Chronic polyarthritis—classification, prevalence, and natural course

- Inflammatory joint disorders are common in the population. Most frequent is rheumatoid arthritis (RA), which is present in nearly 1% of adults. The prevalence of psoriatic arthritis (PsoA) is uncertain, but estimated at 0.1%.
- A large segment of the population with RA faces the risk of developing a destructive joint disorder with functional impairment severe enough to cause problems in managing the rigors of daily life, professional life, and recreational activity.
- Several studies have shown excessive mortality in RA.
- The general opinion held earlier that PsoA is a mild disorder has been contradicted by recent studies showing that PsoA may develop into a destructive, polyarticular disorder having a course similar to that of severe RA.
- Treatment for these disorders is symptomatic, aiming to suppress inflammation and improve function. In this respect, rheumatic surgery plays an important role.

Rheumatic disorders can be classified into non-inflammatory disorders such as arthrosis and soft-tissue syndromes (eg, fibromyalgia syndrome) and inflammatory disorders. Inflammatory disorders can be further classified into systemic rheumatic diseases such as systemic lupus erythematosus and systemic sclerosis (sclerodermas) and inflammatory joint disorders such as rheumatoid arthritis, juvenile chronic arthritis, and spondylarthropathy. Spondylarthropathy is a group or "family" of genetically related disorders including, eg, psoriatic arthritis and ankylosing spondylitis.

An extensive classification of rheumatic disorders was published recently [4].

Chronic polyarthritis

The etiology of inflammatory joint disorders remains unknown. Inflammatory joint conditions are characterized by chronic inflammation of synovial membranes and other structures in and around the peripheral joints and spine, causing a risk for destruction of the involved structures and subsequent functional impairment. Frequently, these disorders are generally referred to as "chronic polyarthritis".

Studies suggest that approximately 2% of the adult population suffer from an inflammatory joint disorder [8].

The inflammatory process may impair the function of joints and their surrounding structures, eg, tendons and muscles. Damage to skin, eyes, and internal organs may occur in cases where the inflammatory process involves structures beyond the musculoskeletal system.

The consequences of inflammation affect a patient's life situation and quality of life to varying degrees. The ability to manage activities of daily living (ADL) and the ability to perform in work and recreational activities may be seriously impaired.

The need for rheumatic surgery may, in principle, exist in all chronic polyarthritis, but appears to be largest in RA and PsoA. Hence, a survey addressing the occurrence and clinical features of these disorders is motivated. First, below we briefly address chronic arthritis in children, a substantially less common condition.

Juvenile chronic arthritis (JCA)

JCA is a heterogeneous group of arthritis in children. Three main forms exist:

- Arthritis in a few joints is the most common type of juvenile arthritis (55% to 75%),
- a polyarticular type (15% to 25%),
- a systemic type accompanied by fever, rash, and

internal organ manifestations (10% to 25%).

The etiology is unknown. The occurrence of JCA was recently studied in western Sweden [11]. The annual incidence was estimated to 11 per 100 000 children and the prevalence to 86 per 100 000 children. Hence, approximately 200 children fall ill annually, and there should be between 1500 and 2000 children with the disease in Sweden.

The course of the disease varies. In the early phase, the prognosis is difficult to assess in the individual case, which motivates careful followup by a multi-disciplinary team including a pediatrician or rheumatologist, physical therapist, occupational therapist, ophthalmologist (children may acquire insidious chronic uveitis), and others. Although most types of juvenile arthritis have a good prognosis, some children acquire an extensively destructive type which may cause severe functional impairment. The problems here are somewhat the same as in chronic arthritis in adults, but involve specific problems related to a growing individual. Hence, this requires the skills of a surgeon specialized in rheumatic surgery and experienced in juvenile arthritis.

Rheumatoid arthritis

Epidemiology

In common language in Sweden, rheumatoid arthritis (RA) is often referred to as "joint rheumatism" or "rheumatic pain". However, much uncertainty still exists as to whether RA is an old or a "modern" disease. The first reliable description of RA did not appear until 1800. Earlier descriptions of RA-type conditions are unreliable as are assessments of paleontological findings.

