In our experience with these and other patients 50% lactulose has been an effective and trouble-free agent in promoting bowel evacuation in elderly as well as younger patients. We suggest that the administration of lactulose after barium-meal examination in the elderly should be a routine in helping to prevent retention of barium and the subsequent morbidity of barium-meal examination.

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Occasional Review

Sjögren's Syndrome

GRAHAM R. V. HUGHES, KEITH WHALEY

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Summary

Sjögren's syndrome is a common accompaniment of rheumatoid arthritis and other connective-tissue diseases as well as several diseases thought to have an immunological basis. Despite the wide spectrum of clinical features and serological abnormalities the condition is, if anything, underdiagnosed. A clinical subgroup of patients with Sjögren's syndrome can be distinguished by their pronounced hypergammaglobulinaemia, widespread and prominent immunological abnormalities, severe salivary gland swelling, and mild or absent arthritis. It is in this group that lymphoma development has been a complication.

Introduction

In 1933 Henrick Sjögren, a Swedish ophthalmologist, wrote a monograph on keratoconjunctivitis sicca.¹ Of the 19 females included in the study 13 had arthritis. While arthritis associated with keratitis filamentosa had been described in 1889² it was Sjögren who in this and subsequent studies drew attention to the widespread changes seen in this disorder.

The full triad of Sjögren's syndrome consists of keratoconjunctivitis sicca (dry eyes), xerostomia (dry mouth), and a connective-tissue disorder—usually rheumatoid arthritis.³ The term "sicca syndrome" is reserved for cases in which only the first two features are present. The syndrome with its wide spectrum of clinical features and immunological abnormalities provides a link between the various connective-tissue disorders and in turn between these disorders and malignancy of the lymphoreticular system.

Pathological Features

In the salivary glands the most characteristic change is a diffuse lymphocyte infiltration (Fig. 1). This in turn may lead to

FIG. 1—Labial gland biopsy specimen from a patient with Sjögren's syndrome. (X116.) (Courtesy of Dr. David Evans, department of pathology, Hammersmith Hospital, London.)

destruction and loss of salivary tissue. In the more severe cases lymphoid follicles complete with germinal centres may be seen. Proliferation of the myoepithelial cells lining the ducts may lead to the so-called epimyoeplithelial islands (Morgan-Castleman islands),⁴ though these are by no means confined to this disease.

Lymphoid infiltrates may be seen in the lacrimal glands, the mucus secreting glands of the conjunctivae, the nasal cavity, pharynx, larynx, trachea, and bronchi, leading to atrophy of these glands. The sweat glands and vagina may also show secretory insufficiency and chronic inflammatory infiltrates.

Clinical Features

Keratoconjunctivitis Sicca.—The commonest complaint (see Table) is not of dryness but of grittiness or a burning sensation of the eyes. Other symptoms include tiredness with difficulty in opening the eyes, dryness or occasionally redness, photophobia, and discharge. On examination dilatation of the bulbar conjunctival vessels, pericorneal injection, discharge, and dullness of the conjunctiva and cornea may be seen. Lacrimal gland enlargement is uncommon. The symptoms and signs of keratoconjunctivitis sicca are not specific for the condition and therefore the diagnosis must be made by showing diminished lacrimation, as shown by the Schirmer tear test, and finding filamentary

Department of Medicine, Hammersmith Hospital, London W12 OHS
GRAHAM R. V. HUGHES, M.B., M.R.C.P., Senior Registrar and Clinical Tutor

Department of Pathology, University of Glasgow, Glasgow W.2
KEITH WHALEY, M.D., M.R.C.P., Lecturer

