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Detecting Psoriasis Arthritis Early in the Disease Course – Why This is Important and How Dermatologists and Rheumatologists Can Successfully Cooperate?

Peter Härle

*Katholisches Klinikum Mainz, Klinik für Rheumatologie und Physikalische Therapie
An der Goldgrube 11, Mainz
Germany*

1. Introduction

Psoriatic arthritis (PsA) was first recognized as a specific rheumatic entity in 1964 by the American Rheumatism Association (later American College of Rheumatology) (Blumberg, 1964). In the forthcoming years it has become clear that PsA belongs to the spondyloarthritis (SpA) family that comprises several heterogeneous clinical conditions. These are Ankylosing Spondylitis, Reactive Arthritis (which occurs after bacterial infections), Spondyloarthritis associated to Chronic Inflammatory Bowel Diseases (Crohn's disease and Ulcerative Colitis), Undifferentiated Spondyloarthritis, and juvenile forms (figure 1). The term spondyloarthritis relates to inflammatory manifestations of peripheral and spinal joint structures. The Spondyloarthritis are defined by classification criteria (Sieper, 2009; Zeidler 2011, Rudwaleit 2011). The main clinical manifestation will trigger the main group for each disease entity may have varying degrees of articular, spinal, and extraarticular manifestations. Furthermore, extraarticular inflammatory manifestations may also occur at different intensity levels. However, it needs to be emphasized that classification criteria are not diagnostic criteria. Classification criteria were developed for clinical studies in order to include rather homogenous disease manifestations. In daily clinical practice it may occur that although the classification criteria are not fully met, the patient still may be allocated to a certain disease entity.

Peripheral joint manifestations	Spinal manifestations	Extra-articular Manifestations
Arthritis	Spondylitis	Uveitis, Scleritis, Conjunctivitis
Enthesitis	Enthesitis	Psoriasis
Bursitis	Sacroiliac joint arthritis	Urethritis
Tendosynovitis	Facet joint arthritis	Inflammatory bowel disease
Erosive-proliferative joint destruction	Bony ankylosis	Periodontitis with dental loss

Table 1. Clinical manifestation of the Spondyloarthritis, which may be present in all the different disease entities (Fig. 1).

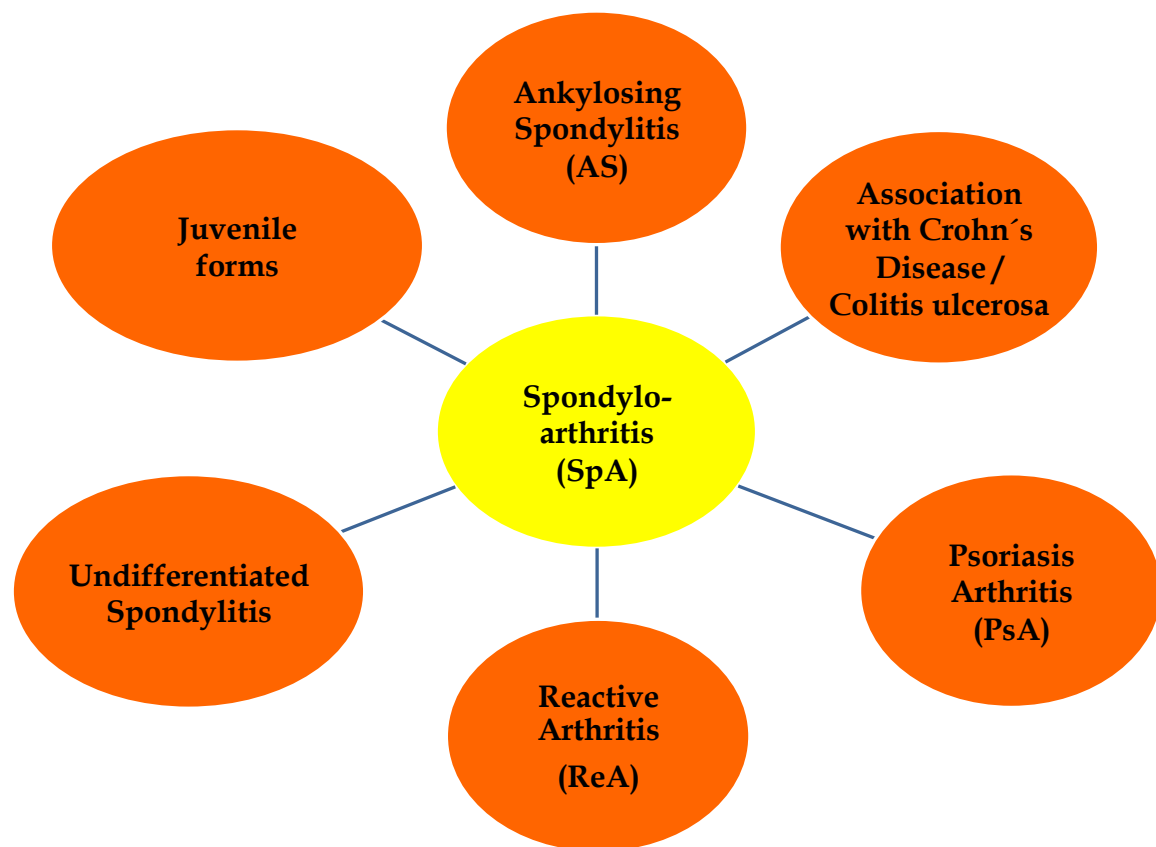


Fig. 1. Clinical entities of Spondyloarthritis. The overall disease group is the Spondyloarthritis, which comprises 6 distinct diseases. Psoriasis Arthritis is one disease entity of the group. Common abbreviations are given in parenthesis.

