SP0017 LESSONS LEARNED FROM LYME DISEASE: ONLY PERSISTENT BACTERIA OR AUTOIMMUNITY

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10.1136/annrheumdis-2001.81

Antibiotic treatment-resistant Lyme arthritis is a chronic inflammatory joint disease, associated with a limited number of MHC alleles, including HLA DRb1*0401. A marked antibody and T cell response to outer surface protein A (OspA) of *Borrelia burgdorferi*, the causative agent of Lyme disease, is often seen during prolonged episodes of arthritis. An autoimmune mechanism has been implicated due to the lack of the *Borrelia burgdorferi* antigen in the target organ and apparent cross-reaction at the T cell level between the bacterial OspA and a self-protein, LFA-1aL. To directly test this hypothesis, we isolated and cloned T cells specific for the immunodominant epitope of OspA, OspA165–174, from five DRb1*0401+ patients, using OspA-class II tetramers. These clones were tested for their ability to respond to peptide containing the human homologue of OspA165–174, LFA-1aL332–340, as determined by proliferation and cytokine production. All of the T cell lines responded to minute concentrations of OspA165–174 by proliferation and secretion of IFN- γ and IL-13. In contrast, larger concentrations of LFA-1aL326–345 were required for stimulation, and only 10% of the clones proliferated vigorously. With this stimulation, approximately half of the cell lines secreted IL-13 but produced no IFN- γ . LFA-1aL-tetramers required a 2.5- to 25-fold higher concentration to stain dual reactive clones than OspA tetramer. Our analysis at the clonal level demonstrate that LFA-1aL326–345 behaves as an analogue for the OspA peptide, but a greater concentration of the LFA-1 peptide is required and an altered cytokine response is elicited. Thus, a single bacterial-specific T cell may respond to a cross-reactive human protein, LFA-1aL, indicating a role for molecular mimicry, and thus, autoimmunity, in treatment resistant Lyme arthritis.

Review session N° 2 – Thursday 14 June, 10.00-11.45/South Hall

SP0019 HOW THE CLINICIAN CAN USE THE COCHRANE LIBRARY

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10.1136/annrheumdis-2001.82

Objectives To demonstrate online searching of The Cochrane Library for clinicians and illustrate how The Cochrane Library can be used in practice.

The Cochrane Library is the single best source of updated systematic reviews of health care interventions. There are now 37 published Cochrane reviews relating to Musculoskeletal Diseases. The abstracts can be accessed for free on the internet and lay summaries written in consultation with consumers are also available on the internet (www.arthritis.ca). The first part of this workshop will demonstrate how to use text words to search for consumer and scientific abstracts available for free on the internet. In addition, the web interface for the full Cochrane Library will be shown.

The second purpose of this workshop is to provide examples of how to use Cochrane reviews in clinical practice. For example, the University of Ottawa has developed hospital-wide access to the Cochrane Library, and these can be accessed by clinicians from any computer with an internet connexion. The pooled estimate of efficacy and side effects is the best estimate from all published randomised controlled trials. The direction and statistical significance of this estimate can be easily interpreted. The second part of the workshop will illustrate the interpretation of the magnitude and direction of the pooled estimate. In addition, the workshop will illustrate how these estimates can be used as part of evidence based practice.

SP0022 LOW BACK PAIN AND IMAGING

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10.1136/annrheumdis-2001.83

Low-back pain is a very common but benign and in general self-limiting disease indicating that only a small proportion of the patients will require sophisticated imaging studies. Recent studies have highlighted that a simple relation of structural abnormalities to low-back pain is impossible because similar alterations can be found in symptomatic as well as in asymptomatic individuals. These findings question our current criteria for the diagnosis of low-back pain disorders with regard to their discriminative power in differentiating diseased and non-diseased individuals. Structural abnormalities demonstrated by imaging studies should therefore only be interpreted in the light of the clinical findings. This review has shown that only a few studies contribute to our understanding of the clinical efficacy of imaging studies in the evaluation of low-back pain disorders. There is an absolute need for comprehensive well conducted studies on the impact of specific image modalities on diagnosis and treatment of lumbar spinal disease.

Stem cell treatment of autoimmune disease – Thursday 14 June, 10.00-11.45/Meeting Hall I

SP0023 HAEMOPOIETIC STEM CELL TRANSPLANTATION FOR SEVERE AUTOIMMUNE DISEASE

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10.1136/annrheumdis-2001.84

Reporting on behalf of the EULAR and EBMT Autoimmune Disease Stem Cell Project. High dose immunoablative therapy with autologous haemopoietic stem cell transplantation (HSCT) has been used to treat selected patients with severe autoimmune disease (AD) in over 400 cases world wide. 334 transplants (327 autologous) are registered in the combined EULAR/EBMT data base, target ADs and numbers being: multiple sclerosis-102, SSc-70, RA-41, JIA-35, SLE-25, dermatomyositis-6, Behcets-3, vasculitis 6 and others. Patients were from 78 transplant centres in 22 countries with a median follow up of 16(1–81) months. Four basic conditioning regimens were used in phase I and II pilot studies, with an unmanipulated graft product in 85 cases. A

