Summary

In this dissertation various aspects of the fibromyalgia syndrome are discussed. Fibromyalgia (syndrome) is a common disorder seen in rheumatology practices, and has been known under a variety of names during the years. The introduction to the syndrome and a historical review of fibromyalgia are described in chapter 1 Criteria for the fibromyalgia syndrome have evolved during the years from a wide spectrum of different symptoms to just two criteria:

1. the existence of chronic widespread pain and
2. a number of positive tender points on palpation (11 out of 18).

There have been many different ideas on the possible pathophysiology of this chronic pain syndrome, but no definite answer has been found.

Chapter 2summarizes the different studies that are performed in the search for a, primarily, somatic origin of the syndrome. Through the years one can see that the ideas on pathophysiology of the fibromyalgia syndrome have changed. In the beginning most studies looked for a disease, e.g. dysfunction of the end organ, the muscle. This evolved to more complex mechanisms of immunologic problems, neuromuscular disturbances, microcirculatory changes, sleep cycle disturbances, chronic (virus) infections and finally neuro-immuno-endocrinologic abnormalities. The results of the different studies makes it highly unlikely that there are specific and consistent abnormalities in the muscle tissue in fibromyalgia, and neither is their substantial evidence for abnormalities in energy metabolism. The studies on immunologic factors bring contradictory results, but overall there is no proof that there are immunologic abnormalities in fibromyalgia or that fibromyalgia is (or will develop into) a (auto-immune) connective tissue disorder. Evidence for neuromuscular abnormalities is not found. There is no abnormal muscle tension present in fibromyalgia. An abnormal reaction to cold vasospasm is observed, although there was no relation between these vasospasm and the subjective experiences of Raynaud-like phenomena.

In the sleep-studies an alpha EEG sleep anomaly in patients with fibromyalgia is frequently found. But if fibromyalgia is caused by sleep anomalies, or that fibromyalgia and sleep anomalies are both the result of another, still unknown factor, remains an open question.

Analyzing the different reports and studies on a possible virus or other invader in the etiology of fibromyalgia, the conclusion is that this theory can not be held upright. The studies on neuro-immuno-endocrinologic aspects show different outcomes, although abnormal reactions in the hypothalamic-pituitary-adrenal axis are frequently found. The relation between cortisol and stress in the fibromyalgia syndrome should be further analyzed. Evidence for disturbances in serotonin level and metabolism is found as well, and this also needs further study to establish a possible link with depression (and again stress).

The last part of chapter 2 describes different aspect of aerobic capacity and muscle performance in fibromyalgia. The conclusion is that the basic physiological function

of the muscles is normal during exercise, but patients do not bring their maximal effort in the different test situations. Fibromyalgia patients are physically unfit, but this is due to a deconditioning effect.

In chapter 3different coexisting and modulating factors are discussed. Irritable bowel syndrome is often described as a coexisting factor in fibromyalgia, and so are Raynaud's and Sjögren's syndrome. Patients with fibromyalgia often have a wide variety in symptoms of these different syndromes. The same can be said of the related, or overlapping, syndromes, like the chronic fatigue syndrome and the myofascial pain syndrome. We do not think that these syndromes are separate entities, but it is more like a continuum of different symptoms, with in each patient emphasis on one of more of these symptoms which will define the patient to one of the syndromes.

In chapter 4a study is described of 31P Magnetic Resonance-Spectroscopy (31P MRS) at the site of tender points in the trapezius muscle of patients with fibromyalgia. 31P MRS provides the opportunity to study high energy phosphate metabolism in muscle tissue. We did not find a significant decrease in the high energy phosphate metabolites in the trapezius muscle of fibromyalgia patients, compared to healthy controls. The results of our study do not support the theory that a state of hypoxia causes the muscle complaints in fibromyalgia, providing an organic origin for the syndrome.

Chapter 5describes the results of two physiological (hormonal) stress test, and the relation between the results of these stress test to two psychological tests. This study was conducted as a pilot study and no control group was included. 20 patients were tested with a TRH/LHRH test, and also a CRF/GRF test. The psychological tests were the PBV and STAI. Evaluating the different hormonal test results, there are many abnormal values, but not all in the same direction. We found no correlation between hormonal stress scores and psychological test scores in our study. Patient number in our study was limited and there was a wide variation in the abnormal hormonal stress scores, so this makes it very unlikely to find a correlation.

