
Hyonate[®]

Sodium hyaluronate for the treatment of non-infectious arthritis

Product Information

International Edition



Important note

This product information on Hyonate is based on the available results of controlled international studies. User information is to be found in the instructions for use contained in the Hyonate package inserts which have been approved by the regulatory authority.

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*Movement is integral to life.
But movement would
not be possible
without joints –
one of nature's
perfect solutions.*



The Problem

Non-infectious inflammation of joints, ligaments and tendons in the horse is one of the most commonly occurring medical problems facing riders, trainers and veterinary surgeons.

Lameness originating in the joints of the limbs often results in lengthy interruption of the training and schooling of horses. This may lead to financial loss, particularly in the case of horses used in competition, as they may be out of action for several months. Even if a horse is ridden purely for recreation, such long periods are cause for concern and disappointment. A statistical survey of the reasons for absence from training amongst racehorses revealed lameness to be cause in 67.6% of cases. Over the two year period during which the study was conducted, about 20% of such cases of lameness were attributable to arthritis.

Joints

The joints of a horse's locomotor system are subject to enormous stress. Nature has therefore provided horses with a joint structure capable of accommodating such high demands. In biochemical terms, joints offer the optimum solution, the perfection of which has remained unmatched by any technological reproductions. In spite of this, however, misuse and overuse of joints still gives rise to lameness originating in the synovial joints of the limbs. In the case of horses involved in competition, such lameness is caused by the exertion required of the animal. Lameness in horses used for recreation, on the other hand, is often associated with inexperience on the part of the rider and irregular exercise (e.g. at weekends) interspersed with long periods of inactivity.

Anatomy of a synovial joint (Articulatio synovialis)

The three main components of a joint are as follows (figure 1):

- × the hyaline cartilage (articular cartilage) which covers the bony surfaces of the joint
- × the joint capsule which is made up of two layers:
 - an outer fibrous membrane which merges with the periosteum. It consists of taut connective tissue.
 - an inner highly vascular synovial membrane which lines the joint cavity.

- × the joint cavity containing the synovial fluid.

The mechanical stability of a joint is derived from:

- × the shape of the joint surfaces
- × the design of the bones involved in joint formation
- × the fibrous membrane which, together with the ligaments, forms the supporting structure
- × the tendons and muscles surrounding the joint.

A joint is provided with sensory nerve fibres solely in the joint capsule. In other words, arthralgia only ever originates in the joint capsule.

Synovial fluid

Normal synovial fluid is clear, pale yellow and stringy. The total protein content is approximately 1.8 g/dl, i.e. about 70% below that of the plasma protein content. The molecular weight of the proteins is less than 160,000 daltons. In healthy synovial fluid no fibrinogen is detectable and the total cell count is less than 200/ μ . It is therefore a complex ultrafiltrate of blood plasma additionally containing sodium hyaluronate. The synovial fluid volume correlates more closely with joint circumference than with height. Differences in the composition of the synovial fluid are detectable, however, between horses in training and those at pasture as well as before and after exercise.

As well as supplying nutrients to the hyaline cartilage, the synovial fluid also makes an important contribution to the lubrication and elasticity of the joint surfaces.

These properties are attributable to the presence of the most important constituent of synovial fluid, sodium hyaluronate.

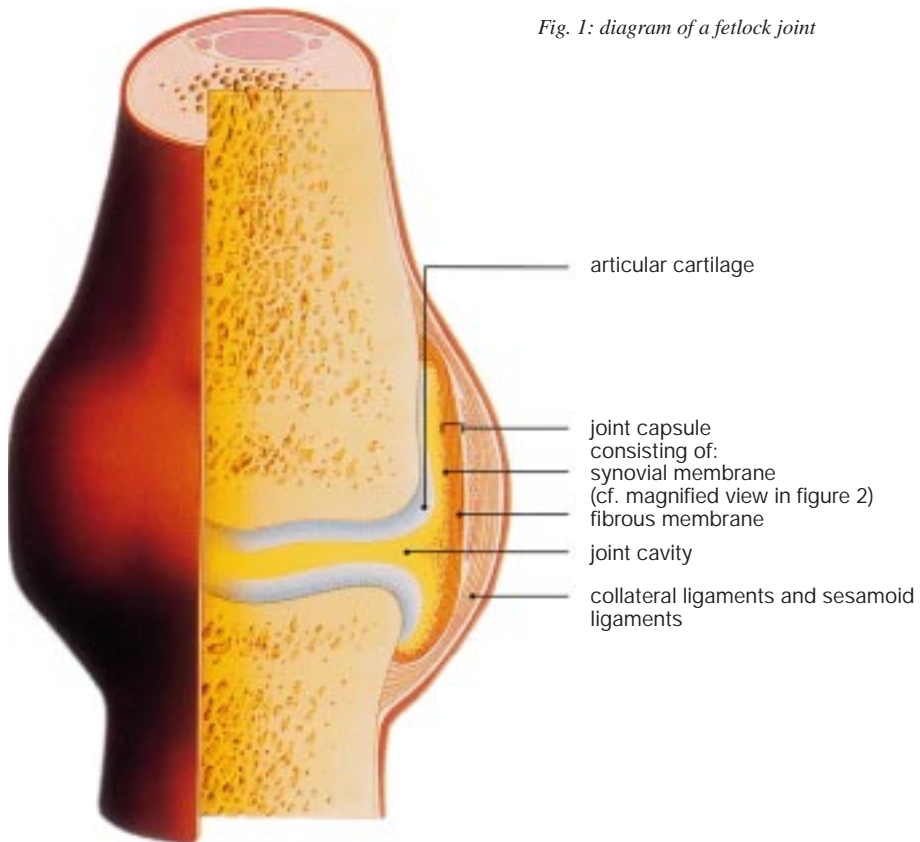


Fig. 1: diagram of a fetlock joint

Synovial membrane

The structure of the synovial membrane is illustrated in figure 2. The purpose of this membrane and of its synoviocytes is, on the one hand, the regulation of the protein and hyaluronate content of the synovial fluid and, on the other, phagocytosis.

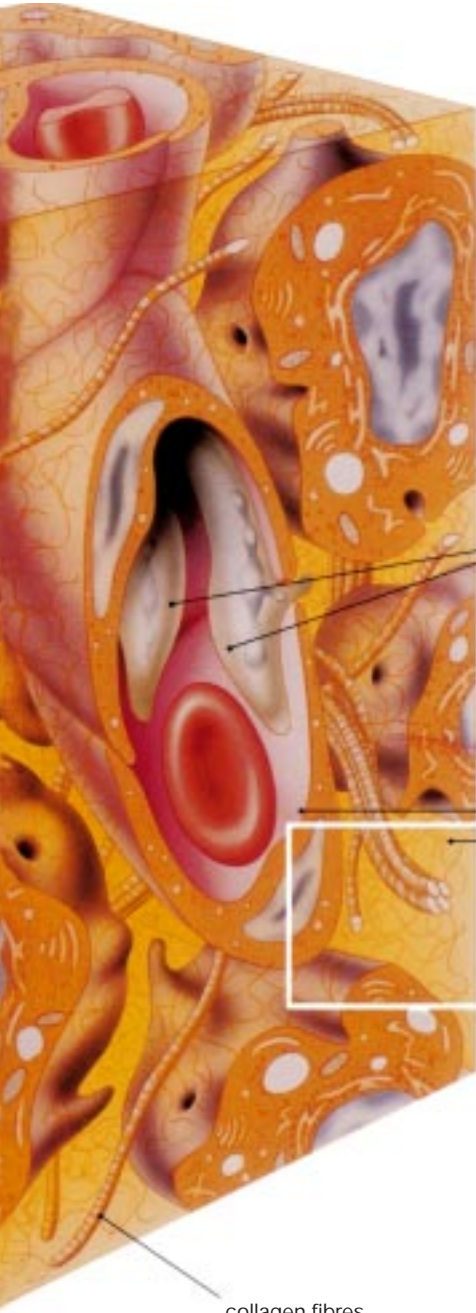
The primary function of the synovial membrane is regulation of the composition of the synovial fluid:

- the structure of the membrane allows smaller molecules to diffuse freely between joint cavity and vascular lumen across the intercellular space. Proteins with a higher molecular weight, on the other hand, are unable to cross this barrier.
- the sodium hyaluronate synthesised by the synoviocytes forms a 3-dimensionally cross-linked network. Since this network is also present in the intercellular space, it acts as a physical barrier to prevent blood cells entering the joint cavity.

