

# Osteoarthritis

The Individual Osteoarthritis Therapy



## Autologous Proteins

- fight the cause in the joint
- protect the cartilage
- improve the joint mobility

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# Foreword

Our modern society envisions a future of autonomy and independence with the freedom to be active no matter our age. Being able to move without pain is of considerable importance in maintaining our independence and quality of life. A painful knee can cause everyday problems and prevent us from being as active as we would like. Many activities, such as jogging, playing golf or tennis or skiing can put enormous strain on the knee joint. The pain of osteoarthritis can make it impossible to participate in these activities. Joint pain can make routine activities, such as stair climbing, walking and shopping difficult. Preserving the health of our joints is fundamental to maintaining our independence and freedom at any age.

Even though osteoarthritis is a very common disease, its treatment was extremely dissatisfying in the past. Usually, the treatment consisted of treating the pain, until it was time for joint replacement surgery. How can the mechanisms of this disease be influenced? What can we do, in order to prevent this disease or stop its progression? These questions have been important to me, ever since the beginning of my orthopedic career 20 years ago and formed the motivation for me to be an active researcher of this disease looking for new ways.

The basics of Molecular Orthopedics were of special interest to me. Molecular Orthopedics deals with the translation of the cells' language, as well as understanding musculoskeletal disorders, thus, leading to new treatment concepts.

Ideas concerning this type of research were also from Prof. Christopher Evans (Harvard University, U.S.A.) and Prof. Paul Robbins (University of Pittsburgh, U.S.A.), with whom I have been working together intensively over the past twenty years.

Together with the biologist Dr. Julio Reinecke, it was possible to develop a new form of treatment speaking the language of the cartilage cells: the Orthokine-Therapy. This was very particular, as the treatment of the underlying causes of osteoarthritis has been made possible. In the meantime, I was able to prove the following together with my colleagues at the Center for Molecular Orthopedics in Düsseldorf/Germany: the Orthokine-Osteoarthritis-Therapy is effective and well tolerated. Independent clinical trials at other research centers around the world confirmed our positive experience with this new form of therapy.

This information booklet shall provide with current well-founded information, concerning modern treatment forms of osteoarthritis. This is extremely important, for it is clear that the outcome of treatment is best, the more the patient knows of the underlying causes of his or her disease. Thus, the great threat this disease forms for us loses its meaning, as activity and quality of life are maintained.

Prof. Dr. med. Peter Wehling

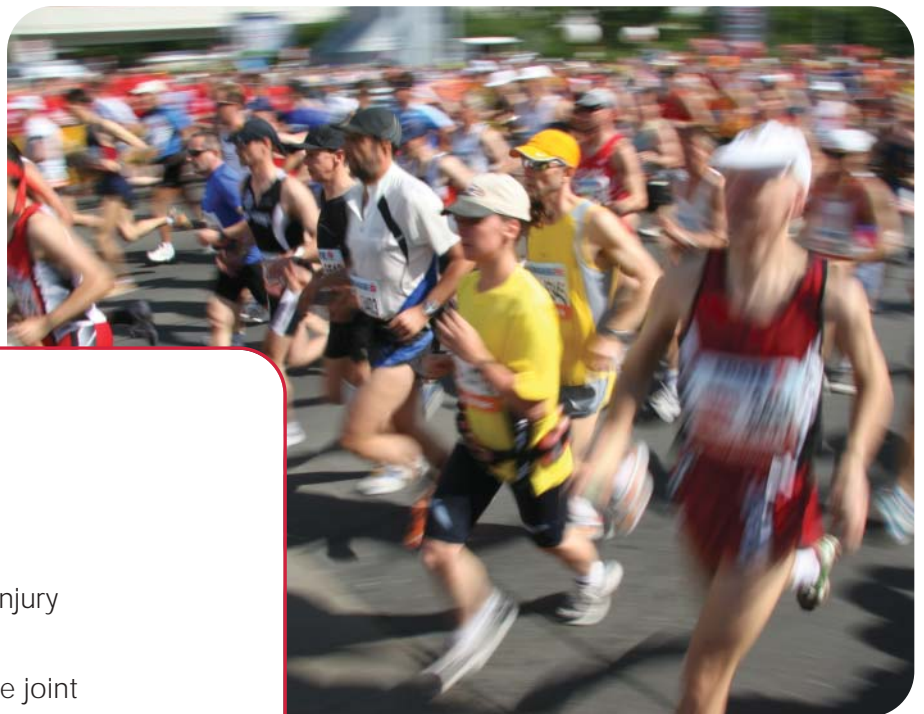


# Osteoarthritis: A Widespread Illness

As we get older, natural wear and tear slowly takes its toll on our body. Unfortunately, our joints are not exempt from this process, and arthritis is often the result. There are many different types of arthritis, the most common of which is osteoarthritis.

The fact is that within most developed countries about 10% of the population suffers from osteoarthritis. In these countries, approximately every 3rd visit to a doctor's practice is due to pain experienced during movement. Millions of days of work are missed each year as a direct result of this joint disease. The percentage of people with arthritis, unfortunately, increases with age.