Clinical Features of Sjögren's Syndrome

Eyes	Nervous System
Keratoconjunctivitis sicca	Cranial nerve lesions
Conjunctivitis	Peripheral neuropathy
Corneal vascularization	Respiratory System
Lacrimal gland enlargement	Tracheitis, bronchitis, Pneumonitis
Mouth	Atelectasis
Xerostomia	Pleural effusions
Dental caries	Diffuse interstitial pulmonary fibrosis
Parotid gland enlargement	Blood Vessels
Recurrent parotitis	Raynaud's phenomenon
Ear, nose, and Throat	Hyperglobulinaemic purpura
Epistaxis	Blood
Nasal septal perforation	Anaemia
Sinusitis	Thrombocytopenia, leucopenia
Serous otitis media	Hyperglobulinemia
Gastrointestinal tract	Autoantibodies
Dysphagia	General
Oesophageal webs	Drug hypersensitivity
Atrophic gastritis	Lymphoma development
(Pancreatitis)	
Genitourinary tract	
Renal tubular defects	
Interstitial nephritis	
Vaginitis sicca	

or punctate keratitis on slit-lamp examination of the cornea after the instillation of rose bengal dye into the conjunctival sac.

Xerostomia.—Unlike keratoconjunctivitis sicca there are no specific criteria for the diagnosis of xerostomia. Severe xerostomia with atrophy of the oral mucosa and a board-like, red fissured tongue is uncommon. Even when there is severe damage to the major salivary glands the minor salivary glands of the oral cavity may secrete enough saliva for the inside of the mouth to appear moist. Nevertheless, the absence of a pool of saliva around the base of the lingual frenulum is sufficient to suggest the diagnosis. Because of the lack of saliva dental caries is often early and may progress rapidly* (Fig. 2).

FIG. 2—Gross dental caries associated with xerostomia in Sjögren's syndrome.

Other Sicca Components.—Lack of adequate exocrine and mucus secretions may lead to other widespread problems. Dryness and crusting of the nose may be extremely uncomfortable; epistaxes and nasal septum perforation may occur.⁶ Eustachian tube obstruction may lead to persisting otitis media and deafness. Involvement of the larynx may lead to hoarseness, and bronchial disease to persistent cough with difficulty in expectorating thick, tenacious sputum, leading in turn to recurrent pneumonitis and atelectasis. Diffuse interstitial pulmonary fibrosis and pleurisy with effusion are other complications.⁷ Atrophy of sweat glands may cause skin dryness, although this is rare. Dyspareunia due to vaginal dryness may occur.

Alimentary Tract.—Dysphagia is not uncommon and oesophageal webs similar to those found in the Plummer-Vinson syndrome are occasionally seen on barium swallow.⁶ It is not yet known whether these webs are premalignant. Atrophic gastritis may be an associated condition⁷ and pancreatitis, though surprisingly uncommon, may be present subclinically as shown by secretin and pancreozymin tests.⁸ The relation between Sjögren's syndrome and liver disease will be referred to later.

Renal Disease.—The continual sipping of water for mouth dryness may result in polyuria. In Sjögren's syndrome, however, this may also be due to the occurrence of nephrogenic diabetes insipidus, a defect not reversible by pitressin.⁹ Other renal tubular defects are usually present in such cases and include renal tubular acidosis, uricosuria, phosphaturia, and generalized aminoaciduria. Even in the absence of overt renal disease many patients with Sjögren's syndrome have impaired ability to excrete an acid load and to concentrate their urine.¹⁰ While pathological changes such as interstitial nephritis, which may be found in Sjögren's syndrome,¹¹ may be responsible it is possible that in most cases these tubular defects are secondary to hyperglobulinaemia, similar tubular defects being seen in a number of conditions (Waldenström's macroglobulinaemia, multiple myeloma, sarcoidosis) where hyperglobulinaemia is pronounced.

