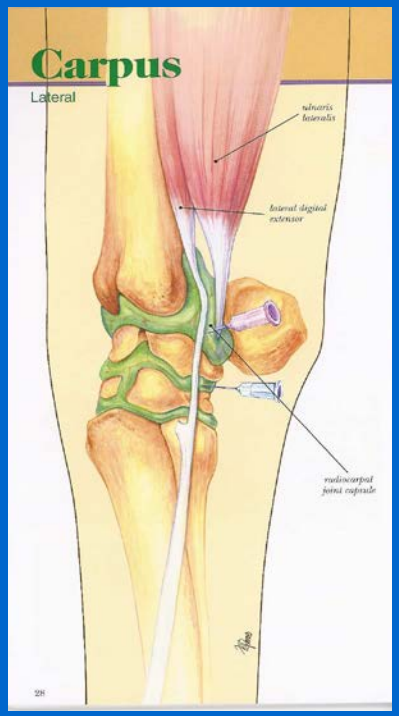

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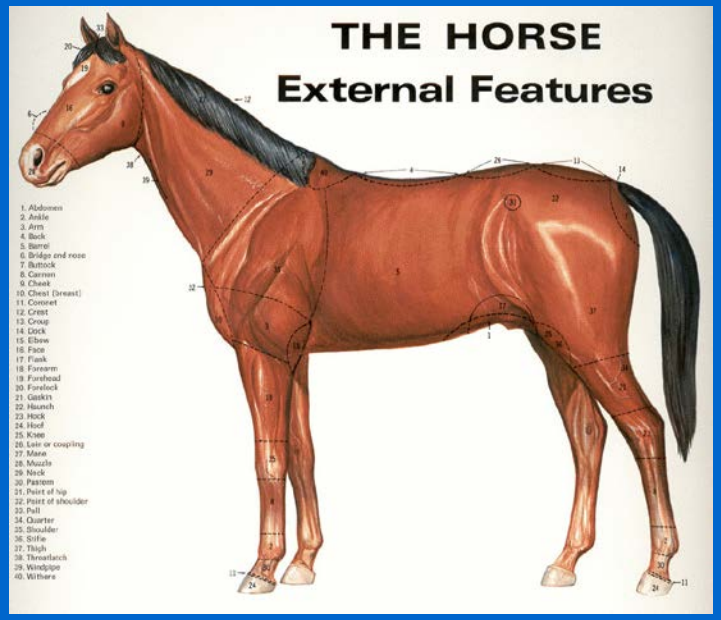