This filtering action allows the synovial membrane to regulate the composition of the synovial fluid. In conjunction with sodium hyaluronate, it guarantees the physiological composition of the synovial fluid and its properties that are crucial to the functioning of the joint.

In addition to synthesis of sodium hyaluronate, the synoviocytes are also capable of phagocytosis of degradation products.





For this purpose they have their own cyto-lytic lysosomal enzymes which also play an important role in the pathogenesis of arthritis.

Fig. 2: diagram (detail) of the synovial membrane

leukocytes (prevented from passing into the joint cavity by the sodium hyaluronate network)

blood vessel

sodium hyaluronate chains

collagen fibres



Sodium hyaluronate

The sodium hyaluronate synthesised by the synoviocytes is the sodium salt of hyaluronic acid. It occurs naturally in the form of the salt. Although generally referred to as **hyaluronic acid** this term is therefore strictly speaking incorrect.

Sodium hyaluronate is a sulphate-free glycosaminoglycan made up of repeating disaccharide units of N-acetylglucosaminoglycan and sodium glucuronate (figure 3).

The resulting long chains form a 3-dimensionally cross-linked network and are the crucial determinant of the properties of the synovial fluid.

The high affinity of sodium hyaluronate for water, which is enclosed rather than bound within the three-dimensional structure, is responsible, in particular, for the known high viscosity of the synovial fluid. Recent studies have shown that sodium hyaluronate exerts its lubricant effect primarily on the membrane separating

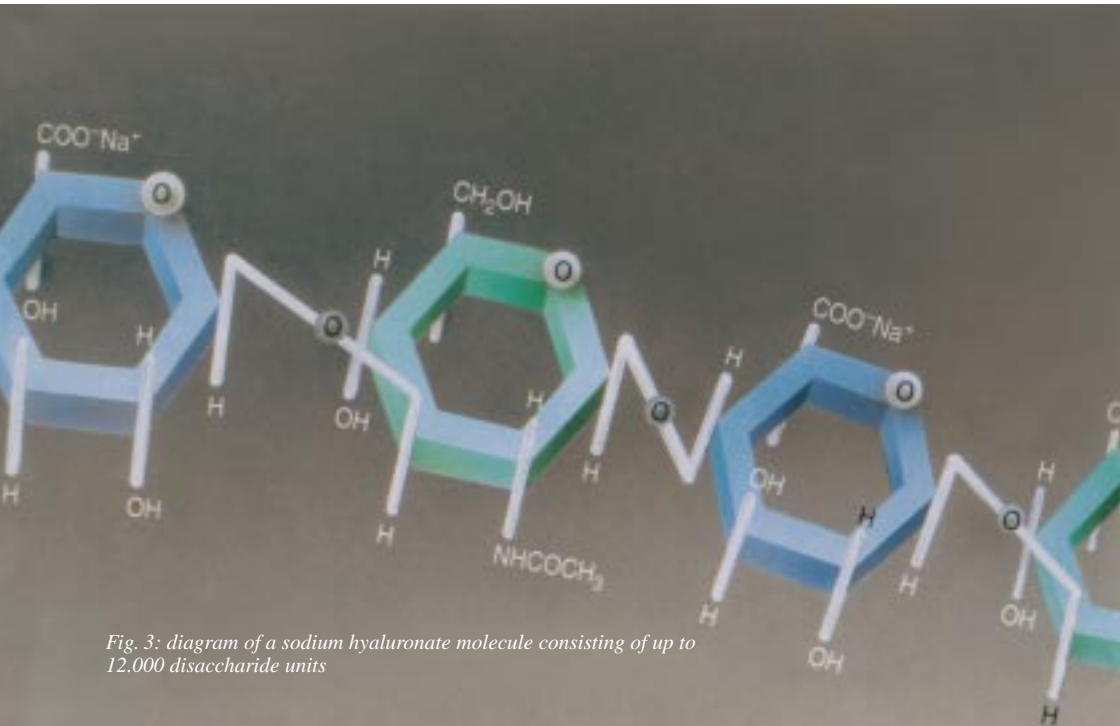
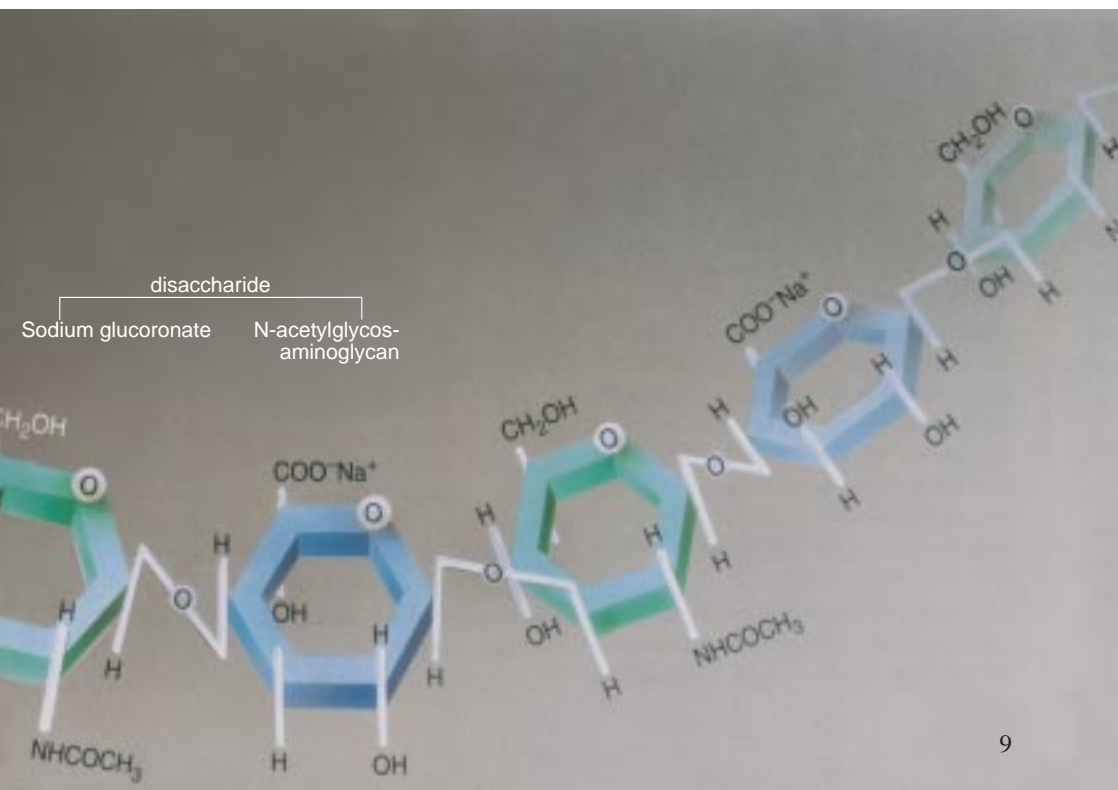


Fig. 3: diagram of a sodium hyaluronate molecule consisting of up to 12.000 disaccharide units

the synovial fluid from the soft tissue (capsule) of the joint which has a more powerful retarding action than the joint surfaces. This is explained by the fact that the viscous sodium hyaluronate molecules pass directly from the intercellular space of the synovial membrane into the synovial fluid, thus forming an elastic, fluid transition from capsule to joint cavity.