Typical signs of osteoarthritis are abrasion of the joint's cartilage, pain, inflammation, and a reduction in joint mobility. Osteoarthritis generally develops slowly taking many years to cause symptoms. Once symptoms arise, osteoarthritis is already well established. Osteoarthritis can affect any joint, but most commonly occurs in the neck, low back, knee, hip and hands. Some experts maintain that osteoarthritis is simply part of the aging process. This however, is of no comfort for those suffering its symptoms.



## Risk Factors:

- Excessive physical strain
- Too little movement
- Overweight/Obesity
- Damage to cartilage through injury
- Broken bones
- Inflammation or infection of the joint
- Bone diseases
- Nervous disorders
- Metabolic illnesses (e.g. diabetes)
- Natural posture problems like knocked knees or bowed legs
- Genetic factors

# Causes for Osteoarthritis

Osteoarthritis always involves the degeneration of the joint's articular cartilage. This may have originated from damage caused by overstraining the joint, incorrect posture, or any other inappropriate pressure on the joint. It may have occurred during sports, during an accident, or perhaps due to meniscus removal. There are many possibilities.

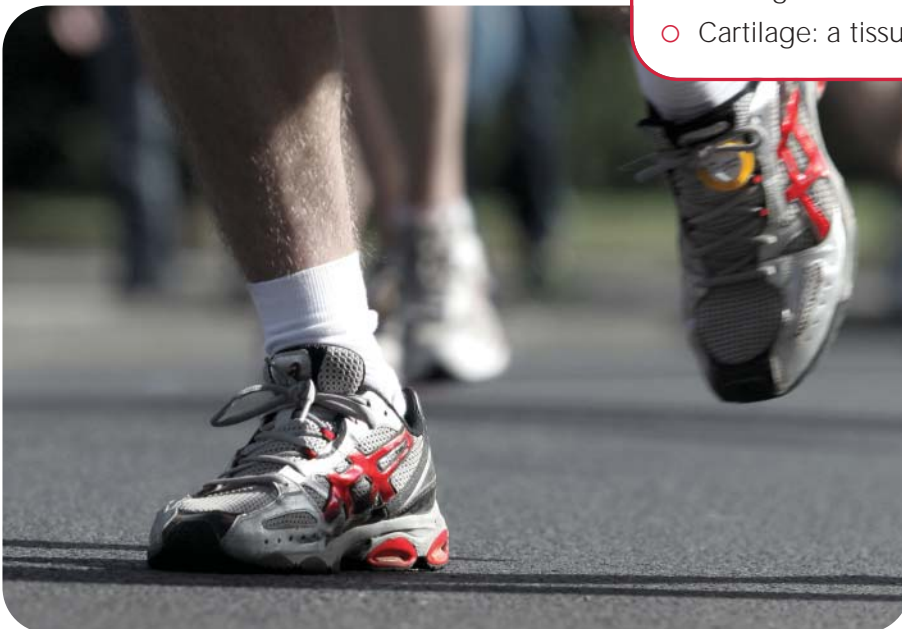
Factors that increase the chance of developing arthritis include being overweight, doing hard or repetitive physical work and participating in sports and physical activity. Posture problems or deformities like bowed legs or knocked knees may also lead to premature wear and tear.

As we grow older our cartilage loses its elasticity. It roughens, grows brittle and may crack easily. At this stage, normal movement produces friction causing the cartilage to wear down at an accelerated rate. If fragments of loose cartilage worn off by the mechanical degenerative process remain within the joint and irritate the synovial membrane, inflammation and

swelling of the joint will also occur. This is referred to as "activated osteoarthritis". Changes caused by inflammation of the synovial membrane may also decrease the nourishment supplied to the cartilage, accelerating the disease. Some choose to view osteoarthritis as a natural part of the aging process; after all, most other parts of the human body seem to wear out over the course of time – why should joints be any different? But just as everyone ages at a different rate, the onset of osteoarthritis and its rate of development differs from individual to individual.

## Main Points:

- Osteoarthritis is a chronic illness of the joints
- It can affect any joint in the body
- The knee is particularly susceptible to osteoarthritis
- Damage tends to begin within the articular cartilage
- Cartilage: a tissue without blood vessels

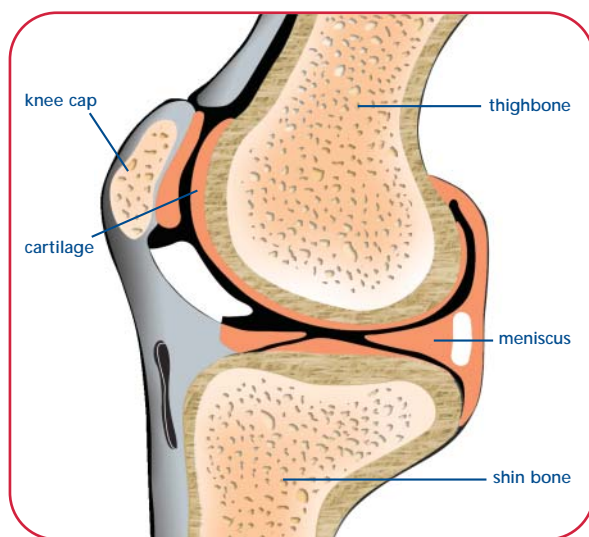


# The Knee Joint – a Miracle

Osteoarthritis also called degenerative joint disease is a chronic disease, which can occur in any joint within the body. The most common expression – osteoarthritis of the knee – is estimated to afflict 50% of people over the age of 55; almost 100% of those over 75. Our knee joints perform tens of thousands of movements every day – day in, day out – absorbing uncountable sudden shocks while giving us support and stability. When the enormous strains placed on the knee are considered, it is no wonder that knees are most at risk.

