336. IN VIVO EVIDENCE FOR APOPTOSIS IN THE BONE MARROW IN SLE
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Background: Impaired clearance of apoptotic cells has been implicated in the pathogenesis of SLE. Apoptotic cells are likely to be a key source of autoantigens since they express many of the nuclear autoantigens relevant to SLE in surface blebs and apoptotic bodies. The clearance of apoptotic cells is usually a very rapid process such that few cells are usually seen in the extracellular environment in vivo. We have analysed all bone marrow (BM) trephines taken from patients in our unit with SLE and severe haematological involvement, with particular reference to evidence of apoptosis in vivo in the marrow.

Methods: All BM aspirates and trephines were analysed from patients with SLE and peripheral cytopenias from 1993-2003. Clinical data was obtained for each patient, including serology and peripheral blood counts at the time of BM examination.

Results: Eleven patients fulfilling ACR criteria were studied (10 F, 1 M; age range 23-50). Haematological disease developed from 1-10 years (median 4) after SLE was diagnosed. Neutropenia was present in 7/11 patients, CNS disease in 3. Three patients had received azathiprine (AZA) prior to BM examination, but none had a reticulocytosis. Anti-nRNP was positive in 7, anti-Ro in 5, anti-C1q in 4 and anti-dsDNA in 9/11. On BM trephine, hypocellularity was observed in all cases. Megakaryocyte clusters were present in 5 with a plasmacytosis in 2. Megakaryocytes were present in 6 and increased reticulin in 5/11. Apoptotic bodies, identified by their characteristic morphology, were present in 7/11 BM. Four of these patients were receiving AZA. Apoptotic bodies were most abundant in a 42 yr old female with SLE previously well-controlled on prednisolone and methyl-prednisolone, CYC and recombinant human G-CSF.

Conclusions: The most frequent BM findings of hypocellularity and plasma-cytosis were consistent with two previous published series. The most striking abnormality in our series however was the presence of multiple apoptotic bodies in several patients, not previously reported. The demonstration of apoptotic bodies in vivo in patients with SLE is unusual and supports the notion that the marrow may be a target organ in the disease. Further, its abundance suggests that normal clearance mechanisms are defective and/or overwhelmed in such cases.

337. THE Y-LINKED AUTOIMMUNE ACCELERATOR (YAA) GENE IS SUFFICIENT TO BREAK IMMUNOLOGICAL TOLERANCE
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Background: Systemic Lupus Erythematosus (SLE) shows a greater sex bias than other autoimmune diseases such that 9 out of 10 patients are female. A sex bias is also observed in some murine models of SLE. In (NZBxW/F) mice, the bias is towards female disease, whereas in BXSB mice, early onset of disease is observed in the males. The Y-chromosome of BXSB has been demonstrated to contain an autoimmune accelerating (Yaa) gene, however the identity of this gene remains unclear.

Methods: We have generated Y-chromosome consomic mice on the non-autoimmune prone background strain, C57BL/10 (B10). A detailed analysis of male consomic B10.Yaa mice aged 4 to 12 months was performed including kidney histology, autoantibody profile, splenomegaly and FACS analysis of peripheral blood and splenocytes. Aged matched B10 male mice were used as controls.

Results: Antibacterial antibodies were significantly elevated in B10.Yaa from 4 months of age (p<0.0001). Antinuclear antibodies (ANA) were found to be significantly elevated from 8 months of age (p=0.013), at which time point there was no significant splenomegaly at autopsy (p=0.011). However, we found no evidence of anti-ds or anti-ssDNA antibody production, and kidney histology remained entirely unremarkable, even to 18 months of age. Previous reports had indicated that there was no Yaa effect in non-autoimmune prone strains, but this was made on 6-8 week old mice. In the 18 month old mice, there was a significant increase in glomerulonephritis scores and anti-dsDNA titre only. We have therefore re-examined C57BL/6 (B6) Y-consonic mice, and demonstrated that peripheral tolerance has also broken down in these mice. B6.Yaa mice also develop ANA and antichromatin antibodies, but do not progress to glomerulonephritis.

Conclusions: Yaa, far from being a mere accelerator of autoimmunity, is capable of causing a breakdown in tolerance in both B10 and B6 mice. This effect does not require a background which is already pre-disposed to the development of autoimmunity. The consomic mouse strain presented here will be an invaluable tool to aid in the identification and functional analysis of the Y-chromosome gene. The identity of Yaa will direct the interrogation of human Y-chromosome genes, and their X-chromosome homologues. These X-homologues may direct the sex bias observed in human SLE.

338. COULD B CELLS HAVE THE POTENTIAL TO CONTROL LUPUS-LIKE SYNDROME IN MRL/lpr?
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Background: The severe autoimmune syndrome of MRL/lpr mice closely resembles human systemic lupus erythematosus. The disease is characterised by autoantibody production, hypergammaglobulinemia and progressive lymphadenopathy. It has been previously shown that B cells producing IL-10 play a key role in protecting against autoimmunity. As IL-10 deficient mice develop an exacerbated disease we speculate that B cells producing IL-10 might also play an important regulatory role in this animal model.

Methods: To ascertain the importance of B cells in the attenuation of autoimmunity in MRL/lpr mice, B cells from 9 week old MRL/lpr mice were purified with anti-CD43 magnetic beads and passed through a separation column (negative selection). B cells were incubated for 48 hours with antibodies against CD40 and IgM or medium alone, and transferred to 9 week old MRL/lpr mice. Urine proteinuria was assessed semiquantitatively using albumin reagent strips. Serum anti-dsDNA IgG, IgG2a and IgG1 was measured by ELISA. To assess cytokine production, cells were activated with PMA, ionomycin and Brefeldin A in 5 with saponin washed, fixed, permeablised and stained with APC-anti IFNγ, IL10 or TNFα.

Results: B cells activated with antibodies against CD40 and IgM for 48h produced more IL10 and less IFNγ compared to cells incubated with medium. Transfer of B cells incubated with antibodies against CD40 and IgM into 9 week old MRL/lpr mice decreased proteinuria and anti-dsDNA antibody titre, enhanced their survival, and decreased the IFNγ levels by comparison with controls.

Conclusions: These data have showed that B cells activated with IgM and CD40 antibodies play a key role in controlling autoimmunity in MRL/lpr.

339. SOLUBLE L-SELECTIN LEVELS CORRELATE WITH GENOTYPE AND A CLINICAL SUBSET OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
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Background: Alterated function of selectin glycoprotein adhesion molecules may modulate severity and organ-specific manifestations of autoimmune and inflammatory disease via changes in leucocyte trafficking. Serum concentrations of selectin molecules have been suggested as useful biomarkers in systemic lupus erythematosus (SLE). In addition, the selectin locus lies on human chromosome 1q24, within an interval linked with SLE.

Methods: Using a ELISA method, soluble L- and E-selectin were measured in the sera from 278 European-Caucasian lupus patients compared to 230 healthy siblings. Using generalised linear models, correlations were sought between disease phenotype and soluble selectin levels. Using SNP markers typed in nuclear SLE families, haplotypes were constructed across the selectin genes and genotype-phenotype associations sought using family-based methods.

Results: We identified increased levels of soluble L-selectin (sL-selectin), but not soluble E-selectin (sE-selectin) in 278 European-Caucasian lupus patients compared to 230 healthy siblings. Using generalised linear models, correlations were sought between disease phenotype and soluble selectin levels. Using SNP markers typed in nuclear SLE families, haplotypes were constructed across the selectin genes and genotype-phenotype associations sought using family-based methods.

