problems of dealing with chronic disease is that for a medical student the condition is seen as a particular window, i.e. the 10 days in hospital following an exacerbation of rheumatoid arthritis or the 7 days for an operation in a disease which may last a lifetime. Continuity is something that is hard to find in modern teaching hospital where average bed stay might be down to 5 days. Since there is evidence that exposure to disabled persons consistently leads to the development of more positive attitudes to disability [11], students might be ‘attached’ to a patient with a chronic rheumatoid complaint in the first year of their medical course and asked to follow that patient throughout their course, even if it just meant contact with them three or four times a year.

The incorporation of questions on musculoskeletal disease in examinations provides an important (if not unfortunate) reason for students to focus on this specialty. Although knowledge can be tested through standard or extended multiple-choice questions, clinical skills are best tested using some form of objective structured clinical examination. The Objective Structured Clinical Examination can also be extended, as has been demonstrated by Cannell et al. [12] using a standardized patient where history and physical examination can be videotaped. This experience seems to provide a valid way of assessing a range of clinical competencies in musculoskeletal disease.

Medical school curricula should be evolving ‘beasts’. They need constant review, refinement and change as knowledge expands and new diseases emerge. At a recent conference on undergraduate education in musculoskeletal diseases [13], considerable support was given to the idea that rheumatologists and orthopaedic surgeons might work more closely together in developing joint training programmes. Musculoskeletal diseases present one of the last bastions of general medicine. They cover an enormous spectrum of disease, from the severe and acute scleroderma crises through to the chronic musculoskeletal pain syndromes. Core knowledge in the basic diseases is required, but even more important is the ability to clinically assess a patient both in terms of their disease and disability, and to master the skills required to provide support and guidance for a patient with a chronic disabling illness.

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SJÖGREN’S SYNDROME REVISITED: AUTOIMMUNE EPITHELITIS

EPONYMS have been used in the medical literature either to honour the first person who described the disease or the location where the disorder was first described. In that respect, Sjögren’s syndrome (SS) was named after the Swedish ophthalmologist who pointed out that dry eyes and dry mouth constitute local manifestations of a rather systemic syndrome. Clinical and pathogenetic studies suggest that a descriptive term for SS should be used.

The major histopathological lesion of this syndrome is a round cell infiltrate which affects the exocrine glands; in the early lesions, it begins around ductal epithelial cells, whereas in advanced lesions the infiltrate extends and replaces the functional tissue [1]. This results in glandular dysfunction and manifests clinically with dry eyes, mouth, nose, airways, atrophic gastritis, subclinical pancreatitis and dry skin. This is called ‘glandular’ SS. Since exocrine glands are primarily affected and the syndrome presents tissue autodestruction by the invading lymphocytes, as well as a plethora of autoantibodies, Talal [2] provided the term ‘autoimmune exocrinopathy’. In a quarter of the
patients, however, the lymphocytic infiltrates extend beyond the exocrine glands and affect parenchymal organs such as the thyroid, liver, kidneys and lungs. Thus, this name does not completely describe the syndrome. Careful analysis on clinical and immunopathological grounds shows that the major cell affected in both glandular and extraglandular syndrome mainly concerns the epithelium.

The histopathological lesion of the kidneys resembles that seen in the exocrine glands (focal infiltrates around tubular epithelium which extend and occupy the interstitium), resulting clinically in a tubular defect with or without acidosis [3]. Lung disease in SS is slowly progressive, affecting mainly the airways and the interstitial space, rarely leading to severe interstitial disease [4]. In a recent study of non-selected and consecutive patients with SS, almost all of the patients presented with expiratory airflow indices compatible with mild small airways obstruction, and this was correlated with a reduced alveolo-arterial oxygen difference. Chest radiography revealed a pattern compatible with minimal to mild interstitial disease. Computerized chest tomography in patients with major radiographic findings showed that the main lesion consisted of thickened bronchial walls, while the mild interstitial pattern was located around bronchi. Transbronchial biopsy performed in patients with follicular bronchiolitis on tomography showed that the lymphocytic infiltrates were around bronchi adjacent to the bronchial epithelial cells, while in some patients an interstitial spillover co-existed. These findings suggest that initially the round cell infiltrates start in the large airways around exocrine glands and subsequently, as the disease progresses, extend to the peripheral airways. The initial lesion leads to destruction of the large airways exocrine glands which clinically presents as ‘xerotrachea’, while in the later stages in a small number of patients spilling of lymphocytes from peribronchial areas to the interstitium leads to the subclinical interstitial disease [5].

