



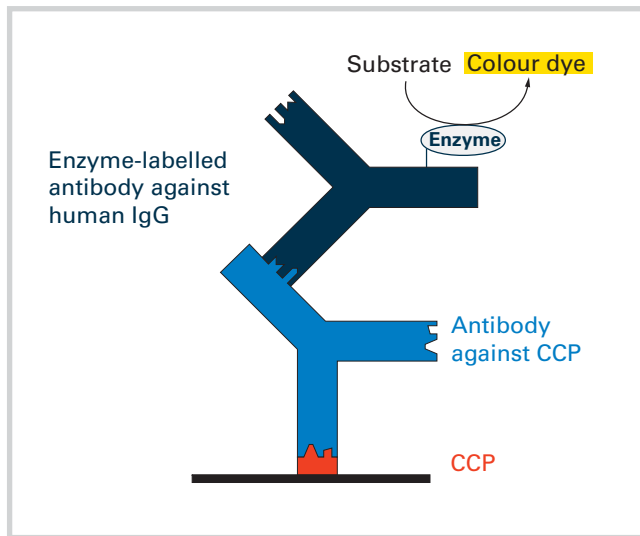
The EUROIMMUN-Anti-CCP ELISA

Experienced clinicians use the **EUROIMMUN Anti-CCP ELISA** for the detection of antibodies against CCP. The test meets the high requirements of the European Quality Standards EN ISO 9001 and 13485.



Positive and negative reactions in the Anti-CCP-ELISA

Reagent wells coated with highly purified, synthesized CCP antigen are the main component of the EUROIMMUN Anti-CCP ELISA. These wells are incubated with diluted patient serum, whereby specific antibodies in positive samples bind to the immobilized antigen. To visualise the bound antibodies, a second incubation step is performed using enzyme-labelled anti-human IgG, which catalyses a colour reaction.



Test principle of the EUROIMMUN Anti-CCP ELISA



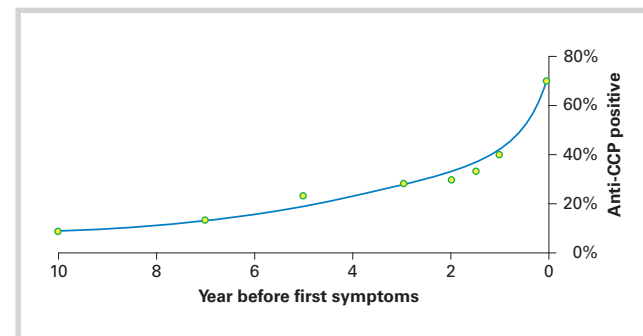
Treatment, advantages of early diagnosis

Rheumatoid arthritis is treated on an individual basis depending on clinical symptoms, disease severity and joint changes that have already taken place:

- **With drugs:** reduction of pain, inhibition of inflammation
- **Operative:** removal of joint damage
- **Supportive:** physiotherapy

Today, the **severe consequences** of the disease can usually be **avoided** by implementing consequent therapy in the early stages. Many rheumatoid arthritis patients who now suffer from severe symptoms would have been able to lead an almost normal, pain-free life if they had been treated appropriately from the start. The first months of the disease are the most critical. In these months, however, the disease course is so untypical that a precise clinical diagnosis cannot be made and medical treatment is started only when it is too late.

Two state-of-the-art methods can help diagnose fresh rheumatoid arthritis: **nuclear magnetic resonance tomography**, which rheumatologists and radiologists can perform, and the revolutionary determination of **anti-CCP antibodies** by the medical laboratory. In a large proportion of patients antibodies against CCP are present years before the first symptoms occur.



Antibodies against CCP before rheumatoid arthritis starts

Already at the start of the disease when the first joint damage occurs, the determination of antibodies against CCP in a blood sample can **clarify** a diagnosis of rheumatoid arthritis in 80% of patients. If the result is positive, treatment can begin **immediately**, and in many cases severe, permanent joint damage can be avoided. A negative result does not exclude the disease.



Where can your anti-CCP value be measured?

Due to the high diagnostic hit rate, the analysis of antibodies against CCP offers four out of five of patients the chance to identify their disease in the early stages and to begin treatment straightaway. Testing for rheumatoid factors on the other hand does not enable either a reliable or an early diagnosis.