Chapter 6reports on a study on the relationship between weather conditions and fibromyalgic complaints. Patients with fibromyalgia often state that weather conditions modulate their complaints. We related the subjective symptoms of pain, stiffness, sleep and mood in fibromyalgia patients (reported in weekly diaries), to objective meteorological data (from the Dutch Meteorological Institute at Airport Eelde). Correlation analyses showed no relation between the subjective complaints and meteorological factors. The subjective symptoms pain, stiffness and fatigue, however, showed a strong intercorrelation. One explanation for the discrepancy between the patients' belief on one side and objective findings in this study on the other side, could be found in the attribution theories. Patients with pain feel less helpless if they can relate their pain to some external condition, i.e., the weather, thus justifying it.

Chapter 7describes different aspects of tender points in fibromyalgia, like mode of examination and identification of positive tender points, the concept of tender points especially in relation to fibromyalgia and compared with other diagnoses, furthermore

the aspect of reliability of tender points in fibromyalgia and last aspect is the value of a tender point count as a treatment outcome variable. The tender points play a crucial role in determining if a patient with wide spread chronic pain will be classified as a fibromyalgia patient. A change in number of tender points is not generally accepted as an useful outcome parameter in evaluating therapy programs in fibromyalgia. A relation between number of positive tender points and severity of the syndrome is not established.

The results of a study are presented, in which the total number and specific localizations of the tender points in individual fibromyalgia patients were consistent in time. In our study we found no differences in number of tender points in fibromyalgia patients in the course of 18 months, and the score of each individual tender point pro patient was consistent as well. Patients with a high number of tender points also have a high number of positive control points. This would mean that in fibromyalgia there is a generalized lowered pain threshold, and also women have a lowered pain threshold compared to men.

Chapter 8summarizes the results of several epidemiological studies. There are a few population based studies, with prevalence numbers of 0.66% up to 11.2%. This last number reflects all persons with wide spread pain in a general population in England. The latest prevalence study mentions a prevalence of 2% in a general population of 18 years and older. It is very difficult to determine the prevalence in the general population and part of this problem is that fibromyalgia is too heterogenous to be one disease or illness. There are no reliable data on the prevalence in primary care populations. The prevalence in clinical or hospital populations depends strongly on referral patterns, but most studies mention a prevalence of 5-20%. Although fibromyalgia is thought to be most frequently seen in women between 30-50 years, the syndrome also is diagnosed in children and elderly people.

In this chapter an attempt is made to evaluate the severity and socio-economic impact of the fibromyalgia syndrome. Musculoskeletal conditions are among the leading diseases when it concerns social and economic costs to individual and society as well. They score high in measures of disabilities, restriction of activity, use of vocational rehabilitation, and medical costs. They score relatively low, compared with other diseases, as a cause of death. The impact of the fibromyalgia syndrome is not the same in all countries, because there are many differences in social and medical securance and insurance systems, offers for jobs, unemployment rates, attitude to work and attitude to (psychosomatic) diseases.

In chapter 9some clinical aspects and the natural history of the fibromyalgia patient group in our studies (n=144) are highlighted. A description is made of several aspects of the medical consumption and literature on these aspects is reviewed. There is a high percentage of female patients in fibromyalgia, a phenomenon for which there is no good explanation. In our population 90% of the patients is female, which is comparable to the findings of other researchers. The perceived severity of the complaints make that fibromyalgia patients feel that they are handicapped and the vast majority of patients (70%) in our study population state that their complaints are

worsening over time. Fibromyalgia complaints emerge gradually and spontaneously in most patients (66% in our patient group).

Chapter 10 contains a review of literature on psychological aspects in fibromyalgia. The relation between fibromyalgia and anxiety and depression is highlighted. There is no compelling evidence for psychological abnormality in fibromyalgia as an etiological factor. Depressive symptoms and anxiety are present, but are most likely an accompanying factor in a chronic medical condition. Furthermore the relation between pain, the most prominent complaint in fibromyalgia, and psychological aspects are studied in more detail. "Learned helplessness", inadequate behavioral responses, reinforcement of pain behavior, social modelling and cognitive aspects are modulating factors in pain experience and pain behavior. There is a reciprocal relationship between stress and pain at one hand and psychological factors at the other. Whether these psychological factors can be considered as etiologic is still open to discussion.

In chapter 11 psychological aspects of fibromyalgia are compared with those of chronic and nonchronic pain. Three groups, a chronic pain group (n=99), a nonchronic pain group (n=34) and a fibromyalgia group (n=36) are compared, using a standardized interview and psychological questionnaires (SCL-90, IBQ and CIPI). It appeared that the chronic pain group and the nonchronic pain group can be easily distinguished from each other on basis of criteria of an advisory committee (Gezondheidsraad) of the Dutch Ministry of Health. The scores of the fibromyalgia group and the chronic pain group were very similar. This leads to the conclusion that many psychological aspects in fibromyalgia can be considered as aspects of having chronic pain complaints.