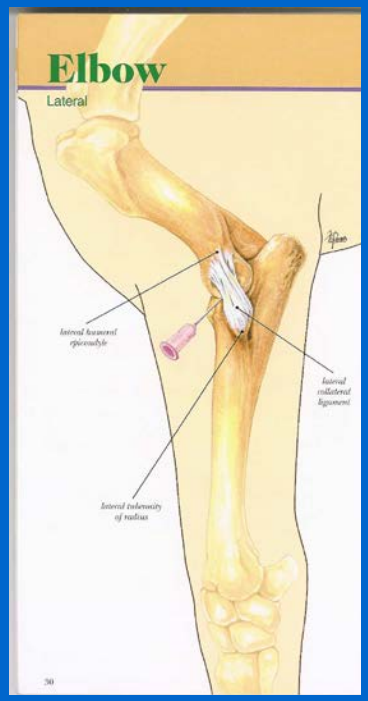

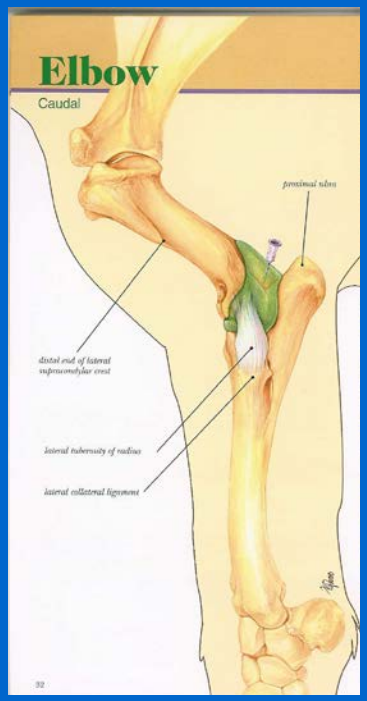

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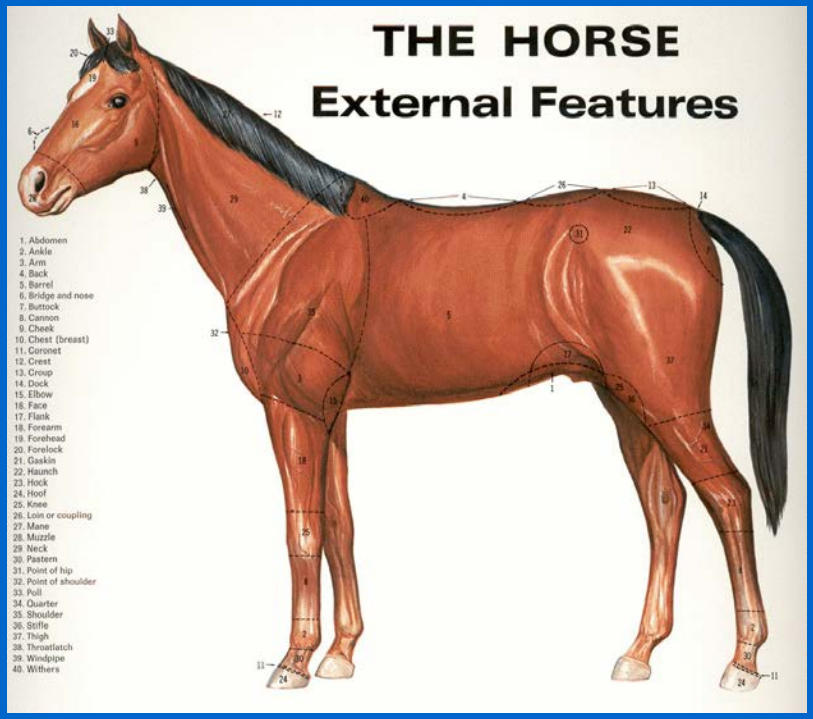

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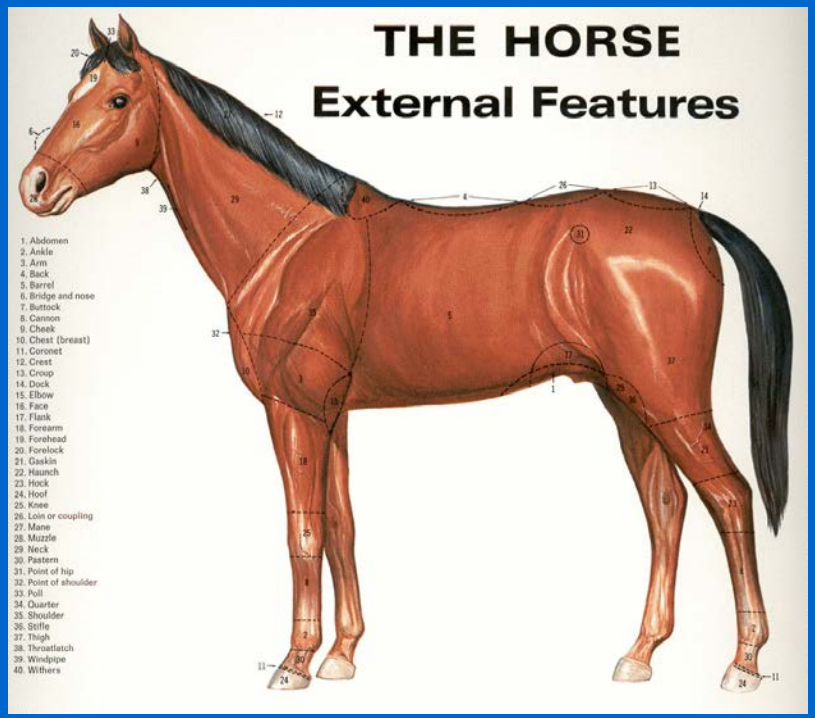

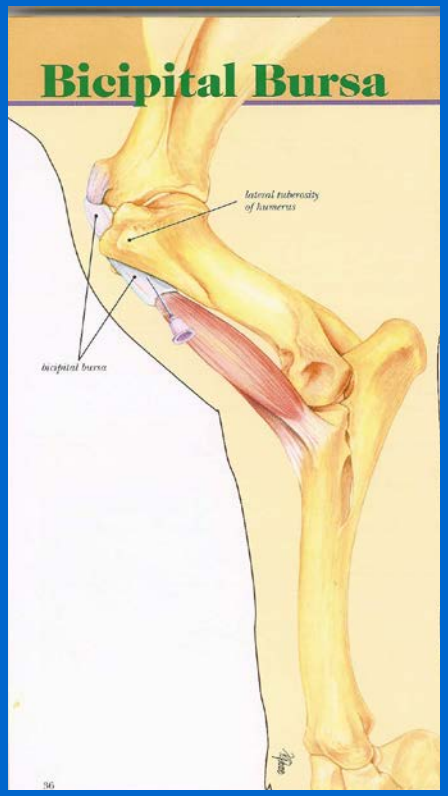

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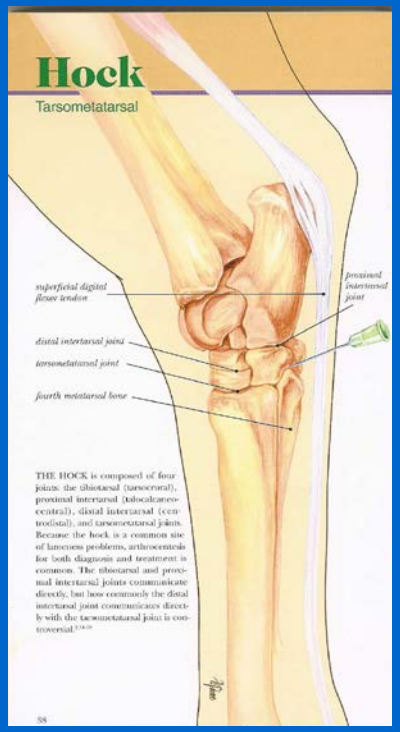