## The biggest joint of the body

Your knee joint works like a versatile hinge: you can bend and stretch it, and twist your lower outwards or inwards. Where the thighbone and shinbone meet at the knee the bones are covered in an elastic layer of gristle (articular



The knee joint shows complex structures. Therefore it is particularly delicate.

cartilage). This articular cartilage acts like a protective shock absorber, stopping the bones grinding against each other. It also greatly decreases friction during movement. The ends of the bones, including the articular cartilage, are enclosed in a "capsule" of connective tissue, holding the joint together. There is a thin film on the inside of the capsule containing blood vessels and nerves called the 'synovium'. The synovium produces lubricating fluid that also supplies nourishment to the cartilage. Last, but not least, the kneecap protects the interior knee from injury from outside.

Several structures are responsible for the stability of the knee joint.

- **Ligaments**

The ligaments are attached to the sides of the thighbone and shinbone, which ensure lateral stability (side to side motion) when the knee is extended.

- **Cruciate ligaments**

The two cruciate ligaments protect the knee joint from dislocating forwards or backwards and impart additional twisting stability.

- **Menisci**

The two half-moon shaped strips of very flexible cartilage that sit between the thighbone and the shinbone are called menisci. The function of the menisci is to spread the weight of the body over a wide area, lessening the stress on the contacting articular cartilage of the thigh and shinbones. In a healthy knee the menisci carry an estimated 50% of the weight. If for any reason a meniscus needs to be removed, the result is a significant increase in stress on the cartilage. As you can see, the knee joint is a complex structure. With so many functions and parts, the knee runs a high risk of showing early symptoms of wear and tear.

# Cartilage Tissue: A Unique Structure

All types of osteoarthritis involve damage to the articular cartilage. Damaged cartilage can no longer function properly. In order to continue supporting your body's weight, the stress from this damaged area must be transferred to the healthy surrounding cartilage. This ultimately overloads the healthy area and causes degeneration of the entire joint surface. Eventually the joint cartilage is incapable of weight-bearing without pain and inflammation. If normal levels of activity are maintained, the degeneration of the articular cartilage progresses to end stage bone on bone unless some form of effective treatment is provided.

The articular cartilage within the joint is unique, for normal, healthy articular cartilage tissue is not supplied with blood vessels. In other words, the cartilage cells do not have direct access to blood vessels, depriving them of nourishment through the blood stream. This means that the cartilage cells depend upon the surrounding lubricating fluid.

In order to remain nourished, the articular cartilage must be bathed in lubricating fluid. The weightbearing motion of walking and exercising during daily activity is necessary to distribute the fluid. When under stress, waste materials are squeezed out of the cartilage, and when the pressure is relieved, new lubricant with fresh nourishment is spread throughout the joint. The principal way the immune system operates and communicates with other tissues is through your blood stream. Because the articular cartilage has little contact with the blood stream, it has little contact with the immune system. The body's defenses reach the cartilage in a round-about way through the lubricating fluid. This lack of circulation to the cartilage creates a problem in delivering ingested medications into the joint. Higher concentrations of drugs in the blood stream are often required to achieve the desired effect. Drugs that can be introduced directly into the joint circumvent this problem and can affect the cartilage instantly.

## Important:

- Minor cartilage damage can lead to serious harm!
- Remember weight-bearing and movement of the knee joint is necessary to nourish the cartilage and removes harmful substances!



