-79_2Medicine

Volume 79(2), March 2000, pp 103-108

Thyroid Disease in Primary Sjogren Syndrome: Study in a Series of 160 Patients

[Article]

Ramos-Casals, Manuel M.D.; Garcia-Carrasco, Mario M.D., Ph.D.; Cervera, Ricard
M.D., Ph.D.; Gaya, Joan M.D., Ph.D.; Halperin, Irene M.D., Ph.D.; Ubieto, Irene
M.D.; Aymami, Ana M.D.; Morla, Rosa M. M.D.; Font, Josep M.D., Ph.D.; Ingelmo,
Miguel M.D., Ph.D.
From Systemic Autoimmune Diseases Unit (MR-C, MG-C, RC, RMM, JF, MI), Hormonal
Laboratory (JG), and Department of Endocrinology (IH), Department of Medicine,
Institut d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Hospital
Clinic, School of Medicine, University of Barcelona; CAP Molins de Rei (IU, AA),
Molins de Rei, Barcelona, Catalonia, Spain; and Rheumatology Department (MG-C),
Benemerita University School of Medicine, Puebla, Mexico.
Supported by Grants SAF96-0120 from the Comision Interministerial de Ciencia y
Tecnologia, FIS 97/0669 and FIS 99/0280 from the Fondo de Investigaciones
Sanitarias. M. Ramos-Casals is a Research Fellow sponsored by a grant from the
Hospital Clinic.
Address reprint requests to: Dr. Ricard Cervera, Unitat de Malalties Autoimmunes
Sistemiques, Hospital Clinic, C/Villarroel, 170, 08036-Barcelona, Catalonia,
Spain. Fax: 34-93-451 52 72; e-mail: cervera@medicina.ub.es .
Abbreviations used in this article: ANA, antinuclear antibodies; ATD, autoimmune
thyroid disease; CI, confidence interval; NATD, nonautoimmune thyroid disease;
OR, odds ratio; SS, Sjogren syndrome; TgAb, antithyroglobulin antibodies; TPOAb,
antithyroid peroxidase antibodies; TSH, thyroid-stimulating hormone.

Outline

Introduction

Sjogren syndrome (SS) is an autoimmune disease that mainly affects exocrine glands and usually presents as a persistent dryness of the mouth and eyes due to functional impairment of the salivary and lacrimal glands (6). In the absence of an associated systemic autoimmune disease, patients with this condition are classified as having primary SS. The histologic hallmark is a focal lymphocytic infiltration of the exocrine glands, and the spectrum of the disease extends from an organ-specific autoimmune disease (autoimmune exocrinopathy) (28) to a systemic process (musculoskeletal, pulmonary, gastric, hematologic, vascular, dermatologic, renal, nervous system involvement, and lymphoproliferation) (1, 4, 8, 10, 22, 23). Because of this heterogeneity, some researchers have attempted to identify subsets of patients that would permit more reliable prediction of the course of primary SS in the affected individuals (11, 24, 25).

Considering the developmental, functional, and pathologic similarities of the thyroid and salivary glands (18), of particular interest is the association of thyroid disease and SS, which may have not only clinical but also etiopathogenic significance. The first studies of this association were included in general descriptions of the clinical picture of SS, whether primary or secondary (2, 31). These studies found the association of both diseases in 10%-14% of patients and showed that clinical thyroid disease was not common in SS, although similar studies (14) have shown a higher prevalence (50%). Since these initial reports, studies on the prevalence and clinical significance of thyroid disease in patients with primary SS have been scarce and generally performed in small series of patients without an age/gender-matched control group (9, 12, 14, 16, 20). We conducted the present study to determine the prevalence and clinical significance of thyroid disease in a large series of patients with primary SS.

Methods

Patients

We investigated 160 consecutive patients (147 women and 13 men; mean age, 60 yr;
range, 23-87 yr) seen in the Systemic Autoimmune Disease Unit. All patients fulfilled 4 or more of the preliminary diagnostic criteria for SS proposed by the European Community Study Group in 1993 (30). Moreover, presence of a positive minor salivary gland biopsy result (lymphocytic infiltrates grade 3 or
4 according to Chisholm-Mason's classification [5]) or a positive immunologic test (antinuclear antibodies [ANA] with a titer > 1/40, rheumatoid factor, anti-Ro/SS-A or anti-La/SS-B antibodies) was required for the diagnosis of SS.
None of these patients presented clinical or immunologic evidence of other systemic autoimmune disease, and all were classified as having primary SS.