In clinical practice, articular and extraarticular manifestations overlap quite frequently among the SpA diseases. Initially, the clinical manifestations of PsA were collected and a set of manifestations was proposed as classification criteria by Moll and Wright in 1973 (Moll, 1973). These described clinical features were considered to be "Psoriatic Arthritis". However, over the following years, 6 modified classification criteria for PsA (Bennet, 1979; Dougados, 1991; Fournie, 1999; Gladman, 1987; McGonagle, 1999; Vasey, 1984) have been proposed by different research groups in order to differentiate between the different disease entities (Taylor, 2002). As in the Moll and Wright criteria proposal, these criteria mainly have been established in groups of patients with classical and fully developed disease manifestations. The validity of these criteria have never been formally proven in studies. Formal prove of PsA criteria was done in 2006 with the publication of the CASPAR (Classification of Psoriasis Arthritis Study Group)-Criteria (Taylor, 2006) as a joint project of the EUAR and ACR. As with the other above mentioned 7 criteria sets, the CASPAR criteria also were established in a group of patients with long standing psoriasis arthritis (mean disease duration of greater than 10 years (Taylor, 2006). As we know that chronic inflammatory arthritis like Rheumatoid Arthritis (RA) and PsA can destroy joints and cause significant disability (see Tab. 1) we need to diagnose arthritis before destruction of tissue has taken place. For this reason, in RA, arthritis classification criteria have just been revised to also classify early RA (Aletaha, 2010). Next to the new RA early classification criteria, the newly proposed classification criteria for spinal spondyloarthritis now include MRI

diagnostics of the sacroiliac joints (Rudwaleit, 2009). Bone marrow edema around the sacroiliac joints seen in MRI in water sensitive sequences, i.e. STIR (short tau inversion recovery, T1 plus contrast media) detects inflammatory processes significantly earlier than actual joint destruction can be seen on conventional X-ray films.

However, we still do not have validated early PsA criteria and early PsA most times does not present with the classical, fully developed clinical picture as is described in our textbooks.

This book chapter is dedicated to discuss why we need to detect PsA early and will answer the question of how patients with psoriasis can be screened for possible early peripheral and spinal arthritis manifestations. Suggestions on how cooperation between dermatologists and rheumatologists can be effectively set up will be given at the end.

2. Why is early detection of inflammatory processes important?

2.1 The earlier the better or time is joint function

Early detection and treatment of chronic inflammatory joint disease has been shown in numerous reports to correlate with better long-term outcome in rheumatoid arthritis (van der Bijl, 2007; Verstappen, 2007). Severity of joint destruction and loss of quality of life in PsA has been shown to be similar to RA (Husted, 2001; Rahman, 2001). Therefore, many aspects in PsA may be compared with aspects in RA. As depicted in figure 2, the chronic inflammatory process begins with an undulating situation of clinical and subclinical manifestations of joint pain with or without swelling. A trigger event then sets off the clinical manifest chronic inflammatory course. Joint destruction begins very early after this event. If the inflammatory process is not stopped, the natural disease course will occur with more or less destruction of joint structures.