Sodium hyaluronate therefore has various properties:

- it guarantees the viscosity of the synovial fluid through its 3-dimensional structure(lubrication)
- it assists with the filtering function of the synovial membrane (regulation of composition of synovial fluid)
- it is a constituent of hyaline cartilage
- it plays a role in the supply of nutrients to the cartilage.



- sodium hyaluronate also has a number of anti-inflammatory properties which have been confirmed in in vitro and in vivo tests:
 - inhibition of the phagocytic activity of granulocytes
 - inhibition of lymphocyte activity (proliferation, migration)
 - reduction of the release of prostaglandin
 - inhibition of the action of interleukin
 - reduction of the release of free radicals.

Hyaline cartilage

The three main requirements of the hyaline cartilage in joints are as follows:

- load-bearing capacity
- elasticity
- lubrication.

Cartilage tissue is made up of cartilage cells (chondrocytes) and well-hydrogenated ground substance. 70—80% of hyaline cartilage consists of water. In adults, the ground substance predominates, whilst the chondrocytes are distributed individually but usually uniformly throughout the ground substance. Since hyaline cartilage has no blood vessels or nerve fibres of its own, it is supplied exclusively via the synovial fluid by means of a vacuum pumping mechanism and diffusion as well as from the bone marrows.

A prerequisite for provision via this mechanism and for the overall functioning of the cartilage in the joint is its elasticity.

The ground substance of hyaline cartilage is made up largely of collagen fibres and proteoglycan aggregates. This complex composition ensures the required degree of elasticity and the high resistance to stress.

The collagen fibres are responsible for the strength of the cartilage. They run individually or in bundles in all directions throughout the cartilage. The ends of these fibres form the smooth, firm articular surface (cf. figures 7 and 8).

The proteoglycan aggregates consist of long sodium hyaluronate chains and a number of proteoglycans. This gives the cartilage its elastic properties. In so doing, the sodium hyaluronate serves as a base for the proteoglycans, the protein cores of which are bound to it at right angles. A number of glycosaminoglycan side-chains, each bearing abundant negative charges, accumulate on the protein core of the proteoglycans. Their mutual repulsion and their ability to bind water guarantees the elasticity of the cartilage (figure 4).

- From this explanation it is evident that sodium hyaluronate plays a crucial role in the physiology of joints. If the described interaction between joint capsule, synovial fluid and cartilage is impaired in any way, arthritis occurs. Changes in the quantity and quality of the sodium hyaluronate play a pivotal role in both the pathogenesis and the repair stage of arthritis.

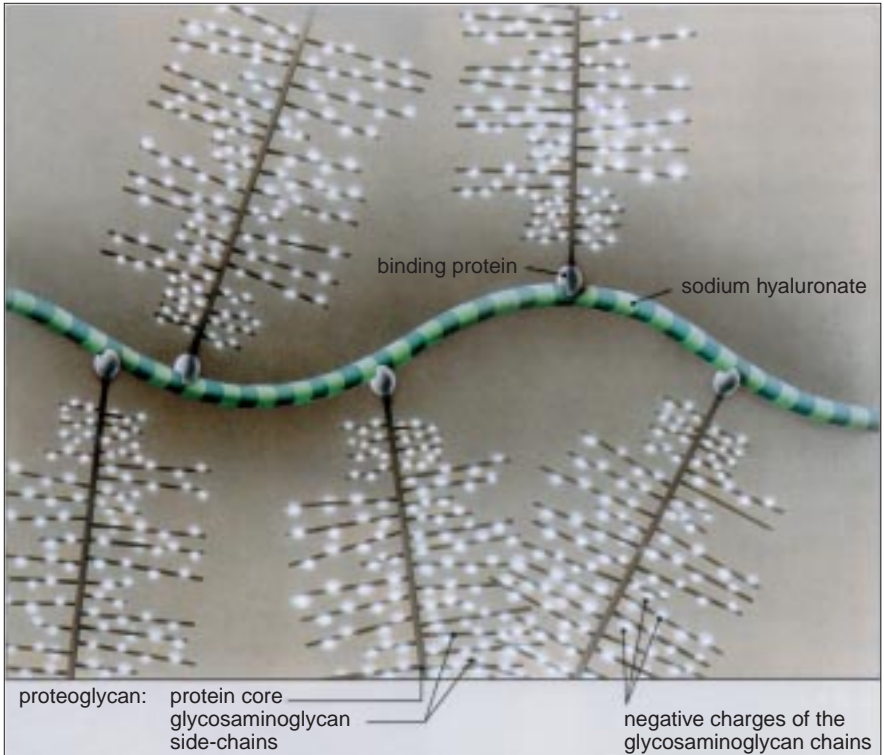


Fig. 4: diagram (detail) of a proteoglycan aggregate in joint cartilage

Arthritis

Arthritic diseases can be divided essentially into infectious and non-infectious inflammation of joints. Because of differences in the aetiology and treatment of these two types of arthritis, only the non-infectious types are dealt with in detail here. Non-infectious arthritis can be classified on the basis of severity as follows:

- mild synovitis
(painless joint effusion)
- synovitis, capsulitis
- chronic degenerative arthritis or osteoarthritis.

Non-infectious forms of arthritis are caused by trauma or wear and tear. Such abnormal stresses causes varying degrees of damage to the hyaline cartilage and/or the joint capsule.

Even minor irritation can trigger a pathological mechanism resulting in cartilage damage.

Pathophysiology

As well as directly damaging the cartilage, trauma may also result in damage to synoviocytes and/or chondrocytes. This releases catabolic enzymes which reduce the hyaluronate content of the synovial fluid and break down the collagen and proteoglycan in the cartilage. These changes in the ground substance of the cartilage result in a loss of elasticity and disrupt the supply of nutrients to the cartilage as a whole.