All patients underwent a complete history and physical examination, as well as
diagnostic tests for SS applied according to the recommendations of the European
Community Study Group (30). All patients were specifically questioned on the presence of a past history of thyroid disease as well as on the current presence
of clinical manifestations suggestive of hyper- or hypothyroidism. A careful examination of the neck was performed in all patients and thyroid echography and/or scintigraphy was performed in those patients in whom a goiter or a thyroid nodule was suspected clinically.

Control group patients

To ensure that age and gender were similarly distributed in primary SS and control groups, we sorted the 160 SS patients in ascending order according to age and alternatively selected the odd cases. Each odd case was individually matched with a control subject of the same age and sex, consecutively selected
from a primary care center in our geographic area. Thus, we selected 80 control
subjects, but 5 refused to participate in the study and we finally obtained a control group of 75 individuals (66 women and 9 men; mean age, 61 yr; range, 23-80 yr) with a demographic profile similar to the 160 SS patients. Control subjects were selected if they did not have referred clinical manifestations of
SS and did not receive medications that might alter the thyroidal profile (lithium, iodine, amiodarone, phenylbutazone, sulfonamides, glucocorticoids, fenclofenac, or furosemide).

Hormonal studies

The following hormonal studies were performed in all patients and controls at the time of the study. Triiodothyronine (T3) and free thyroxine (FT4) were determined using a heterogeneous competitive magnetic separation assay (Technicon Immuno 1 System, Bayer Corporation, Tarrytown, NY). The normal ranges
were 0.6-1.6 ng/dL for T3 and 0.8-2.0 ng/dL for FT4. Thyroid-stimulating hormone
(TSH) was determined using a sandwich immunoassay format (Technicon Immuno 1 System, Bayer Corporation, Tarry-town, NY) with a sensitivity of 0.03 mIU/L. The
normal range for TSH was 0.4-4.0 mIU/L. Clinical hypothyroidism is defined by the finding of a decreased serum concentration of FT4 with an increase in

serum
TSH. Subclinical hypothyroidism is defined by the finding of an increase in serum TSH concentration with normal serum FT4 and T3 concentrations. Clinical hyperthyroidism is defined by the finding of an increased serum concentration of
FT4 or T3, or both, but decreased serum TSH. Finally, subclinical hyperthyroidism
is defined by normal serum FT4 and T3 concentrations but decreased serum TSH in
an asymptomatic individual.

Immunologic studies

Serum autoantibodies against thyroglobulin (TgAb) and thyroid peroxidase (TPOAb)
were determined by an automatic ELISA system in which the autoantibodies react
with specific antigen linked to a solid phase and to Protein-A labeled with enzyme (Enzymun-Test, Roche-Boehringer, Manheim, RFA). The existence of an autoimmune thyroid disease (ATD) was based on the presence of TgAb and/or TPOAb
in high titer (>136 IU/mL for TgAb and >36 IU/mL for TPOAb). Other immunologic
tests included determination of ANA (indirect immunofluorescence using mouse liver as substrate), precipitating antibodies to the extractable nuclear antigens Ro/SS-A and La/SS-B (counterimmunoelectrophoresis), and rheumatoid factor (ELISA).

Statistical analysis

We used conventional chi-square and Fisher exact tests to analyze qualitative differences, the Student test for comparison of means in large samples of similar variance, and the nonparametric Mann-Whitney U test for small samples.
The odds ratio (OR) was calculated for assessing the risk of appearance of each
variable, with a confidence interval (CI) of 95%. Values of quantitative variables are expressed as mean +/- standard error of the mean. A value of p

Results

Thyroid disease in patients with primary SS

Fifty-eight (36%) of the 160 patients with primary SS had evidence of thyroid disease (Table 1). Fifty-seven were female and 1, male. At the time of protocol,
the mean age of the patients was 60 years (range, 24-80 yr) and the mean disease
duration of SS was 81 months (range, 12-180 mo). None of these patients was treated with medications that might alter the thyroidal profile (lithium, iodine, amiodarone, phenylbutazone, sulfonamides, glucocorticoids, fenclofenac,
or furosemide).

TABLE 1. Thyroid disease in 160 patients with primary Sjogren syndrome

---

Autoimmune thyroid disease: Autoimmune thyroid disease (ATD) was diagnosed in 32
(20%) of the 160 patients with primary SS. Twenty patients showed an altered hormonal profile: 18 showed hypothyroidism (15 subclinical hypothyroidism and 3
clinical hypothyroidism) and 2 hyperthyroidism (both subclinical hyperthyroidism).
The remaining 12 patients were euthyroidal (6 of them previously had hypothyroidism
and received substitutive treatment).