Results: We have identified increased levels of soluble L-selectin (sL-selectin), but not soluble E-selectin (sE-selectin) in 278 European-Caucasian lupus patients compared to 230 healthy siblings. Using generalised linear models, correlations were sought between disease phenotype and soluble selectin levels. Using SNP markers typed in nuclear SLE families, haplotypes were constructed across the selectin genes and genotype-phenotype associations sought using family-based methods.

Results: We have identified increased levels of soluble L-selectin (sL-selectin), but not soluble E-selectin (sE-selectin) in 278 European-Caucasian lupus patients compared to 230 healthy siblings. Using generalised linear models, correlations were sought between disease phenotype and soluble selectin levels. Using SNP markers typed in nuclear SLE families, haplotypes were constructed across the selectin genes and genotype-phenotype associations sought using family-based methods.
340. THE ROLE OF CD4 T CELLS IN THE LOSS OF TOLERANCE IN A MURINE MODEL OF SLE

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Background: SLE is an autoimmune disease, the hallmark of which is the loss of tolerance to self. We have identified a number of chromosomal regions in the mouse model, BXSB, that are linked to aspects of disease severity. In previous studies, we have investigated the properties of a number of congenic strains bearing different, previously identified, disease loci on the background of the non-autoimmune strain C57BL/10 (B10). Two of these congenic strains are particularly arginine residues are important. Further studies are required to demonstrate whether these sequence changes that alter the binding properties of B3 alter its pathogenicity.

Methods: To characterize the role played by CD4 T cells in disease onset and progression, the functional capacity of splenic and peripheral blood CD4 cells were assessed in the two congenic lines prior to, at the onset of, and post, disease manifestation. CD4 purity was determined by two colour flow cytometry (FACS); the cytotoxic secretion profile (T helper subset) by cytokine ELISA and finally CD4 proliferation in response to polyclonal stimulation by both the incorporation of 5-thymidine and FACS analysis to determine cell population size and distribution.

Results: Significant differences were revealed in B10.Yaa.Bxs1/4 and B10.Yaa.Bxs2/3 compared to each other and to the control strains for all parameters measured. At 2 months of age the autoimmune prone mice revealed a higher percentage of actively dividing cells than their non-autoimmune counterparts. At 6 months the pattern was reversed, with CD4 cells from autoimmune mice only weakly responding to activation stimuli. Prior to disease onset, FACS analysis revealed higher percentage populations of CD3 T cells in all autoimmune mice compared to controls. However, as disease progressed the percentage of CD4 cells declined rapidly in all autoimmune mice, followed by a decrease in the percentage of CD4 cells. In both cases the loss occurred first in B10.Yaa.Bxs2/3. The decline in T cells was also apparent from IHC analysis of splenic sections. Cytokine secretion patterns also differed. At 2 months of age the autoimmunotype mice revealed a higher percentage of CTL activity than CTL activity, with the presence of nucleosomes.

Conclusions: These data suggest profound CD4 T cell functional differences that correlate with defined genetic intervals and different phenotypes.
Poster Session 3. SLE and antiphospholipid syndrome

343. CYTOTOXIC EFFECTS INDUCED BY MINOCYCLINE SUPPORT A COMMON MEIOSIS-PERIODASE MEDIATED PATHOGENIC MECHANISM FOR DRUG-INDUCED LUPUS

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Background: Many drugs associated with drug-induced lupus have been shown to be susceptible to oxidative transformation by the enzymatic action of myeloperoxidase (MPO). Lupus inducing drugs are chemically disparate, but it has been suggested that MPO mediated metabolism may represent a common pathogenic pathway. Minocycline is a tetracycline derivative most commonly used for the treatment of inflammatory acne and for the treatment of rheumatoid arthritis. The aim of this study was to investigate if minocycline could act as a substrate for MPO and be converted to cytotoxic metabolites.

Methods: To ascertain if minocycline could act as a substrate for MPO, the effect of adding increasing amounts of minocycline on MPO activity was determined using H2O2 as the primary and o-dianisidine as a secondary substrate. The MTT cell cytotoxicity assay was employed to assess if MPO could convert minocycline to reactive metabolites. The viability of EL4 cells was evaluated using the MTT assay. The impact of minocycline with or without the addition of neutrophils activated with opsonized zymosan.

Results: Minocycline was found to inhibit MPO activity when H2O2 was used as a primary substrate and o-dianisidine as a secondary substrate (47% inhibition at 100uM). Analysis of enzyme kinetic data indicated that it was a non-competitive inhibitor (Km=7.3). In the presence of activated neutrophils minocycline was found to be cytotoxic to target EL4 cells. Cytotoxicity increased in the presence of increasing concentration of drug.

Conclusions: These results show that minocycline is a competitive inhibitor for MPO when H2O2 is used as a primary and o-dianisidine as a secondary substrate, indicating that minocycline is a potential substrate for MPO. Cell cytotoxicity assays suggested that activated neutrophils are able to transform minocycline to cytotoxic products. Further work is needed to establish if this possible pathogenic mechanism is driven by MPO metabolism.

344. PATIENTS’ PERCEPTION OF SYSTEMIC LUPUS ERYTHEMATOUS DISEASE ACTIVITY

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Background: Disease activity assessment is one of the core components in management of systemic lupus erythematosus (SLE). The difference between patients’ and physicians’ SLE disease activity ratings has been described and some variables were examined as possible sources of the discrepancy. We hypothesized that health-related quality of life (HRQoL) can influence the perception of disease activity.

Methods: Thirty Caucasian SLE patients (29 (96.7%) women, age 16 to 59, and disease duration 1 to 12 years) with various clinical features consented to participate in the study. Disease activity was assessed with the Systemic Lupus Activity Measure (SLAM); damage was evaluated with SLICC/ACR Damage Index (SDI); HRQoL was measured with EQ-5D visual-analog scale (VAS). Physicians also rated global disease activity using a 10 cm anchored visual analog scale (PGA). Patients assessed disease activity using Lupus Activity Self-assessment Tool (LAST), which consists of 10 questions on SLE-related symptoms weighted from 0 to 3 on Likert-type scale according to their severity and an anchored 11-point (0 to 10) numerical rating scale for patient global disease activity, all questions ask about symptoms observed in 10 days prior to administration. Minimal LAST score is 0 and maximum is 40 points. Statistical tests included Spearman’s rank correlation and ANCOVA.

Results: Median SLAM score was 6.5 (range 0 to 23), median SDI was 5 (range 0 to 5), mean (SD) EQ-5D VAS ratings were 54.7 (17.27) and median 45.0 (range 20 to 81). The LAST scores showed non-normal distribution, mean (SD) LAST scores were 10.3 (6.8), median 12.5 points (range 0 to 21). The LAST scores showed strong positive correlation with both SLAM (r=0.616, p<0.0005) and PGA (r=0.650, p<0.0005) and no correlation with SDI. EQ-5D VAS ratings negatively correlated with SDI (r=0.421, p=0.021) and with the LAST scores (r=0.396, p=0.03) while no correlation with SLAM or PGA was observed.

SDI and EQ-5D VAS ratings were included in ANCOVA model with the LAST scores as dependent variable. Interaction between SDI and EQ-5D VAS appeared to be a significant parameter in the model as well as SDI scores alone, while EQ-5D VAS was a non-significant parameter. Each of significant parameters accounted for 16% of total variation. When PGA was included in the model, disease activity remained the only significant parameter for predicting the LAST score.