Please ask your doctor if an anti-CCP determination is advisable. Your doctor can take a blood sample for analysis. Your doctor should make sure that the laboratory uses an anti-CCP ELISA of the "second generation" with authentic CCP as the target antigen, as offered by only a few competent manufacturers.

Further advice

Rheumatology Societies offer advice and practical help to persons suffering from rheumatic diseases. Please contact your local society.

Provided by:



- Immunofluorescence
- Enzyme immunoassays
- Histology and cytology
- Recombinant techniques
- Analysis systems
- Autoimmune diseases
- Infectious diseases
- Allergology
- Antigen detection
- Genetic characteristics

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ANTI-CCP

A serological test for early recognition and diagnostic confirmation of Rheumatoid Arthritis



Early phase of rheumatoid arthritis

With a new serological test rheumatoid arthritis can be reliably diagnosed in 80% of cases: in the laboratory **autoantibodies against CCP** (cyclic citrullinated peptide) are investigated. Compared to "rheumatoid factors" antibodies against CCP are more closely associated with rheumatoid arthritis and are therefore more suitable for diagnostics.

Antibodies against CCP already occur in the **early phase** of the disease, and in many unclear cases their detection plays an important role in the decision to **start specific treatment early**. This can make patients' lives more bearable by preventing many severe late symptoms.



The term **“rheuma”** encompasses a group of diseases that affect the motoric apparatus (joints, muscles, tendons) and are accompanied by pain and restricted movement. The group includes:

- Arthrosis (destruction of joints)
- Fibromyalgia (soft tissue rheumatism)
- Gouty arthritis (through increase in the level of uric acid)
- Collagenosis
- Rheumatoid arthritis

Symptoms of rheumatoid arthritis

Rheumatoid arthritis, also called (primary) chronic polyarthritis, is an inflammatory disease of connective tissue. It is a chronic progressive condition, which occurs in phases and manifests above all in the joint mucous membranes (synovial membrane: synovialitis), from which it proceeds to the cartilage and bones. At first the small joints are affected symmetrically, with time also the large joints. If the disease is left untreated, severe damage often occurs. Aside from the joints, various organs can also be involved (heart: myocarditis, lungs: pleuritis, nerves: polyneuritis, eyes: keratoconjunctivitis sicca). 1% of the population is affected by rheumatoid arthritis, women three times more frequently than men. The disease can occur at any age, with the highest frequency occurring between 35 and 45 years and after 60 years.

Initial symptoms of rheumatoid arthritis are:

- **Stiff joints** (in the morning, longer than 15 minutes)
- **Swelling of joints** (soft, often spindly deformation of the finger joints)
- **Joint pain** (at night and in the morning)
- **Tiredness/exhaustion**

In later stages of the disease the following joint changes can often be observed:

- **Swan neck deformity:** bending of the finger joints in a forwards direction
- **Rheumatoid nodules:** rubber-like lumps in the region of the joints
- **Ulnar deviation:** bending of the fingers towards the little finger



Swan neck

Rheumatoid nodules

Ulnar deviation



An experienced rheumatologist can diagnose a distinctive case of rheumatoid arthritis without the aid of the laboratory. The disease is identified by means of anamnesis and physical examination of the patient. Additionally, changes in bone structure typical for rheumatoid arthritis can be seen on an X-ray image.



Rheumatoid arthritis



Healthy hand

Diagnosis is more difficult in patients with less pronounced symptoms, especially in the **early phase of the disease**. But a definitive diagnosis is of decisive importance in these patients because it is still possible to treat the disease and avoid the severe late consequences of rheumatoid arthritis.

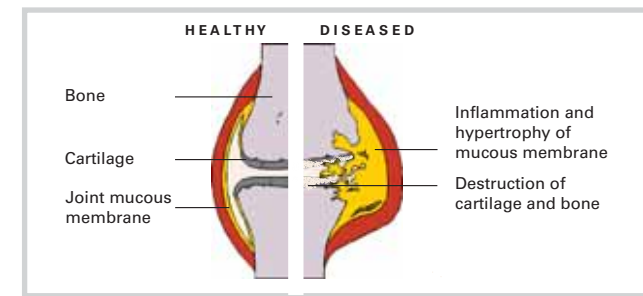
Patients with rheumatoid arthritis can now benefit from a new scientific breakthrough: a laboratory test that can reliably identify the disease in the early stages in four out of five cases – the determination of **antibodies against CCP**.