The RA diagnosis lacks pathognomonic features and hence must be based on criteria. Agreement has been reached on diagnostic criteria (see below) of high sensitivity and specificity. This has increased the potential for better studies concerning incidence and prevalence.

RA occurs world-wide, in all climates, and affects all ethnic groups to varying degrees.

The average age of onset in most studies is somewhat over 50 years. There is no apparent difference between younger and older individuals as regards the intensity and course of disease, at least not during the early phase. Women are affected twice as often as men.

Incidence

The data reported on the incidence of RA in western (Caucasian) populations varies. Whether this is due mainly to methodological problems or to actual differences in different populations is unclear. North American studies show similar data with an annual incidence of approximately 50 new cases per 100,000 inhabitants [3]. A recent study from England, which is the first prospective incidence study of RA, reports a substantially lower incidence with 25 new cases per 100,000 inhabitants [22]. An opinion suggesting that RA is a secular disease with a declining incidence is interesting, but has to be corroborated [13].

Prevalence

Current studies of western Caucasian populations report a prevalence just below 1% of the adult population [13]. Other ethnic populations have shown higher and lower figures [6,16].

An earlier Swedish study found a prevalence as high as 2.7% [1]. New studies of interest include an ongoing study in the Swedish county of Halland.

Etiology and pathogenesis

A good overview of etiology and pathogenesis in RA is found in a current textbook on rheumatology [15]. Only a few general viewpoints will be presented here. The etiology of RA remains unknown. The general opinion is that the development and manifestations of the disease are a result of one or more disorders in the immune system. The factors which cause the immune system to stimulate, react, and induce tissue damage are not completely known.

The predominant theory today is that the endogenous or exogenous antigen which triggers the disease initially comes into contact with the immune system. This contact, given certain genetic conditions, causes the antigen to be presented to the central cells (T-lymphocytes) of the immune system which activate for the purpose of eliminating the agent in question. Activation results in the production of antibodies, cytokines, proteases, and other tissue damaging agents. This further

causes new cells to penetrate from the blood stream to the synovial membrane, further stimulating and maintaining inflammation.

Certain bacteria, viruses (exogenous), and cartilage tissue (endogenous) have been suggested as antigen candidates. The required genetic pattern is probably quite complex. Certain HLA antigens (so-called shared epitopes) seem to play a central role in antigen presentation.

The resulting tissue damage may affect the synovial membrane, cartilage, and bone. The synovial membrane goes through major changes, becomes hyperplastic, is infiltrated by lymphocytes, macrophages, fibroblasts, and plasma cells. Vascularization increases, especially of capillaries and post-capillary venules.

The synovial tissue spreads toward the cartilage and forms so-called pannus tissue – a destructive tissue surface. This is where the attack on cartilage and bone takes place (often first apparent in "bare areas" at the edges of the joint where bone borders directly on synovial membrane). X-ray images visualize this by the erosions characteristic for RA.

Clinical profile

Symptoms and clinical profile are determined by the inflammatory process within and outside of the musculoskeletal system and the consequences caused by inflammation.

Disease onset

RA usually presents as a symmetric polyarthritis with involvement of hands and toes. Approximately half of the patients develop RA acutely and many can state the day and location of the first symptoms. Others have a more insidious onset, where the first symptoms cannot be dated any closer than to a given month. In some cases, onset occurs as a palindrome, where the patient over time, sometimes several years, experiences episodic attacks of transient monoarthritis in different joints, before the profile of permanent arthritis occurs.

Most patients develop RA with involvement of the small joints in hands and feet, but onset may also occur in large joints, eg, knees and hip. The disease usually spreads over a longer period of time, and often symmetrically, ie, simultaneously involving the same joint on both sides of the body.

As mentioned above, RA usually debuts with polyarthritis, sometimes with tenosynovitis, possibly with symptoms similar to those of carpal tunnel syndrome. In some cases, particularly in men, the disease may involve symptoms outside of the locomotor system (eg, pleuropneumonia) which, usually after a longer time, develops into arthritis.

Disease progression

The destructive joint process causes, to varying degrees, pain and deformity in peripheral joints, affects the joint system of the cervical spine, and involves a risk for atlas-dens instability. Other common consequences of synovitis include, eg, median nerve compression, tendon rupture, and ruptured Baker's cyst.