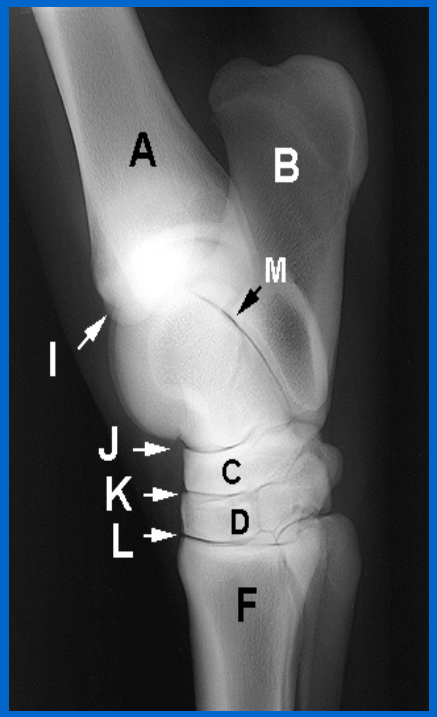

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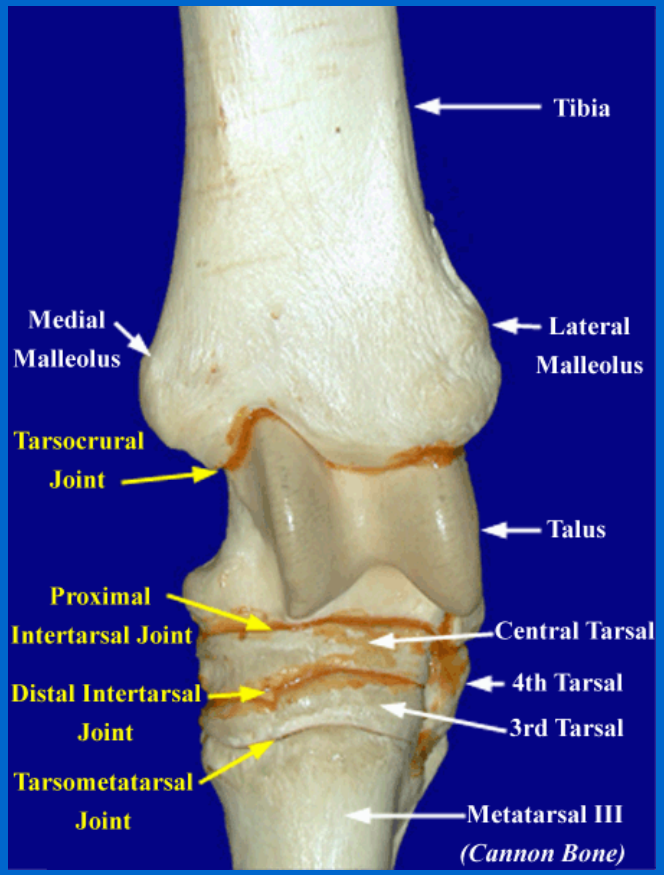

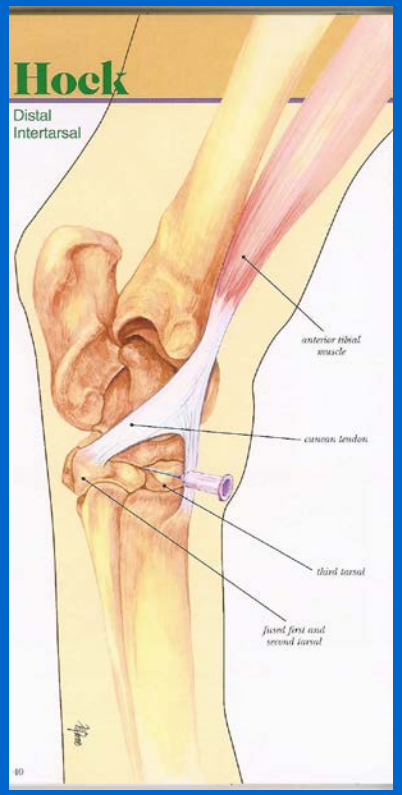

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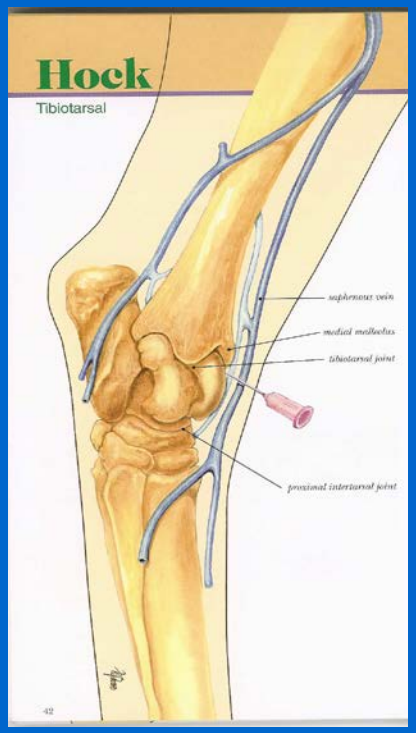