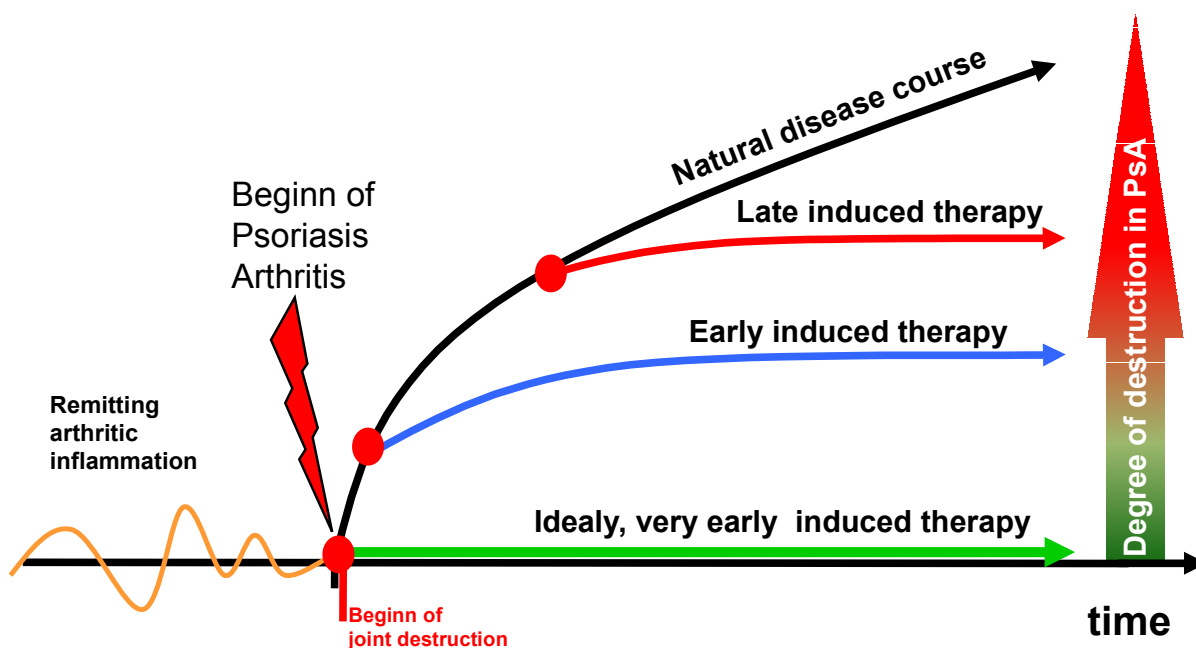


Fig. 2. Time course of the development of PsA. The earlier detection and treatment of arthritis takes place, the better the outcome in the following years will be, adapted according to (Machold, 1998).

However, if we treat to the target of remission and control the inflammatory process, it is possible to prevent or slow down the destructive process. We have plenty of evidence for this targeted approach for RA as reviewed elsewhere (Schoels, 2010). Furthermore, recommendations for physicians (Smolen, 2010) and patients (de Wit, 2011) on how to treat to the target of remission have recently been published. Very likely, the targeted approach is also true for PsA, because PsA also shows destructive disease courses and we use the same outcome measures than for RA. However, this has not yet been formally proven as has been for RA.

Inflammation of articular structures always is coupled with loss of function. Early in the disease course inflammation and loss of function correlate very well. This means, if inflammation is suppressed, function is completely regained. However, the longer the inflammatory process goes on, the more fibrotic and destructive changes occur which are not reversible (Aletaha, 2006). This implies that effective suppression of inflammation will not result in full regain of function anymore (figure 3). Furthermore, fibrotic tissue may cause destruction by itself thus uncoupling the destructive process from classic immune mediated mechanisms (Neumann, 2006).

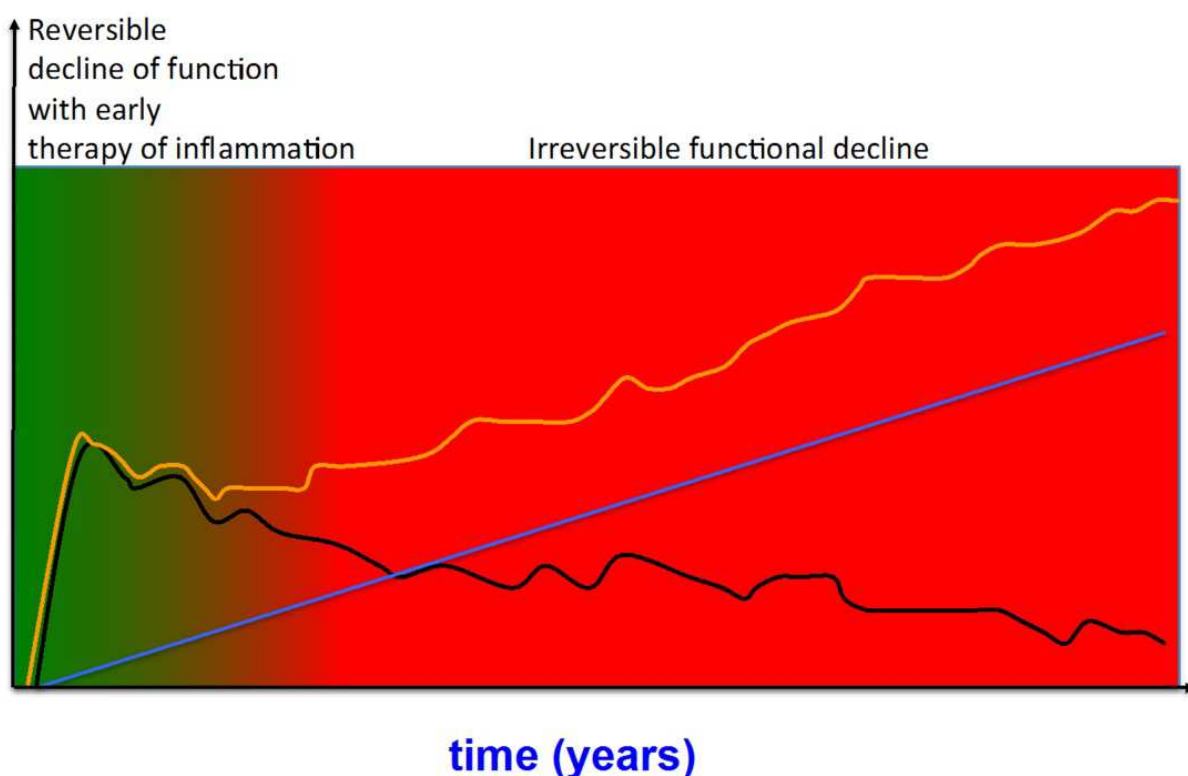


Fig. 3. Correlation of inflammation (black), loss of function (yellow) and joint destruction (blue) with time. Very early in the inflammatory process loss of joint function is tightly correlated with the degree of inflammation. In this phase, complete reduction of joint inflammation will restore joint function. However, the longer the inflammatory process goes on, the more destruction of joint structures will occur along with continuously more irreversible loss of function and destruction. Finally, there may occur an uncoupling of inflammation and irreversible joint destruction with loss of function, adapted according to (Kirwan, 2001).