RA is a systemic disease and may involve any organ. Subcutaneous nodules, skin changes such as vasculitis with purpura and vasculitis induced leg ulcers occur as do pericarditis, pleuritis, and lung fibrosis. Keratoconjunctivitis and dryness of the mouth are viewed as expressions of a secondary Sjögren's syndrome.

Systemic vasculitis or "malignant RA" is a serious condition having a course that involves vasculitis and/or sensorimotor neuropathy (mononeuritis multiplex) and a risk for developing vasculitis in mesenteric, coronary, and cerebral vessels. It is associated with a high mortality risk.

The natural history of RA has not been sufficiently studied. The literature – prospective population studies and clinical observation studies – is inadequate and somewhat contradictory.

An attempt to interpret the data available was recently presented by Pincus, who distinguishes the following three types of RA based on the course of the disease [19]:

- Type I RA. Self-limiting, monocyclic RA. This type is unusual and found in only a minority of patients with RA at specialized rheumatology units.
- Type II RA. Slowly progressive disease, which can be controlled by adequate treatment. This type is found in approximately 25% of RA patients managed at rheumatology departments.
- Type III RA. This type is serious, continuously progressive, markedly destructive, and consti-

tutes most of the RA cases in specialized rheumatology services. Most cases of serious systemic disease are found here, and this group is mainly responsible for the increase in RA mortality.

However, one must keep in mind that the course of RA may vary widely and is difficult to predict in the individual case. An individual with seemingly mild RA may suddenly develop a severely destructive disease. On the other hand, a disease progression involving joint destruction and extra-articular symptoms may go into remission with well preserved function.

Diagnosis

A diagnosis of RA is established on the basis of medical history, physical examination, clinical chemistry and immunology examinations, and radiology findings.

A fundamental condition for establishing the diagnosis is the detection of synovitis, the presence of which is usually indicated by medical history, but it must be verified by a physician. When synovitis cannot be positively confirmed, an RA diagnosis is nearly impossible to establish.

Analysis of the character, location, scope, and consequences of synovitis, along with other disease characteristics, leads to a correct diagnosis.

Diagnostic criteria

Since the cause of RA is unknown, and since there are no disease characteristics with 100% sensitivity and specificity, the diagnostic value of various constellations of symptoms and examination findings have been developed and tested. The criteria generally used internationally were accepted in 1987 by the American College of Rheumatology (ACR) [2]. These criteria are mainly intended to classify RA for epidemiologic and other scientific purposes, but they are also valuable in diagnosing individuals. Compared to earlier criteria, a current study shows that they define a more clinically relevant population. The criteria are as follows:

1. Morning stiffness in involved joints for at least 1 hour.
2. Arthritis for at least 6 weeks in three or more defined joints or joint areas.
3. Arthritis in the joints of the hands.
4. Symmetrical arthritis.
5. Rheumatoid nodules.
6. Positive rheumatoid factor test.
7. Radiology changes typical for RA with periarticular decalcification, cartilage reduction or erosion.

A clinical profile including at least four of the seven criteria is considered consistent with the diagnosis of RA. The criteria have been tested and found to have high sensitivity and specificity.

Laboratory and radiology examinations

Considering the number of so-called "rheuma tests" available, it may seem strange that there are so few laboratory indicators for diagnosing RA.

Acute phase reactants such as ESR and CRP are of interest to demonstrate and monitor inflammation, but obviously provide no information about its cause.

Detection of rheumatoid factor (RF), an antibody directed at endogenous IgG, is one of the few laboratory tests which can reliably support suspicions of RA. Rheumatoid factor can be determined by a sheep red blood cell test, ELISA test, etc. The results are expressed in International Units and reference values vary among laboratories. Approximately 60% to 80% of the test results have been positive in most studies of early RA.

Most patients with RA have a haploid or diploid set-up of certain specific HLA DR-alleles ("shared epitopes"). Demonstration of these epitopes may have significance for diagnosis, assessment of the severity of the disease, and selection of specific therapy strategies [12].