Conclusions: Damage and HRQoL appear to influence patients’ perception of SLE disease activity, but such influence seems to be small. Strong correlation between patients’ and physicians’ estimates of disease activity further supports the idea of patient-derived SLE disease activity measure.

345. AUTOMMUNE LIVER DISEASE IN JUVENILE AND ADULT POPULATIONS WITH SYSTEMIC LUPUS ERYTHEMATOUS

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Background: Clinically significant autoimmune liver disease (AILD) is perceived as unusual in systemic lupus erythematosus (SLE). Biopsy proven serious chronic liver disease (primary biliary cirrhosis (PBC), chronic active hepatitis (CAH) and cirrhosis) has been reported in as few as 5% of adult SLE patients. In contrast there is sparse data on liver disease in the juvenile SLE population. We were thus interested to see the prevalence of these conditions in our cohort of patients and importantly if there were any differences between the adult and juvenile SLE cohort.

Methods: A retrospective review of case notes was performed in the juvenile SLE cohort (n=74) and an existing database in the SLE adult population (n=401) searched to identify patients with hepatic involvement.

Results: Table 1 below summarises our results of adult and juvenile patients with SLE and biopsy proven AILD. Of particular note, the prevalence of AILD was significantly different (p<0.005 on Chi Square testing) between the adult (1.2%) and juvenile (12.2%) populations.

Table 1. A comparison between adult and juvenile patients with SLE and biopsy proven AILD

<table>
<thead>
<tr>
<th></th>
<th>Adult (n=401)</th>
<th>Juvenile (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of SLE patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with biopsy proven AILD</td>
<td>5 (1.2%)</td>
<td>9 (12.2%)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– CAH</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>– PBC</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>– CAH &amp; Cirrhosis</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Serology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– ANA</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>– cDNA</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>– SMA</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>– AMA</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>– LKM</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Liver Failure</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>SLLE diagnosed first</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>AILD diagnosed first</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Time to develop SLE (months)</td>
<td>22 (range 1-56)</td>
<td>60 (range 1-145)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time to develop AILD (months)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>–ANA</td>
<td>Anti-nuclear antibody</td>
</tr>
<tr>
<td>–dsDNA</td>
<td>Double stranded DNA</td>
</tr>
<tr>
<td>–SMMA</td>
<td>Smooth muscle antibody</td>
</tr>
<tr>
<td>–AMA</td>
<td>Anti-mitochondrial antibody</td>
</tr>
<tr>
<td>–LKM</td>
<td>Liver kidney microsomal antibodies</td>
</tr>
</tbody>
</table>

Conclusions: In one of the largest cohorts of SLE patients in this country we were fascinated to note the differences in the presentations of biopsy proven liver involvement in the adult and juvenile population. Clearly autoimmune liver involvement is significantly more prevalent in the juvenile cohort and strikingly, in these patients, liver involvement always precedes the development of SLE in contrast to the adult cohort. The most common liver pathology appears to be a chronic active hepatitis in both groups however there appears to be a difference in the autoantibody profile between them.

346. AN AUDIT OF VACCINATION AND INFECTION PROPHYLAXIS IN SLE

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Background: Infectious diseases, associated with disease activity or immunosuppressive therapy, are a significant cause of morbidity and mortality among SLE patients. Up to 30% of all deaths in SLE can be attributed to infection and approximately 50% of all SLE patients will suffer an infection during the course of their disease. Prophylactic therapy, including vaccination is thus a vital tool for preventing infection. Our aim was to audit current immunisation practice among patients attending a lupus clinic.

Saturday, 22 April 2005
Methods: Consecutive patients attending a lupus clinic over a 2-month period were asked to complete a short questionnaire. This included questions regarding side-effects of medication (in the past 12 months and ever required hospitalisation), current drug treatment and immunisation history (against influenza in the last 12 months, pneumococcus in the last 6 years and tetanus in the last 10 years).

Results: Fifty-one patients (all female) were included. The mean (SD) age was 47 (13) years, of whom 84% were Caucasian. Thirty-two (63%) had required antibiotics in the past 12 months and 14 (27%) had been hospitalised due to infection during the course of their disease. Twenty-nine (57%) were currently taking prednisolone, and 5 (10%) were currently taking ≥20mg/day. Sixteen patients (31%) were on immunosuppressive therapy (methotrexate, azathioprine or mycophenolate mofetil). Thirty patients (59%) had been vaccinated against influenza in the past 12 months, 16 (31%) against pneumococcus in the past 6 years and 20 (39%) against tetanus in the past 10 years. Of those currently on immunosuppressive therapy or prednisolone at a dose ≥20 mg/day, 14 (70%), 6 (30%) and 8 (40%) were vaccinated against influenza in the past 12 months, pneumococcus in the past 6 years and tetanus in the past 10 years respectively.

Conclusions: Infection is a significant cause of morbidity among patients with SLE and greater muscle-skeletal morbidity in those taking immunosuppressive therapy and/or prednisolone. In particular, extra vigilance is required with SLE. Despite this, a significant minority are not being appropriately vaccinated against influenza, pneumococcus and tetanus.

347. NON-CAUCASIAN ETHNICITY IS ASSOCIATED WITH HIGHER RATES AND A DIFFERENT PATTERN OF DAMAGE IN A MULTITELENI IC UK LUPUS COHORT

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Background: Assessment of damage in SLE is an important outcome measure that allows one to assess the burden of morbidity in particular groups of patients. Damage has been observed to be higher in certain ethnic subgroups and the pattern of damage accrual has also been suggested to differ according to ethnicity. The aim of this study was to examine the prevalence and pattern of damage in a multiethnic lupus cohort attending a single UK centre.

Methods: Women with SLE (1998 ACR criteria) attending an outpatient clinic were assessed. Damage was assessed by the Systemic Lupus International Collaborating Clinics Damage Index (SDI) by medical interview and chart review. Ethnicity was defined according to patient self-assignment using census definitions.

Intergroup differences in SDI were calculated using Mann-Whitney and Kruskal-Wallis tests. Chi-squared and Fisher's exact tests were used for categorical variables.

Results: Of 162 patients studied, 131 (84.5%) were Caucasian and 24 (15.5%) were non-Caucasian. There were 6 South Asians; 2 Black Africans; 11 Black Caribbeans; 3 Chinese and 2 Persian patients. The mean (SD) age and disease duration of the whole group were 47 (11) and 11 (9) years respectively. Non-Caucasians, compared to Caucasian mean (SD) 40 years [12] vs. 48 years [10] and a shorter disease duration [mean (SD) 9 years [4] vs. 12 years [5]]. Overall, 66 (42.6%) had at least one item of damage, this included 50 (38.5%) Caucasians with damage compared to 16 (67%) non-Caucasians (p=0.039). In the whole group the median (range) SDI was 0.5 (0-4). Caucasians had lower overall scores than non-Caucasians (0 [0-4] vs. 1 [0-4], p=0.03). South Asians had the highest median SDI scores (1.5 [0-4]). Musculoskeletal and neuropsychiatric damage were the commonest damage items in the whole group. Caucasians had significantly more peripheral vascular disease (deep vein thromboses) (p=0.03) and non-Caucasians significantly more musculoskeletal (cavitation, chest wall pain) and psychiatric (post-traumatic stress disorders) (p=0.003) and skin (extensive scarring/rash) (p=0.03) damage.