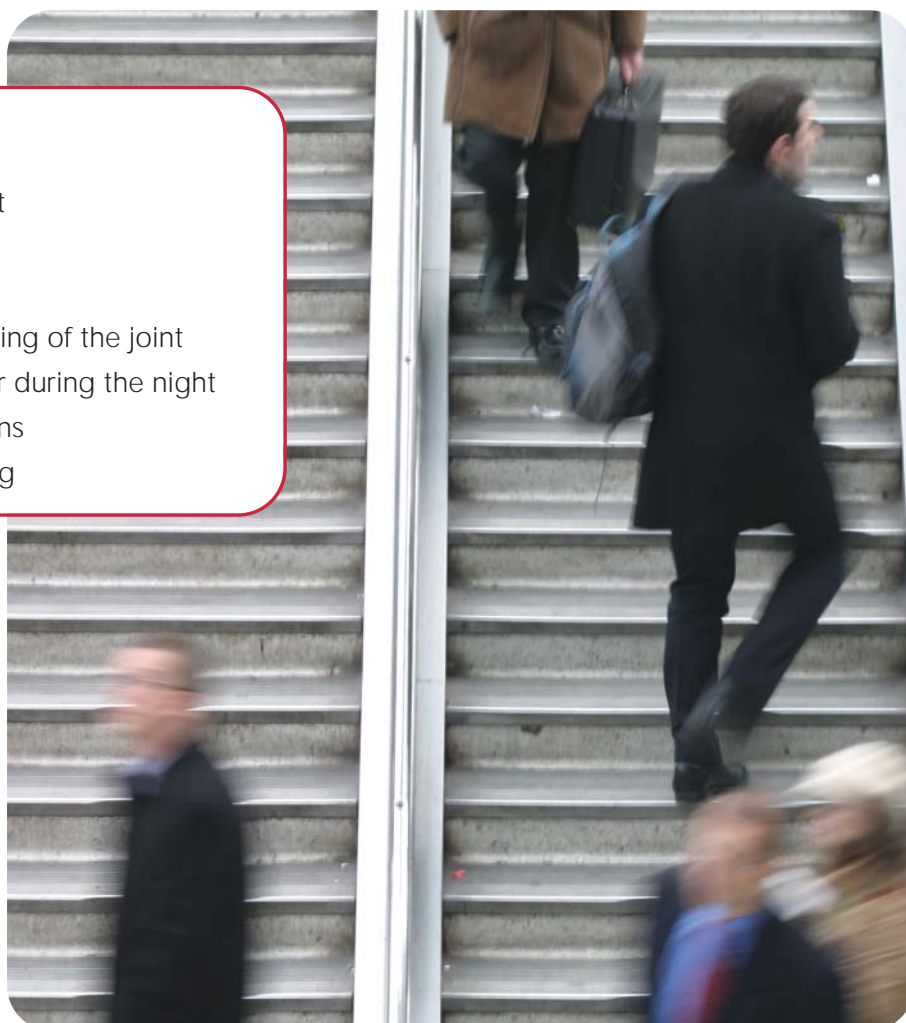
# Common Symptoms of Osteoarthritis

The first sign of osteoarthritis is often pain on initiating movement particularly after sitting for a while. Another important indicator is pain when extending the joint. As the disease progresses, the symptoms become more severe. Early morning pain and stiffness are common along with pain during the onset of weight-bearing and movement. After the joint has 'warmed up' the pain usually goes away, but it comes back again after a long period of activity. The joints may also make noise, like creaking or cracking, they may sometimes sound like Velcro tearing.

Patients often say that the pain is particularly severe during wet and cold weather. Signs of decreasing joint function include the onset of pain when the joint is at rest or during the night. An individual suffering from osteoarthritis of the knee joint may have difficulty going down stairs or getting in and out of vehicles. Should there be severe damage to the cartilage, the bone beneath the cartilage may also be affected.

## Common Symptoms:

- Pain at the onset of movement
- Pain through weight-bearing
- Restricted mobility
- Fluid within the joint and swelling of the joint
- Pain when the joint is at rest or during the night
- Sensitivity to weather conditions
- Noises like creaking or cracking





# Painful Alarm Signs

Pain and inflammation are the most important symptoms; they represent the awareness that the body has been injured or is being disturbed. The greater the number of cartilage cells being destroyed, the worse the pain and inflammation becomes. This alarm system mobilizes all available defence and rescue mechanisms in order to repair the damage as quickly as possible.

Unfortunately, osteoarthritis is a chronic disease, which means the conflict within the joints becomes a perpetually smouldering situation. The rescue operation may be on its way, but it seems that our rescue forces are incapable of preventing further damage to the cartilage. More pain and inflammation usually follow from the normal wear and tear of everyday life.

## When Joint Pain Becomes Unbearable

As the pain worsens, we attempt to treat the joint by resting it. This lack of use only speeds up the process of destroying cartilage by preventing nourishment from getting through and waste from being removed. Simultaneously, the ligaments that support the joint weaken and the muscles atrophy. In order to avoid pain, we “use the joint differently”. Muscle imbalances changes in the joint’s capsule occur, both leading to further restriction of movement. This significantly reduces joint nourishment and increases the load on the already damaged cartilage. Conventional treatment adds to the progression of disease by diminishing pain without stopping the degenerative process. When the pain is absent, we tend to put more pressure on the joint again, thus, causing further cartilage damage. Conventional treatment merely prevents us from feeling the damage as it occurs.



### Important:

- Contact your doctor at the first sign of joint pain occurring at the beginning of movement, weight-bearing or upon awakening.

# Stages of the Disease

## Early Stages

Osteoarthritis begins with damage to the joint's articular cartilage, possibly by a preceding injury to the joint, such as twisting, collision with another object or by simply overloading the joint. This first damage is often so minor that it is seldom noticed, but it does lead to major changes. The damaged cartilage can no longer carry its share of the load on the joint and must rely on the surrounding healthy cartilage to carry an extra share of the burden. This simple damage to the cartilage may progress to true osteoarthritis.

## Intermediate Stages

In the intermediate stages the cartilage layer becomes thinner and roughens. During the course of time, deeper, more irregular clefts form within the cartilage, leading to shifting the load onto the remaining healthy cartilage. When first reporting their symptoms to the doctor, many patients are already at this intermediate stage of disease; the pathological alterations are significant not yet as serious as they can become. As degeneration continues, holes and fissures develop, some extending to the bone beneath the surface of the articular cartilage.

