Abstract 204 Table 2 Clinical characteristics (n,%)

Muco-cutanous	108 (72%)
Arthritis	100 (66.7%)
Renal disease	72 (48%)
Leukopenia/lymphopenia	94 (62.7%)
Hemolytic anaemia	13 (8.7%)
Thrombocytopenia	28 (18.7%)
Serositis	30 (20%)
Nervous system disease	11 (7.3%)
Anti-phospholipid Syndrome	24 (16%)

Abstract 204 Table 3 Treatment (n,%)

Steroid/pulse treatment	149 (99.3%)/38 (25.3%)
Hydroxycholoroquine	150 (100%)
Azathioprine	107 (71.3%)
Mycophenolate mofetil	55 (36.7%)
Cyclophosphamide (iv)	45 (30%); 10±4.5 cycles
Rituximab	15 (10%)
Warfarin	31 (20.7%)
Intravenous immunglobulin (IVIG)	3 (2%)
Plasmapheresis	2 (1.3%)

hypertension, 21 (14%) had avascular necrosis, 6 (4%) had malignancy. SLE is an autoimmune disease requiring multi-faceted approach.

205 ANNEXIN II-BINDING IMMUNOGLOBULIN G LEVEL CORRELATES WITH CLINICAL AND RENAL HISTOLOGICAL DISEASE ACTIVITY IN LUPUS NEPHRITIS

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Background and aims Annexin II mediates anti-dsDNA antibody binding to mesangial cells and downstream inflammatory and fibrotic processes. We investigated the relationship between annexin II-binding IgG and clinical or histological activity in lupus nephritis.

Methods Serial serum samples from 28 patients with Class III/IV±V lupus nephritis were studied. Annexin II-binding IgG level was measured with an in-house ELISA. Glomeruli were isolated from NZBWF1 mice, gene and protein expression of annexin II and its binding protein p11 were investigated by real-time PCR and cytochemical staining respectively. Ultrastructural localization of annexin II was determined by electron microscopy and immunogold staining.

Results Annexin II-binding IgG level was associated with anti-dsDNA level and disease activity in 42% of lupus nephritis patients. Annexin II-binding IgG level correlated with Activity Index ($r=0.44$, $p=0.04$), leukocyte infiltration score ($r=0.52$, $p=0.02$), and karyorrhexis/fibrinoid necrosis score ($r=0.66$, $p=0.002$) in renal biopsies, and also with the amount of mesangial electron-dense deposit scored semi-quantitatively ($r=0.63$, $p=0.009$). Glomerular annexin II and p11 expression increased with disease progression in NZBWF1 mice, and annexin II was found on the surface of mesangial cells and in the mesangial matrix, co-localising with electron-dense deposits.

Conclusions Our data demonstrated an association between annexin II-binding IgG level and clinical/histological disease activity in proliferative lupus nephritis. Co-localization of annexin II with electron-dense deposits suggests a pathogenic role for annexin II.

206 INCREASED URINARY HEPARANASE LEVELS ARE ASSOCIATED WITH ACTIVE LUPUS NEPHRITIS

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Background and aims Heparan sulfate in glomerular basement membrane is crucial for charge-selective filtration. Heparanase, an endoglycosidase that cleave heparan sulphate, is reported to be up-regulated in several proteinuric diseases. We investigated the association of urinary heparanase level with renal indices in patients with systemic lupus erythematosus (SLE).

Methods Urinary samples were collected from 76 patients with lupus nephritis (LN; 51 active and 25 inactive), 63 SLE patients without renal involvement and 28 healthy individuals (HC). Heparanase levels were measured by ELISA and normalised by urinary creatinine level (mU/mg).