Conclusions: In a UK multiethnic cohort, we have found a significantly higher prevalence of damage in SLE patients of non-Caucasian ethnicity. The highest levels of damage were observed in the South Asian population. In addition, the pattern of damage was different according to ethnicity. Further work is needed to understand the contribution of genetic, e.g. response to therapy and baseline clinical phenotype, and environmental factors, e.g. sociodemographic factors and compliance with medication, to these differences.

348. LUPUS NEPHRITIS IN AN AFROCARIBBEAN POPULATION IN BARBADOS

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Background: Lupus nephritis [LN] was observed to be a major cause of morbidity and mortality in patients with systemic lupus erythematosus [SLE] followed in the rheumatology clinic of the Queen Elizabeth Hospital in Barbados. Barbados, a 166 square-mile island in the Caribbean, with a population of 268,790 of whom 94-97% are AfroCaribbean has this single public tertiary care centre at which rheumatology services became available in 1995. Based on the following the profiles the clinical features of 53 cases of lupus nephritis diagnosed and followed by the rheumatology service from 1995 to 2004.

Methods: Fifty-three cases of LN occurring in newly diagnosed patients with SLE between 1995 to 2004 were identified for observation.

Results: Of the 53 cases of LN followed, 52 were AfroCaribbean [F=45; M=7] and one was a woman of mixed race. The age range was 4-45 years. Mean age of onset of disease was 29 years. 50% of patients had LN as a presenting feature of SLE and 96% of patients with LN developed this complication within 3 years of diagnosis of SLE. Based on their clinical presentation, patients with LN could be divided into 4 categories. Normal renal function with <3g proteinuria [29%]; normal renal function with >3g proteinuria [12%]; renal impairment with >3g proteinuria [15%]; renal impairment with >3g proteinuria [44%]. Patients with normal renal function, regardless of the degree of proteinuria, had a good response to prednisolone and azathioprine [over 80%] with no development of chronic renal failure and no deaths attributed directly or indirectly to renal disease.

Patients with renal impairment and proteinuria of varying degrees were initially treated with Azathioprine in 60% of cases with response noted in only 20%. In patients treated with cyclophosphamide, both initially and for azathioprine-resistant failure, only 50% responded. Patients failing cyclophosphamide generally tended to be the subset with delayed presentation and acute renal failure. Experience with mycophenolate mofetil [MMF] was limited because of cost issues and 3 of 4 patients treated with the drug in 2004 developed septic complications within weeks of initiation of therapy with the ill advised dose of 500mg bid. Deaths occurred in 20% of patients, all as a result of complications of renal failure and sepsis.

13 renal biopsies were performed in the 53 patients, 11 in the 31 patients with renal impairment. Just over a third of biopsies were reported as Type I. Just over 60% of patients tested positive for antDNA antibodies, a conservative figure since not all patients were able to be tested.

Conclusions: AfroCaribbean patients with lupus nephritis was observed to develop this complication typically within 3 years of diagnosis of SLE. Most patients present with renal impairment and greater than 3 g proteinuria and are at risk of developing chronic renal failure if not treated early with cyclophosphamide.

349. VITAMIN D DEFICIENCY IN SLE

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Background: Patients with SLE are often photosensitive and may use sun block whenever UVB exposure is predicted.

The main source of vitamin D is from the skin when exposed to ultraviolet light (UVL). In patients with SLE, sun exposure is decreased due to photosensitivity, therefore, decreased vitamin D levels can be expected. The main cause of vitamin D deficiency is insufficient exposure to UVB; however, patients with SLE are at risk of developing vitamin D deficiency due to decreased sun exposure. This study aimed to measure vitamin D levels in SLE patients and to compare these levels to healthy controls.

Methods: Vitamin D and bone turnover markers were measured in 31 patients with SLE. Patients were questioned regarding symptoms of vitamin D deficiency, exposure to sunlight, use of sun block and consumption of vitamin D supplements.

Results: There were no significant differences in 25(OH) vitamin D or 1,25-dihydroxyvitamin D between patients with SLE who used sun block, patients with SLE who did not routinely use sun block and healthy controls.

Vitamin D concentrations.

Vitamin D deficiency was however common occurring in 22 subjects (63% of patients who used sun block (46%), 7 of 10 patients who did not (38%) and 7 of 11 controls (63%)).
Conclusions: These results indicate that vitamin D insufficiency is common in SLE and that these patients use sun block, also in the control population. There is a trend towards lower 25(OH) vitamin D3 in patients who use sun block. The results are limited due to the small number of subjects involved. The high rate of hypovitaminosis D in controls is consistent with several studies reporting that vitamin D deficiency is common even in young, healthy adults. Symptoms of vitamin D deficiency are common amongst patients with SLE. In this study they do not correlate with vitamin D deficiency therefore screening based on symptoms is unlikely to be helpful. Vitamin D deficiency appears to be common in patients with SLE. This may be exaggerated in patients who use sun block. Therefore we would advocate screening patients with SLE for vitamin D deficiency.

350. SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), RHEUMATOID ARTHRITIS AND OTHER CONNECTIVE TISSUE DISEASES – CLINICAL FEATURES AND SEROLOGICAL RESULTS IN OUTPATIENTS FROM SINGAPORE AND SYDNEY

D.A. Kandiah. Department of Rheumatology and Immunology, Singapore General Hospital, Singapore, Singapore, Singapore

Background: Patients with Connective Tissue Diseases (CTD) of Asian origin appear to have more end-organ damage than Caucasian patients. This may be due to the effect of these different diseases necessitating the use of strong immunosuppressive therapy, which in turn results in morbidity and mortality from infection.

Methods: Patients with CTD seen by one Rheumatologist at his hospital outpatient clinic were assessed for organ involvement and serology. Comparisons were made with a white population.

Results: Seventy-seven patients with a high ANA titre (> 400) were included in the analysis. Data on the patients’ age, gender, racial origin, diagnosis, use of Prednisolone, Disease-modifying/Immunosuppressive therapy, and organ involvement were collected. Similarly, 94 patients with Rheumatoid Arthritis were assessed.

The mean age of the population was 44 years (range 15-80 years). There were 79.5% females. The most common clinical manifestations were polyarthralgia (53.4%), skin rashes (51.1%) and cytopenia (40.9%). dsDNA antibodies were found in 54.5%, and 51.1% had ACL antibodies. Anti-Ro was the most commonENA antibody (30.6% recorded). There was a strong association between Ro/SSB antibodies and serositis with pleural and pericardial effusions (p=0.03). Younger patients had more skin rashes (p=0.007), nephritis (p=0.008) and cytopenias (p=0.033). Older people had more interstitial lung disease (p=0.002). The highest use of Prednisolone was for cytopenias (p=0.001), vasculitis (p=0.01), nephritis (p=0.006) and serositis (p=0.012). Strong immunosuppressants were used for nephritis (p=0.001), vasculitis (p=0.011) and cytopenias (p=0.031). Both the SGH and Sydney-based populations had a similar age and gender distribution. Only 25.6% of patients in Sydney satisfied the diagnosis of SLE compared with 57.1% of the Singaporean cohort (p=0.005). Only 28.2% of the Sydney patients were on Prednisolone compared to 82.9% of the Singaporean patients (p=0.001).

Conclusions: This study shows that CTD manifestations in Asian patients are more severe and need strong treatment. A similar analysis for patients with Rheumatoid Arthritis showed a different correlation between Rheumatoid Factor and clinical manifestations. This needs to be taken into consideration in the development of new treatments.