## Advanced Stages

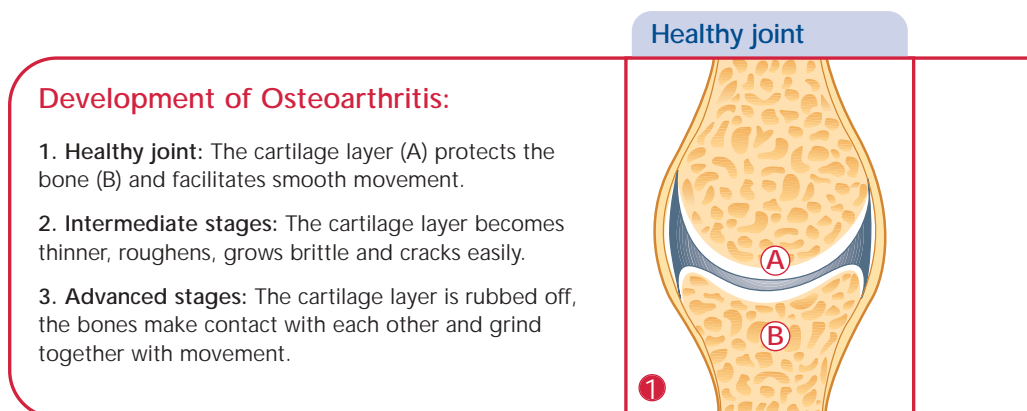
As the degenerative processes continue, the cartilage layer is eventually rubbed off or simply dissolves, exposing the underlying bone. Without the protective cartilage on the articular surface, the bones rub against each other. This advanced stage of cartilage decay leads to increasing stiffness of the joint. When the joint becomes too painful or too stiff to move, the joints function can only be restored through total joint replacement surgery.

## Diagnosis

Nowadays, thanks to the modern imaging technology known as Magnetic Resonance Imaging (MRI), pathological changes within the joint's cartilage can be detected and analysed more easily.

Doctors classify the progression of osteoarthritis according to its severity, using categories of stage I (onset) to stage IV (advanced). Analysis is necessary because the type of treatment depends on the stage of the osteoarthritis.

Patients with mild to intermediate arthritis still have so many healthy cartilage cells remaining, that a new therapy utilising the body's own proteins is the key to significantly slowing down or even stopping the degenerative process.



# Molecular Orthopedics

The field of Molecular Orthopedics has revealed the biological causes of musculoskeletal diseases. Thus, this field has made biological treatment possible. This field derives important facts from the following specialties: orthopedic surgery, molecular biology and physiology. As the field of Molecular Orthopedics deals with researching osteoarthritis, it has enabled us to understand the depth of this disease. Thus, scientists have discovered a fundamental cause of joint disease. The protein Interleukin-1 (IL-1) is one of the chief evildoers concerning osteoarthritis, as it forms an inflammatory agent.

It bears the capability of changing other cells' function, as it is a mediator of our immune system. This can form a positive function, when it comes to opening a quick pathway for our body's repair troops, so that they may reach the place of destruction in time. On the other hand, IL-1 may also lead to damage, inflammatory processes and joint pain. These negative influences form main causes of the development and progression of cartilage damage leading to osteoarthritis. Nevertheless, the mere knowledge of one cause is not sufficient enough for treatment.

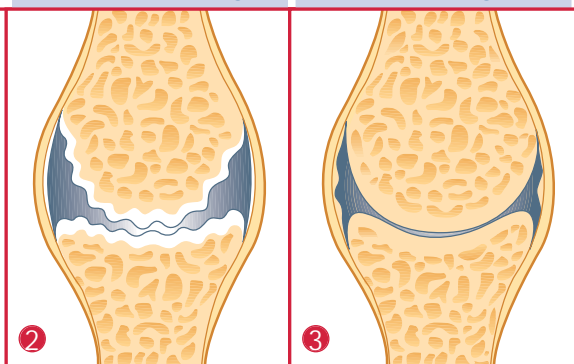
At the end of the 80's, an American research group was able to find the main protein against osteoarthritis: the Interleukin-1-Receptor-Antagonist (IL-1Ra). This is the natural counterpart of IL-1. IL-1Ra prevents the destructive influences of the evildoer IL-1, as IL-1Ra is the good guy defending the cartilage.

There are proteins available within our bodies that can fight the destructive processes within the arthritic joint.



Intermediate stages

Advanced stages



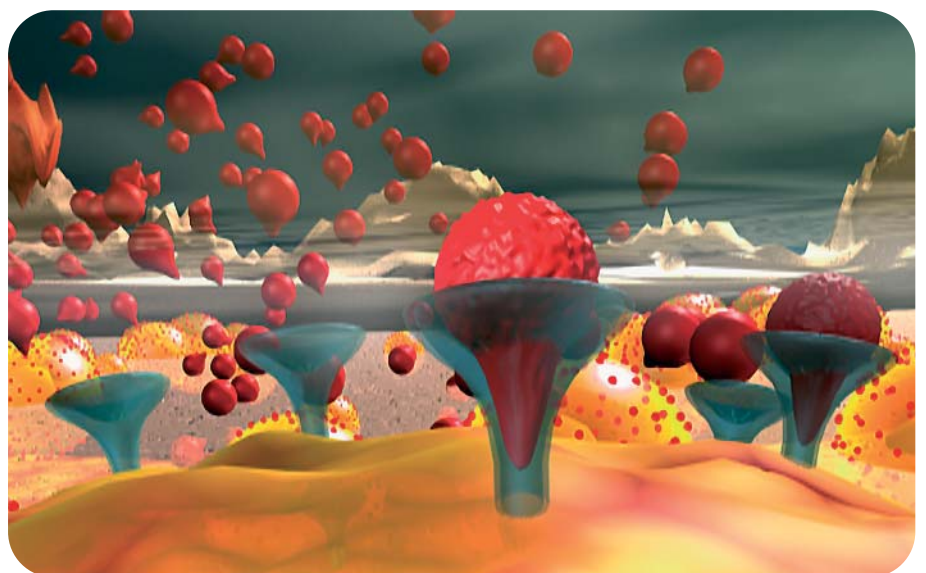
# Harmful Proteins Destroy the Cartilage

Then why, if everyone has these defence mechanisms within their body, do people have osteoarthritis? Basically, all the chemical processes occurring within our bodies have a single aim: to maintain a naturally balanced state between destructive and protective elements. There is no creation without destruction or in the case of a worn or injured joint, there is no repair without destructive and protective elements. Balance between these elements guarantees health.