Fig. 5: arthroscopic view of a healthy fetlock joint

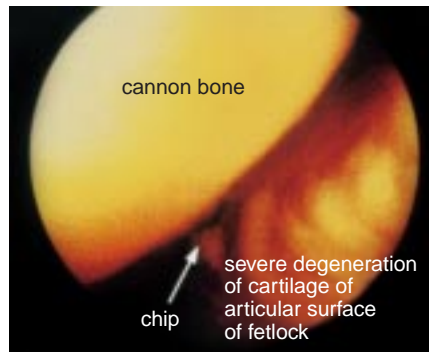
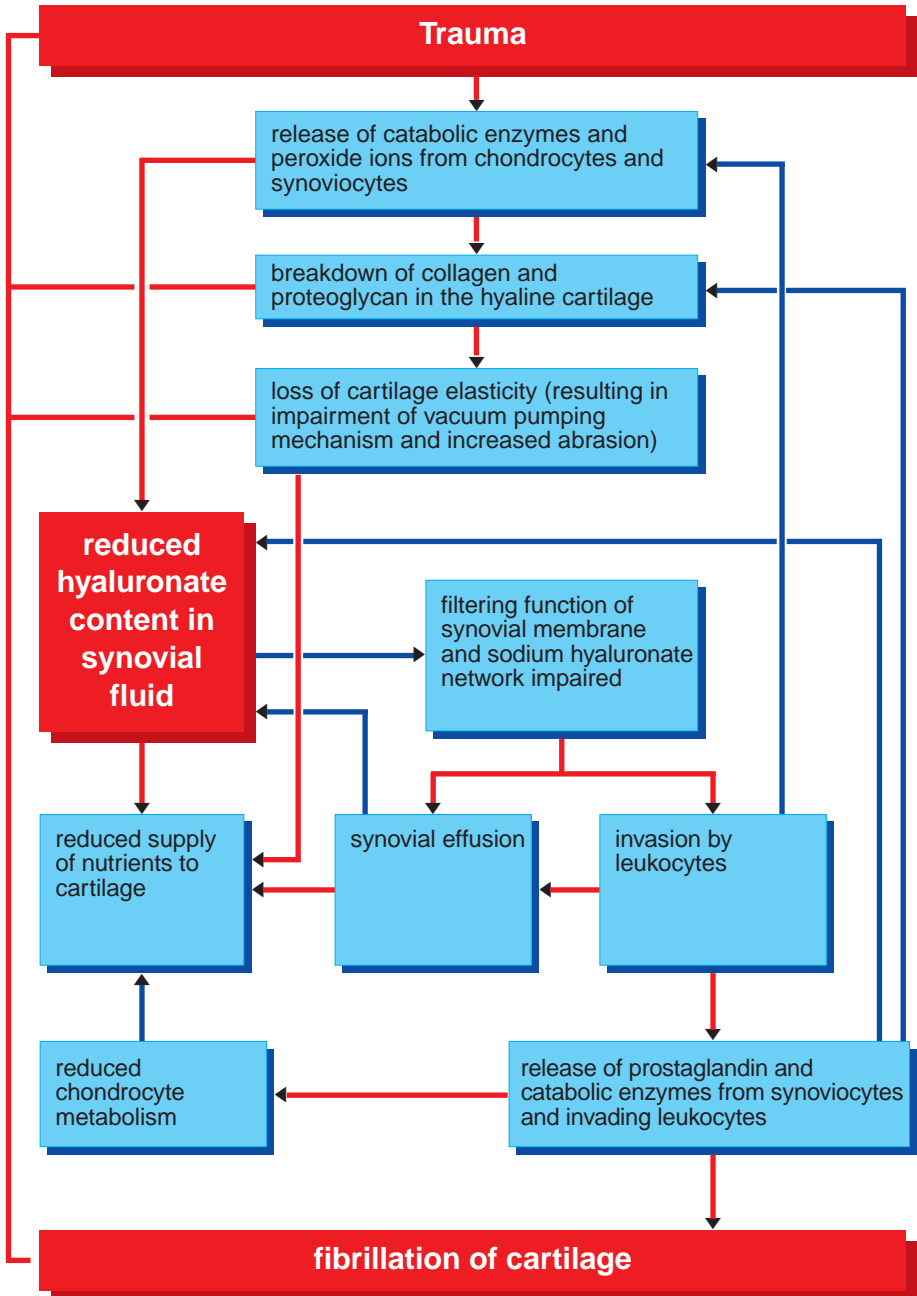


Fig. 6: arthroscopic view of an arthritic fetlock joint

The reduction in the sodium hyaluronate content of the synovial fluid means that its functions, such as the provision of the cartilage with nutrients, are further impaired.



The complex filtering action of the synovial membrane, in which sodium hyaluronate plays a crucial role, is also impaired. As a result, leukocytes and detrimental material pass into the joint cavity. The leukocytes in turn release other mediators of inflammation and catabolic enzymes. This cascade further reduces the sodium hyaluronate content and thus also the elasticity of the cartilage as well as further impairing the filtering function of the inflamed synovial membrane.

This further intensifies degeneration of the normally well structured cartilage (fig. 8) both directly and indirectly. e.g. through increased abrasion, resulting in fibrillation of the cartilage through exposure of the collagen fibres forming the surface of the joint (figures 9 and 10).

An additional factor is the increased amount of fluid in the joint cavity as a result of the inflammation and the impaired filtering action. This increases the intra-articular pressure in the synovial membrane and further enlarges the intercellular spaces, promoting synovial effusion. Quite apart from the reduced mobility of the joint, the pressure of the synovial effusion may cause the capillary network to collapse. This further hinders the healing process because of the reduced blood supply to the synovial membrane. The entire functioning of all joint structures is impaired as a result and a partly self-sustaining process takes place, leading to a vicious circle. These processes are illustrated in the diagram on page 13.

Therapy

The primary aim of any therapy of joint diseases is to restore normal function of the joint as soon as possible, i.e. to allow the horse to return to exercise. This means that the degenerative processes in the joint have to be stopped and the repair of the tissue and the synovial fluid promoted. A number of treatment options are available for use either singly or in combination. The various factors determining which form of therapy the vet may select are as follows:

- the affected joint itself
- the age of the patient
- the duration of the inflammation (acute/chronic)
- the severity of the inflammation
- the purposes for which the horse is used
- the special requirements of the horse's owner.

The available treatment options are described briefly below.

Rest

In order to reduce the risk of further tissue damage where the function of a joint is already impaired, temporary (though by no means complete) immobilisation or rest is a valuable aid to therapy. This also allows the degenerative process to come to a halt and repair processes to begin.

A common natural limitation on such forms of therapy is the understandable wish of the owner or trainer, particularly in the case of competition horses, to shorten the healing process.

Fig. 7: scanning electron microscopic view of unchanged cartilage surface enlargement: 4300 x



Physiotherapy/ stimulation therapy

Cooling has proved a useful first aid measure if initiated within 48 hours of the occurrence of the trauma. At later stages, mildly rubefacient and absorption-promoting ointments can be used.

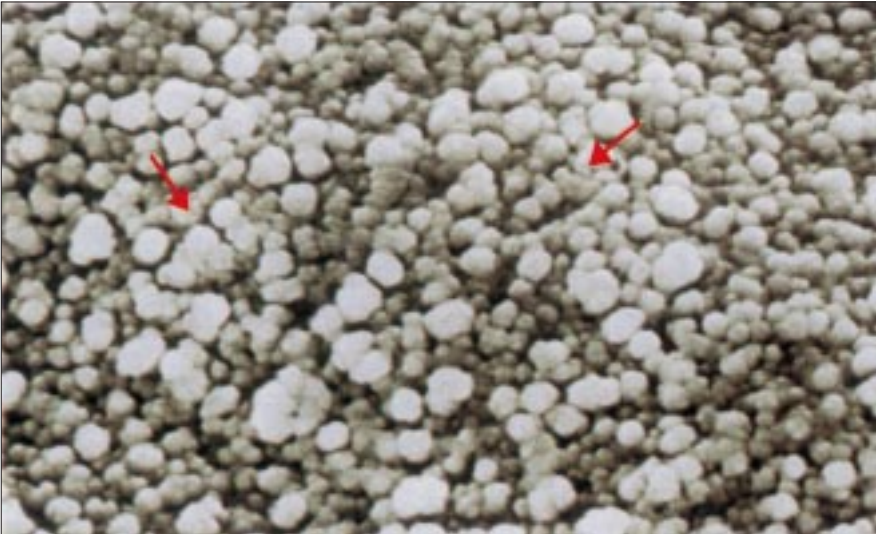
Controversy currently surrounds the stimulation techniques for inducing hyperaemia through blistering and thermocautery which were formerly in widespread use for the treatment of chronic arthritis. The main benefit of such therapeutic techniques is now considered to lie in the several

months of enforced rest with the acceptance also of the animal's owner.