351. NEUROLOGICAL MANIFESTATIONS OF CONNECTIVE TISSUE DISEASES: CORRELATION WITH SEROLOGICAL MARKERS

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Background: Patients with Connective Tissue Diseases (CTDs) are well known to have neurological events. These patients need to be identified when they present with their neurological manifestations so that treatment can be tailored to the underlying conditions as well as to the neurological problems.

Methods: In this study, patients followed-up by one Rheumatologist in a Hospital-based Clinic were assessed for their clinical manifestations and serological blood tests. Clinical events were confirmed by physical assessment and investigations.

Results: Eighty-three patients were followed up from October 2003 to the end of August 2004. 77 of these patients had SLE, and the other 12 had other CTDs. 21 patients had neurological events. The 15 SLE patients had seizures (5), vascular events (4), personality changes, anxiety and confusion (3), migraine (1) and myasthenia gravis (1). The 3 Primary Sjogren’s Syndrome patients had associated myasthenia gravis, paraesthesiae and definite optic neuritis and transverse myelitis. The other 3 patients had epilepsy (Primary APS), personality disorder (Mixed CTD) and vascular events (Scleroderma). There was a greater occurrence in the age of the total population versus the patients with CNS disease (Mean 44 ± 40 years). There was no difference as well in the gender (79.5% vs. 76.2% females) and race. In the assessment of the serological features, only one test stood out. 54.8% of all patients had anti-cardiolipin antibodies by ELISA testing. Of the 21 patients with CNS manifestations, 86.7% had ACL antibodies [Odd Ratio 3.52 (95% CI 1.15-10.8)].

Conclusions: Patients presenting with neurological events need to be assessed for autoimmune diseases especially if there are less than 50 years of age and female. But 2 of the patients with ACL antibodies and neurological manifestations were on a vascular protectant with Warfarin, Aspirin and Hydroxychloroquine the most commonly used, alone or in combination.
positivity was defined as having, on the day of the study, a positive test for either ACL or lupus anticoagulant.

Results: We studied 62 patients, the median (range) age and disease duration were 48.5 (21-73) and 11 (1.0-40) yrs respectively. Twenty four (39%) were positive for ACL. Patients with ACL tended to have a shorter disease duration (7.0 (1.0-23) vs 12.5 (1.0-40), P = 0.08) but there was no difference in age. The numbers on steroids did not differ between groups, however those with ACL were less likely to be on antimalarials (52% vs 26%, P = 0.001). Patients with ACL had significantly higher SLEDAI (P = 0.03) and a higher proportion had a category A or B BILAG score (29% vs 13%). ACL positive cases had significantly higher levels of triglycerides (P = 0.010), VLDL-cholesterol (P = 0.017), LDL-cholesterol (P = 0.02) and ox-LDL (P < 0.001) (Table).

Conclusions: ACA in women with SLE are associated with an adverse lipid profile and increased ox-LDL. ACA may therefore be associated with inflammatory mechanisms that promote an atherogenic lipid profile and increase susceptibility of LDL to oxidation. Prospective studies are needed to study this relationship further and to investigate the potential for therapy such as antimalarials to modulate this pathway.

354. PREVALENCE OF CONVENTIONAL AND LUPUS-SPECIFIC RISK FACTORS FOR CARDIOVASCULAR DISEASE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) - A CASE CONTROL STUDY

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Background: Patients with SLE are significantly more likely to suffer a myocardial infarction or a stroke than age-matched controls. We sought to compare the prevalence of conventional and lupus-specific risk factors in patients with SLE who have suffered a cardiovascular event with their prevalence in matched control subjects with SLE, but no cardiovascular disease.

Methods: 29 patients with SLE and cardiovascular disease attending one of two specialist SLE clinics, all fulfilling the revised ACR criteria, were enrolled. For each patient two ethnically matched controls were obtained, one matched for age and one for duration of SLE. Data regarding risk factors were collected for the time immediately preceding the relevant cardiovascular event, or at an equivalent time for the controls. The chi-squared test was used to analyse differences in the prevalence of each risk factor between patients and controls at these time points.

Results: The patients’ mean age at event was 47.7 years (range 21-69 years) whilst their mean disease duration was 12.0 years. 24 were female and 5 male. 21 were Caucasian, 5 Asian and 3 of Caribbean origin. Significant differences were found in the prevalence of: elevated blood pressure immediately prior to event (37.9% of patients vs 15.5% of matched controls; P = 0.019); treatment for hypertension (58.6% vs. 22.4%; P = 0.0008); family history of cardiovascular disease (48.3% vs. 25%; P = 0.022); elevated IgG antiphospholipid antibody (52% vs. 16.1%; P = 0.0049); presence of lupus anticoagulant (41.2% vs. 6.9%; P = 0.0026); and treatment with hydroxychloroquine (20.7% vs. 51.8%; P = 0.0056). Differences in the prevalence of smoking (37.9% vs. 18.5%; P = 0.053) and menopausal status (59% vs. 34.1%; P = 0.010) were also significant. Differences in the prevalence of statins (37.9% vs. 18.5%; P = 0.053) and menopausal status (59% vs. 34.1%; P = 0.010) were also significant.

Conclusions: ACL positive cases had significantly higher levels of triglycerides, VLDL-cholesterol, LDL-cholesterol and ox-LDL. ACL positive cases had significantly higher levels of triglycerides (P = 0.010), VLDL-cholesterol (P = 0.017), LDL-cholesterol (P = 0.02) and ox-LDL (P < 0.001).

Poster Session 3. SLE and antiphospholipid syndrome

355. THE ROSE ANGINA QUESTIONNAIRE POORLY DISCRIMINATES SUBCLINICAL ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: To investigate if the Rose Angina Questionnaire (RAQ), a validated measure of the prevalence of angina in the general population, is associated with other markers of coronary heart disease (CHD) risks and/or subclinical atherosclerosis in SLE.

Methods: Patients with SLE (197 revised criteria) were identified from outpatient clinics. All patients underwent a complete history and physical examination, with assessment of classic CHD risk factors, prevalent cardiovascular disease and a carotid doppler examination to measure intimal media thickness (IMT) and the presence of carotid plaque. Each patient had postal administration of the Rose Angina Questionnaire.

Results: 200 female patients were questioned, 146 (73%) were complete and suitable for analysis. In this group the median and interquartile range (iQR) of age and disease duration were 48 years (43-56) and 10 years (4-18) respectively. Ten percent had a history of CHD (5) or stroke/transient ischaemic attack (14). Cases of Rose angina were more prevalent in SLE compared to controls (20.7% vs. 51.8%; P = 0.0056). Differences in the prevalence of smoking (37.9% vs. 18.5%; P = 0.053) and menopausal status (59% vs. 34.1%; P = 0.010) were also significant. Differences in the prevalence of statins (37.9% vs. 18.5%; P = 0.053) and menopausal status (59% vs. 34.1%; P = 0.010) were also significant.

Conclusions: In this study of women with SLE we found no association of the RAQ with risk factors for cardiovascular disease, subclinical or known clinical cardiovascular disease. This is in contrast to other measures of subclinical atherosclerosis that have been used in this population. While a prospective study is required to assess CHD outcomes in these patients, our initial results suggest that the Rose Angina Questionnaire is not a useful screening tool to identify subclinical atherosclerosis in women with SLE.

