will be briefly illustrated in the lecture. The following concepts will be clarified as well: characteristics of the origin of pain (cause attribution), characteristic of the controlling of pain (locus of control), individual illness experiences and the cognitive and emotional reactions to pain.

REFERENCES

- 1 Saner H. Die Anarchie der Stille. Lenos, 1990
- 2 Melzack R, Wall PD. Pain mechanisms: a new theory. *Science* 1965

Awareness of people with rheumatism/ arthritis – Friday 15 June, 14.00-15.30/Club A-B-C-D

SP0159 PERSONAL IMPORTANCE OF A GOOD RELATIONSHIP TO A THERAPIST FROM A PATIENT'S POINT OF VIEW

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For a patient, it is very important, how the relationship to a therapist looks and feels like. First of all, patient and professional have a business-relationship: the professional offers a kind of 'service' and gets money for it, and they have an agreement what is included and so on. So the customer (patient) is the one who can 'buy or refuse'; the professional has to respect the wishes. They have to work out conditions, that are ok for all parties. They have to define expectations and roles; possibilities and limits of it.

Of course the relationship also has more components:

Arthritis makes you feel small, dependent and insecure. So one effect of the relationship should be, that the patient feels more self-confident, to get supported in its own personality.

Therapists aren't really experts for the illness; for the 'technical part', yes; but not for the other components. Every patient is the expert of his own illness; nobody can feel, how it feels like, and whether it feels better or worse; nobody else can finally say, which therapy, remedy or diet really helps you the best. Therapists can help us to have an overview of the possibilities we have and they can tell us what experience (positive and negative-ones) have been made with them; but proof and decide we have ourselves. The most important thing is, that a therapist should show me a way to an easier way of life, that is realistic and not too complicated.

That also means, that therapists should inform us in an objective way, to really help us decide, which way we choose.

And: if we decide in another way, the professional suggested: he should accept it fully and not judge or treat the patient worse than before.

The example of my personal relationship to 'my' therapists will be given at the meeting.

Communication and partnership – Friday 15 June, 16.00-17.30/Club A-B-C-D

SP0178 SURGERY IN THE PATIENT WITH RHEUMATOID ARTHRITIS

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The person with Rheumatoid Arthritis has a higher than average chance of undergoing surgery at some stage in the disease process. Surgery is not without risks and a benefit/risk assessment is essential in all patients for selection.

This presentation will address care of the patient with RA before and after surgery from a multi-disciplinary view point. General considerations prior to surgery will be mentioned. Potential problems specific to the person with RA include care of the cervical spine during intubation, infection both due to low haemoglobin and drug therapy, care of the skin and other joints whilst recumbent and management of drug therapy. These will be analysed along with possible management protocols and strategies.

Pre and post surgical intervention physiotherapy is a luxury for some patients, for those with RA it is an essential component of the continued care of this group.

Intl. scientific forum for young rheumatologists – Thursday 14 June, 10.30-12.30/Meeting Hall V

OP0139 REGULATION OF CD154 IN SYSTEMIC LUPUS ERYTHEMATOSUS

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CD40-ligand (CD154) is expressed on the surface of activated CD4 T cells and as a soluble cytokine. CD154 is a critical regulator of the immune response via its interaction with CD40 on various cell types, and, therefore, it is not surprising that its expression is tightly controlled. Current reports have described abnormal expression (increased and prolonged levels) of CD154 in adult patients with systemic lupus erythematosus (SLE), similar to observations in lupus-prone mice. We have recently confirmed these findings in paediatric SLE patients. Normally, like several tumour necrosis factor cytokine family members, CD154 expression is primarily controlled at the level of gene transcription and mRNA stability. Moreover, regulatory defects in intracellular signalling pathways that may effect cytokine mRNA levels have recently been described in CD4 T cells from patients with SLE. Using real-time quantitative PCR we have found that CD154 mRNA levels are increased in SLE patients versus matched controls. Preliminary results from nuclear run-on assays also suggest that increased CD154 transcription plays a role in CD154 hyper-expression in SLE. The CD154 *cis*-element (s) responsible for this increase in transcription is unknown. Although we had previously identified a relatively weak proximal 5' flank transcriptional promoter, very little is known about

the *cis*- and *trans*-regulatory elements that contribute to CD154 gene expression. We have recently identified a NFκB-responsive transcriptional enhancer element located within and just downstream of the 3' CD154 untranslated region. Moreover, using nuclei from primary human CD4 T cells, we have identified a novel DNase I hypersensitive site located approximately 1 kb upstream of the proximal promoter. This novel site is flanked by several potential T cell transcription factor binding sites and, thus, may function as a transcriptional enhancer. We are currently comparing the transcriptional activities of these various CD154 *cis*-regulatory elements in T cells from SLE patients and controls in order to identify region (s) that contribute to enhanced CD154 expression in SLE. Ultimately, we hope to be able to target the *cis*- or *trans*-regulatory elements that lead to the abnormal expression of CD154 in SLE and various other autoimmune disorders.