The magnetic field technique is based on similar lines to the heat treatment principle.

Non-steroidal anti-inflammatory drugs (NSAIDs)

This class of drugs includes a number of substances, the best known of which are the cyclo-oxygenase inhibitors, phenylbutazone, naproxen, flunixin and acetylsalicylic acid. They act essentially by inhibit-



*Fig. 8: scanning electron microscopic view of unchanged cartilage surface. The arrows indicate the ends of the collagen fibrils emerging on the surface (light dot-like pattern)
enlargement: 22300 x*

ing the formation of prostaglandins (potent mediators of inflammation). In addition to their anti-inflammatory action, these substances also have a desensitising effect on pain receptors. In view of these advantages, drugs of this class are routinely used to treat diseases of the musculoskeletal system in the horse.

Although this class of drugs was originally considered virtually harmless, attitudes have now changed. Adverse drug reactions such as ulcers in the gastrointestinal tract and nephritis, particularly in foals, are now known to occur. Furthermore, the

pharmacokinetics of the drugs mean that the onset of action in the affected joint is often delayed after oral administration as therapeutic concentrations are attained only slowly in the affected joint.

Corticosteroids

Intra-articular administration of corticosteroids for the treatment of arthritic diseases was first described in 1955 and has since been widely used with success as initial therapy. The risks associated with



*Fig. 9: scanning electron microscopic view of cartilage surface exhibiting arthritic changes. The collagen fibrils are clearly exposed with loss of ground substance
enlargement: 6400 x*

such drugs must always be included in therapeutic considerations, however.

Corticosteroids exhibit potent anti-inflammatory activity and therefore bring about the fastest relief of symptoms. There is always a risk, however, that apparently cured, symptom-free horses with damaged and not fully regenerated cartilage will be put back into training, possibly resulting in severe damage to the joint. Corticosteroids are also known to have a directly or indirectly harmful effect on cartilage as a result of impairment of cartilage metabolism. The expression *Cortisone joint* is derived from early experience of indiscriminate use of steroids and is used to describe irreversible joint defects.

Peroxide mutase

Peroxide radicals, which are present in the initial stage of inflammation and give rise to further inflammatory processes as well as breaking down hyaluronate, are bound by this substance. In view of its mode of action, it is used as concomitant therapy in acute stages of arthritis.

PSGAG

PSGAG (polysulphonated glycosaminoglycans) or mucopolysaccharidic sulphuric acid ester was marketed for human use as a chondroprotective agent in the treatment of osteoarthritis of the knee up until the end

of the 1980s. With its efficacy already in dispute, this substance then had to be withdrawn from the market in Germany, for instance, in view of the occurrence of a number of severe adverse reactions.

PSGAG is now licensed in some countries for the treatment of non-infectious arthritis in the horse. Its mechanism of action is said to involve activation of the synthesis of collagen, proteoglycan and sodium hyaluronate. Conflicting reports exist of the efficacy of PSGAG which has to be administered 5 times i. a. or 7 times i. m. per course of treatment.

Sodium hyaluronate

Following the realisation that sodium hyaluronate is both quantitatively and qualitatively diminished in arthritic joints, use of hyaluronate for intra-articular therapy commenced in 1970. Considerable experience of use of this class of substance is now available. Success has been achieved with intra-articular administration of sodium hyaluronate both alone and in combination with corticosteroids. Sodium hyaluronate has proved particularly successful in shortening the healing period and is therefore one of the most widely used drugs for indications such as:

- synovitis/capsulitis
- acute arthritis and post-operative treatments.

Sodium hyaluronate is also used for treating chronic degenerative changes, but the clinical results are less convincing than in the case of acute arthritis.

In view of the pivotal role played by sodium hyaluronate in joint function and in the pathogenesis of arthritis, provision of arthritic joints with pure grade sodium hyaluronate obviously appeared to represent one of the most important therapeutic measures initially.

The reasoning behind this was based on the assumption that externally administered sodium hyaluronate would replace only the hyaluronate broken down by inflammatory enzymes. However, it is now known that externally administered hyaluronate is metabolised between 36 and 96 hours after administration and absorbed from the joint. This makes it difficult to

explain the action of the locally administered substance, which sometimes lasts several weeks, solely in terms of the purely chemical/physical mechanism described above. The precise mode of action of sodium hyaluronate has still not been satisfactorily explained in detail but is increasingly thought to involve a pharmacological mechanism in view of the number of proven properties.

It is generally agreed that administration of sodium hyaluronate has a beneficial effect on the following:

- improvement of lubrication
- improvement of permeability regulation via the synovial membrane
- positive effect on the composition of the synovial fluid, partly as a result of activation of the synoviocytes to synthesise increased amounts of hyaluronate



Fig. 10: scanning electron microscopic view of cartilage surface exhibiting severe arthritic changes (as in figure 8) showing the presence of granulocytes (arrow). enlargement: 3900 x

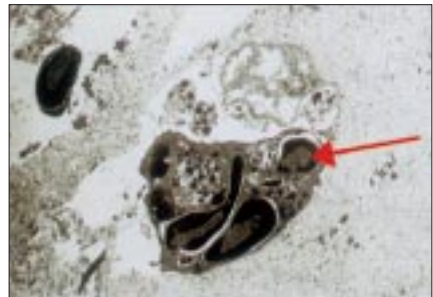


Fig. 11: electron microscopic view of granulocytes that have entered the cartilage (arrow). The cartilage is severely degenerated, as in figure 10, partly through the action of catabolic enzymes in the granulocytes, enlargement: 2900 x

- improvement of the nutrient supply to the cartilage
- direct anti-inflammatory effects (see page 10)

Since 1987, there have been a number of published reports of successful treatment of acute tendonitis and tenosynovitis with sodium hyaluronate. This group of products is now increasingly being used for this indication.

To summarise, sodium hyaluronate has been successfully used for the following indications:

- simple hydrarthrosis
- degenerative joint diseases
- synovitis/capsulitis
- following arthroscopic interventions
- chip fractures
- follow-up therapy after irrigation of infected joints
- treatment of acute and chronic tendonitis/tenosynovitis.



The solution – Hyonate

As outlined in the previous sections, sodium hyaluronate plays a crucial role in the physiology of joints. In joints exhibiting arthritic changes, both the quantity and the quality of this essential constituent of synovial fluid are markedly reduced. It is therefore essential to restore hyaluronate metabolism to normal as quickly as possible, thereby interrupting the complex pathological mechanism described above, so that healing processes can take place.

Conventional sodium hyaluronate products are obtained by extraction from cockerel combs.