356. ENDOTHELIAL DYSFUNCTION AND CIRCULATING MARKERS OF ENDOTHELIAL DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS

S.V. Shevchuk, M.A. Stanislavchuk, N.V. Zaichko. Rheumatology, Vinnytsia National Medical University, Vinnytsia, Ukraine

Background: Increased prevalence of cardiovascular morbidity and mortality due to atherosclerosis has been observed in patients with systemic lupus erythematosus (SLE). This increased prevalence cannot be explained by the presence of the traditional cardiovascular risk factors such as hypertension, hyperlipidaemia et al. Therefore, other risk factors must be present in patients with systemic lupus erythematosus. Although the mechanisms have not been fully unravelled, endothelial cell (EC) activation through autoantibodies seems to be one of the factors involved. EC activation results in the formation of an oxLDL, which is a positive marker of atherosclerosis. Prospective studies are needed to elucidate the role of endothelial dysfunction in cardiovascular disease.

Methods: 63 patients with SLE and 21 healthy controls were examined for sVCAM-1, sCD62L, circulating von Willebrand factor (vWF) and anti-dsDNA antibodies with specific ELISA kits. We measured disease severity by SLEDAI and SLAC/ARC in patients with SLE. Endothelial function was evaluated using brachial artery reactivity.

Results: We found significantly elevated levels of sVCAM-1, sCD62L and vWF (P < 0.05) in patients with SLE compared to controls. The flow-mediated dilatation (endothelial dependent dilatation) was significantly impaired in SLE patients when compared to controls. The endothelium-dependent dilatation was not related to SLEDAI or SLAC. The results were similar for sVCAM-1 and vWF. We found a positive correlation between the levels of sVCAM-1 and vWF. The increase of sVCAM-1 and vWF reflects a state of persistent endothelial cell activation.
357. TREATMENT ADHERENCE IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: The treatment of SLE is difficult and represents a significant therapeutic challenge. There is no specific treatment and although several drugs can modify the disease sufficiently for the patient's symptoms to be tolerable or vital organs to be protected from permanent damage, none are curative. Poor adherence can lead to frequent relapses and potential organ damage, increased clinic visits and hospital admissions; erroneous conclusions about the efficacy of the treatment; wasted drug costs for the NHS and costs to the patient in lost time in work. However, there is a lack of empirical work concerning adherence in this group of patients. Therefore, this study was undertaken to evaluate adherence to treatments in SLE.

Methods: An anonymous self-report questionnaire was administered to consecutive SLE patients attending an outpatient clinic at a district general hospital. The adherence questionnaire asked how often they took their medications as prescribed, believed their medication to be very important and reported troublesome treatments to be. The treatments evaluated are listed in the table below.

Results: Fifty females with SLE took part in the study. They had a mean age of 51 years (range 23-80 years) and had been diagnosed with SLE for a mean of 11 years (range 1-28 years). For each of the treatments, the table below shows the percentages of patients who always took their medication as prescribed, believed their medication to be very important and reported that their medication was very troublesome.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Always take as prescribed (%)</th>
<th>Very important (%)</th>
<th>Very troublesome (%)</th>
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</thead>
<tbody>
<tr>
<td>Oral steroids</td>
<td>94</td>
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<td>6</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>83</td>
<td>52</td>
<td>4</td>
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<tr>
<td>Azathioprine</td>
<td>100</td>
<td>50</td>
<td>13</td>
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<tr>
<td>Methotrexate</td>
<td>80</td>
<td>20</td>
<td>20</td>
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<tr>
<td>NSAIDs</td>
<td>68</td>
<td>48</td>
<td>5</td>
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<tr>
<td>Bone protection</td>
<td>61</td>
<td>52</td>
<td>0</td>
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<tr>
<td>Aspirin</td>
<td>77</td>
<td>51</td>
<td>3</td>
</tr>
<tr>
<td>Sun protection</td>
<td>41</td>
<td>77</td>
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</table>

There were no correlations between age and adherence for any of the treatments studied. However, patients with longer disease duration tended to have a higher level of adherence to methotrexate, hydroxychloroquine, bone protection and aspirin (Spearman coefficients all > 0.4).

Conclusions: Adherence rates were treatment specific. Adherence to immuno-modulatory therapy was relatively high whereas sun protection behaviours were low. As photosensitivity is an important aspect of the disease this represents a major concern. Patients' beliefs about their treatments are important and should be evaluated to aid the effective management of the disease.

358. THE LOW GLYCAEMIC INDEX DIET IN SYSTEMIC LUPUS ERYTHEMATOSUS: FEASIBILITY, SAFETY AND TOLERABILITY

S.I. Yeo, R.J. Davies, K. Avloniti, M. Lomer, G. Hughes, D. O'Cruz. The Lupus Research Unit, The Rayne Institute, St Thomas' Hospital, London, United Kingdom

Background: Systemic lupus erythematosus (SLE) is an autoimmune connective tissue disease characterised by multi-system organ involvement. Although accelerated atheroma is well described in SLE, the mechanism is not fully understood. Specifically, there is evidence that the inflammatory process may be contributing to the pathogenesis of atheroma. However, the potential role of diet in SLE and the mechanism by which diet may modify the disease process is unclear. In this pilot study we aimed to evaluate adherence to a low glycaemic index diet and its effects on disease activity in patients on low dose prednisolone with stable SLE.

Methods: We included 23 patients with SLE who fulfilled the inclusion criteria of the study. The patients were randomly assigned, by minimisation, to a conventional low-calorie diet (Low Cal) or a low glycaemic index diet (Low GI). They were assessed at baseline and six weeks, by a clinician and dietitian. Compliance and adverse effects were determined through self-reporting, food diaries and once-weekly telephone consultation with the dietician. Validated tools of assessment for disease activity, fatigue, and sleep were applied at these time-points (BILAG, ECLAM, SLEDAI, Fatigue Severity Score (FSS) and Pittsburgh Sleep Quality Indices (PSQI), respectively).

Results: Twelve and 11 subjects were assigned to Low Cal and Low GI, respectively. One withdrew from the Low Cal and 3 withdrew from the Low GI (not statistically significant; Chi-squared test). There were significant reductions in weight for both groups (Wilcoxon signed rank test). However, the difference in mean weight loss between groups was not significant.

There were no correlations between age and adherence for any of the treatments studied. However, patients with longer disease duration tended to have a higher level of adherence to methotrexate, hydroxychloroquine, bone protection, and aspirin (Spearman coefficients all > 0.4).

Conclusions: Adherence rates were treatment specific. Adherence to immuno-modulatory therapy was relatively high whereas sun protection behaviours were low. As photosensitivity is an important aspect of the disease this represents a major concern. Patients' beliefs about their treatments are important and should be evaluated to aid the effective management of the disease.

359. A PILOT STUDY OF A LOW GLYCAEMIC INDEX DIET IN SYSTEMIC LUPUS ERYTHEMATOSUS: WEIGHT LOSS AND CARDIOVASCULAR RISK FACTORS

R. Davies, S.I. Yeo, K. Avloniti, M. Lomer, G. Hughes, D. O'Cruz. The Lupus Research Unit, The Rayne Institute, St Thomas' Hospital, London, United Kingdom

Background: The aim of this study was to assess the feasibility and tolerability of a low glycaemic index diet on weight and cardiovascular risk factors in systemic lupus erythematosus (SLE). Accelerated atheroma with resulting cardiovascular and cerebrovascular events accounts for the second peak in mortality seen in SLE. Reduction in dietary carbohydrate load may lower weight and improve biomarkers of cardiovascular risk so forming a useful tool in the prevention of atheroma.