Disease signifies that the balance within the body has been disturbed, and that an attempt is being made to correct the disturbance and re-establish balance. Once we discover the main cause of imbalance, discovering treatment is not far away.

In the case of osteoarthritis, Interleukin-1 causes cartilage damage, inflammation and pain. Interleukin-1 is the 'destructive' protein. Interleukin-1 receptor antagonist (IL-1Ra) as well as several other cytokines and growth factors make-up the "protective" protein that counters the action of IL-1 and helps to maintain the healing balance.

The joints of healthy individuals show a natural balance between destructive and protective proteins. People with healthy joints maintain a state of equilibrium between these factors whereas those with osteoarthritis have a preponderance of destructive proteins.





# Treatment Possibilities for Osteoarthritis

Pain and loss of mobility form the greatest problems and need for treatment, as far as degenerative joint disease is concerned. The mild to moderate stages of arthritis are usually treated non-operatively. Surgery is recommended for severe cases of arthritis.

## Non-operative Treatment

The goal of treatment with medication is to ease pain and to improve joint function. Analgesic treatment involves gentle and strong pain medication. NSAIDs are the most common form of medication, as they are anti-inflammatory and analgesic. Many of these analgesics lead to a temporary improvement of symptoms, but they tend to show many side-effects, in the long run. Substances, such as glucosamine are used, in order to support the metabolism within the articular cartilage. This type of medication is supposed to ease arthritic symptoms and delay the destruction of the articular cartilage.

## Intra-articular Injections

Injections containing corticosteroids, hyaluronic acid or proteins are often used when treating arthritis. The advantage of this form of treatment is, that it is possible to install a high drug concentration directly into the joint. This means, that we may profit from a high drug concentration, on the one hand, without affecting the entire organism, on the other hand. Intra-articular injections play an important role in routine orthopedic treatment, for they are tolerated very well, when applied in accordance with appropriate safety measures.

## Corticosteroids

Corticosteroid injections are recommended, when we are dealing with acute inflammatory arthritic symptoms, for they act as strong analgesic and anti-inflammatory agents. Joint effusions can be treated quite effectively with this medication. However, it is important to keep in mind that corticosteroids possibly lead to cartilage damage, although they show many good effects.

## Hyaluronic Acid

Hyaluronic acid is a natural content of the joint fluid. It is responsible for joint lubrication and shock absorbance. It can also be used as a drug, in order to lubricate the joint, thus, improving joint function, especially when it comes to degenerative arthritic changes of the knee joint.

## Supplementary Treatment Forms

Besides medication, there are other forms of treatment meant to stabilize the joint and improve joint and muscle function. Physical therapy and acupuncture are most important, in this respect. Acupuncture is very effective, when it comes to treating pain syndromes caused by arthritis. Individual treatment forms may involve underwater movement therapy, hot packs, cold packs, electro-therapy, as well as baths and other types of packs.

## Surgery

In some cases, it is only possible to improve pain symptoms by taking care of the mechanical problem. As the stage of arthritis progresses from mild to moderate, arthroscopic surgery is performed, in order to smooth out the articular cartilage and remove damaged particles. Total joint arthroplasty has been proven to be effective, especially when treating the final stage of arthritis of the hip and knee joints.

# Orthokine-Therapy against Osteoarthritis

The concept of the Orthokine-Therapy is to derive the body's own inhibiting agents and growth factors from the blood stream and to inject them into the afflicted joints afterwards.

First, the physician must draw blood from the patient, using a special syringe. This syringe contains special beads leading to the induction of the blood cells, so that they produce protective proteins during a complicated mechanism. The blood samples must be stored 6 to 9 hours at body temperature in an incubator, so that the proteins can multiply.

After this time, the biochemical process is complete. During this interval the quantity of inhibiting agents, such as IL1-Ra, increases to about 100 times as much as it was in the beginning.