Several studies show that more than 50% of patients who have had an x-ray of the hands and feet, have obvious changes indicating a bone-cartilage injury involving cartilage reduction and erosion within 2 years from the first symptoms [7]. Possibly MRI may prove to be a more sensitive instrument to detect early signs of joint destruction.

Synovial fluid examination in RA is mainly of value in differential diagnosis. In the future, however, it is hoped to be able to identify markers in synovial fluid (or synovial biopsy) for diagnosis, severity of illness, and choice of therapy.

Prognosis

Long-term studies of patients followed from onset of disease up to 25 years have been published

[20]. The results of these studies indicate that RA has a significantly poorer prognosis than previously thought. However, it is important to emphasize that these studies are based on clinical patient data with an obvious tendency to select more severe cases. A recently published prospective long-term study of patients with new onset of RA is also of interest, and suggests that the prognosis is not necessarily as poor as indicated by previous studies [5]. Nevertheless, RA is undeniably a serious disease which causes severe functional impairment and negatively affects the patient's life

Several studies show excessive mortality from RA, mainly resulting from cardiovascular disease [23]. The higher mortality rates particularly affect patients with severe, disabling RA, which is often complicated by the involvement of vital internal organs [18].

Spondylarthropathy

The term spondylarthropathy (SA) was introduced during the 1970s to better describe and understand a group of rheumatic disorders which have appeared to be heterogeneous conditions, but which have many clinical and genetic features in common.

Spondylarthropathy is said to be present in patients with [9]:

1. arthritis which is either asymmetrical or most pronounced in the lower extremities
   or
2. back pain resulting from an inflammatory cause
   plus one or several of the following symptoms:

- positive family history,
- low-back pain which changes side,
- tendinitis (enthesopathy),
- psoriasis,
- inflammatory bowel disease (IBD),
- urethritis/cervicitis/diarrhea within a month prior to arthritis,
- sacroiliitis.

Psoriatic arthritis, ankylosing spondylitis, pelvospondylitis in IBD, reactive arthritis, and juvenile pelvospondylitis are a few members of the SA family. In an early and incomplete clinical profile, the presence of one or more of the above symptoms may lead the diagnostic investigation to the correct final diagnosis.

The genetic marker HLA B27 often appears in individuals with SA. The diagnostic value of determining HLA B27 is, however, limited since most people in the population with this tissue type neither have, nor will contract, SA. However, there is much speculation concerning the etiological significance of this factor.

The occurrence of SA is not well known. An "educated guess" is that its prevalence is similar to that of RA, ie, approximately 0.75% of the total population.

Patients with SA may require rheumatic surgery. Psoriatic arthritis is a destructive joint disease where rheumatic surgery assessment and treatment is often considered, and is therefore discussed further here.

Psoriatic arthritis

The association between psoriasis and arthritis was first described in 1818. A few earlier case descriptions were, however, suggestive of psoriatic arthritis (PsoA). In the middle of this century, a more systematic approach to this problem was initiated, and now there is general agreement on the existence of a mutual relationship between skin disease and joint involvement, although the nature of the association remains a mystery.

Epidemiology

Two studies, one Finnish and one North American, estimated the annual incidence of PsoA at 6 per 100 000 adults, Population-based studies of prevalence in PsoA are lacking [21]. Psoriasis occurs in approximately 1% to 3% of our population. Different studies suggest that between 5% and 35% of individuals with psoriasis have an arthritis associated with the skin disease. These discordant figures are due, in part, to differences in the definition of PsoA, and reflect the great uncertainty concerning the prevalence of this joint disease.

Etiology and pathogenesis

The etiology of PsoA is unknown. Associations have been found between PsoA and different HLA antigens. The tissue type HLA B 27 is, eg, associ-

ated with all clinical types of PsoA, not only with the pelvospondylitis type (see below).

Some research suggests that previous streptococcal infection may be an introduction to a clinical profile involving guttate psoriasis and arthritis. Furthermore, patients with AIDS may have severe outbreaks of psoriasis, at times with severe arthritis.

There is speculation whether trauma may play a part in the induction of PsoA, but reliable evidence is lacking.