2.2 Chronic inflammation confers a cardiovascular risk factor by itself

An upcoming discussion is that chronic inflammatory processes enhance the cardiovascular risk to a similar extent like the classical known risk factors diabetes, hypertension, hyperlipidemia, obesity, smoking and genetics (van Halm, 2009). This implies that treatment of inflammation may be similar important to the treatment of the classical cardiovascular risk factors in order to reduce the overall cardiovascular risk. Prospective studies on reduction of cardiovascular risk by anti-inflammatory treatment are still pending but it was shown retrospectively that effective reduction of inflammation with combination therapy of methotrexate and anti-TNF (Tumor Necrosis Factor) medication may reduce the risk for the first cardiovascular event (Cugno, 2010).

As in RA the cytokine TNF plays an important role in the pathophysiological mechanism of Ps and PsA. The prothrombotic effects of TNF in cardiovascular disease are discussed in a recent review and may play an important role in the about 4 fold enhanced cardiovascular risk compared with the normal population (Jacobsson, 2005). However, Ps and PsA patients seem to additionally have an increased prevalence of cardiovascular risk factors such as smoking, hypertension, raised levels of homocysteine, excessive alcohol consumption and metabolic syndrome compared to the normal population (Tobin, 2010). Therefore, it cannot be finally answered to what extent chronic inflammation of the skin, joints, and spine in Ps/PsA add to an enhanced cardiovascular risk.

2.3 Health care costs of PsA are high

Another reason for early detection of PsA is health care costs. PsA shows increasing costs with the duration of the disease. This seems to mainly be due to the rising risk of work disability. However, the association of work disability and disease duration has not very well been studied up to day. Only 3 studies were published on this topic (Mau, 2005; Verstappen, 2010) and one review gets to the conclusion that the data is too heterogeneous to draw hard conclusions (Tillett, 2011). Nevertheless the study of Mau et al. describes a reduction of the standard employment rate in PsA patients from 0,94 to 0,7 within 5 years. Functional status seems to be the most important factor to predict total costs. Zink et al. summarize that patients with a poor functional status of 50% (HAQ of more than 1,7) cost more than double compared to patients with a good functional status (functional status of 70% or HAQ less than 1,2) (Zink, 2006).

2.4 Psychosomatic comorbidity is important to consider

Finally, the psychological and psychiatric comorbidities resulting from the cutaneous stigmatization and the painful, debilitating arthritic manifestations of joint and spine add to the disease burden of PsA (Devrimci-Ozguven, 2000; Esposito, 2006). There seems to be no difference in depression rate among sex and age of patients with PsA. Effective therapy of cutaneous manifestations and arthritis may reduce depressive disorders, which will significantly reduce health costs and therefore needs to be balanced against the high costs of modern treatment with biologics.

3. How can patients with PsA be identified in daily clinical routine?

In clinical practice, psoriatic patients with a dominant skin manifestation primarily consult dermatologists and patients with a dominant peripheral or spinal manifestation primarily

consult rheumatologists or orthopedics. However, the vast majority of Ps patients gather within the dermatology setting. Therefore, it seems rational to screen patients for arthritic manifestations in the dermatology setting.

From July 2005 until October 2008, we validated and established the self-administered patient-screening questionnaire GEPARD (GERman Psoriasis ARthritis Diagnostic questionnaire) to detect PsA in psoriatic patients seeking primarily dermatologic care (Härle, 2010) (Tab. 2 and www.kkm-mainz.de/rheumatologie). In order to keep the questionnaire simple, only dichotomous answers (yes/no) were used. The twelve questions were derived from discussions about appropriate questions among the authors and additional advice provided by other experienced rheumatologists. Questions number 1 to 4 relate to clinical signs of arthritis but do not necessarily impose a momentary active state of arthritis by asking if the patient ever had these signs. It was considered that these questions take into account the remitting and relapsing nature of PsA. We considered the detection of these patients being especially important in the context of a longitudinal follow-up of fluctuating arthritis, which might eventually lead to establishing prognostic parameters for PsA. Questions number 5 to 8 pertain to arthritis in a more indirect way by relating to the discomfort caused by joint pain or dysfunction. Questions number 9 to 13 relate to the clinical signs of inflammatory back pain which can be associated with PsA. An additional

#	Question	Yes	No				
1	<i>Have you ever had joint pain accompanied by swelling?</i>						
2	<i>Have you ever had a completely swollen digit or toe?</i>						
3	<i>Have you ever had joint pain accompanied by redness of that joint?</i>						
4	<i>Do your joints feel stiff after waking up in the morning?</i>						
5	<i>Have you ever thought of having a joint disease?</i>						
6	<i>Have you ever consulted a doctor because of your joint problems?</i>						
7	<i>Have you ever received the diagnosis of "arthritis"?</i>						
8	<i>Do you take pain medication for your joint pain?</i>						
9	<i>Do you suffer from back- or buttock pain? If yes, does/is this pain.... (please, answer questions 8a to 8d)</i>						
10	<i>... most intense in the early morning hours?</i>						
11	<i>... improve through exercising or moving around?</i>						
12	<i>... persist while resting?</i>						
13	<i>... accompanied by back stiffness in the morning hours?</i>						
14	<i>If you answered one of the above questions with "YES": Since when do you have these complaints?</i>						
	More than 1 week	More than 1 month	More than 3 months	More than 6 months	More than 1 year	More than 3 years	More than 5 years