Methods: We recruited 23 women with SLE, meeting the ACR criteria. Other inclusion criteria were 18-65 years, body mass index (BMI) > 25 and a stable dose of prednisolone 5-20mg/d. Using minimisation patients were randomly assigned to a low glycaemic index diet (Low GI), or a calorie restricted diet (Low Cal) for six weeks. Compliance was determined by entry and exit food diaries and self-reporting during weekly telephone consultations with a dietician. Entry and exitfast blood samples were taken to determine lipid profile, glucose, insulin, urate, hsCRP, fibrinogen and homocysteine levels. An oral glucose tolerance test was performed.

Results: Twelve and 11 subjects were assigned to Low Cal and Low GI, respectively. One withdrew from the Low Cal and 3 withdrew from the Low GI (not statistically significant; Chi-squared test). There were significant reductions in weight for both groups (Wilcoxon signed rank test). However, the difference in mean weight loss between groups was not significant.

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There were no correlations between age and adherence for any of the treatments studied. However, patients with longer disease duration tended to have a higher level of adherence to methotrexate, hydroxychloroquine, bone protection, and aspirin (Spearman coefficients all > 0.4).

Conclusions: Adherence rates were treatment specific. Adherence to immuno-modulatory therapy was relatively high whereas sun protection behaviours were low. As photosensitivity is an important aspect of the disease this represents a major concern. Patients' beliefs about their treatments are important and should be evaluated to aid the effective management of the disease.

360. A NOVEL, EFFICIENT, EXPRESS SYSTEM OF DOMAIN I OF HUMAN BETAZ HYDROXYPROTEIN IN E.COLI

Y. Ioannou1, I. Gilles1, N. Lambririades1, D.S. Latchman2, D.A. Isenberg1, 1Centre for Rheumatology, University College London, London, United Kingdom; 2Institute of Child Health, University College London, London, United Kingdom

Background: Domain I (DI) of human beta2 glycoprotein I ($\beta$2GPI) is thought to contain crucial antibody binding epitopes for antiphospholipid antibodies (aPL), which are critical to the pathogenesis of the antiphospholipid syndrome (APS). DI has recently been studied therapeutically for its use in APS as a tolerogen. An efficient system of DI production would thus facilitate further molecular studies of how pathogenic aPL interact with antigen and may
open up other therapeutic avenues. Expression in E. coli is often the expres-
sion of choice as bacterial expression systems will aid future production and studies of DI, helping to further elucidate its role as an antigenic target in the pathogenesis of APS.

361. ARGinine RESIDUES ARE CRITICAL IN THE BINDING OF HUMAN MONOCLONAL ANTI-PHOSPHOLIPID ANTIBODIES TO β2Glycoprotein I

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Background: Previously, we reported that specific arginine (Arg) residues in the heavy chain (VH) of a human pathogenic β2GPI-dependent antiphos-
pholipid antibody (aPL), IS4, and light chain (VL) of a human anti-DNA anti-
tibody, B3, were important in conferring their ability to bind cardiolipin (CL). We were unable to demonstrate binding to β2GPI, due to the low yield of antibody in the transient expression system. To improve the yield of IgG, we developed a stable expression system to examine the importance of specific Arg residues in IS4VH and paired VL in binding to native β2GPI and domain (D1D1) of β2GPI alone, which we hypothesised to contain the immunodominant epitopes for aPL.

Methods: VH and VL cDNA were cloned into the same plasmid contain-
ing the CDRs of VH and VL of pathogenic aPL. Ease, efficiency and relatively inexpensive cost of this pro-
duction system will aid future production and studies of DI, helping to further elucidate its role as an antigenic target in the pathogenesis of APS.

Conclusion: This is the first description of prokaryotic expression of soluble forms (CDR3s) of VH and VL sequences, with proven binding to human monoclonal aPL. Ease, efficiency and relatively inexpensive cost of this pro-
duction system will aid future production and studies of DI, helping to further elucidate its role as an antigenic target in the pathogenesis of APS.

Poster Session 3. SLE and antiphospholipid syndrome

S.R. Sangle, D.P. D'Cruz, G.R.V. Hughes. Lupus Research Unit, The Rayne Institute, St Thomas' Hospital, London, United Kingdom

Background: We have observed a number of patients with arterial/venous thrombotic events and/or pregnancy morbidity who but remain persistently negative for antiphospholipid antibodies (aPL).

Objective: To determine the prevalence of pregnancy related morbidity and thrombotic events in patients who were suspected of having APS but were persistently aPL negative.

Methods: We studied 80 patients who were referred for investigation of pos-
sible APS. All had negative aPL. Human monoclonal anti-DI antibodies were important in conferring their ability to bind cardiolipin (CL).

Results: Of four Arg residues in IS4VH CDR3 substituted to serines, two at positions 100 and 100g had a moderate influence on the strength of CL, β2GPI and 2GPI at good levels, with proven binding to pathogenic human 2GPI. Expres-
sion of the native human cDNA sequence of DI in the same construct under identical conditions yielded 35% less his-tagged DI compared to the recombinant optimised sequence.

Conclusion: This is the first description of prokaryotic expression of soluble forms (CDR3s) of VH and VL sequences, with proven binding to human monoclonal aPL. Ease, efficiency and relatively inexpensive cost of this pro-
duction system will aid future production and studies of DI, helping to further elucidate its role as an antigenic target in the pathogenesis of APS.

362. SERoNegaTive ANTI-PHOSPHOLIPID (HUGHES) SYNDROME

S.R. Sangle, D.P. D'Cruz, G.R.V. Hughes. Lupus Research Unit, The Rayne Institute, St Thomas’ Hospital, London, United Kingdom

Background: To determine the possible factors associated with non-renal hypertensive in patients with antiphospholipid syndrome (APS).

Methods: We screened 130 patients with APS and hypertensive. All pa-
tients fulfilled Sapporo criteria for APS. Hypertension was confirmed by per-
 sistent readings of BP > 140/90 mmHg and all were on hypotensive ther-
 apy. They were screened for fasting insulin, lipids, hs CRP and homocys-
ete levels. Renal pathology was excluded by estimation of proteinuria, frag-
mented RBC & casts in the urine, creatinine and if necessary renal biopsy. All patients BMI, steroid intake and smoking habits were recorded. Twenty-two patients had Primary APS and 108 had secondary APS.

Results: Of the 130 patients 107 were Caucasians, 13 were Afro-Caribbean, 8 were Asians and 2 from Southeast Asia. The median age was 41 years (20-80). Raised hs CRP levels were found in 22 (28.6%), patients, raised fasting insulin was in 16 (20%) of patients. Erythrocyte sedimentation rate (>5.6 mm/h) was found in 58 (75.4%) patients. High level of LDL was found in 9.1% (7) patients. Homocysteine levels were high in 6 (7.6%) patients. Two patients were on Prednisolone > 7.5 mg/day for more than 6 months. Of 9 patients with raised BMI (>25) 4 were diabetic type II), 2 had high fasting Insulin and elevated cholesterol.

