(EULAR) Social Leagues + International Organisation of Youth with Rheumatism (IOYR).

SP0047 ASSESSING THE NEEDS OF THE INDIVIDUAL

N Price. Locomotor Directorate, North Staffordshire Hospitals NHS Trust, Stoke on Trent, UK

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The shift away from service driven to needs lead service delivery will be explored.

The needs of the individual during the phases of disease progress will compare perceived versus actual. Contribution of the multidisciplinary team at all stages will be highlighted.

The move to patient/individual self-efficacy and the effect on relationships with health professionals provide an arena for potential conflict. The health professionals perception of the individuals needs are often not compatible with the actual needs of the individual.

The results of an in depth interview, with a patient, will explore their needs and whether they have been met. (An interview audited tool will be used).

Financial constraints, shortage of health professionals, the political agenda, compliance of the individual and "patient power" will highlight the areas of unmet needs.

The needs of carers and service providers are often neglected at the expense of the "individual". The conflict of the carer and individual will also be addressed.

Does the individual know best?

REFERENCES

- 1 Arthritis Impact Measurement Scales (AIMS)
- 2 Health Assessment Questionnaire (HAQ)
- 3 SF – 36 Health Survey
- 4 The NHS and Community Care Act 1990

SP0049 RAISING PRIORITY FOR THE NEEDS OF THE INDIVIDUAL

AD Woolf. Department of Rheumatology, Royal Cornwall Hospital, Truro, UK

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Musculoskeletal conditions (MSC) have an enormous and growing impact recognised by WHO Europe in "Health 21" yet national health care priorities in most European countries do not include them. The aim of the Bone and Joint Decade is to redress this imbalance by advocacy supported by evidence. To improve the outcome for the individual greater priority has to be given to the provision of existing proven interventions that meet the needs and wishes of the person with a MSC, and better interventions need to be developed through research. Education of public, people with MSC, health care providers, politicians and health professionals is fundamental to changing the negative perception of what can be achieved and in improving standards of care. Any campaign to meet these objectives needs to be supported by relevant data of the impact of MSC and evidence based solutions to reduce this. Key messages that highlight the issues, priorities and these solutions need to be developed for the decision-makers and any other relevant audiences. These messages should be conveyed by the powerful alliance of those with MSC and those who provide their care. The potent image of advocates must be used to attract media attention that is central to the strength of any campaign. Finally targets must be set

to measure the success of any campaign. The Bone and Joint Decade is identifying the burden of MSC with the WHO and developing evidence based strategies for prevention with the support of the EU. National and local campaigns are necessary that use this evidence to achieve change and fulfil the aim of the Decade, which is to improve the health-related quality of life for those with musculoskeletal conditions.

T-Cell activation and MHC – Thursday 14 June, 16.00-17.30/South Hall

SP0050 THE ROLE OF HLA IN RHEUMATOID ARTHRITIS: INDUCTION OF AGGRESSION OR FAILURE TO PROTECT?

¹R De Vries, ¹E Zanelli, ²F Breedveld. ¹Immunohematology and Blood Transfusion, Leiden, The Netherlands; ²Rheumatology, Leiden University Medical Center, Leiden, The Netherlands

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Genetic factors contribute both to the development and the course of Rheumatoid Arthritis (RA). The contribution of inherited genetic variability has been estimated 60%. Moreover, stochastic processes during the development of the T and B lymphocytes repertoire or so-called somatic genetic diversity may be responsible for an as yet unknown fraction of the remaining 40% of the factors contributing to the pathogenesis of RA.

Thus far, the only known inherited genetic factors are encoded by the HLA system. These factors contribute about 40% of the inherited genetic variability and also contribute to the somatic genetic diversity. The main contribution of the HLA system is conferred by the HLA class II region and HLA-DR genes are certainly involved but HLA-DQ genes also may have a contribution. Perhaps most importantly: certain HLA-DR genes may provide dominant protection. HLA genes not only contribute to the development but also the course and severity of RA. There is also evidence for dominant protection against the development of erosions. We observed that this effect may be relatively short-lasting and overruled by a very early start of treatment with DMARDS (Yard *et al.*, submitted for publication). These observations suggest that pharmacogenomics may offer possibilities for a tailor-made optimal treatment for individual RA patients. The standard hypothesis for an association of an HLA class II allele with an auto-immune disease is that auto-reactive T cells recognise certain self-epitopes that are exclusively or preferentially presented by that particular HLA class II allele. The Shared Epitope (SE) hypothesis (Gregersen *et al.* 1987) is a paradigm of this. More than 20 years of intensive research along these lines have however yielded little evidence for this concept. Therefore, we have developed an alternative hypothesis. In this hypothesis auto-reactive T cells do not play a role in the initiation but in the regulation of the disease process (Zanelli *et al.*, Rheumatology, in press). Our model is an extension of the one proposed by Thomas and Lipsky (Immunology Today 1996; 17: 559–560). It starts with activation of synoviocytes by a trauma or an infection. Usually this results in a local inflammation that resolves in a few days, but in the presence of one or more (yet to be identified) genetic factors (not HLA class II) an aberrant activation of synoviocytes results in a chronic inflammation. As proposed by Thomas and Lipsky chemo-attraction of dendritic

cells (DC) and/or the transformation of synoviocytes to follicular DC may play a key role in this process. In our model a so-called amplifier gene stimulates this chemo-attraction of and/or the differentiation to DC's. The DC's present self-peptides not to disease-inducing but to regulatory auto-reactive T cells that have been recruited also to the inflamed synovium. These regulatory T cells recognise self-peptides such as DERAA peptides from the HV III region of certain HLA-DR alleles presented by DR or DQ molecules. This DC-regulatory T cell interaction is an essential checkpoint for the control of the inflammation and is controlled by HLA class II genes. In the absence of protective HLA alleles and therefore self-reactive regulatory T cells this checkpoint fails and this results in a local loss of tolerance and a (severe) chronic arthritis (RA).