Nonautoimmune thyroid disease: Nonautoimmune thyroid disease (NATD) was diagnosed in 26 (16%) of the 160 patients with primary SS. Seventeen patients showed an altered hormonal profile: 7 showed hypothyroidism (4 subclinical hypothyroidism and 3 clinical hypothyroidism) and 10 showed hyperthyroidism (3
subclinical hyperthyroidism and 7 clinical hyperthyroidism). The remaining 9 patients showed a morphologic thyroid disease with euthyroidism. The diagnoses
in these patients were multinodular goiter in 5, diffuse goiter in 3, and thyroid adenoma in 1.

Considering those patients with altered hormonal profiles, a different hormonal
pattern was observed when ATD patients were compared with NATD patients. Patients with ATD showed mainly hypothyroidism (18/20, 90% versus 7/17, 41% in
patients with NATD, p = 0.001, OR 12.86, CI 1.87-138.09), and those with NATD showed mainly hyperthyroidism (10/17, 59% versus 2/20, 10% in patients with ATD,
p = 0.001, OR 12.86, CI 1.87-138.09).

Relationship between thyroid disease and other features of SS

Clinical and immunologic manifestations of primary SS in patients with and without thyroid disease are shown in Table 2. A higher frequency of female patients was found in patients with thyroid disease than in those without (57/58, 98% versus 90/102, 88%, p = 0.03, OR 7.60, CI 1.06-330.47), but no statistical differences were found between the groups concerning age at protocol
or mean disease duration. The prevalences of glandular and extraglandular manifestations during the course of the disease were also similar in both groups, but when immunologic profiles were compared, patients with thyroid disease showed a higher prevalence, compared with those without thyroid disease,
of antiparietal cell autoantibodies (33% versus 12%, p = 0.002, OR 3.65, CI 1.50-9.05), TgAb (30% versus 5%, p

---

TABLE 2. Clinical and immunologic manifestations of primary SS in patients
with and without thyroid disease

Comparison of thyroid disease in patients with primary SS and controls

Table 3 shows the prevalences of the different types of thyroid disease in patients with primary SS and in controls of similar age and gender. No significant differences were found when comparing the prevalences of both ATD and NATD in patients with primary SS and in controls, respectively (32/160, 20%
versus 13/75, 17% for ATD and 26/160, 16% versus 7/75, 9% for NATD).

TABLE 3. Epidemiologic characteristics and prevalence of thyroid disease
in patients with primary SS and in control group

Discussion

In our study, we found a similar prevalence of thyroid disease in patients with
primary SS and in a control group of similar age and gender. Although thyroid disease was more common in patients with SS than in the control group, the difference (36% versus 27%, respectively) did not reach statistical significance.
Patients with primary SS and thyroid disease were preferentially women, and showed the same glandular and extraglandular manifestations of SS as those without thyroid disease, but we found a higher prevalence of several autoantibodies
(antiparietal cell-Ab, TgAb, and TPOAb) in patients with thyroid disease.

The thyroid and salivary glands have a number of interesting functional similarities, including the uptake and concentration of iodine by both glands (18). Histopathologically, the lymphocytic infiltrates of lacrimal and salivary
glands that are found in SS are similar to those of the thyroid gland in Hashimoto thyroiditis (13, 17). These observations may suggest a common pathogenetic mechanism for thyroid and salivary gland disease in SS (3). It is
possible that antigens shared by the salivary and thyroid glands are responsible
for the apparent association of autoimmune disease directed to each organ. In addition, a similar genetic background could predispose individuals to both diseases (26). Foster et al (9) studied the prevalences of thyroid disease and
antithyroid antibodies in family members of patients with primary SS and found
that they were increased in first- and second-degree relatives and in patients
with primary SS, with a significant relationship among TPOAb, hypothyroidism, ANA, and HLA-DR3 phenotype.

The prevalence and characteristics of thyroid disease in patients with primary
SS have been evaluated by several uncontrolled studies (9, 12, 14, 15, 16, 20,
21) (Tables 4 and 5). These studies showed percentages of thyroid dysfunction ranging from 10% to 45%, but at least 90% of the patients studied were women whose average age was about 50 years. Thus, that thyroid disease is more common
in patients with primary SS than in the general population of similar age and

gender could not be ascertained from these studies because of the high expected
rate of thyroid disease in this population (middle-aged individuals, mainly women) (7, 29). It is noteworthy that our study shows that patients with primary
SS have a prevalence of thyroid disease similar to that of a control group of similar age and gender (36% versus 27%, respectively). Moreover, the prevalences
of both ATD and NATD were similar in SS patients and controls.