Liver involvement in SS patients is rare, but the co-existence of liver disease and the presence of circulating antimitochondrial antibodies in patients' sera points to the possibility that liver pathology might be autoimmune and similar to that of primary biliary cirrhosis. In fact, the main histopathological finding in the liver biopsies of patients with SS and antibodies to mitochondria and/or elevated liver enzymes is a pericholangial lymphocytic infiltration similar to that found in stage I of primary biliary cirrhosis [6].

The aforementioned observations on kidney, lung and liver in SS patients strongly suggest that the extraglandular autoimmune insult is due to the attraction of lymphocytes by epithelial cells from the renal tubules, the bronchi and the cholangial ducts. In fact, all these cells have been shown to share a common antigen: carbonic anhydrase II [7]. Cellular and humoral responses against this molecule were found in patients with SS and chronic pancreatitis [8, 9]. Furthermore, autoimmune sialoadenitis was induced in mice by intradermal immunization with human carbonic anhydrase II [10]. These observations are of interest, but further work is needed to evaluate the relationship of this antigen with the autoantigens to which an autoimmune response is known in SS patients.

SS extends from benign lymphoproliferation which, as we have described, concerns glandular and parenchymal organs, to malignant lymphoproliferation which affects B lymphocytes. Recent work has revealed that these cells arise mainly from mucosa-associated lymphoid tissue [11]. This observation further strengthens the hypothesis that chronic activation of lymphocytes by mucosal epithelial cells leads to lymphoid malignancy.

Immunopathological studies suggest that all immunocytes occupying the minor salivary glands of SS patients are activated and most of them are T cells bearing the phenotype of memory cells [12]. B cells constitute the one fourth of the invading lymphocytes, while monocytes-macrophages are very poorly represented in the lesion; which cell then plays the antigen-presenting cell role in the lesion of the exocrine glands in SS patients? In fact, ductal and acinar epithelial cells of the labial salivary glands overexpress class II HLA molecules. Recent preliminary observations revealed that these cells also inappropriately express the nuclear antigen La/SSB on their surface [13]. Furthermore, studies of imprints of conjunctival cells with monoclonal antibodies demonstrated that these cells also inappropriately express class II molecules and La/SSB autoantigen in their membranes [12]. Studies of the proto-oncogene mRNA expression of the minor salivary glands of SS patients showed that c-myc was only expressed from the epithelial glandular cells and not from the activated lymphocytes.

Evaluation of cytokines by in situ hybridization in labial salivary glands revealed that the RNA message of proinflammatory cytokines (IL-1 and IL-6) comes not only from the infiltrating lymphocytes, but also from the epithelial cells [14]. Finally, insertion of proviral retroviral sequences in the epithelial cells of primary SS patients was found. Thus, the epithelial cells in patients with SS present altered characteristics and these characteristics are selectively expressed by these cells. The significance of the epithelial cells is further attested to in the autoimmune sialoadenitis which develops in tax transgenic mice. This model reveals that the tax gene is epitheliotropic; after insertion of the gene, the epithelia enlarge and subsequently lymphocytes are attracted which produce the Sjögren’s-like picture in these animals [15]. On the basis of the summarized clinical and immunopathological studies, the term used for Sjögren's syndrome should reflect both the pathogenetic process and the major cell which probably initiates it. The term 'autoimmune epithelitis' precisely expresses both.

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