

# Pulmonary function abnormalities in Sjögren's syndrome and the sicca complex

ILIA SEGAL, GERSHON FINK, ISRAEL MACHTEY, VIKTOR GURA, AND SHIMON A SPITZER

*From the Pulmonary Section, Beilinson Medical Center, Petah Tiqva and Tel Aviv University Sackler School of Medicine, Rheumatology Clinic, and Nephrology Unit, HaSharon Hospital, Petah Tiqva, Israel*

**ABSTRACT** The frequency of pulmonary involvement in a group of 20 patients with Sjögren's syndrome or the sicca complex was evaluated with pulmonary function studies. In 12 patients pulmonary functional abnormalities were demonstrated. The most common abnormality was airway obstruction. Nine out of 13 patients with the limited variant of the disease (sicca complex) and three out of seven patients with the complete syndrome had abnormal pulmonary function.

Sjögren's syndrome is a chronic autoimmune disorder, characterised by keratoconjunctivitis sicca (dry eyes), xerostomia (dry mouth), and a connective tissue disorder, usually rheumatoid arthritis. The term "sicca complex" is reserved for cases in whom only the first two features are present.

Until recently only isolated cases of pulmonary involvement in patients with Sjögren's syndrome have been reported.<sup>1,2</sup> Strimlan *et al*<sup>3</sup> found pulmonary involvement in 9% of patients with Sjögren's syndrome. They showed mainly a restrictive ventilatory defect, low diffusing capacity or both, related to interstitial or pleural changes on chest radiography. Newball *et al*<sup>4</sup> found evidence of airway disease in six out of 13 patients evaluated. They concluded that certain patients with Sjögren's syndrome develop an unusual type of chronic obstructive airway disease which is probably the result of a chronic inflammatory process similar to that seen in their salivary and lacrimal glands. The authors suggested that the restrictive ventilatory defect seen in Sjögren's syndrome might be associated with the connective tissue disorder rather than with the sicca complex.

The purpose of this study is to report the types of pulmonary functional defects seen in 20 patients with Sjögren's syndrome.

## Methods

Twenty non-smokers, 19 women and one man,

Address for reprint requests: Dr SA Spitzer, Pulmonary Section, Beilinson Medical Center, Petah Tiqva, Israel.

who were diagnosed as suffering from Sjögren's syndrome or sicca complex, underwent clinical examination, chest radiography, and standard pulmonary function tests. Keratoconjunctivitis sicca was present in 19 out of 20 patients and included positive Shirmer test and punctate ulcers on cornea and conjunctiva found by slit lamp or fluorescent staining. Xerostomia was present in all patients and included diminution of salivary flow, positive sialography, and focal lymphoplasmacytic infiltrates and chronic fibrosing sialadenitis on lower lip or parotid biopsy. Connective tissue disease was present in seven patients (35%). Five patients met the criteria for the diagnosis of rheumatoid arthritis, one for dermatomyositis, and one for scleroderma.

Spirometry was performed with a Godart water spirometer. The FRC was determined with the helium dilution technique and thoracic gas volume (TGV) and airways resistance (Raw) were determined plethysmographically. Flow volume curves were determined by an Ohio spirometer and recorded on a Hewlett-Packard x-y recorder. Carbon monoxide diffusing capacity was determined by the steady state method. Arterial blood gases were measured in duplicate with standard electrodes (Radiometer, Model BMS-3).

## Results

The anthropometric and clinical characteristics of the patients are listed in table 1. The group consisted of 19 women and one man with a mean age

Table 1 Anthropometric and clinical characteristics of 20 patients with Sjögren's syndrome

