CHAPTER 1

General introduction
The condition that is now known as Sjögren’s syndrome (SS) has been studied for over a century. Still it poses the clinician a great challenge as its manifestations extend beyond the clinical scope of any of the involved specialists hence requiring multidisciplinary treatment and research. Classified as an autoimmune disorder of the exocrine glands, SS is generally regarded as the second most common rheumatic disorder, exceeded in incidence only by rheumatoid arthritis. The occurrence of SS, however, is not well established due to a lack of uniform diagnostic criteria and differences in diagnostic techniques.

Having SS has a great impact on the patient’s physical, mental, and social well being. Physically, patients may suffer from exhausting fatigue, persistent daily discomfort of dry eyes and mouth and many other complaints related to either general autoimmune processes, or exocrine gland inflammation throughout their body. Mentally, patients have to cope with a chronic, disabling disease that is mostly invisible (to friends and relatives), is poorly known, and is often initially misdiagnosed, or remains undiagnosed for other reasons for periods of five to ten years. Socially, patients are impaired because they cannot take part in many activities due to either ocular problems (sun-, wind- and smoke intolerance), oral problems (difficulties with speaking, eating, wearing a denture) and a great lack of energy. Many patients have to reduce their level of employment or even resign from their job due to complaints related to SS. The diagnostic procedure itself of SS is also very demanding for the patient, because many tests are currently required for a proper diagnosis. Large variability in disease expression, an insidious onset of the disease, and its resemblance with many other conditions necessitates a variety of tests for establishing the diagnosis. With respect to our understanding of SS, it is striking that we are still dealing with a syndrome instead of a disease; after a century of experience with this relatively common disorder, there is still much to discover. A true organ-specific autoantibody with pathognomonic significance for example, as ultimate proof of the autoimmune nature of SS, has not yet been identified. Pathognomonic signs that would otherwise disclose SS are also lacking, rendering clinicians dependent upon a variety of tests that, combined, reach a certain probability for the presence of this syndrome. Since the tear and salivary glands are both well accessible for clinical evaluation, an oral and an ocular component of SS can be distinguished diagnostically. Current treatment modalities for SS are predominantly symptomatic. To date, objective methods to estimate disease activity are lacking, which renders the evaluation and introduction of new therapeutic agents difficult.
Clinicians are thus confronted with a very common debilitating disease that 
provokes diffuse sicca complaints, as well as general complaints. The disorder is 
often difficult to recognise and requires quite some effort to be diagnosed properly. 
After the diagnosis has been established, there is generally no other treatment than 
alleviating the symptoms.\textsuperscript{13,14}

The main objective in this thesis is to optimise current diagnostics and to obtain 
clinical outcome parameters in SS. In 200 patients, the oral component of SS has 
been studied extensively during the past three years by a multidisciplinary research 
team, in order to improve and simplify the process of diagnosing SS, and to obtain 
methods to evaluate drugtherapy. All studied patients were diagnosed in 
accordance to the revised European classification criteria for SS. Specific objectives 
were to shorten the diagnostic delay, reduce the diagnostic work-up, and, in 
addition, to find clinical parameters which assess disease activity and progression. 
An early diagnosis of SS has two main advantages. Firstly, that the complaints can be 
related properly to the underlying disease, which is often very important for the 
patient. Secondly, an early diagnosis allows clinicians to consider preventive 
measurements for ocular and oral damage that may be necessitated by impaired 
function of tear- and salivary glands. With improved and simplified procedures, the 
diagnostic work-up will become more concise resulting in better general 
acceptance by patients and clinicians. This will yield clinically and scientifically 
relevant advantages, for it facilitates clinical diagnostics and it optimises external 
validity of research results. With valid outcome parameters of SS, specific disease 
effects of drug therapy can be monitored, thus clinical trials can be evaluated more 
accurately.

The oral tests that were selected for evaluation in this thesis each assess the disorder 
differently, by analysis of saliva, serum, and glandular duct-architecture. The selected 
diagnostic tests are: sialometry and sialochemistry assessing salivary gland function 
(chapter 3); measurement of serum salivary isoamylase activity assessing turnover of 
salivary gland cells (chapter 4); and sialography visualising specific alterations of 
salivary gland duct architecture (chapter 5). After the different tests for the oral 
component of SS have been evaluated individually, a comparison was made 
between the tests for the oral and the ocular component (chapter 6). Two rather 
unusual cases are presented in the next chapter (chapter 7), demonstrating the risk 
of misdiagnosing SS in relation to current diagnostic criteria. In chapter 8, 
conclusions of the individual studies are combined and placed into a wider context.
REFERENCES