This model has several important implications for the immunotherapy of RA:

- We may stop the search for a unique target antigen for disease-inducing T cells
- Immunotherapy that is exclusively targeted at T cells may have an adverse effect
- Immunotherapy strategies for RA should either be targeted at the re-establishment of a normal phenotype in synoviocytes or on restoring a functional immunoregulatory loop.

SP0051 HSP REACTIVE T CELLS AS INFLAMMATION REGULATORS

¹W Van Eden, ¹L Paul, ¹U Wendling, ¹P Van Kooten, ¹J Bos-de Ruijter, ¹R Van der Zee, ²B Prakken. ¹Department of Infectious Diseases and Immunology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands; ²Department of Pediatric Immunology, University Hospital for Children and Youth, Utrecht, The Netherlands

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Immunisation with heat shock proteins has protective effects in models of induced arthritis. Analysis has shown a reduced synovial inflammation in such protected animals. Adoptive transfer and immunisation with selected T cell epitopes (synthetic peptides) have indicated the protection to be mediated by T cells directed to conserved hsp epitopes. This was shown first for mycobacterial hsp60¹ and later for mycobacterial hsp70.^{2,3}

Fine specificity analysis showed that such T cells were cross-reactive with the homologous self hsp. Therefore protection by microbial hsp reactive T cells can be by cross-recognition of self hsp overexpressed in the inflamed tissue. Preimmunisation with hsp leads to a relative expansion of such self hsp cross-responsive T cells. The regulatory nature of such T cells may originate from mucosal tolerance maintained by commensal flora derived hsp or from partial activation through recognition of self hsp as a partial agonist (Altered Peptide Ligand) or in the absence of proper costimulation. Recently, we reported the selective upregulation of B7.2 on microbial hsp60 specific T cells in response to self hsp60.⁴ Through a preferred interaction with CTLA-4 on proinflammatory T cells this may constitute an effector mechanism of regulation. Also, regulatory T cells produced IL10.

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- 2 Tanaka S, Kimura Y, Mitani A, Yamamoto G, Nishimura H, Spallek R, Singh M, Noguchi T, Yoshikai Y. Activation of T cells recognizing an epitope of heat-shock protein 70 can protect against rat adjuvant arthritis. *J Immunol.* 1999;**163**:5560–65

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- 4 Paul AG, van Der Zee R, Taams LS, van Eden W. A self-hsp60 peptide acts as a partial agonist inducing expression of B7-2 on mycobacterial hsp60-specific T cells: a possible mechanism for inhibitory T cell regulation of adjuvant arthritis? *Int Immunol.* 2000;**12**:1041–50

SP0052 DETECTION OF ANTIGEN-SPECIFIC T CELLS

P Bowness. MRC Human Immunology Group, IMM, John Radcliffe Hospital, Oxford, UK

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Antigen-specific T cells are thought to drive the inflammatory response in a number of rheumatic diseases including RA and the spondyloarthropathies. T cells recognise specific combinations of antigenic peptides bound to of HLA molecules, and subsequently proliferate and perform effector functions including cytokine secretion. Techniques have been developed to detect these T cells (usually *ex vivo* or *in vitro*), based upon their antigenic specificity, their function, and their clonality. Some techniques combine these attributes. Recently fluorescent-labelled multimers (usually tetramers) of synthetic HLA/peptide combinations have been used to stain T cells of defined antigen specificity. The use of HLA /peptide tetramers has greatly increased our understanding of the role of T cells in viral infections and given some insight into rheumatic diseases. Other techniques have been developed that detect cytokines produced in response to specific antigens (i.e. detecting function), or that detect populations of T cells carrying the same or related T cell receptors. Our ability to detect antigen-specific T cells has important implications for our understanding of disease pathogenesis, and for monitoring disease progress. These methodologies also offer therapeutic potential.

Polymyalgia rheumatica – Thursday 14 June, 16.00-17.30/Small Hall

SP0053 EUROPEAN DIAGNOSTIC CRITERIA FOR POLYMYALGIA RHEUMATICA

H Bird. Clinical Pharmacology Unit, University of Leeds, Leeds, UK

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A variety of separate diagnostic criteria sets exist for polymyalgia rheumatica. These include those proposed in 1979,¹ 1981² and 1989.³ All differ slightly, the optimum criteria still having to be determined.

In 1997, the Polymyalgia Rheumatica Special Interest Group was established under the auspices of the EULAR Standing Committee for International Clinical Studies. Twenty participating centres throughout Europe between them promised to make available 200 new patients each year for the comparison of criteria sets. In parallel patients, where suitable, were recruited to a study to evaluate, for the first time, response criteria for this condition. It was hoped that both studies would lead to more accurate assessment of the several drugs then being claimed to be steroid sparing agents.