TABLE 4. Prevalence of thyroid disease in patients with primary Sjogren syndrome, present report and previous studies

---

TABLE 5. Prevalence of positive antithyroidal autoantibodies and autoimmune thyroiditis in patients with primary Sjogren syndrome, present report
and previous studies

The most frequent hormonal profile observed in our SS patients with thyroid disease was subclinical hypothyroidism, detected in 19 (51%) of the 37 patients
with altered hormonal values. Subclinical hypothyroidism is a relatively common
disorder caused by the same disorders that result in overt hypothyroidism. The
most common cause, responsible for about 50% of cases, is autoimmune or Hashimoto thyroiditis (27). The overall prevalence of these findings in the general population is 2%-8% (2.8% in men and 7.5% in women) with a particularly
high prevalence, up to 16%, in women older than 60 years of age (27). In our control group (mainly women, with a mean age of 60 years) we found a similar prevalence (17%). Early investigators believed that these findings characterized
a stage of hypothyroidism that preceded the clinical presentation of disease. We
also believe that, in most of our SS patients, an increase in serum TSH represents the earliest detectable stage of hypothyroidism. When patients with
subclinical hypothyroidism are studied over a period of years, 20%-50% of individuals appears to develop overt clinical hypothyroidism within 4-8 years.
Furthermore, those patients who also have higher titers of antithyroid antibodies have a higher risk of developing clinical hypothyroidism. In patients
older than 65 years of age, the presence of an increase in serum TSH and antithyroid antibodies predicts that about 80% of individuals will develop clinical hypothyroidism within 4 years (27). A prospective follow-up of our

subclinical SS patients is required to confirm the development of overt clinical
thyroid disease.

Subclinical hyperthyroidism occurs less frequently than subclinical hypothyroidism.
The reported prevalence in the general population ranges from 1% to 12%, and the
most common causes of hyperthyroidism are Graves disease, nodular goiter, and thyroiditis (27). To our knowledge, the association between primary SS and Graves disease has been described anecdotally (15), and hyperthyroidism has been
scarcely described in SS patients (19, 20, 21, 31). In this study, we found hyperthyroidism in 12 (8%) of 160 SS patients, thus hyperthyroidism in primary
SS is more frequent than previously thought. Furthermore, only 2 of our patients
showed autoimmune hyperthyroidism, a rare association previously described by Perez-E et al (20). Most of our hyperthyroidal patients had NATD, while hypothyroidal patients had mainly ATD.

In conclusion, a high prevalence of thyroid disease was found in a large series
of patients with primary SS, although no significant differences were demonstrated
when we compared this prevalence with that of a control group of similar age and
gender. Subclinical hypothyroidism is the most frequent thyroidal profile found
in patients with ATD, while patients with NATD had mainly hyperthyroidism. Our
results indicate that middle-aged women (with or without SS) should be screened
periodically for thyroid function.

Summary

We studied 160 consecutive patients (147 female and 13 male) with primary Sjogren syndrome (SS) to determine the prevalence and clinical significance of
thyroid disease in a large series of patients with primary SS from our unit and
to compare the prevalence and significance with those in 75 individuals without
SS from a primary care center. Serum levels of thyroid hormones (free thyroxine,
triiodothyronine, and thyroid-stimulating hormone) and autoantibodies against thyroglobulin (TgAb) and thyroid peroxidase (TPOAb) were measured in all SS patients and in 75 control patients.

Fifty-eight (36%) of the 160 patients with primary SS had evidence of thyroid disease. Autoimmune thyroid disease (ATD) was diagnosed in 32 (20%) patients and
nonautoimmune thyroid disease (NATD) in 26 (16%). No significant differences were found when these prevalences were compared with those in control patients.
On the other hand, comparing those patients with altered hormonal profiles, patients with NATD showed mainly hyperthyroidism (10/17, 59% versus 2/20, 10% in
patients with ATD, p = 0.001). Finally, when clinical and immunologic manifestations
of SS were analyzed in patients with and without thyroid disease, respectively,

we found that patients with thyroid disease had a higher prevalence of female gender (98% versus 88%, p = 0.03), antiparietal cell autoantibodies (33% versus
12%, p = 0.002), TgAb (30% versus 5%, p

In conclusion, thyroid disease occurred in more than one-third of patients with
primary SS; the main cause was ATD, which was present in 20% of the patients studied. We note that no significant differences were observed when the prevalence of thyroid disease (either ATD or NATD) was compared with that in a
control group of similar age and gender. Our results indicate that middle-aged
women (with or without SS) should be screened periodically for thyroid function.