Number	Sex	Age (yr)	Height (cm)	BSA	Associated immune disease	Chest x-ray pattern	Shirmer test	Reduced salivary flow rate	Sialography	Slit lamp	Salivary gland biopsy
1	F	71	139	1.43	No	Normal	+	+	No	+	+
2	F	71	150	1.50	No	Hyperinfl	+	+	+	+	No
3	F	63	156	1.61	No	Normal	+	+	No	+	+
4	F	63	167	1.87	RA	Hyperinfl	+	+	No	No	+
5	F	70	145	1.53	No	Normal	+	+	+	+	-
6	F	70	160	1.55	No	Hyperinfl	+	+	No	No	+ Parotid
7	F	70	159	1.64	RA	Hyperinfl	+	+	-	+	+
8	F	64	160	1.65	No	Normal	+	+	No	+	No
9	F	34	176	1.72	No	Normal	+	+	No	No	+
10	F	72	146	1.50	No	Normal	+	+	+	+	No
11	F	63	157	1.65	No	Normal	+	+	No	+	+
12	F	61	150	1.44	Hashimoto Thyroiditis	Normal	+	+	No	+	+ Parotid
13	F	79	148	1.47	RA	Normal	+	+	No	+	No
14	F	50	150	1.52	RA	Normal	+	+	No	-	+
15	F	54	158	1.65	No	Normal	+	+	+	+	No
16	F	42	166	1.83	Dermatomyositis	Normal	+	+	No	-	+
17	F	57	158	1.62	No	Reticulo nodular	+	+	+	No	+ Parotid
18	F	67	153	1.45	Scleroderma	Small lungs ground glass	+	+	-	+	+
19	M	70	170	1.77	LIP	Diffuse alveolar	+	+	+	No	+ Parotid
20	F	64	164	1.66	RA	Normal	-	+	No	+	+

RA=rheumatoid arthritis; LIP= lymphoid interstitial pneumonia; += positive test; -= negative test; No=test not performed.

of 65.7 years and age range of 34-79 years. The diagnostic tests included Shirmer test, which was positive in 19 out of 20 patients. Slit lamp examination revealed erosions on the corneal and conjunctival epithelium in 13 out of 15 patients examined. The two patients with negative slit lamp examination had a positive Shirmer test. Mixed salivary flow rate was decreased or absent in all the patients. Lower lip (minor salivary gland) or parotid biopsy revealed massive lymphoid infiltration with acinar atrophy and fibrosis in 14 out of 15 patients. Abnormalities related to narrowing of the ducts and acinar atrophy were demonstrated on sialography in six out of eight patients studied.

Chest radiographs were abnormal in seven patients. The most common abnormality was hyperinflation in four cases. Reticulonodular pattern was demonstrated in one patient, who was suffering from recurrent pulmonary infections. Small lungs with "ground glass" appearance were found in patients suffering from scleroderma. Chest radiographs of the only male patient demonstrated a diffuse interstitial infiltration. Trephine drill biopsy of the right lung in this patient revealed the pathological picture compatible with lymphoid interstitial pneumonia (LIP).

The laboratory findings revealed anaemia with haemoglobin less than 12 g/dl in six patients, sedimentation rate in excess of 50 mm/lh in seven patients. Rheumatoid factor was present in 15 patients (75%) and antinuclear factor in eight out of 18 studied. Increased levels of IgA were demon-

strated in eight patients, while seven had increased levels of IgM and four of IgG.