Table 2. The GEPARD questionnaire targets arthritic complaints of peripheral joints and spinal manifestations in addition of duration of arthritic symptoms thus enabling early detection of PsA. The patient alone answers the questionnaire. The physician or assistant counts the positive answers. The cut-off value of equal or more than 4 positive answers showed a sensitivity of 89% and a specificity of 73% to detect PsA in Ps patients

question related to the time period since the first occurrence of complaints lasting from one week up to more than 5 years in order to detect early PsA manifestations. In the statistical evaluation of the study, we calculated a cut-off value of greater than or equal to 4 positive answered questions. This cut-off showed a sensitivity of 89% and a specificity of 73% to detect PsA in Ps patients (Härle, 2010).

In the final evaluation, we clinically evaluated 54 patients. These patients were selected by the GEPARD questionnaire from dermatology outpatient clinics. We found 43 patients who had some arthritic manifestations according to clinical examination, ultrasound, x-ray, MRI, and Technecium-Szintigraphy. This accounts for 79,6% patients being positive for PsA manifestation. This percentage of PsA among patients with Ps is in line with earlier publications (Sadek, 2007). Furthermore, 23 patients were first diagnosed as having PsA.

According to the time duration of arthritic complaints we found 57% suffering over 4 years but 43% of patients below 4 years (figure 4) which may still be considered as being early arthritis. From these patients with complaints of less than 4 years 80% could be classified for PsA just by clinical examination according the CASPAR criteria without the use of sonography, x-ray, MRI, or szintigraphy (figure 5). Considering that the initial screening process was exclusively based on patients' answers, without evaluation by a physician, the GEPARD patient - questionnaire is well suited for routine clinical usage. In addition, the screening tool does not consume additional time from the dermatologist but still enables him to identify patients who need to be referred to a rheumatologist for further evaluation of arthritic manifestation.

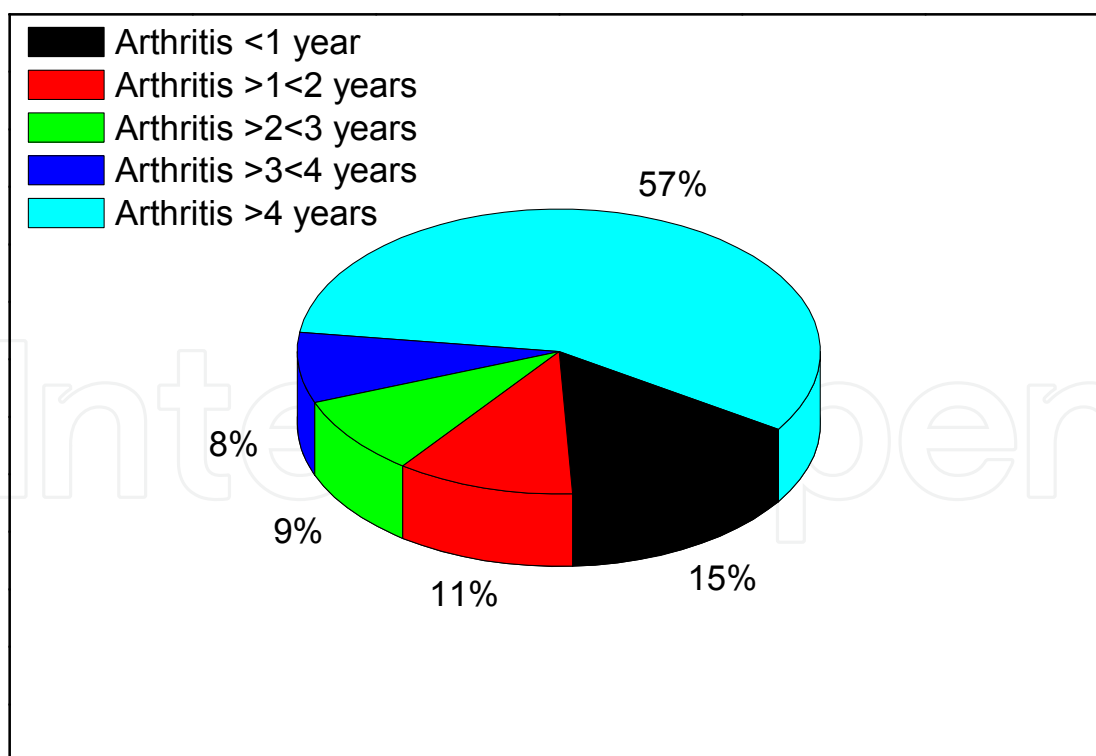


Fig. 4. Pie chart of arthritis duration according to the GEPARD patient-questionnaire. Forty-three percent suffered of symptoms of less than 4 years. Less than 4 years is considered to be early arthritis.