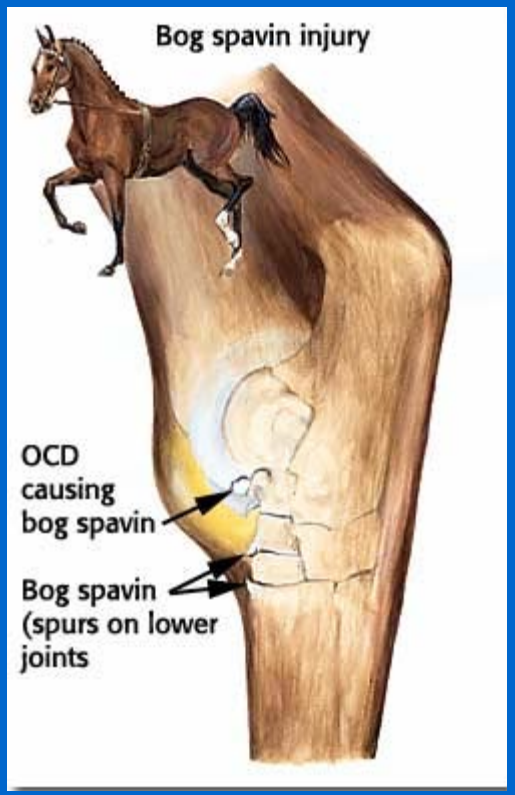

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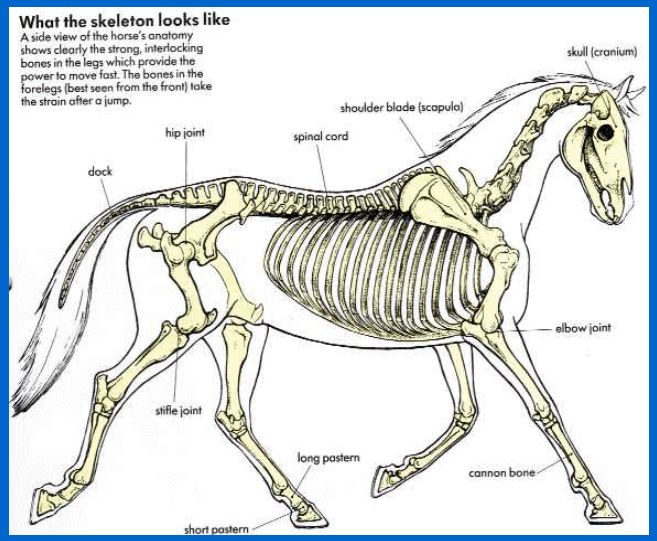

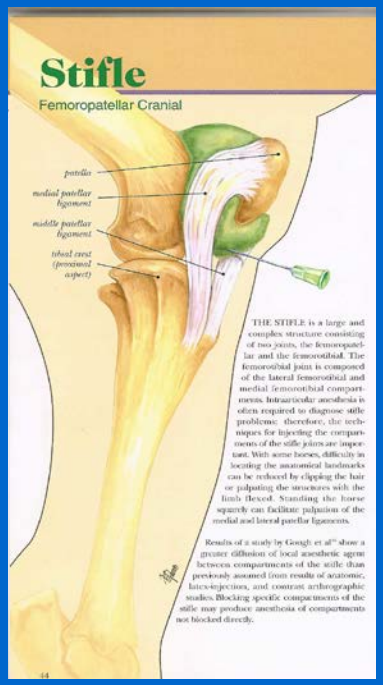

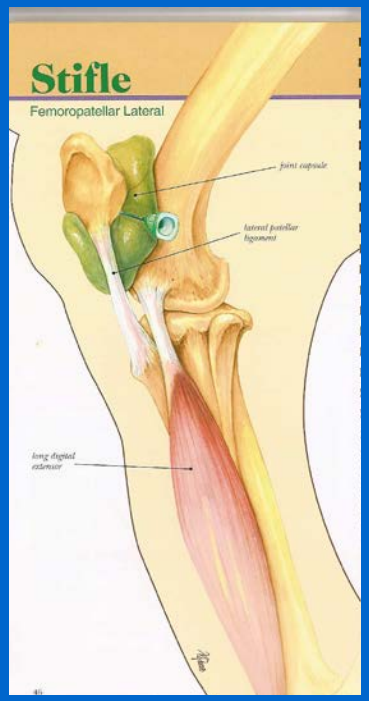

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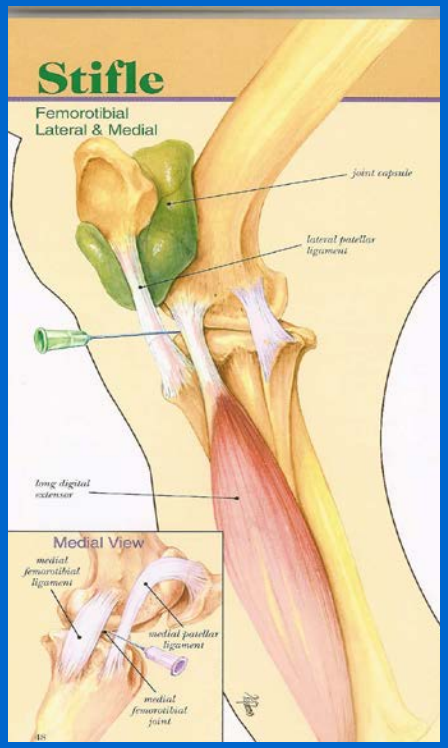