References

1. Anaya JM, Gutierrez M, Espinosa LR. Sindrome de Sjogren primario. Manifestaciones
clinicas extraglandulares. Rev Esp Reumatol 21: 337-42, 1994.

2. Bloch KJ, Buchanan WW, Wohl MJ, Bunim JJ. Sjogren's syndrome. A clinical, pathological and serological study of sixty-two cases. Medicine (Baltimore) 44:
187-231, 1965. Bibliographic Links

3. Bouanani M, Bataille R, Piechaczyk M, Salhi SL, Pau B, Bastide M. Autoimmunity
to human thyroglobulin. Respective epitopic specificity patterns of anti-human
thyroglobulin autoantibodies in patients with Sjogren's syndrome and patients with Hashimoto's thyroiditis. Arthritis Rheum 34: 1585-93, 1991. Bibliographic
Links

4. Cervera R, Garcia-Carrasco M, Font J, Ramos M, Reverter JC, Munoz FJ, Miret
C, Espinosa G, Ingelmo M. Antiphospholipid antibodies in primary Sjogren's syndrome: Prevalence and clinical significance in a series of 80 patients. Clin
Exp Rheumatol 15: 361-65, 1997. Bibliographic Links

5. Chisholm DM, Mason DK. Labial salivary gland biopsy in Sjogren's syndrome. J
Clin Pathol 21: 656-60, 1968. Bibliographic Links

6. Daniels T, Fox PC. Salivary and oral components of Sjogren's syndrome. Rheum
Clin Dis North Am 18: 571-89, 1992.

7. Ericsson UB, Lindgarde F. The epidemiology of thyroid disorders in a coast community in southern Sweden. J Clin Epidemiol 43: 645-50, 1990. Bibliographic
Links

8. Font J, Ramos-Casals M, Cervera R, Bosch X, Mirapeix E, Garcia-Carrasco M, Morla RM, Ingelmo M. Antineutrophil cytoplasmic antibodies in primary Sjogren's
syndrome: Prevalence and clinical significance. Br J Rheumatol 37: 1287-91, 1998. Bibliographic Links

9. Foster H, Fay A, Charles KP, Walker D, Griffiths I. Thyroid disease and

other
autoimmune phenomena in a family study of primary Sjogren's syndrome. Br J Rheumatol 32: 36-40, 1993. Bibliographic Links

10. Garcia-Carrasco M, Ramos M, Cervera R, Font J, Vidal J, Munoz FJ, Miret C,
Espinosa G, Ingelmo M. Hepatitis C virus infection in "primary" Sjogren's syndrome: Prevalence and clinical significance in a series of 90 patients. Ann
Rheum Dis 56: 173-75, 1997. Bibliographic Links

11. Garcia-Carrasco M, Cervera R, Rosas J, Ramos-Casals M, Morla RM, Siso A, Font J, Ingelmo M. Primary Sjogren's syndrome in the elderly: Clinical and immunological characteristics. Lupus 8: 20-23, 1999. Bibliographic Links

12. Hansen BU, Ericsson UB, Henricsson V, Larsson A, Manthorpe R, Warvinge G. Autoimmune thyroiditis and primary Sjogren's syndrome: Clinical and laboratory
evidence of the coexistence of the two diseases. Clin Exp Rheumatol 9: 137-41,
1991. Bibliographic Links

13. Hashimoto H. Zur Kenntniss der lymphomatosen Veranderung der Schilddruse (Struma lymphomatosa). Arch Klin Chir Berl 97: 219-48, 1912.

14. Karsh J, Pavlidis N, Weintraub BD, Moutsopoulos HM. Thyroid disease in Sjogren's syndrome. Arthritis Rheum 23: 1326-29, 1980.