The active ingredient in Hyonate is pure sodium hyaluronate. It is manufactured by Bayer using a new biotechnological process and is of a particularly high degree of purity as a result of this innovative production method.

This unique production technique rules out any possibility of contamination with foreign animal protein.

The purity of the sodium hyaluronate in Hyonate has allowed an innovative mode of administration to be developed. In addition to the conventional intra-articular route, which is a very demanding administration technique, Hyonate can also be administered intravenously as an alternative. This mode of administration, approved for use with a sodium hyaluronate product for the first time, was made possible as a result of intensive Bayer research and of the revolutionary production technique.

The advantages of intravenous over intra-articular injection, which requires special expertise and is not entirely without risks, are obvious.

For the first time, two options are available for therapy with sodium hyaluronate.

Composition

Hyonate is a viscous, crystalline solution containing 10 mg of highly purified sodium hyaluronate per ml.

Indications

Hyonate is used for the treatment of non-infections arthritis in the horse.

Administration

Hyonate can be administered intravenously (i. v.) or intra-articularly (i. a.).

Dosage

a) acute arthritis

- intravenous injection
dosage: 4 ml (40 mg) i. v.
May be repeated once or twice as necessary at weekly intervals.
- intra-articular injection*
Hyonate can also be administered intra-articularly as an alternative to intravenous administration.
dosage: 2 ml (20 mg) i. a.
May be repeated once or twice as necessary at weekly intervals.

*explanation page 22

b) chronic arthritis

Practical experience has shown that it is better to administer Hyonate by means of intra-articular injection for the treatment of chronic arthritis. This means that the active substance is administered directly to the affected site, i.e. the arthritic joint.

- intra-articular injection*
dosage: 2 ml (20 mg) i. a.
May be repeated once or twice as necessary at weekly intervals.

Safety

The active substance, sodium hyaluronate, is a naturally occurring substance in the horse. No evidence of adverse events has been recorded either in field studies or in toxicological investigations.

Hyonate was injected weekly at 3 to 5 times the recommended dosage for 9 weeks. No local or systemic side-effects were detected after either intravenous or intra-articular injection. Haematological and histological investigations performed on animals treated in this manner revealed no pathological findings either.

* *Strict aseptic technique should be observed when injecting Hyonate. As with any intra-articular procedure, proper injection site disinfection and animal restraint are important.*

Excess joint fluid should be aseptically removed prior to articular injection. Care should be taken not to scratch the cartilage surface with the top of the injection needle. Diffuse swelling lasting 24 to 48 hours may result from movement of the needle while in the joint space.

To achieve best results in case of intra-articular administration the horse should be given three days stable rest after treatment before gradually resuming normal activity.

Efficacy

The efficacy of Hyonate both for i.v. and i.a. therapy has been proven in experimental and field studies.

Efficacy in induced arthritis

Standardised conditions for blinded studies with control groups were created by means of artificially induced arthritis in a tolerance model. Both forms of therapy were tested on a standardised horse population in a number of experiments using this model.

The results of investigation of the efficacy of i.v. Hyonate were as follows.

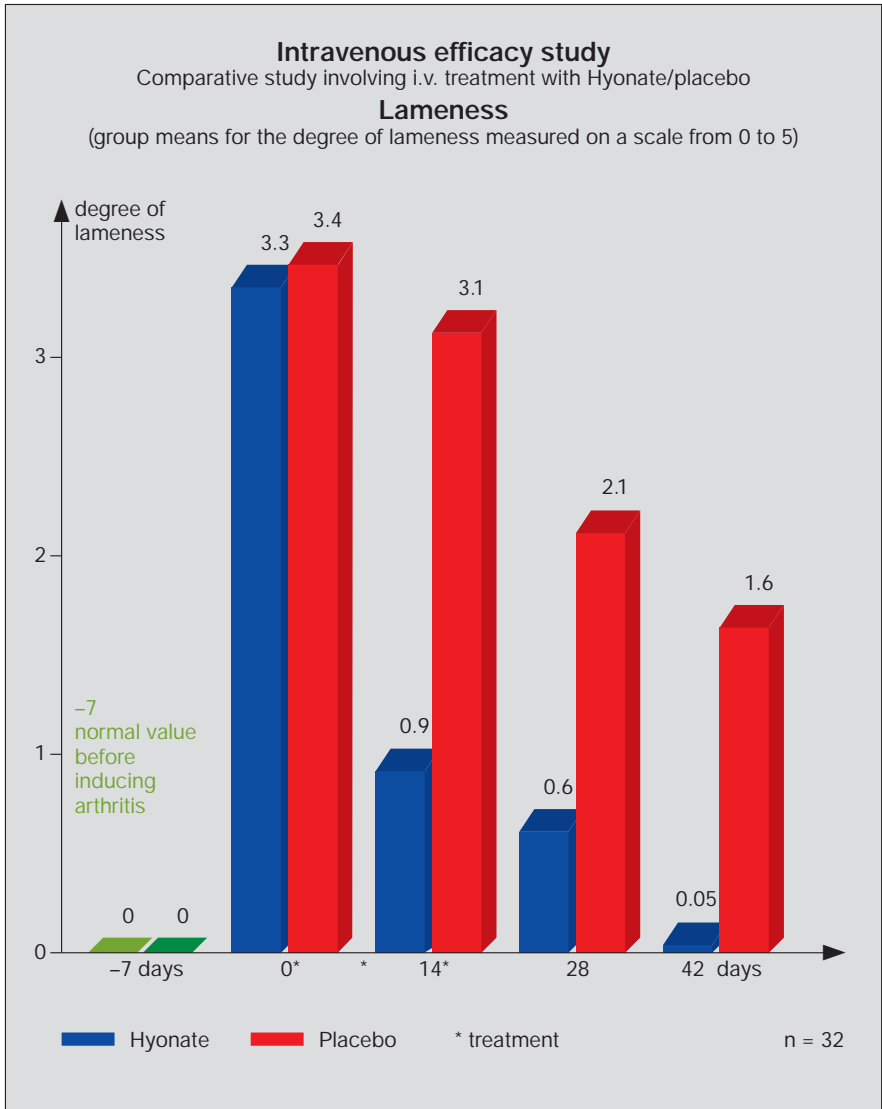
After arthritis had been induced in the carpus, the experimental horses were treated intravenously in a blind trial either with placebo or Hyonate (4 ml) on day 0. Treatment was repeated twice at weekly intervals. The study involved 32 animals.