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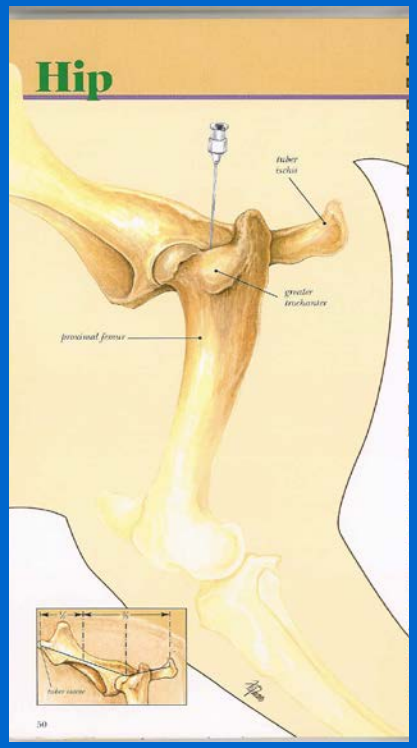
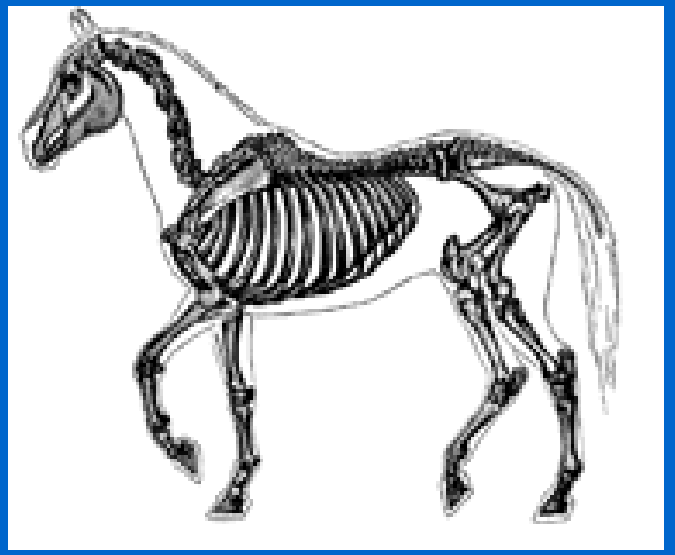
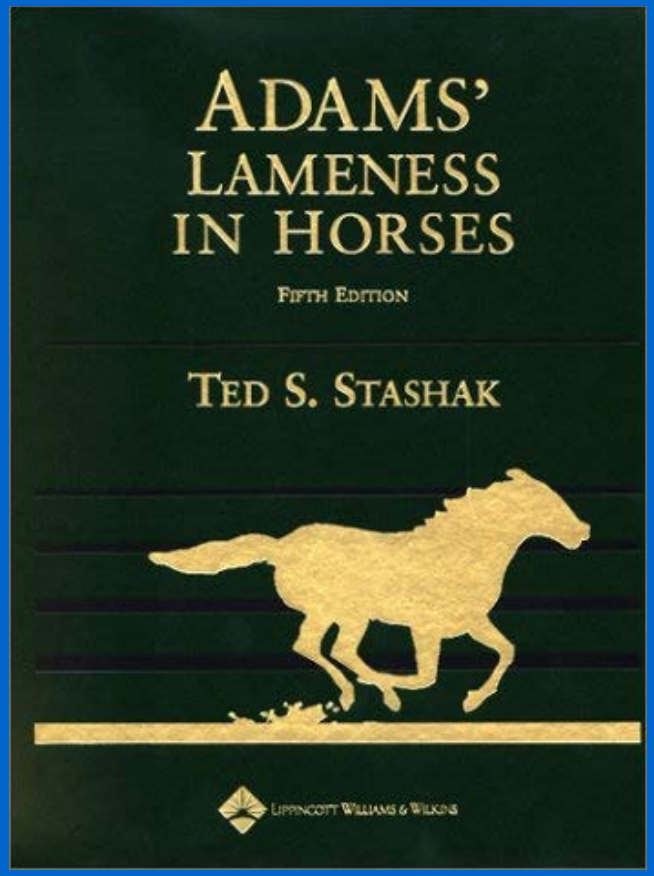