Circulatory Changes.—Raynaud's phenomenon occurs in up to 25% of patients with Sjögren's syndrome. It is not due to cryoglobulinaemia, which is rarely found. Hyperglobulinaemic purpura is not infrequently seen.¹² Arteritis may occur in severe Sjögren's syndrome and is probably responsible for the peripheral and occasional cranial neuropathies which may also complicate the course of this disease.^{3, 13}

Haematological Changes.—Anaemia and leucopenia are common, the latter not necessarily accompanied by splenomegaly. Mild thrombocytopenia and eosinophilia may also be seen.³

Drug Allergy.—A predisposition to drug allergy has been noted in Sjögren's syndrome. Bloch *et al.*³ found that 71 out of 83 patients with Sjögren's syndrome treated with gold salts developed an allergic skin rash. Williams *et al.*¹⁴ in a survey of penicillin allergy in patients with rheumatoid arthritis, found that in rheumatoid patients without Sjögren's syndrome the incidence of penicillin allergy was not significantly higher (16.7%) than in control patients (12.8%). In patients with rheumatoid arthritis and Sjögren's syndrome the incidence rose to 40.7%. These findings in themselves argue for the routine testing of all rheumatoid patients for Sjögren's syndrome.

Diagnosis

Schirmer's Test.—This test is the simplest screening test for keratoconjunctivitis sicca and should be a standard investigation in all rheumatic disease patients. Its beauty lies in the "all-or-nothing" response usually obtained. The test employs five

FIG. 3—Schirmer's test. Wetting of less than 15 mm of the blotting paper in five minutes is regarded as abnormal.

35-mm filter paper strips* (standardized commercially produced papers are available) bent 5 mm from one end and hooked over the lower eyelid at the junction of the middle and outer thirds. The length of the wetting is measured at five

*Tilden Yates Labs. Inc., Wayne, New Jersey 07470, U.S.A.

minutes; less than 15 mm is regarded as abnormal (Fig. 3). The Schirmer test is a crude index of the tear secretion. Subnormal results may be obtained in warm, dry atmospheres and very occasionally in apparently healthy middle-aged and elderly persons. If the Schirmer test gives equivocal results it can be repeated during the inhalation of ammonia to stimulate lacrimation. Irritation produced by the blotting paper in a normal eye generally results in wetting of the whole paper within one to two minutes.

Slit-lamp Examination.—The instillation of a drop of rose bengal dye into the conjunctival sac facilitates the detection of superficial corneal scarring, though the staining obtained is not of itself specific for keratoconjunctivitis sicca. Slit-lamp examination provides the most sensitive test for filamentous keratitis. This investigation showed abnormalities in all 57 patients in the early series reported by Bloch and Bunim.⁷

Tests of Salivary Function.—In view of the difficulty in the clinical detection of xerostomia it is perhaps not surprising that a battery of tests of salivary gland function have been devised, including salivary flow measurements,¹⁵ sialography,⁷ and radioisotope scintiscanning.¹⁶ Of these tests the measurement of parotid salivary flow during lemon juice stimulation is the most sensitive index of salivary gland dysfunction.

Labial Gland Biopsy.—Labial gland biopsy has become an important procedure in the diagnosis of Sjögren's syndrome following the observation that pathological changes occurring in the major salivary glands are mirrored in the minor salivary glands in the lip.³ These glands can often be felt as small pin-head-sized lumps inside the lower lip. Under local anaesthesia the gland can be removed through a small incision. While providing histological evidence of Sjögren's syndrome similar changes are seen in up to 25% of patients with rheumatoid arthritis without overt evidence of Sjögren's syndrome,^{17, 18} perhaps arguing for a spectrum of salivary changes in rheumatoid disease, of which the full-blown sicca syndrome represents an extreme. The borderline between focal and diffuse histological lesions may be indistinct; Waterhouse and Doniach,¹⁹ in a pathological study of salivary glands in a series of 525 necropsies, found focal lymphocytic lesions in over half of the women studied and in a quarter of the men. A raised prevalence and severity of adenitis in the salivary and lacrimal glands was found in subjects with rheumatoid arthritis. They pointed out the analogy with autoimmune thyroiditis in which non-progressive focal lesions are far more prevalent than diffuse primary myxoedema.