15. Kelly CA, Foster H, Pal B, Griffiths I. What is the incidence of thyroid disease in primary Sjogren's syndrome [abstract]. Br J Rheumatol 29: 36, 1990.
Bibliographic Links

16. Loviselli A, Mathieu A, Pala R, Mariotti S, Cau S, Marongiu C, Mazzoleni AP,
Maggio P, Martino E. Development of thyroid disease in patients with primary and
secondary Sjogren's syndrome. J Endocrinol Invest 11: 653-56, 1988. Bibliographic
Links

17. Manthorpe R, Frost-Larsen K, Isager H, Prause JU. Sjogren's syndrome. A review with emphasis on immunological features. Allergy 36: 139-53, 1981. Bibliographic Links

18. Mason DK, Harden RM, Alexander WD. The salivary and thyroid glands. A comparative study in man. Br Dental J 122: 485-89, 1967.

19. Mitani Y, Shigemasa C, Taniguchi S, Tanaka T, Yoshida A, Mashiba H. Clinical
course of silent thyroiditis in a patient with Sjogren's syndrome. Concomitant
changes of antithyroid and antinuclear antibody. Arch Intern Med 148: 1974-75,
1988. Bibliographic Links

20. Perez-E B, Kraus A, Lopez G, Cifuentes M, Alarcon-Segovia D. Autoimmune thyroid disease in primary Sjogren's syndrome. Am J Med 99: 480-84, 1995. Bibliographic Links

21. Punzi L, Ostuni PA, Betterle C, De Sandre P, Botsois C, Gambari PF. Les affections thyroidiennes dans le syndrome de Gougerot-Sjogren primitif. Rev Rhum

(Ed Fr) 63: 943-48, 1996.

22. Ramos-Casals M, Cervera R, Yague J, Garcia-Carrasco M, Trejo O, Jimenez S,
Morla RM, Font J, Ingelmo M. Cryoglobulinemia in primary Sjogren's syndrome: Prevalence and clinical characteristics in a series of 115 patients. Semin Arthritis Rheum 28: 200-5, 1998. Bibliographic Links

23. Ramos-Casals M, Garcia-Carrasco M, Font J, Cervera R. Sjogren's syndrome and
lymphoproliferative disease. In: Shoenfeld Y, Gershwin E, eds. Cancer and autoimmunity. Elsevier: Amsterdam, 2000 (in press).

24. Ramos-Casals M, Cervera R, Font J, Garcia-Carrasco M, Espinosa G, Reino S,
Pallares L, Ingelmo M. Young onset of primary Sjogren's syndrome: Clinical and
immunological characteristics. Lupus 7: 202-6, 1998. Bibliographic Links

25. Ramos M, Cervera R, Garcia-Carrasco M, Miret C, Munoz FJ, Espinosa G, Font
J, Ingelmo M. Sindrome de Sjogren primario: Caracteristicas clinicas e inmunologicas en una serie de 80 pacientes. Med Clin (Barc) 108: 652-57, 1997.
Bibliographic Links

26. Scofield RH. Autoimmune thyroid disease in systemic lupus erythematosus and
Sjogren's syndrome. Clin Exp Rheumatol 14: 321-30, 1996. Bibliographic Links

27. Surks MI, Ocampo E. Subclinical thyroid disease. Am J Med 100: 217-23, 1996.
Bibliographic Links

28. Talal N. Clinical and pathogenetic aspects of Sjogren's syndrome. Semin Clin
Immunol 6: 11-20, 1993.

29. Vanderpump MP, Tunbridge WM, French JM, Appleton D, Bates D, Clark F. The incidence of thyroid disorders in the community: A twenty-year follow-up of the
Wickham survey. Clin Endocrinol 43: 55-68, 1995. Bibliographic Links

30. Vitali C, Bombardieri S, Moutsopoulos HM, 0Balestrieri G, Bencivelli W, Bernstein RM, Bjerrum KB, Braga S, Coll J, de Vita S, Drosos AA, Ehrenfeld M, Hatron PY, Hay EM, Isenberg DA, Janin A, Kalden JR, Kater L, Kontinnen YT, Maddison PJ, Maini RN, Manthorpe R, Meyer O, Ostuni P, Pennec Y, Prause JU, Richards A, Sauvezie B, Shiodt M, Sciuto M, Scully C, Shoenfeld Y, Skopouli FN,
Smolen JS, Snaith ML, Tishler M, Todesco S, Valesini G, Venables PJW, Wattiaux
MJ, Youinou P. Preliminary criteria for the classification of Sjogren's syndrome. Arthritis Rheum 36: 340-47, 1993.

31. Whaley K, Webb J, McAvoy BA, Hughes GR, Lee P, MacSween RN, Buchanan WW. Sjogren's syndrome. 2. Clinical associations and immunological phenomena. Q J Med 42: 513-48, 1973. Bibliographic Links

---

Accession Number: 00005792-200003000-00004