The pathogenesis shows substantial similarities with RA. However, compared to RA, a stronger tendency has been shown toward the development of fibrosis of the inflamed synovial membrane. The clinical significance of this is, however, doubtful.

Clinical profile and diagnosis

PsoA usually debuts around the ages of 30–40 years, usually following the skin disease (70%), but sometimes concurrently with (15%) or before (15%) the disease. PsoA occurs at similar rates in men and women. In children, a type of juvenile chronic arthritis similar to psoriatic arthritis has been described.

Fingernail psoriasis is more frequent in psoriasis patients with arthritis than in individuals with the skin disease alone. The extent or intensity of psoriatic disease does not otherwise appear to be a marker for any specific course of the arthritis.

During the 1970s, a proposal for classifying different types of PsoA was presented [17]. This was widely disseminated and is still in use, despite some deficiencies. The following clinical profiles can be distinguished:

- Classic psoriatic arthritis limited to the distal interphalangeal joints (DIP joints) of the fingers and toes. The nail next to an involved DIP joint often shows psoriatic changes.
- Arthritis mutilans with advanced destruction, mainly in the hands and feet.
- Asymmetric mono- or oligoarthritis, which may affect any joint, but usually fingers, toes, knees, ankles.
- Symmetric polyarthritis, similar to RA.
- Pelvospondylitis, which may differ from ankylosing spondylitis by later onset, milder course, in some cases predominant problems from the cervical spine, and often deviating radiological profile.

This classification illustrates the variety of clinical manifestations of PsoA. Common symptoms also include: *enthesopathy* (inflammation of the area where tendons, ligaments, fascia, and anulus fibrosus connect to bone), which occasionally occurs as a component of a *dactylitis* (swollen fingers or toes due to a combination of synovitis, periostitis, and tendinitis/enthesitis).

The diagnosis is based on medical history and clinical examination. Diagnosis is easy when a patient with obvious psoriasis develops arthritis in distal interphalangeal joints in addition to one or more other joints. Diagnosis is more difficult when onset occurs in an occasional joint, eg, a knee in a patient without obvious psoriasis. Detection of an elusive psoriasis (eg, discrete spots in the axilla, umbilicus, scalp, or intergluteally) and findings of fingernail psoriasis or dactylitis may be decisive.

Radiology may be of assistance (combination of osteolysis and new bone formation in peripheral joints and tendon attachments, and characteristic distribution of changes in the spine), but the laboratory does not offer a test that would support a clinical suspicion of PsoA.

Prognosis

For many years, PsoA has been regarded as a relatively mild disease apart from unusual cases of mutilating arthritis. Hence, previous studies have shown that patients with PsoA, compared to patients with RA, developed less serious functional impairments and reported fewer sick days. However, this perception should be reevaluated given recent data from longitudinal and other studies.

A current study where 63% presented with mono- or oligoarthritis and 25% with polyarthritis, shows that after several years of followup the group with polyarticular disease (including occasional individuals with arthritis mutilans) had increased to 67% [14]. This clearly indicates that many cases of early oligoarthritis progress to polyarthritis. This trend also appeared in the smaller group (10%) which debuted with pelvospondylitis. The trend is important to the prognosis, as demonstrated by the fact that polyarticular illness was most closely associated with functional prob-

lems and need for potent drugs.

Another longitudinal series points in the same direction [10], where the number of patients with polyarthritis increased from 20% to 40% of all PsoA during a 5-year period. Attention to functional problems and care needs also increased.

These studies indicate that PsoA is not nearly as mild a disease as previously thought. Further prospective studies are needed to build a better foundation for diagnosis and prognostic assessment at an early phase of the illness.

Special perspectives on joint surgery in patients with PsoA

The indications for joint surgery in patients with PsoA do not differ substantially from those in patients with RA. Patients with PsoA are thought to run a theoretically higher risk of superficial and deep wound infection resulting from contamination by staphylococci and streptococci from infected psoriatic plaques. Furthermore, the tendency for fibrosis in PsoA mentioned above has been thought to carry a risk for postoperative ankylosis. However, a recent literature review suggests that these theoretic risks do not motivate restrictions against joint surgery in patients with PsoA [24].

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