Chapter 12 contains a report of a study in which a group fibromyalgia patients (n=100) is compared with a group patients with rheumatoid arthritis (n=25) and a group patients with chronic low back pain (n=22), using visual analogue scales for pain intensity, quality of sleep and a global estimate of overall complaint. Furthermore the groups were compared on tender point scores and scores on several psychological questionnaires: SCL-90R, Amsterdamse Biografische vragenlijst (ABV), Maudsley Marital Questionnaire (MMQ), Utrechtse Coping Lijst (UCL) and Prestatie Motivatie Test (PMT; Achievement Motivation Test). Results show that fibromyalgia patients perceive their problems as more severe than both other groups and that the amount of psychological distress is larger. Fibromyalgia patients also have higher scores on neurotic lability, as measured by the ABV, which may be an indication for a psychological predisposing factor. Fibromyalgia patients differ in their coping styles of both other groups. Fibromyalgia patients have higher scores on the Palliative, Avoidance an Depressive reaction subscale of the UCL. This seems to reflect inadequate coping behavior.

Chapter 13 summarizes the different treatment strategies described in the literature. A major issue in evaluating treatment programs is the choice of reliable outcome measures. This point is not yet resolved and this makes a comparing of the different studies very difficult. NSAID's have no more effect on symptoms in fibromyalgia as

placebo. There is a modest positive effect of tricyclic drugs (amitriptyline) in a subgroup of fibromyalgia patients, especially in regard of sleep disturbances. There have been no controlled studies in regard to physical therapy, however a great deal of fibromyalgia patients follow a kind of physical therapy. The same can be said of allopathic treatment regimens. No substantial proof have emerged that fitness programs alleviate the symptoms of the fibromyalgia patients. In general, study length (and follow-up) was short in most studies, and another observation is that there is a considerable placebo-effect in a number of treatment programs, which makes the outcomes not very reliable.

The fibromyalgia syndrome has to be considered as a chronic pain syndrome, with many implications for social and emotional functioning, and these aspects have to be taken into account as well. This can only work in a multidisciplinary setting with a multidisciplinary approach. Patients have to be an active participant in their own rehabilitation program.

In chapter 14a study is presented in which the effect of treatment of fibromyalgia syndrome with psychomotor therapy, based on behavioral therapeutic principles, and marital counselling is evaluated. Fifty fibromyalgia patients participated in the treatment group and fifty patients participated as nontreatment controls. Treatment goals was to help the patient learning to cope with the disabilities resulting from their fibromyalgia complaints, by means of behavioral therapeutic techniques, relaxation exercises, assertiveness exercises and learning to differentiate between complaints of the syndrome and other bodily and emotional sensations. Pretreatment, posttreatment and follow up assessments were made, based on experience of complaints (VAS-scales), SCL-90, UCL and MMQ. The drop out rate was high (34%), probably related to the way participants were selected. Multivariate analysis of variance showed that there were changes over time for both groups (increase of pain, but decrease of psychological distress and decrease of inadequate forms of coping). An effect for treatment was not found.

In chapter 15the effect of a cognitive-behavioral treatment program is evaluated. Thirty patients were selected in an at random procedure and were asked to participate in the treatment program. Thirty patients served as non treatment controls. Treatment goals were:

1. establish adequate coping skills, based on realistic beliefs and thoughts.
2. Shifting the 'locus of control' of the patients from external into an internal one.
3. Thus, diminishing the negative emotional aspects and feelings of helplessness regarding the pain and the other fibromyalgia complaints.

Assessment took place prior to treatment, after treatment and 6 months after the ending of the treatment program. Outcome variables that were used: SCL-90R, Pijn Cognitie Lijst (PCL), PijnBeheersings Vragenlijst (PBV), visual analogue scales for pain, sleep and global estimates of complaints, tender point score, and an ADL-checklist. As in the study described in chapter 14, the drop out rate is high (33%). No treatment effects were found using multivariate analysis of variance. As a result of the high drop out rate the power of the statistical testing has decreased. Replication with

larger groups, and perhaps other recruitment procedures are necessary.
In chapter 16 an attempt is made to bring together the various aspects of fibromyalgia into one model which is explanatory for the most important interrelated factors. Stress, pain and fatigue are the central aspects of this model. They are influenced by several psychological and psychobiological aspects. Many patients with fibromyalgia complaints seem to be trapped in vicious cycles of reciprocal factors. Much is unknown about early stages of fibromyalgia. Further research, based on longitudinal designs, is necessary. Treatment of fibromyalgia should aim primarily on 'care' aspects, not on cure. It is important that patients with fibromyalgia recover the experience of control over their complaints. Treatment programs should therefore aim on breaking through the vicious cycles in which the patients are trapped, thus giving back the patients responsibility for their own well-being.