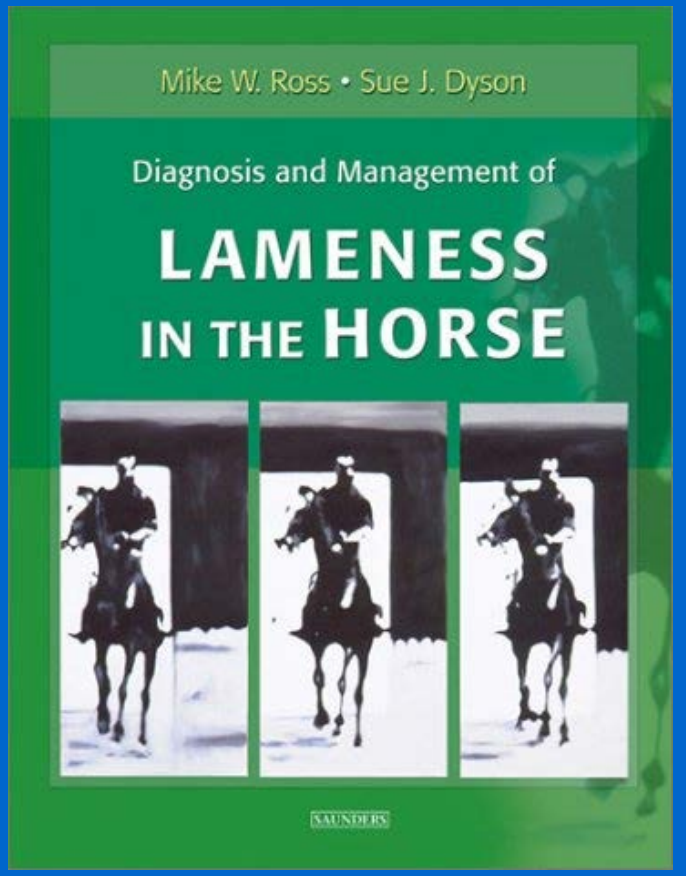


SACRAL JOINT INJECTIONS

Hunter's Bump

GOOD RESOURCES

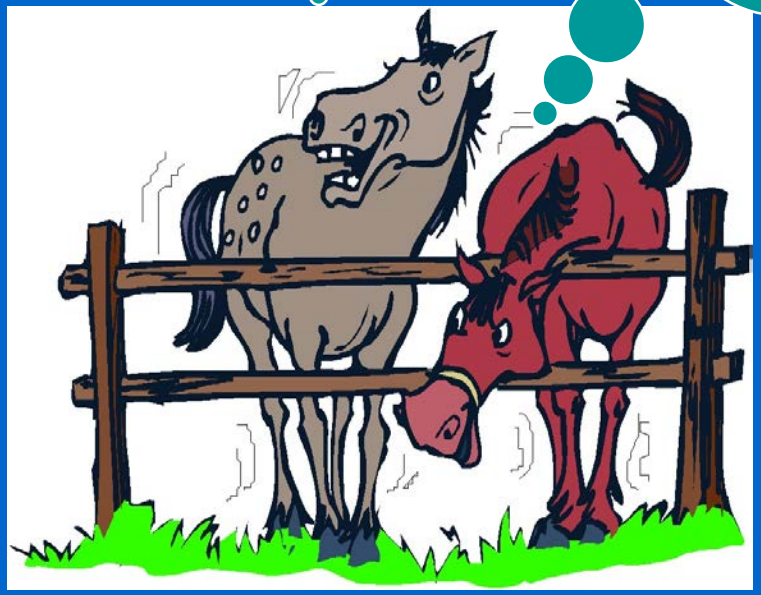




TAKE HOME MESSAGE

Hey, Harry. Look, they keep that thing polished, change the oil, and running like it's new.

Yeah, Mackie. If they had treated us like that, we would still be living the high life with the fancy fillies at the track.