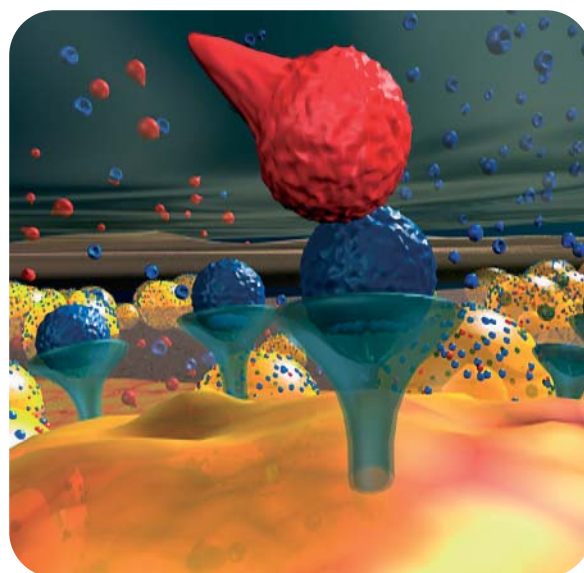
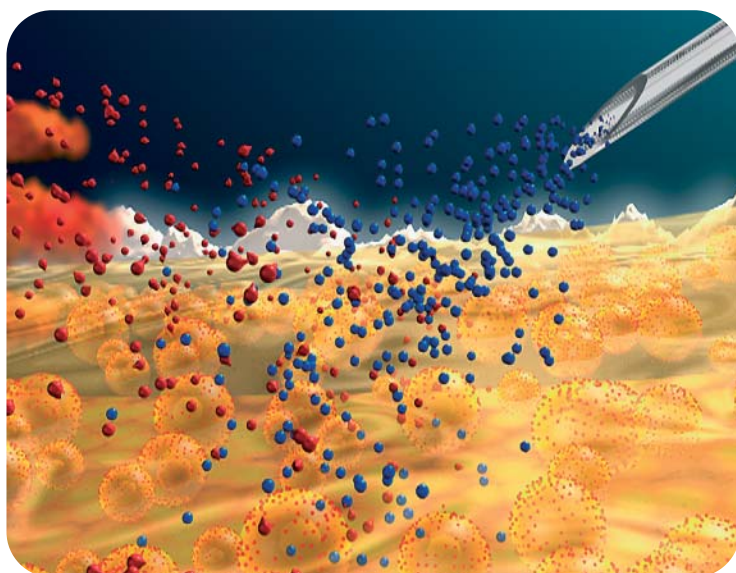
Following incubation the sample is centrifuged to allow the separation of the protein rich serum from the other elements in the blood. The enriched serum is then divided into a number of vials that can be used immediately or deeply frozen for use in the future.

The serum now is ready for joint application. The serum contains a greatly empowered team consisting of the patients own protective proteins, ready for joint injection.

This way the deficiency of protective proteins in patients with osteoarthritis is compensated and the destructive agents are defeated. The protective proteins which act against osteoarthritis dock onto the receptors on the cartilage surface and capsular cells. Thus, these parts of the cells are no longer vulnerable for attack by destructive inflammatory agents.

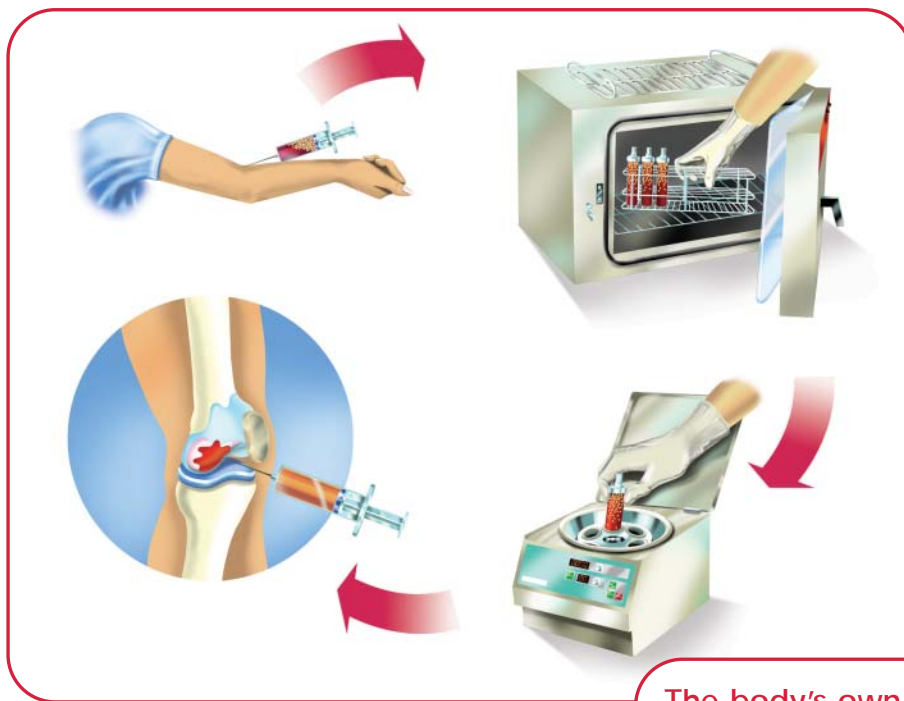
The Orthokine-Therapy provides us with about 100 times the quantity of the body's own osteoarthritis inhibiting agents, which enfold their positive effects within the diseased joint, thus, preventing pain, inflammation, as well as further damage to the articular cartilage.

The Orthokine-Therapy is used in Europe but not yet approved in the United States by the FDA. If patients come from abroad the whole treatment can be carried out in Düsseldorf/Germany in one week starting on Monday until Friday or Saturday.