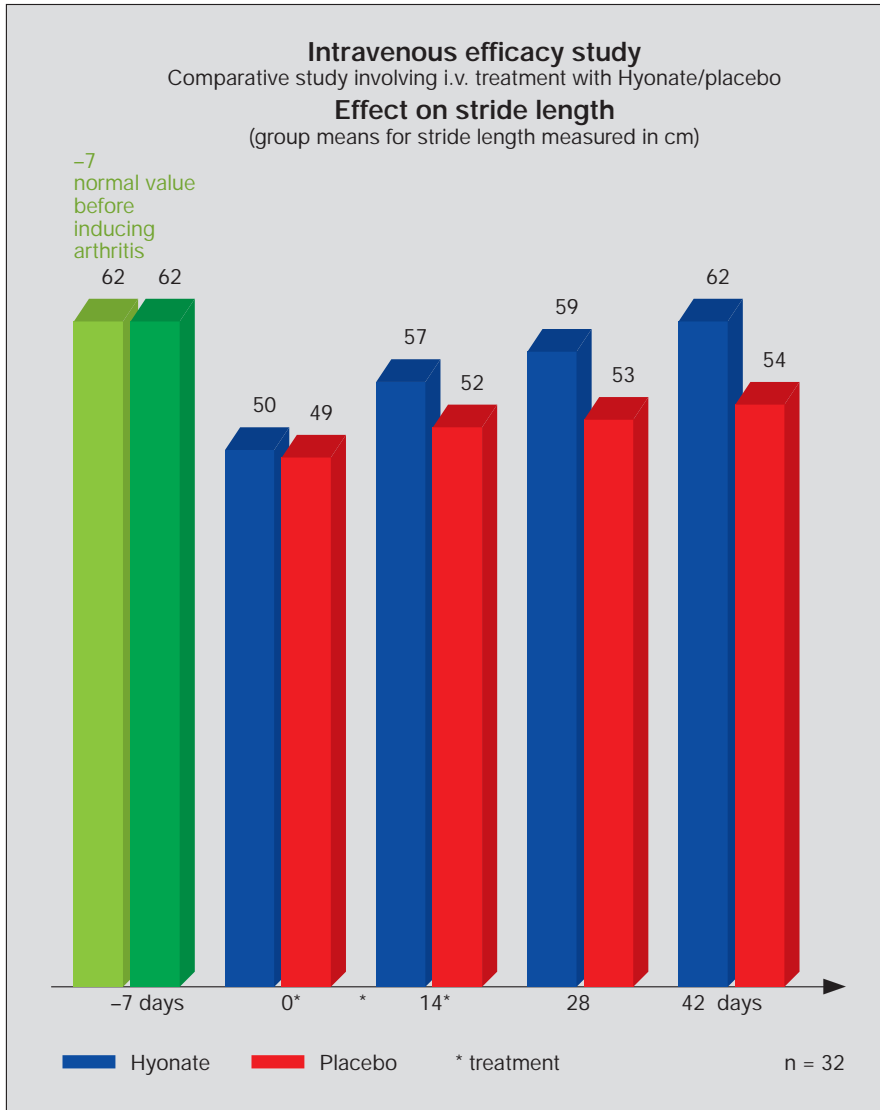
The following parameters were investigated:

- lameness, measured on a scale from 0 (free of lameness) to 5 avoiding use of the leg as much as possible)
- stride length measured in cm
- circumference of joint measured in cm
- mobility of the carpus measured in degrees (maximum degree of flexion of the carpus before pain is felt).

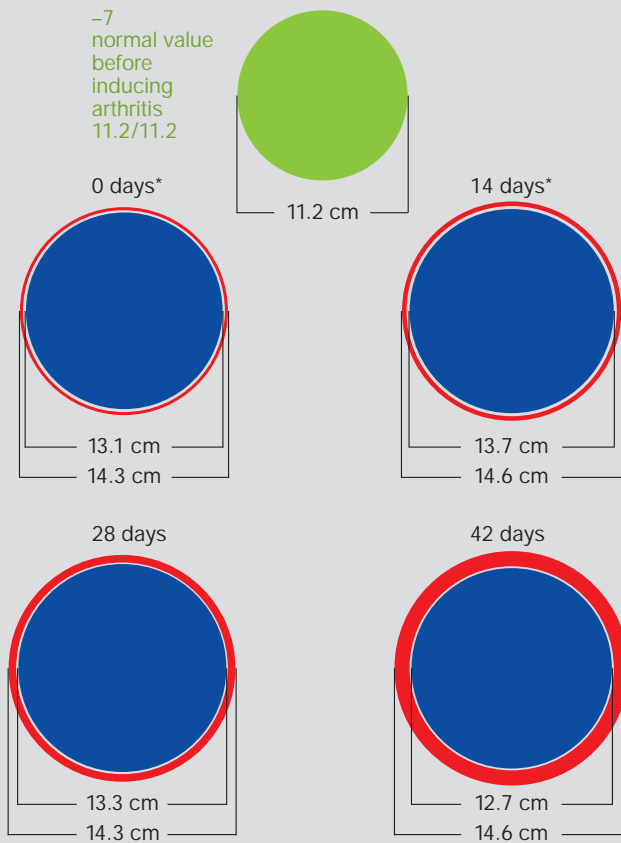
The diagrams on pages 23, 24, 25 and 26 represent the geometric group means on day -7, day 0, day 14, day 28 and day 42.



The results obtained with this tolerance model confirm the efficacy of intravenous Hyonate therapy.





Intravenous efficacy study
 Comparative study involving i.v. treatment with Hyonate/placebo
Effect on joint circumference
 (group means for joint circumference measured in cm)



 Hyonate  Placebo

* treatment

n = 32

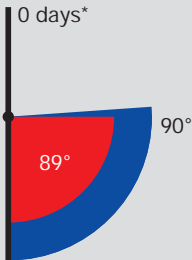
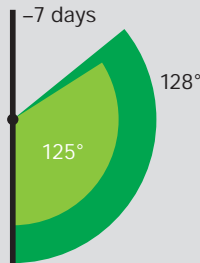
Intravenous efficacy study

Comparative study involving i.v. treatment with Hyonate/placebo

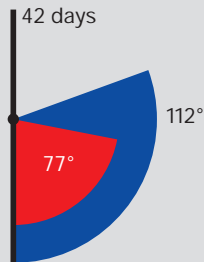
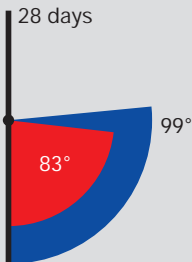
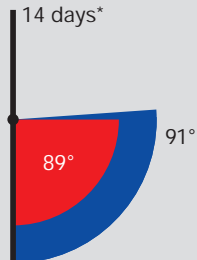
Joint flexibility


(group means for angle of flexion in degrees)

5-7
normal value
before
inducing
arthritis
125°/128°



7 days*



 Hyonate

 Placebo

* treatment

n = 32

Clinical studies

Clinical field studies have been conducted by a number of independent investigators. Animals were included in the studies if they presented at the surgeries with a diagnosis of acute to subacute non-infectious arthritis of the fetlock or the carpus.

They were treated with one of the following:

- Hyonate 4 ml i.v.
- Hyonate 2 ml i.v.
- a conventional, commercial hyaluronic acid product (as a positive control) at a dosage of 2 ml i.a. corresponding to 20 mg sodium hyaluronate.