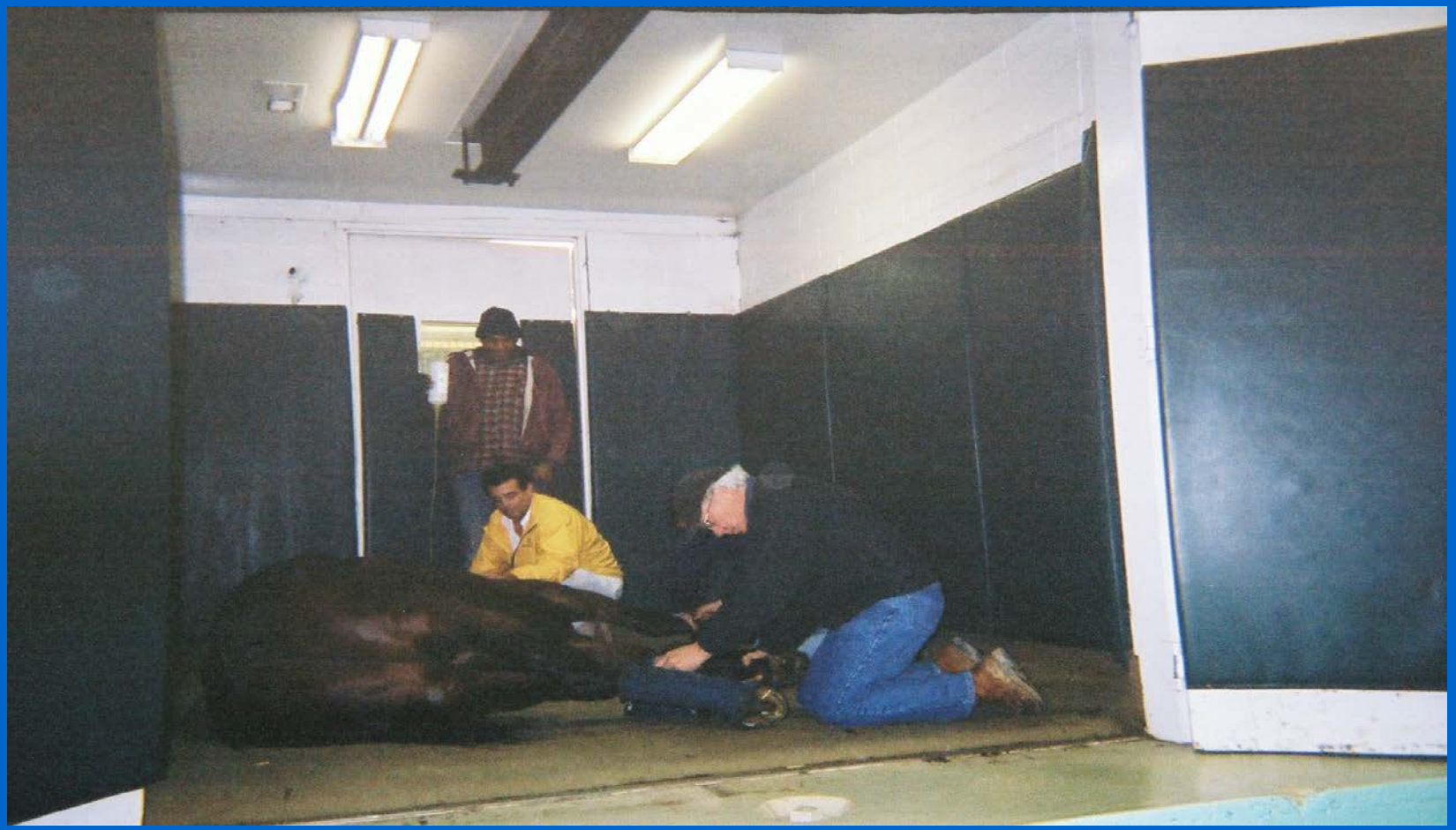


AT THE POST

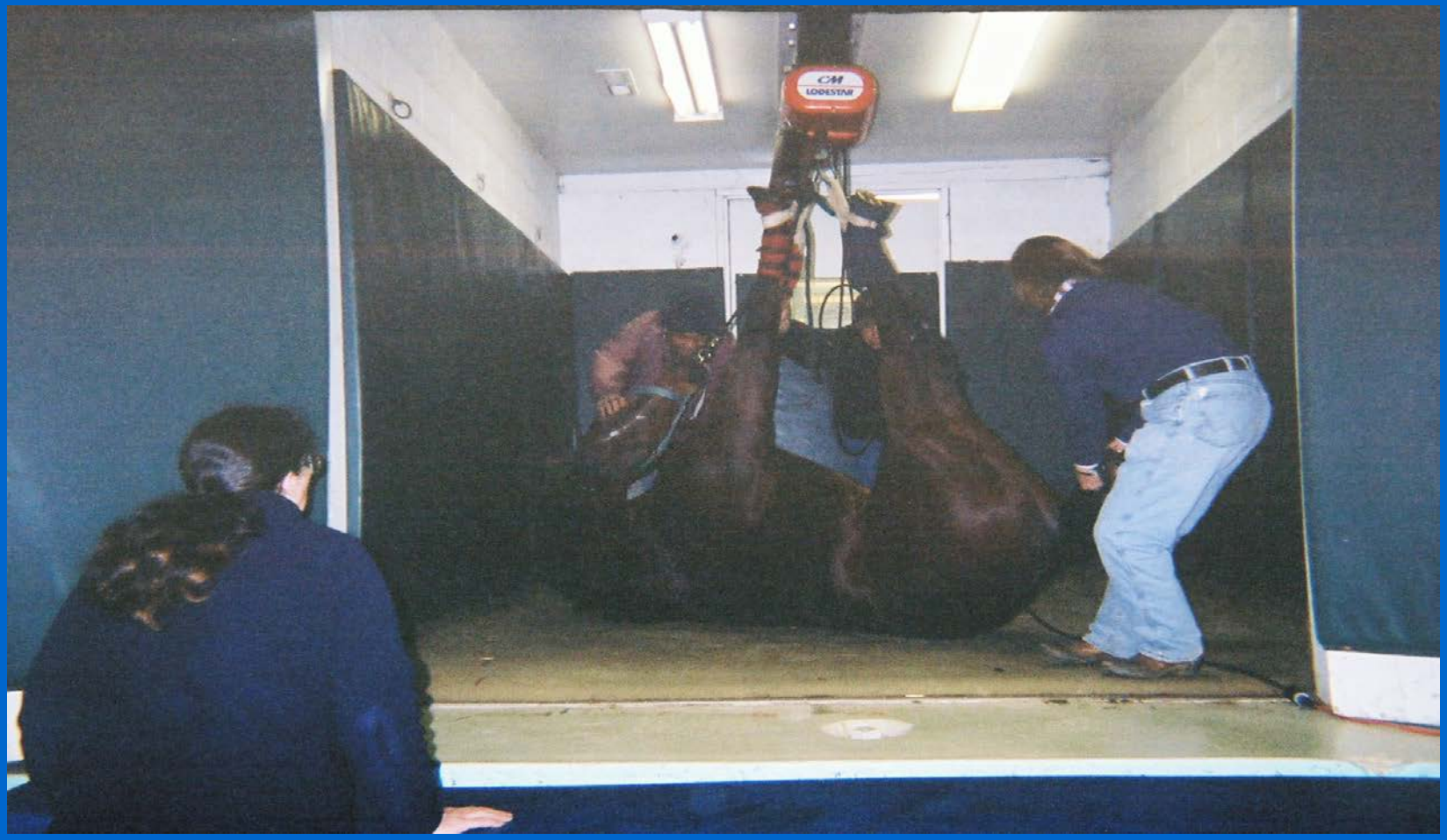
Equine Surgery

Instrument Prep

Induction Anesthetic

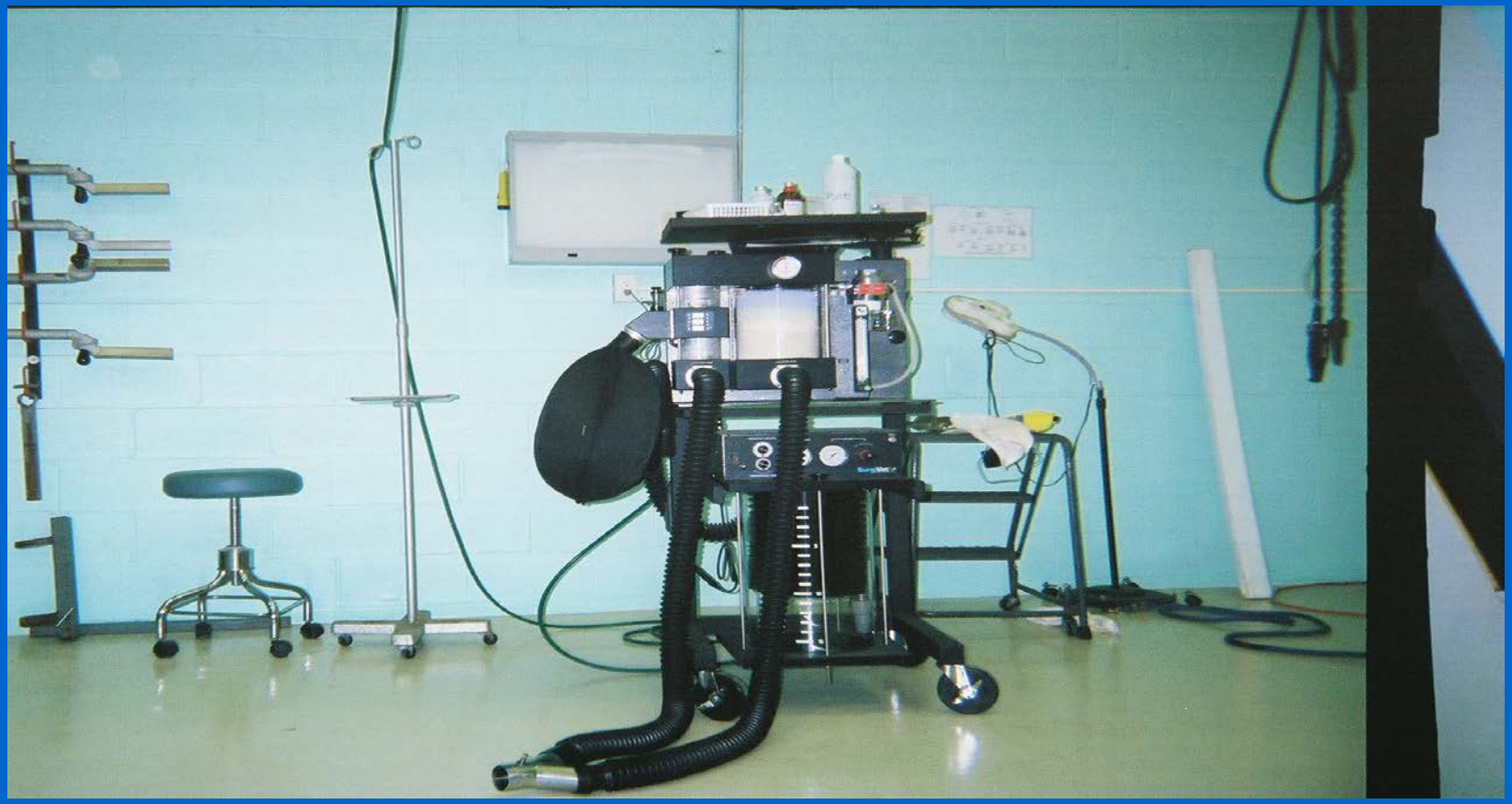


After Induction Horse Is Lifted Mechanically



Horse Is Lowered Onto Surgery Table

Gas Anesthesia Equipment



Prepping Surgical Area

Monitoring Equipment

Surgery – Note Sterile Field

New Frontiers

- Hyperbaric Oxygen Therapy