Pulmonary function tests were normal in eight

Table 2 Pulmonary function tests in 20 patients with Sjögren's syndrome

Number	Parameter	Normal mean $\pm$ SD % of pre- dicted (8 patients)	Obstruc- tive mean $\pm$ SD % of pre- dicted (7 patients)	Restric- tive mean $\pm$ SD % of pre- dicted (3 patients)	Mixed mean and range % of predicted (2 patients)
1	VC	107.8 8.5	84.7 11.6	75.7 10.0	67.0 56-78
2	FRC	106.4 12.5	119.6 11.9	80.0 2.4	85.5 82-89
3	TGV	116.1 10.1	133.9 15.4	82.5 1.5	92.0 84-100
4	RV	106.6 16.3	133.4 21.1	86.0 5.4	99.5 90-109
5	TLC	106.9 7.5	108.0 9.7	78.7 2.4	74.0 67-84
6	RV/TLC	37.3 5.3	47.3 5.5	38.3 6.8	44.5 43-46
7	FEV <sub>1</sub> /FVC %	79.1 3.6	68.1 2.6	81.7 3.7	59.0 50-68
8	FEF <sub>25</sub> %	101.1 10.2	54.9 13.4	105.7 23.3	32.5 15-50
9	Raw	1.604 0.237	2.758 0.536	1.390 0.300	2.85 1.87-3.80
10	sGaw	0.234 0.021	0.130 0.039	0.285 0.005	0.12 0.07-0.16
11	DlCO	111.0 17.8	111.6 31.4	86.0 11.3	63.0 55-71
12	Po <sub>2</sub>	80.9 7.9	69.9 6.6	66.3 5.3	78.5 78-79
13	Pco <sub>2</sub>	32.7 1.9	32.0 3.0	33.3 0.5	30.0 27-33
14	(A-a)O <sub>2</sub>	30.00 9.3	40.00 6.3	42.0 4.5	34.5 30-39

The numbers in the second line of each parameter represent SD.

patients (table 2). In seven patients pulmonary function tests demonstrated obstructive ventilatory defects. Most of the abnormalities were mild to moderate. Airway resistance was elevated and the specific airway conductance reduced in all cases. All but one patient had normal or high carbon monoxide transfer factor. Arterial blood gas analysis showed mild hypoxaemia with hypocapnia caused by alveolar hyperventilation in all patients. Increased alveolar-arterial (A-a) oxygen gradient on room air was observed in all seven patients.

A restrictive ventilatory defect was demonstrated in three patients. The pulmonary diffusing capacity was low in two patients and airway mechanics were normal in all three patients.

In two patients a mixed obstructive and restrictive ventilatory defect was found. There was a reduction in lung volumes with a low VC, FRC, and TLC and a reduction in the FEV<sub>1</sub>/FVC ratio with even more prominent reduction in the late flows. The specific airway and transfer factor were also reduced.

## Discussion

The frequency of pulmonary involvement in Sjögren's syndrome is quite high. Sixty per cent of our patients had pulmonary functional abnormalities of some degree, a similar finding to that of Newball *et al.*<sup>4</sup> The functional derangements in Sjögren's syndrome may be obstructive, restrictive, or mixed. The obstructive ventilatory pattern was the most common and was of mild to moderate severity. In this group in only one patient was the transfer factor diminished without physiological evidence of emphysema. Coury *et al.*<sup>5</sup> and Lemercier *et al.*<sup>6</sup> first reported on the occurrence of obstructive ventilatory defects of various severity in three out of five patients studied. Obstructive ventilatory defect was the only abnormality in six patients studied by Newball.<sup>4</sup> The pathological basis for airway obstruction in Sjögren's syndrome involves lymphoid infiltrates and atrophy of mucous glands of pharynx, larynx and bronchial tree.<sup>3</sup> The involvement of the lower respiratory tract by lymphocytic and plasma cell infiltrates around the walls of small airways gives rise to focal atelectasis, recurrent infections and eventually bronchiectasis.<sup>7-9</sup>

A restrictive ventilatory defect was observed in only three of our patients with Sjögren's syndrome. All three had the complete syndrome. Strimlan *et al.*<sup>3</sup> found a restrictive ventilatory defect with or without decrease in the diffusing capacity in all 18 patients who underwent pulmonary function

studies. It seems that restrictive defects are a common feature of Sjögren's syndrome.<sup>10-11</sup> It is claimed that because the connective tissue disorders such as scleroderma and rheumatoid arthritis frequently have associated interstitial pulmonary fibrosis,<sup>8-10-13</sup> the restrictive defect seen in the complete syndrome is more likely to be associated with the connective tissue disorder, rather than with the sicca complex per se. The spectrum of abnormalities leading to the restriction in Sjögren's syndrome includes also lymphoid interstitial pneumonia (LIP),<sup>14</sup> pseudolymphoma,<sup>15-17</sup> and malignant lymphoma of the lung.<sup>18-20</sup>

A mixed type of pulmonary functional abnormality was observed in two patients, one of whom had the sicca complex and the other the complete variant. This type was the least common ventilatory abnormality seen in our patients and such cases could not be found in the English medical literature.