Some further cases of early rheumatoid arthritis can be identified using a new imaging procedure, **nuclear magnetic resonance tomography**.

Pathogenesis

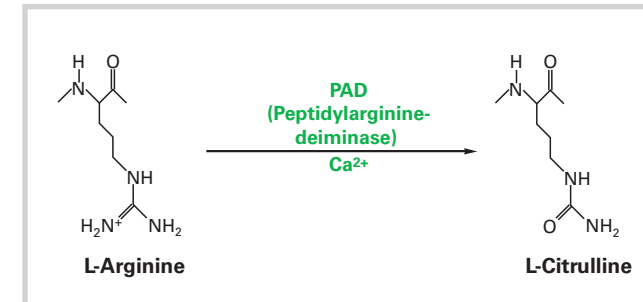
Rheumatoid arthritis is an autoimmune disease. The immune system normally protects an organism from infections with viruses or bacteria, while sparing bodily tissues. In autoimmune diseases this tolerance breaks down and various organs or tissues are attacked by the immune system.

In the case of rheumatoid arthritis the autoaggression is directed against the mucous membranes of the joints. Over time this leads to severe chronic inflammation, which destroys cartilage and bone.



Destruction of joints in rheumatoid arthritis

Medical laboratory diagnostics has delivered new evidence towards understanding the pathogenesis: autoantibodies against proteins containing the rare amino acid citrulline were found in the serum of patients with rheumatoid arthritis. It could be shown that citrullinated proteins were expressed in the mucous membranes of affected joints of rheumatoid arthritis patients, but not in the tissue of healthy persons. The main autoantigen responsible for the inflammatory reaction and tissue destruction has probably now been identified.



Formation of citrulline by the enzyme PAD

Pharmacological researchers are already trying to exploit this new knowledge for the treatment of rheumatoid arthritis. Specifically acting drugs may inhibit the enzyme PAD and stop the formation of citrulline, thus halting the inflammation.

Modern enzyme immunoassays for the diagnosis of rheumatoid arthritis use **cyclic citrullinated peptides (CCP)** as a potent antigen substrate. Antibodies against CCP most likely possess a closer etiological disease association than the longer known rheumatoid factors. The test parameter anti-CCP represents a new, highly specific marker for rheumatoid arthritis.



Laboratory diagnostics

The medical laboratory can help to identify rheumatoid arthritis and also to assess the clinical activity of the disease (unspecific diagnostics).

Unspecific laboratory parameters include:

- **Blood count**
- **Blood sedimentation rate**
- Concentration of **C-reactive protein**

Until a few years ago the only **specific parameter** for rheumatoid arthritis was **rheumatoid factors**, due to lack of a better alternative. These can be detected in 79% of patients with rheumatoid arthritis, but they also occur in many other rheumatic diseases, in infectious diseases and in healthy individuals.

In contrast, **antibodies against CCP** occur almost exclusively in rheumatoid arthritis and are found in 80% of patients. They are not currently known to be associated with any other disease.

Antibodies against CCP are often found in rheumatoid factor-negative rheumatoid arthritis and vice versa. Therefore, the two parameters can complement each other to a certain extent.

The following table illustrates the **superiority of the new parameter anti-CCP over rheumatoid factors**: a positive anti-CCP result is more-or-less proof of rheumatoid arthritis (predictive value: 98%). The result “rheumatoid factor positive” allows only a vague suspected diagnosis, since even in healthy blood donors rheumatoid factors are often detectable in the serum.

Blood samples tested	Positive for anti-bodies against CCP	Positive for rheumatoid factors
Patients with rheumatoid arthritis	80 %	79 %
Patients with other rheumatic diseases	3-8 %	10-73 %
Patients with infectious diseases	1-2 %	22-62 %
Healthy blood donors	0 %	5-10 %
Specificity for rheumatoid arthritis	98 %	63 %

Comparison of anti-CCP antibodies and rheumatoid factors