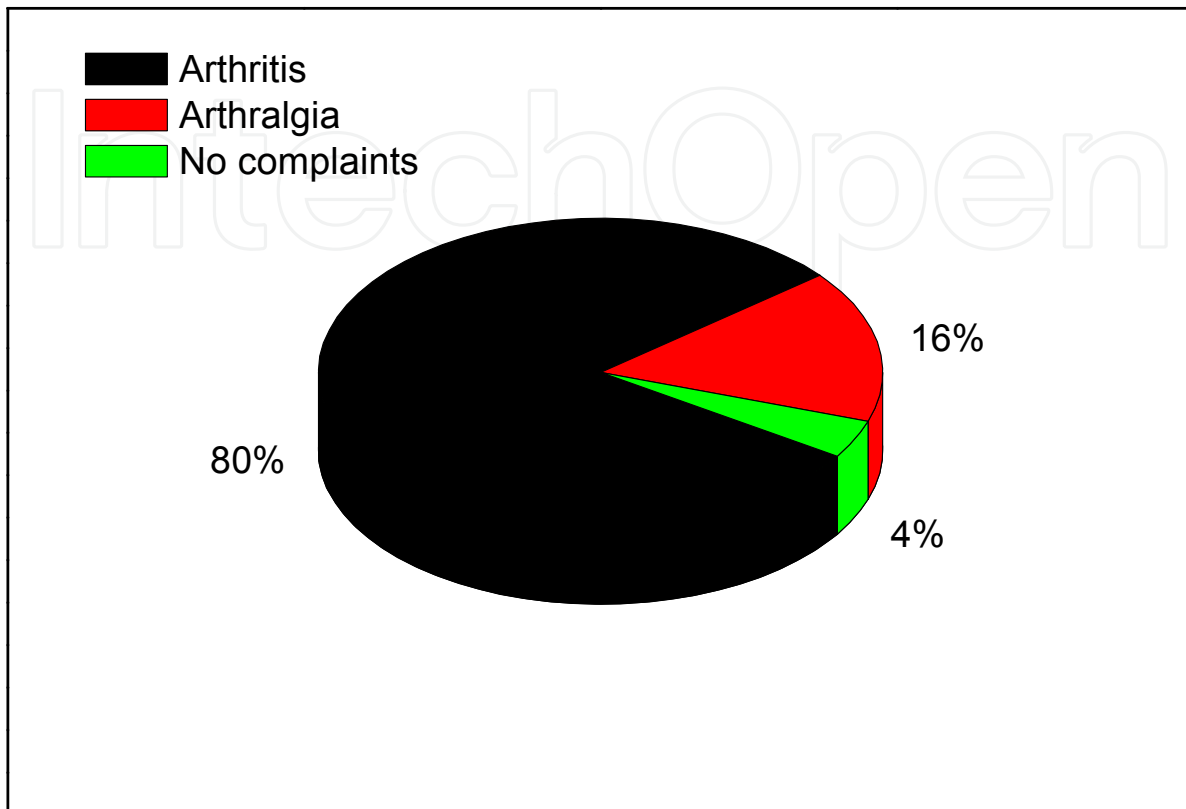


Fig. 5. Distribution of arthritis, arthralgia and no complaints in percent of GEPARD patient-questionnaire early arthritis patients (≤ 4 years). According to the CASPAR classification criteria, eighty percent were classified as having PsA.

4. How could the cooperation between dermatologist and rheumatologist be set up?

As described in the previous paragraphs screening of patients with Ps can easily be done by using the GEPARD patient self-administered questionnaire. In the case of equal or more than 4 positive answers in the questionnaire, the dermatologist may refer the patient to a cooperating rheumatologist. Since the end of the 90s most rheumatologists have set up an early arthritis schedule. With the GEPARD questionnaire the patient is already screened for arthritis and is more likely to have an arthritic manifestation. After the rheumatologic assessment the decision has to be made which discipline is advantageous to take the lead in guidance and treatment of the patient. Usually a cooperative way is chosen, taken into consideration that the general practitioner is the steering physician for the other comorbid and social problems of the individual patient (figure 6).

In the case of leading arthritis, the consultation of the dermatologist is necessary to confirm the diagnosis of Ps by clinical means or by biopsy in unclear situations (figure 7). Furthermore, topical treatment may be instituted if systemic therapy of PsA does not lead to full treatment success of the skin. The same treatment cycle as described before is necessary in order to treat all facets of PsA.