OP0140 CTLA4Ig SUBSTANTIALLY AUGMENTS THE BENEFITS OF CYCLOPHOSPHAMIDE FOR LUPUS NEPHRITIS

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We have recently shown that combining CTLA4Ig with cyclophosphamide (CTX) results in a marked reversal of active lupus nephritis in NZB/NZW mice. To determine whether similar benefit might be obtained with less CTX, we have compared the effect of a single dose of CTX combined with CTLA4Ig with that of continuous CTX and CTLA4Ig administration. Female mice were treated with either continuous CTX (50 mg/kg every 10 days × 7 weeks), continuous CTLA4Ig (50 mg ip 3×/week × 8 weeks), a single ip injection of CTX (50 mg/kg) plus brief CTLA4Ig (50 mg/kg ip 3×/week × 2 weeks), a single dose of cyclophosphamide (50 mg/kg ip) plus continuous CTLA4Ig, continuous CTX + CTLA4Ig, or saline. After 8 weeks, none of the treated mice had died, while 36% of the saline group had significant proteinuria and 18% had died. Mice that had received either continuous CTX, or a combination of prolonged CTLA4Ig with either prolonged or brief CTX had preserved kidney function (>50% vs <10%). However, survival in the CTX alone group was reduced compared with either the continuous CTX+CTLA4Ig or the single dose CTX+continuous CTLA4Ig groups (73% vs 100%). In a subsequent experiment, NZB/NZW mice with either mild or advanced renal disease were treated with low dose CTX (5 mg/kg) or high dose CTX (50 mg/kg) in combination with CTLA4Ig. Although mice with advanced renal disease that received either low dose or high dose CTX plus CTLA4Ig had a reduction in proteinuria compared to controls, the improvement was significantly greater among mice receiving the higher dose of CTX. However, among mice with mild disease, the delay in progression of proteinuria was equivalent in mice that received either low dose or high dose CTX in combination with CTLA4Ig. These results indicate that the benefits of CTX in murine lupus nephritis are amplified or sustained by CTLA4Ig, and that the clinical benefits of combining these agents might be realised while at the same time reducing exposure to CTX.

REFERENCE

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OP0141 ACTIVATED FIBROBLAST-LIKE CELLS IN ASEPTIC PROSTHESIS LOOSENING – SIMILAR OR DIFFERENT FROM RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS?

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Aseptic prosthesis loosening (APL) is an active process that is linked to the development of a synovial-like interface membrane (SLIM) at the bone-implant interface. Growing evidence suggests that the synovial membrane in rheumatoid arthritis (RA) and this SLIM share certain similarities. However, the mechanisms of SLIM formation as well as the cellular and molecular events in the activation of fibroblast-like cells remain elusive. Recently, we have established a novel animal model of SLIM formation that is based on the implantation of joint arthroplasties into intracranially self-stimulated (ICSS) Wistar rats. Data from this animal model as well as from human SLIM samples suggest that there is a subset of activated fibroblast-like cells present also in the SLIM of APL. These prosthesis-loosening fibroblasts (PLF) not only show a similar growth pattern as RA-synovial fibroblasts (RA-SF) but also exhibit features of cellular activation found in RA. Among them, the up regulation of transcription factors and the resistance against Fas-induced apoptosis are most prominent. Although PLF express a number of matrix degrading enzymes and secrete soluble factors that stimulate neighbouring cells, their role in the degradation of bone has been restricted to that of supporting bystanders. Based on most recent results, we report that PLF from the SLIM around loose joint prostheses display a highly aggressive, RA-like phenotype when implanted into SCID mice, are capable of resorbing bone *in vivo* without the help of osteoclasts and release large amounts of acidic components. As demonstrated by RT-PCR, *in situ* hybridization and immuno electron microscopy, these cells express a specific proton pump (v-ATPase) on their cell surface that may account for their ability to decalcify bone. By quantitative real time PCR, an increased expression of this v-ATPase is found in prosthesis loosening fibroblasts and rheumatoid synovial fibroblasts as compared to normal or osteoarthritic cells. Inhibition of the v-ATPase with specific inhibitors results in a decrease of pericellular acidification. Investigating the exon structure of its catalytic β1 subunit, we were able to describe a hitherto unknown v-ATPase splice variant that appears to be regulated differently in prosthesis loosening fibroblasts as compared to rheumatoid and osteoarthritic cells. The expression of specific v-ATPases on their cell membranes including novel splice variants may provide the means by which these cells are able to decalcify bone prior to its degradation. Further studies will have to clarify whether the capability of PLF to resorb bone constitutes a rather unique feature of these cells or is linked also to cellular activation in RA.