Association with Other Connective-tissue Diseases

Rheumatoid arthritis is the most frequent disease accompanying the sicca syndrome. The overall incidence of the Association is not known. In the series of 57 patients with Sjögren's syndrome studied at the National Institutes of Health, Bethesda, 30 had rheumatoid arthritis, 2 had possible rheumatoid arthritis, 3 had scleroderma, and 4 had polymyositis. Conversely, reports of the incidence of keratoconjunctivitis sicca in rheumatoid arthritis have ranged from 10% to 58.4%, the high figure being obtained from a survey of 250 patients using careful slit-lamp examination.¹⁵ A true assessment of the frequency of the association is made even more difficult by the high incidence of arthralgias and mild non-erosive arthritis in patients with the sicca syndrome alone.

Lymphoreticular Neoplasia

In 1951 Rothman *et al.*⁴⁰ described Sjögren's syndrome in association with lymphoblastoma and hypersplenism. Talal and Bunim²¹ in Bethesda subsequently reported the development of extrasalivary reticulum cell sarcoma in three out of 58 patients with Sjögren's syndrome together with a further patient

with raised IgM levels and atypical lymphoid infiltrates in the lymph nodes and lung. The Bethesda group went on to report eight other cases with extrasalivary lymphoid abnormalities; two had primary (Waldenström's) macroglobulinaemia and five had a significant increase of serum IgM.^{21, 22}

Some evidence suggests that irradiation of the parotid glands is a predisposing factor.²² Generally such neoplastic change has an extrasalivary distribution, although recent studies have shown that such malignant transformation may originate within the salivary glands.²³ Reticulum cell sarcoma occurs most commonly, although lymphosarcoma, Waldenström's macroglobulinaemia, and pseudolymphoma are also seen. Benign lymphoproliferation, which occurs as a part of the spectrum of Sjögren's syndrome, may be difficult to distinguish from its malignant counterparts.

Patients with Sjögren's syndrome developing lymphomas have had several clinical features in common. In general the sicca syndrome has been severe and long standing and there has been an increased incidence of lymphadenopathy, splenomegaly, leucopenia, vasculitis, neuropathy, Raynaud's phenomenon, and purpura hyperglobulinaemia.²² Arthritis in these cases has been noticeably mild or absent.

Other pointers to this group have been very high titres of rheumatoid factor and other autoantibodies and a disproportionate increase of IgM compared with IgG. Hypogammaglobulinaemia has been noted during the development of reticulum cell sarcoma and cryoglobulinaemia in reticulum cell sarcoma or pseudolymphoma.²¹ Thus Sjögren's syndrome provides another link between disease affecting immunological responses and the development of neoplasia. Whether or not such malignant change results from a loss of immunological surveillance in Sjögren's syndrome remains hypothetical.

Immunological Changes

Sjögren's syndrome ranks second only to systemic lupus erythematosus in its abundance of serum autoantibodies, both organ-specific and non-organ-specific. Hypergammaglobulinaemia, usually polyclonal, is almost the rule in this disease. Depending on the method used 75-100% of patients can be shown to have rheumatoid factor in their sera,³ even in the absence of rheumatoid arthritis. Antinuclear antibodies are found in roughly two-thirds of patients with Sjögren's syndrome, a speckled or nucleolar pattern being common.²⁴ Tests for lupus erythematosus cells are positive in about 10%.³ The measurement of anti-DNA antibodies has provided help in the differential diagnosis of Sjögren's syndrome and systemic lupus erythematosus.^{25, 26} While antibodies to native, double-stranded DNA are found in all cases of clinically active systemic lupus erythematosus they are not present in Sjögren's syndrome, even in the presence of positive antinuclear factor tests.²⁴ Antibodies to denatured DNA, on the other hand, are occasionally found in high titre in Sjögren's syndrome.²⁷