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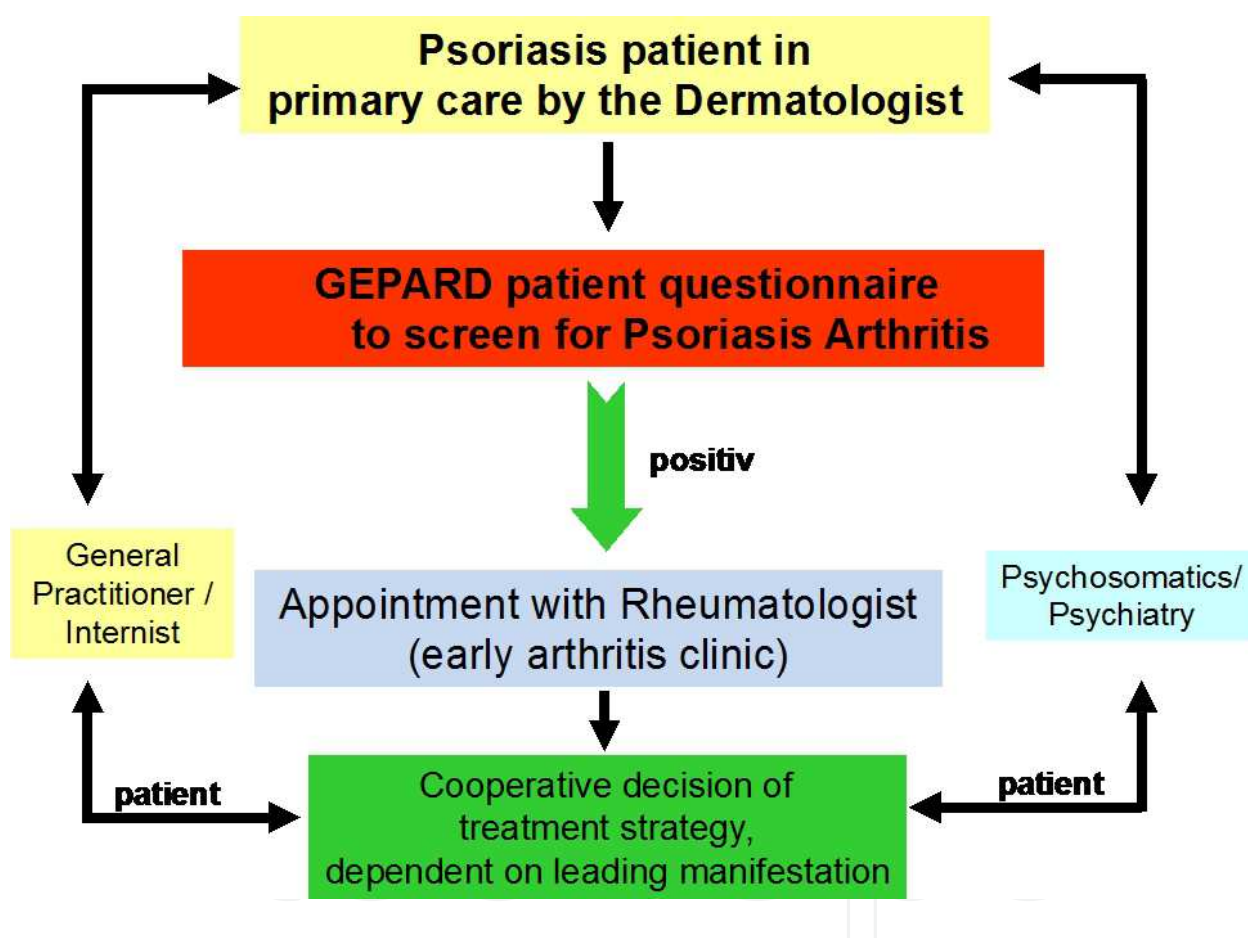


Fig. 6. Flow chart of possible cooperation among the medical disciplines. Screening starts in the dermatology practice by using the GEPARD patient self-administered questionnaire.