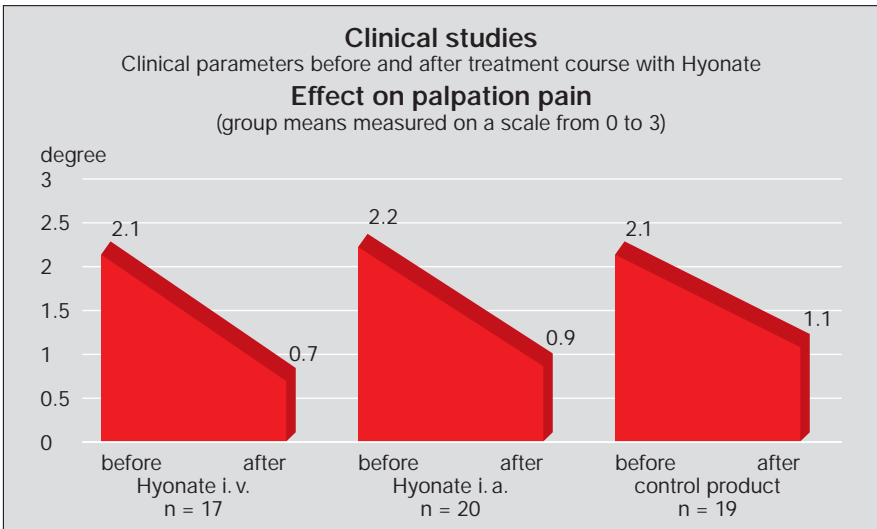
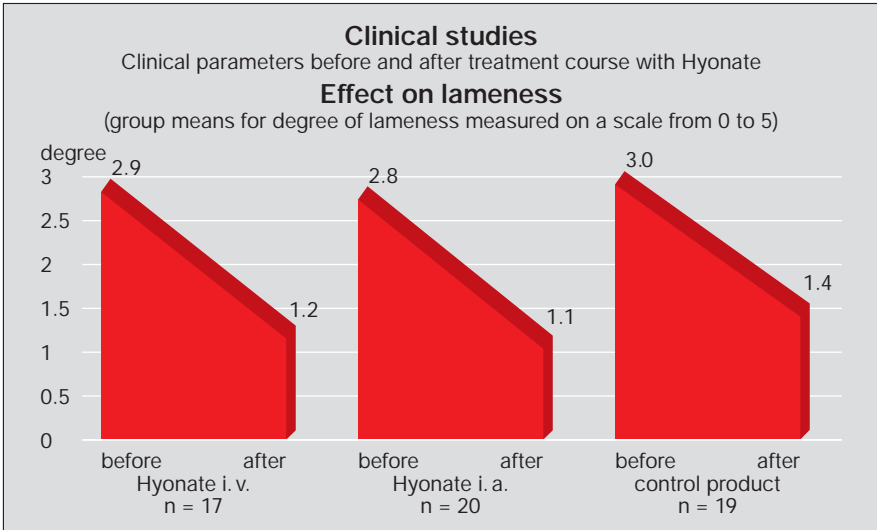
The animals were treated 1—3 times at weekly intervals without varying either the product or the mode of administration. None of the animals in this study received concomitant therapy with other medication. The study involved 56 horses. In order to guarantee objectivity, the findings and the progress of treatment were documented by a different veterinary surgeon who was unaware what treatment the animals were receiving. There were no significant differences between the groups in terms of the frequency with which the treatment needed to be administered.

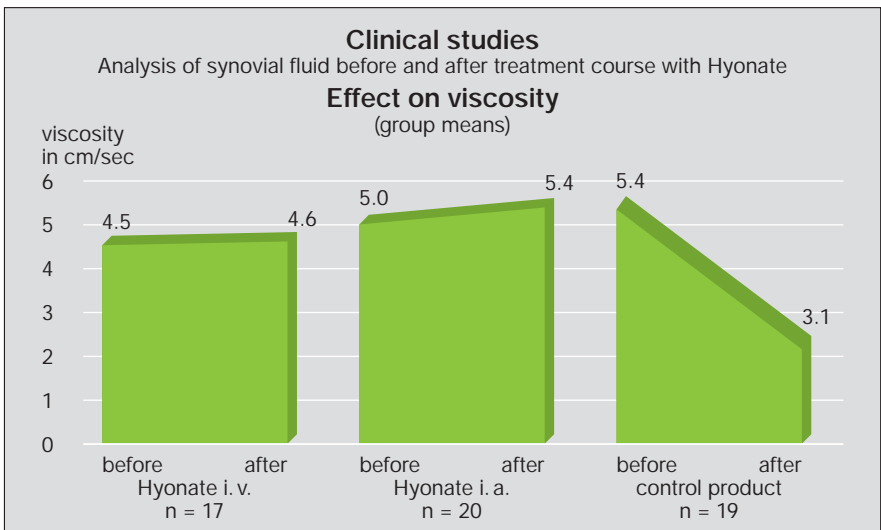
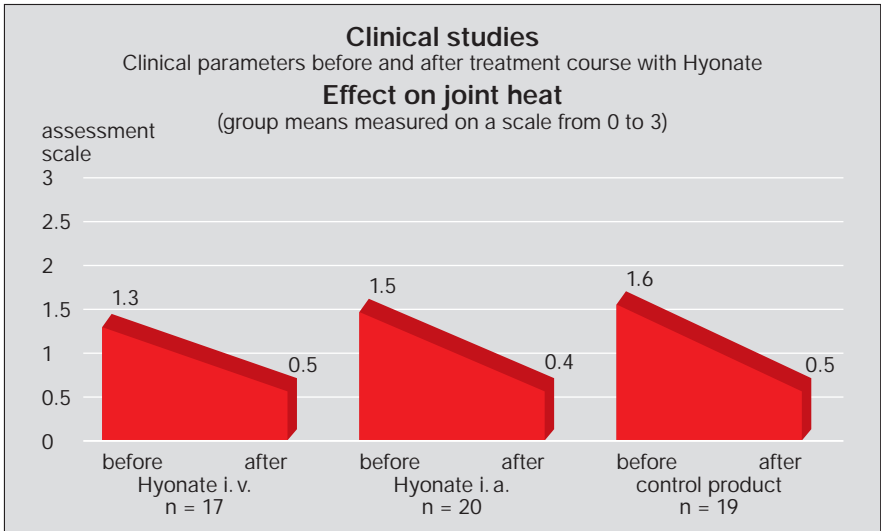
The success of treatment was validated by measuring the following parameters before and after completion of therapy:

- lameness measured on a scale from 0 (free of lameness) to 5 (avoiding use of leg as much as possible)
- joint heat measured on a scale from 0 (normal) to 3
- pain on palpation measured on a scale from 0 (painless) to 3
- viscosity of the synovial fluid measured in cm/sec.

The diagrams on pages 28 and 29 show the group means before and after treatment. The lameness, pain and joint heat parameters indicate that clear and rapid improvement has taken place. The results can be considered particularly encouraging as the last findings were recorded a mere 1 week after the final treatment had been administered, i.e. at the most 4 weeks after treatment commenced. Full healing could not be expected to have occurred by then. Furthermore, none of the horses received concomitant medication. In comparative terms, the results obtained with both Hyonate i.v. and Hyonate i.a. are as good as, if not better than, those obtained in horses treated with a conventional control product.

Other parameters such as joint circumference and the protein and hyaluronate content of the synovial fluid were also measured during these studies. In these cases normal values were recorded on completion of treatment, further underlining the therapeutic efficacy of Hyonate after both intravenous and intra-articular administration.





In a larger scale field study conducted at 4 veterinary centres, 72 horses with lameness of the carpus or fetlock attributable to arthritis were included in a comparative study.

This study also involved 3 different treatment groups:

- Hyonate 4 ml i.v.
- Hyonate 2 ml i.a.
- conventional, commercial product at a dosage of 2 ml i.a. (as positive control)

The animals were treated 2—3 times at weekly intervals.

The overall success of treatment in the individual groups is shown in the table below.

	very good/good outcome	slight improvement	no improvement
Hyonate i.v. (n = 21)	90% (19)	5% (1)	5% (1)
Hyonate i.a. (n = 25)	96% (24)	0% (0)	4% (1)
control product i.a. (n = 26)	88% (23)	8% (2)	4% (1)

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Picture references

- Fig. 8—11
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