## References

- 1 Snider GL, Weiss MA. Pulmonary infiltrates in a woman with Sjogren's syndrome. *N Engl J Med* 1975; **293**:136-44.
- 2 Bucher UG, Reid L. Sjogren's syndrome: report of a fatal case with pulmonary and renal lesions. *Br J Dis Chest* 1960; **53**:237-52.
- 3 Strimlan CV, Rosenow EC, Divertie MB, Harrison EG. Pulmonary manifestations of Sjogren's syndrome. *Chest* 1976; **70**:354-61.
- 4 Newball HH, Brahim SA. Chronic obstructive airway disease in patients with Sjogren's syndrome. *Am Rev Respir Dis* 1977; **115**:295-304.
- 5 Coury C, Rulliere R, Delepiere F, Saigot T. Les manifestations respiratoires au cours du syndrome de Gougerot-Sjogren (a propos de deux observations. *Poumon Coeur* 1972; **28**:11-20.
- 6 Lemercier JP, Michel MJ. Les manifestations respiratoires du syndrome de Gougerot-Sjogren. *Sem Hop (Paris)* 1973; **49**:1227-31.
- 7 Bloch KJ, Buchanan WW, Wohl MG, Bunim JJ. Sjogren's syndrome: a clinical pathological and selological study of 62 cases. *Medicine (Baltimore)* 1965; **44**:187-231.
- 8 Cummings NA, Schall GL, Asofsky R, Anderson LG, Talal N. Sjogren's syndrome—newer aspects of research, diagnosis and therapy. *Ann Intern Med* 1971; **75**:937-50.
- 9 Ellman P, Weber FP. Sjogren's disease with dryness of the bronchial mucosa and uncertain lung lesion. *Br Med J* 1949; **1**:304-5.
- 10 Caterall M, Rowell NR. Respiratory function studies in patients with certain connective tissue diseases. *Br J Dermatol* 1965; **77**:221-5.
- 11 Shearn MA. *Sjogren's syndrome*. Philadelphia: Saunders, 1971.

- 12 Denko CW, Bergenstal DM. The Sicca syndrome (Sjögren's syndrome): a study of 16 cases. *Arch Intern Med* 1960; **105**:849-58.
- 13 Whaley K, Williamson J, Chisholm DM, Webb J, Mason DK, Buchanan WW. Sjögren's syndrome I. Sicca component. *Q J Med* 1973; **42**: 279-304.
- 14 Bonner H Jr, Ennis RS, Geelhoed EW, Tarpley TM. Lymphoid infiltration and amyloidosis of lung in Sjögren's syndrome. *Arch Pathol* 1973; **95**:42-4.
- 15 Anderson LG, Talal W. The spectrum of benign to malignant lymphoproliferation in Sjögren's syndrome. *Clin Exp Immunol* 1972; **10**:199-221.
- 16 Talal N, Sokoloff L, Barth WF. Extrasalivary lymphoid abnormalities in Sjögren's syndrome (reticulum cell sarcoma, "pseudolymphoma", macroglobulinemia). *Am J Med* 1967; **43**:50-65.
- 17 Liebow AA, Carrington CB. Diffuse pulmonary lymphoreticular infiltrations associated with dysproteinemia. *Med Clin North Am* 1973; **57**: 809-43.
- 18 Talal N, Bunim JJ. The development of malignant lymphoma in the course of Sjögren's syndrome. *Am J Med* 1964; **36**:529-40.
- 19 Hornbaker JH Jr, Foster EA, Williams GS, Davis JS. Sjögren's syndrome and nodular reticulum cell sarcoma. *Arch Intern Med* 1966; **118**: 449-52.
- 20 Saltzstein SL. Pulmonary malignant lymphomas and pseudolymphomas: classification therapy and prognosis. *Cancer* 1963; **16**:928-55.