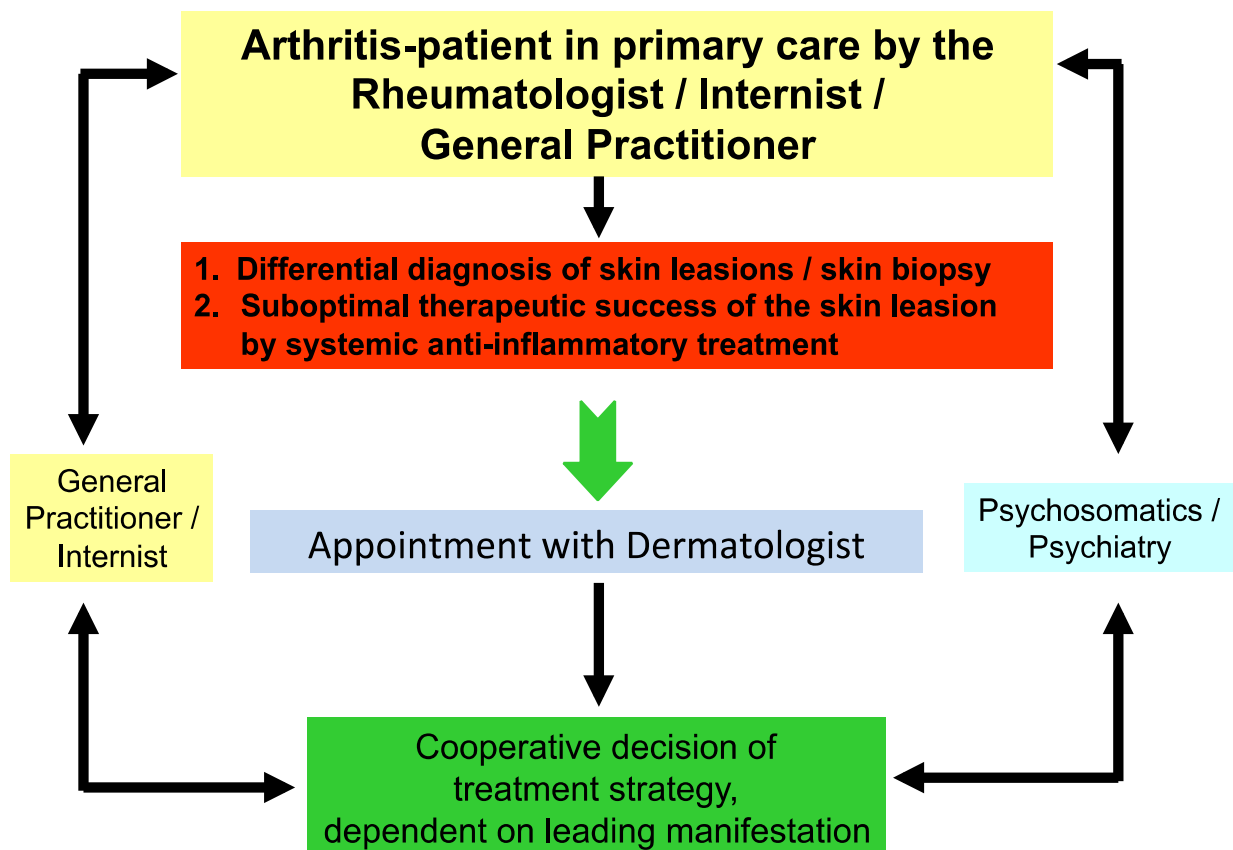


Fig. 7. Flow chart of possible cooperation among the medical disciplines. In the case of suspected psoriatic manifestation or in the case of suboptimal treatment response of Ps by systemic therapy the rheumatologist confers the patient to the dermatologist for further evaluation.

5. Summary

Considering all the many facets of PsA and the different diagnostic and therapeutic strategies is the art of modern medicine and good clinical practice. We need to understand the context of inflammatory skin, joint, and spine manifestations with mental health, extra articular problems and economical considerations. This can only be accomplished by good cooperation between dermatologist and rheumatologist in addition to the comprehensive care by the general practitioner, internist, and psychological disciplines (figure 8).

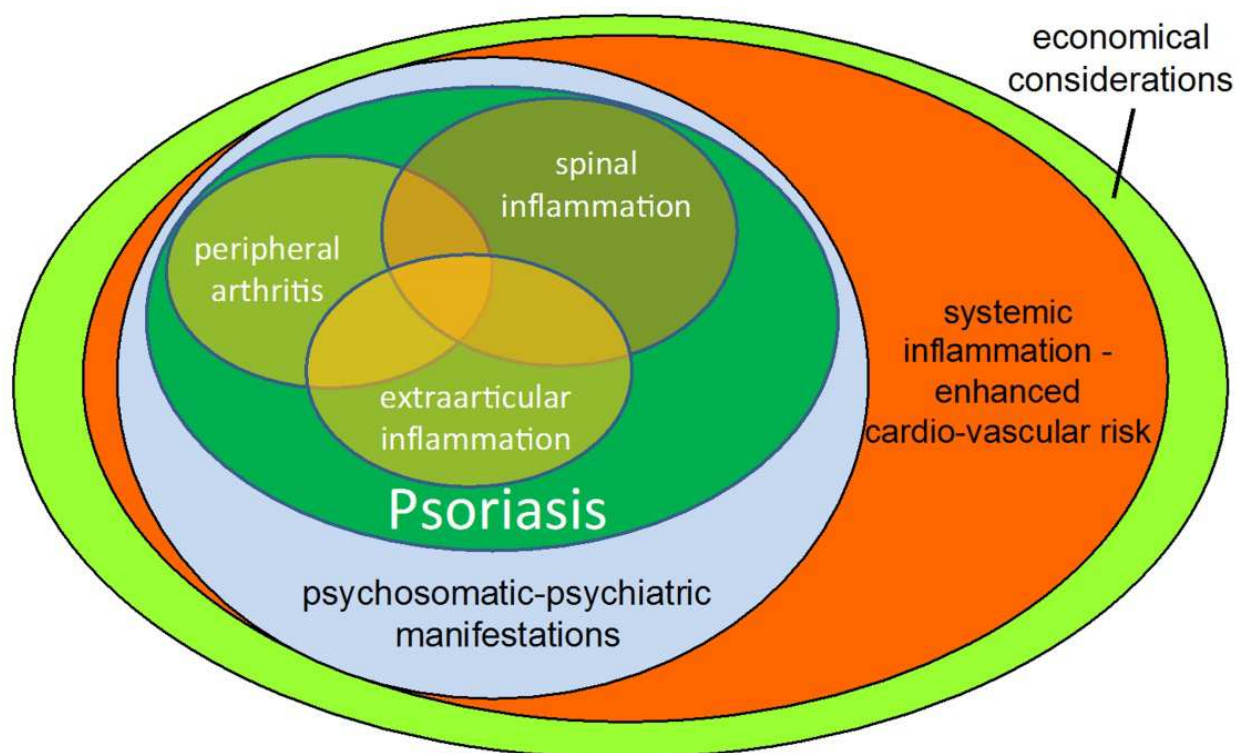


Fig. 8. Interdisciplinary, holistic view of Ps and PsA.

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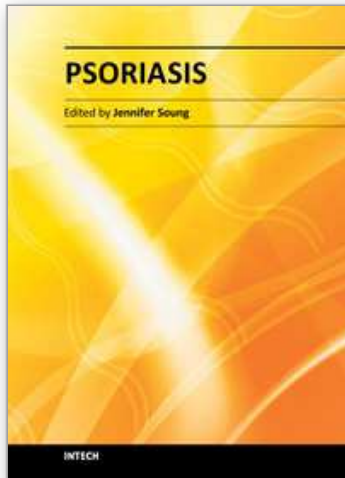
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Slavka Krautzeka 83/A
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Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
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Phone: +86-21-62489820
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