Conclusion: Raised hs CRP, fasting insulin and homocysteine levels suggest that inflammation and/or accelerated atherosclerosis may be associated with non-renal hypertension in patients with primary and secondary APS.
364. VASCULITIS, ANTI-PHOSPHOLIPID ANTIBODIES AND RENAL ARTERY STENOSIS
S.N. Paul, R.S. Sangle, A.N. Bennett, G.N.V. Hughes, D.P. O’Croz. Lupus Research Unit, The Rayne Institute, St Thomas’ Hospital, London, United Kingdom

Background: The presence of antiphospholipid antibodies (aPL) in patients with systemic vasculitis is generally thought to be non-pathogenic. We present five patients with renal artery stenosis (RAS) and primary vasculitis who have positive aPL.

Methods: We present five patients with primary systemic vasculitis (Wegener’s 2, Churg Strauss 2 and unclassified 1) with positive aPL. Three patients fulfilled the Sapporo criteria for Antiphospholipid syndrome. The mean age at time of diagnosis of vasculitis was 45 years (42-56). The mean time from diagnosis of vasculitis to the discovery of RAS was 9.6 years (4-18).

All except one patient was Caucasian. All patients had uncontrolled hypertension (BP >140/90mmHg) despite receiving more than 2 antihypertensive drugs. None were hyperlipidaemic, obese or smokers. Patients with Takayasu’s and/or polyarteritis nodosa were excluded. The median serum creatinine at the time of diagnosis of RAS was 127 µmol/L (range 66-220). One patient had renal involvement secondary to Wegener’s as well as aPL related thrombotic microangiopathy. All received immunosuppressive therapy and their vasculitis disease activity was satisfactory. All patients had positive DRVVT and/or anticardiolipin antibodies. Magnetic resonance angiography was used to scans the renal arteries.

Results: All patients had RAS just distal to the ostium. The lesions were smooth and well delineated and angiography failed to reveal tortuous aortae suggestive of atherosclerosis. One patient underwent renal angioplasty. Her renal function returned to normal post-angioplasty.

Conclusions: Previous reports have suggested that the presence of aPL is non-pathogenic in systemic vasculitis. RAS has not previously been reported in systemic vasculitis associated with aPL. We believe the RAS in these patients is associated with presence of aPL and therefore that the presence of aPL may be pathogenic in patients with systemic vasculitis.

365. OUTCOMES IN THE FIRST YEAR IN POLYMYALGIA RHEUMATICA (PMR): RESULTS FROM A MULTI-CENTRE PROSPECTIVE COHORT STUDY
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Background: Little is known about the impact of disease on the quality of life (QOL) and functional status of patients with PMR. No studies have evaluated QOL in PMR patients before treatment, how QOL changes in response to treatment or the relationship between QOL, clinical and laboratory markers of disease activity.

Methods: We recruited 129 patients with newly diagnosed PMR fulfilling modified Jones and Hazelman criteria (minimum duration of disease was excluded) and without clinical features of GCA. Baseline data were collected before beginning a tapered steroid schedule starting at 15mg oral prednisolone, with deviations at clinician discretion. Follow-up data were collected at 3 and 6 weeks and 3, 6 and 12 months. QOL and functional status were assessed at baseline, 3 and 12 months using the SF-36 and Modified Health Assessment Questionnaire (MHAQ). The SF-36 contains summary scores for physical (PCS) and mental (MCS) components of QOL.

Results: Mean age was 79 years, 59.7% were female and 7 withdrew before 12-month follow-up. Mean PCS 31.5 (95% CI 30.0-32.9) and MCS 38.9 (36.8-40.9) at baseline were substantially lower than norms for 65-74 year-olds in the general population (44.7 and 53.2 respectively). By 12 months mean PCS 43.4 (41.5-45.3) and MCS 50.1 (48.1-52.2) improved significantly (both p<0.001). Mean MHAQ score improved from 1.20 to 0.37 at 12 months (p<0.001). During follow-up 42 (34.4%) patients had their oral steroid dose increased above scheduled (28 relapses, 6 lack of initial response, 2 as a result of symptoms, 3 other). At 12 months 20% reported morning stiffness (EMS) >30 mins, 46% reported pain in their shoulders or thighs and 24 (20%) had ESR >30 mm/hr, 9 (38%) of whom had CRP >10 mg/dl. Improvements in PCS and MCS correlated most highly with improvement in MHAQ (both r=0.51) and less so with EMS (r=0.08 and 0.26), ESR (r=0.16 and 0.27) and CRP (r=0.15 and 0.19).

Conclusions: Our findings demonstrate the impact of PMR on QOL. Conventional treatment with oral steroids improved QOL significantly though there was limited correlation with clinical and laboratory markers of disease activity. Many patients reported shoulder pain at 12-months though two thirds were able to reduce oral steroids at or ahead of a tapered schedule.

366. THE DIFFICULTIES IN THE DEVELOPMENT OF HISTOLOGICAL SCORING FOR INFLAMED TEMPORAL ARTERY IN GIANT CELL ARTERITIS
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Background: The major complication of GCA is vision loss. A recent audit showed a high percentage of visual loss (29%) in biopsy patients. Cytokine patterns in temporal artery biopsies (TAB) such as high interferon-gamma have reported correlation with clinical features of ischaemia. It will be useful to differential patients at higher risk for ischaemic events early, to prevent complications such as vision loss. We undertook this study to determine whether a light microscopic histological score of TAB could reliably quantify the inflammatory response and different histological patterns in GCA.

Methods: A scoring system to quantify inflammatory response in TAB was evolved from a UK-Swedish collaboration. TAB were scored as mild (1), moderate (2), Severe (3) for the following: general degree of inflammation, extent of inflammatory invasion with regard to wall layers and the circumference, presence and the extent of multinucleate giant cells, intimal thickening, fibrous exudation and neovascularisation. Twenty five TAB from biopsy positive GCA were scored twice after a 4-week interval by a consultant histopathologist. The slides were then exchanged between the 2 centres and underwent similar review by the other histopathologist. The histopathologist were blinded to each other’s scores, their own scores as well as clinical data. Intra and inter-observer reliability was assessed using kappas statistics.

Results: Intra-observer reliability showed moderate (k=0.59, 95% CI 0.51-0.66) and good (k=0.77, 95% CI 0.71-0.84) agreement for the two observer reliability showed poor agreement (k=0.16, 95% CI 0.12-0.20). Of the seven parameters of inflammation only intimal thickening produced fair or better inter-observer agreement (k=0.34, 95% CI 0.19-0.48). The agreement for giant cell infiltration was no better than would be expected by chance (k=0.02, 95% CI –0.11 to –0.07). The table shows the percentage of TAB with moderate/severe involvement (scores 2 or 3).

Conclusions: The overall histological scores showed poor inter-observer and intra-observer reliability in GCA. Evaluation of giant cells and neo-vascularisation showed highest variability. We suggest that future histological studies agree the definitions of such abnormalities in a prior consensus training phase.

367. SUDDEN BLINDNESS AND ROLE OF THROMBOTHROMBOTIC FACTORS IN GIANT CELL ARTERITIS - A “TRUE TO LIFE” OBSERVATIONAL STUDY
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Background: Giant Cell Arteritis (GCA) is a form of large vessel vasculitis with cumulative effects necessitating long-term follow up. The disease still lacks precise diagnostic criteria and therapeutic guidelines. There is an association between GCA and other inflammatory conditions such as Anti-cardiolipin (aCL) and Anti-neutrophil cytoplasmic antibody (ANCA). This study was a “true to life” observational study of management of patients with proven GCA in routine clinical practice were reviewed. Their clinical features, serological markers and temporal artery histology were reviewed. An ophthalm-