# The Body's Own Proteins from the BioLab

- The blood samples are taken from the arm vein with a special syringe. The glass beads in the syringe induce the blood cells to synthesize increased amounts of protective proteins that inhibit osteoarthritis.
- The temperature of 37°C in the incubator mimics normal body temperature and creates an optimum environment for protein synthesis.
- A centrifuge separates the amber serum from the blood clot; the serum contains high concentration of proteins that protect against osteoarthritis.
- The serum is filled into several syringes. Generally the patient receives six injections into the afflicted joint or three to six into the afflicted spine area. If patients come from abroad the whole treatment can be carried out in one week.



## The body's own proteins – strong allies against

- Joint pain
- Cartilage destruction
- Inflammation



# When Does the Orthokine-Therapy Help?

The Orthokine-Therapy can be used to treat the following arthritic joints:

- Ankle joint
- Knee joint
- Hip joint
- Shoulder joint
- Wrist and finger joint
- Intervertebral joints (spinal joints)

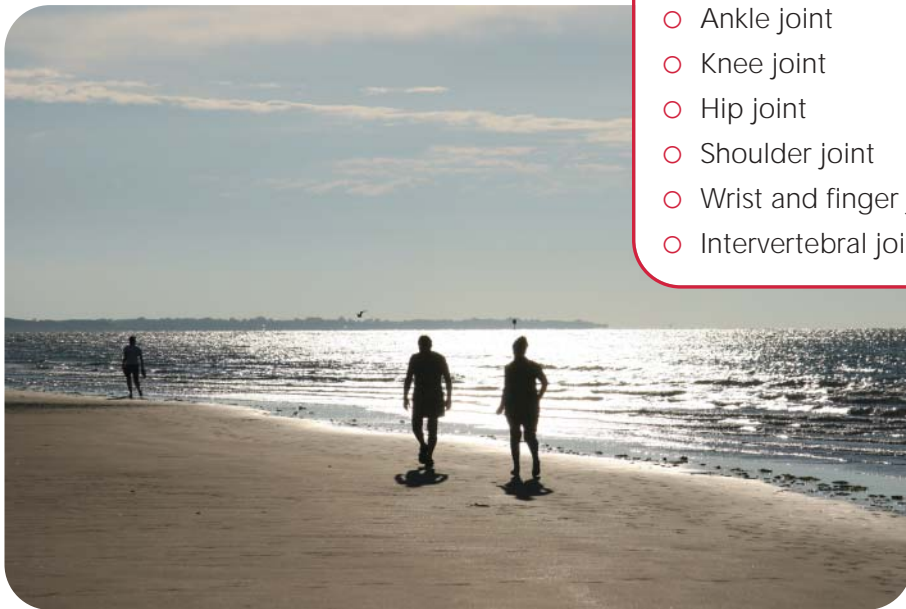
The Orthokine-Therapy provides you with your body's own healing proteins in the treatment of mild to moderate osteoarthritis; it prevents the progression of chronic osteoarthritis directly within the joint. The natural mechanisms of the human body are used to intervene in the destructive process of this disease, a further goal of Orthokine-Therapy is to prevent further damage to your healthy articular cartilage.

Even limited improvement is important in postponing or preventing the need for total joint replacement.

The body's own proteins are strong partners in the battle against osteoarthritis; they form the key to the improving and preserving your quality of life.

## Application of the Orthokine-Therapy

- Ankle joint
- Knee joint
- Hip joint
- Shoulder joint
- Wrist and finger joint
- Intervertebral joints (spinal joints)



## What Can You Expect...

If you have chosen to have the Orthokine-Therapy, you have chosen to support the natural mechanisms within your body with a reinforced supply of your own osteoarthritis antagonist proteins. This means, that you will receive several intraarticular injections into the arthritic joint. They can be applied at a weekly basis, twice a week or according to a different schedule, depending on your symptoms and your doctor's diagnosis of your condition.

The effects of Orthokine are usually revealed after approximately six weeks. Typically, pain is noticeably reduced, inflammation decreases, and the affected joint becomes more mobile. A number of patients find that their symptoms are relieved after the first injection.

The length of the interval of improvement depends on both the stage of the disease, as well as the patient's general physical condition. Usually, the improvement of your osteoarthritis symptoms can last for a period of two years or even longer.

Of course, every patient is different, and that is one reason why the results are never exactly the same for each person. Another reason may be that the reinforcements of antagonist proteins delivered by an injection of Orthokine differ in effectiveness for each patient.



Unfortunately, the osteoarthritis patient cannot sustain the supply of reinforcement antagonist proteins from the own body. When the effects of the Orthokine-Therapy wear off, the old familiar symptoms may return. In that case – depending upon the opinion of your doctor – a further course of Orthokine injections may be necessary.

The Orthokine-Treatment is very safe and tolerable, because it is wholly produced from your own blood cells. Your body knows its own proteins well. It recognises them and accepts them. That explains why no serious side effects have been observed, yet.

Treatment with Orthokine only makes sense if osteoarthritis has not progressed to endstage. If the destruction of the cartilage has reached the stage where there are no more cartilage cells, then even your own antagonist proteins will be powerless. Joint arthroplasty is still the first choice, concerning the final stage of osteoarthritis, in which there is bone to bone contact, as the articular cartilage is no longer present.

Therefore, it is important to react to the first symptoms of osteoarthritis and to consult your doctor, immediately. The earlier the progressive joint destruction is discovered, the better the prognosis becomes. As long as there are still healthy cartilage cells present, the body's own antagonist proteins can do their job and reduce cartilage damage, inflammation and pain.



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