transplant related mortality (TRM) of 9% overall was observed, with inter disease differences (12.5% in SSc and only one TRM in RA). Around 2/3 of patients responded with improvement or stabilisation. In SSc, 69% achieved a 25% or greater improvement in skin score, and in secondary progressive MS, 78% a 3 year progression free survival. Relapse was more common with RA and JIA, mostly being a synovitis easy to control with agents which were ineffective pre transplant. Randomised, controlled prospective trials are underway in SSc (ASTIS Trial: HSCT versus monthly pulse cyclophosphamide)), and planned for RA and MS. Trials in JIA are being discussed and further phase I/II data are required for SLE and vasculitis. These will be presented, together with immune reconstitution data, sometimes predicting relapse, and new developments in HSCT, especially non myeloablative "mini" allograft techniques. This may be applicable to full sibling matched selected patients.

REFERENCE

- 1 Biggs M, Passweg J, Furst D, *et al.* Phase I trial of autologous stem cell transplantation in systemic sclerosis: procedure related mortality and impact on skin disease. *Ann Rheum Dis.* 2001, in press

Ankylosing Spondylitis – Thursday 14 June, 14.00-15.30/Congress Hall

SP0031 GENETIC STUDIES IN FAMILIAL ANKYLOSING SPONDYLITIS: THE NORTH AMERICAN SPONDYLITIS CONSORTIUM EXPERIENCE

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10.1136/annrheumdis-2001.85

Recent genome-wide screens of English families multiplex for ankylosing spondylitis (AS) have suggested genes additional to HLA-B27 to be involved in disease susceptibility, particularly on chromosome 2q and 16q. Another recent study has suggested an association of AS with an allele of the IL-1 receptor antagonist gene (IL-1RA) on chromosome 2q. In order to confirm these findings in an independent group of families, 92 sib pairs concordant for AS by modified New York criteria from 74 North American families from the were examined with eight polymorphic microsatellite markers within the major histocompatibility complex (MHC) and HLA-DRB1, DQA1, DQB1 alleles; four markers on chromosome 2q and three on 16q near the regions previously implicated. Results for the MHC markers were as follows:

Abstract SP0031 Table 1

Marker	Map position (cM) ^a	NPL Statistic	p-value
D6S461	40.14	2.6	0.005

D6S276	44.41	3.09	0.001
D6S105	44.41	2.17	0.015
D6S273	44.96	3.17	0.001
D6S1014	45.5	1.56	0.023
D6S1666	45.5	3.03	0.001
D6S1583	47.71	5.38	8×10^{-6}
DRB1	49.87	3.17	9×10^{-7}
D6S1019	53.81	2.09	0.018

No evidence of linkage was found for the markers on chromosome 2q and 16q. In addition, analysis of 29 single nucleotide polymorphisms (SNP's) from the IL-1 RA gene in 30 AS patients and 48 controls found no evidence of disease association. These data strongly suggest the presence of a second MHC gene operative in predisposition to AS at or near the HLA-DRB1 locus. Additional families are currently being studied and fine mapping studies in progress to confirm and extend these findings.

SP0033 UPDATE ON PSORIASIS AS IT RELATES TO SPONDYLOARTHROPATHIES

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10.1136/annrheumdis-2001.86

Psoriasis is a common disease (affects ~ 2% whites); and up to 10% of these patients have associated inflammatory arthritis [psoriatic arthritis (PsA), including spondyloarthropathy (SpA)], which may, in up to 15% of patients, precede the onset or diagnosis of psoriasis. There are no internationally agreed criteria for the diagnosis of (PsA); it has been broadly defined by Moll and Wright as an "inflammatory arthritis associated with psoriasis, which is usually negative for rheumatoid factor". More precise criteria and a large case-control study comparing patients with PsA with controls without arthritis (despite having had psoriasis for >10 years), properly matched for age, race, gender, geographical area, and for the subtypes of psoriasis/arthritis are needed. It would be advisable to have another control group with inflammatory arthritis without psoriasis.

The sibling recurrence risk (lambda s value) is estimated to be roughly 4 for psoriasis. Self-reported positive family histories for psoriasis among PsA patients have been observed in up to 40% and for PsA in 10%, but the familial aggregation does not follow a simple Mendelian trait. Psoriasis and PsA have not only clinical but also genetic heterogeneity, and multiple susceptibility alleles at different loci may produce the same phenotype, resulting in clinical misclassification of the disease type. There are, as yet unknown, genetic and environmental interactions, and also different combinations of susceptibility genes may predispose to different patterns of psoriasis and PsA (variable disease expression), and not everyone with such genes will develop the disease (variable penetrance). Psoriasis is associated with HLA allele Cw*0602, MICA allele 5.1, corneodesmosin allele 5 (CD*5), OTF3 beta, and HCR (pg8); they are all located on chromosome at the 6p21 region. Associations with chromosomes 17q25, 4q32-35 and 1q (S100A7) have also been reported. Similar studies of affected sib-pair families with PsA are also needed.

Activated T lymphocytes and dendritic cells mediate the disease, but the antigen (s) responsible are not known. Although