ORGAN-SPECIFIC ANTIBODIES

Autoantibodies to thyroglobulin and thyroid microsomes may be found in 25-33% of patients with Sjögren's syndrome.⁷ Although patients having thyroid disease and Sjögren's syndrome are observed occasionally, and despite pathological similarities between thyroiditis and Sjögren's syndrome, the evidence supporting an association between the two disease states is inconclusive. It has been shown that patients with thyroid disease do not have an increased prevalence of Sjögren's syndrome.²⁸

Similarly, the prevalence of gastric parietal cell antibody has been reported to be greater in Sjögren's syndrome.²⁹ Again there is no firm statistical evidence that an association exists between

pernicious anaemia and Sjögren's syndrome despite isolated case reports. Patients with pernicious anaemia do not have an increased prevalence of keratoconjunctivitis sicca.³⁰ Associations between Sjögren's syndrome and liver disease (especially chronic active hepatitis³¹ and fibrosing alveolitis³² have been reported. Mitochondrial antibody (a non-organ-specific antibody) has been detected in the sera of about 6% of patients with the sicca syndrome in titres normally associated with liver disease and has been shown to be associated with histological evidence of liver disease.^{33 34} Antibodies to salivary duct cells can be detected in roughly half of all patients with Sjögren's syndrome though their pathogenic significance is doubtful.³⁵

Management

In most though not all patients suffering from keratoconjunctivitis sicca 0.5% carboxymethylcellulose eye-drops provide symptomatic relief. As most patients have increased bacterial counts in the conjunctivae we frequently begin treatment with a month's course of chloramphenicol eye-drops, carefully observing the patients for the development of drug allergy. The mucolytic agent acetylcysteine shows promise in the treatment of keratoconjunctivitis sicca but needs to be fully evaluated. Some patients resistant to treatment with eye-drops and who have residual tear formation have improved with nasolacrimal duct occlusion. In certain patients, unfortunately, the disease progresses despite all treatment, and complications such as corneal perforation and vascularization occur. These, of course, need expert ophthalmological attention.

The lack of adequate treatment for the dryness of the mouth is reflected in the variety of remedies suggested. Attempts to stimulate salivation with pilocarpine and neostigmine have failed, and patients mostly resort to frequent sips of water and to the use of citric acid or pure lemon juice. The tendency to dental caries makes regular dental treatment doubly important. Occasionally suppurative parotitis may complicate the picture and should be treated with antibiotics. Irradiation of enlarged lacrimal and salivary glands should be avoided in view of the possibility that it may trigger malignant lymphoma development.

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Making Hospital Geriatrics Work

H. M. HODKINSON, P. M. JEFFERYS

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Summary

The first year's work at a new geriatric department at Northwick Park Hospital shows that active policies revolutionize the geriatric service and result in high turnover of patients and no waiting list. Comparison with low turnover/waiting list departments shows the effects of a waiting list in terms of diminished therapeutic benefit and less favourable outcome for patients admitted. The requirements for elimination of the waiting list appear to be well directed policies and adequate and enthusiastic staff. Active geriatrics results in high morale

and could be widely applicable within the present hospital bed resources given the necessary improvements in staffing.

Introduction

This paper looks at the first year of a new geriatric service based on Northwick Park Hospital, a new district general hospital combined with a clinical research centre, which opened in 1970. The geriatric department admitted its first patients in October 1970 and during the following year built up gradually in size to its present 114 beds, 25 in Northwick Park and 89 in two small hospitals in the neighbourhood (Roxbourne and Harrow Hospitals). The department has taken on responsibility for a catchment area of about 140,000 population (17,000 over 65), most of which is in the borough of Harrow with a smaller part in Brent. The area had previously been part of that served by a seriously overburdened geriatric department based on Edgware General Hospital, whose problems were outlined by Binks.¹ In

Northwick Park Hospital, Harrow, Middlesex

H. M. HODKINSON, B.M., M.R.C.P., Consultant Geriatrician

P. M. JEFFERYS, M.B., M.R.C.P., Registrar in Geriatrics (Present address: Maudsley Hospital, London S.E.5.)