Results Urinary heparanase levels were increased in SLE patients than HC ($p<0.001$). Patients with active LN had significantly higher urinary heparanase levels compared to patients with inactive LN and without renal involvement (both $p<0.001$), however, there was no difference between latter groups. Urinary heparanase levels positively correlated with proteinuria (measured by spot urine protein/creatinine ratio) and renal SLEDAI ($\gamma=0.514$, $p<0.001$ and $\gamma=0.365$, $p=0.004$, respectively), but inversely with serum C3 ($\gamma=-0.432$, $p<0.001$), C4 ($\gamma=-0.279$, $p=0.013$), and CH50 levels ($\gamma=-0.336$, $p=0.003$). In 39 patients with active LN whose samples were obtained at the time of kidney biopsy, urinary heparanase levels showed positive correlation with activity index ($\gamma=0.409$, $p=0.011$), but not with chronicity index ($p>0.05$). A cut-off value of 444 mU/mg predicted presence of active LN with sensitivity of 74.5% and specificity of 67.1%.

Conclusions Urinary heparanase levels are increased in patients with active LN and reflect the activity of nephritis, indicating that urinary heparanase can serve as useful biomarker for active LN.

207 SUBCLINICAL DETERIORATION OF LEFT VENTRICULAR DIASTOLIC FUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and aims Systemic lupus erythematosus (SLE) represents diverse cardiac manifestation, but diastolic dysfunction has been reported infrequently. This study is aimed to

investigate the left ventricular diastolic function and the factors related in SLE patients compared with healthy controls.
Methods Thirty consecutive female SLE patients without evidence of cardiac disease were underwent standard transthoracic echocardiography, and were compared with 30 age-matched healthy female controls. Patient characteristics, organ damage and laboratory data were retrieved by medical chart review.
Results In SLE patients, indexes of LV diastolic function differed from control group, with reduced early diastolic filling velocity (E), as well as prolongation of the time taken from the maximum E point to baseline, reduced ratio of early to late diastolic flow velocity (E/A), prolonged ratio of E to early diastolic mitral annular velocity (E') (E/E'). However, the differences did not show statistical significance. Anti-Ro antibody positivity was observed in 43% of SLE patients, and it was correlated with higher E/A ratio significantly (1.3±0.4 vs 1.0 ±0.2, p=0.03). In addition, the SLE patients with hematologic or renal involvement showed more enlarged size of left atrium significantly compared to the patients without any involvement (36±4.3 vs 31±9.2, p=0.01).
Conclusions Although not statistically significant, there was a trend which suggested that patients with SLE have subclinical impaired diastolic function compared with the healthy control. Presence of anti-Ro antibody and systemic organ involvement was related with the diastolic dysfunction markers.

208 EDA+ FIBRONECTIN IN TUBULO-INTERSTITIAL INJURY IN LUPUS NEPHRITIS

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Background and aims Anti-dsDNA antibody plays a critical role in the pathogenesis of lupus nephritis and contributes to inflammatory and fibrotic processes in the kidney. EDA^+ spliced variant of fibronectin (EDA^+ FN), normally only weakly expressed, is markedly increased in pathological conditions. We investigated the effect of human polyclonal anti-dsDNA antibodies on the expression of EDA^+ FN in proximal tubular epithelial cells (PTEC) and the functional consequence.
Methods EDA^+ FN expression in human renal biopsies of Class III/IV±V lupus nephritis was assessed by cytochemistry. Cultured PTEC were incubated with control IgG or IgG anti-dsDNA antibodies isolated from lupus nephritis patients for 24 hour and the expression of EDA^+ FN was investigated. Recombinant human EDA peptide was used to investigate the functional role of EDA^+ FN in PTEC.
Results The results showed that EDA^+ FN was absent from normal kidney tissue but was markedly increased in the tubulo-interstitium in lupus nephritis patients. Cultured PTEC constitutively expressed native FN but not EDA^+ FN. Anti-dsDNA antibodies, compared with serum-free-medium and control IgG, increased EDA^+ FN expression by 5.8- and 5.6-fold respectively ($p<0.05$ for both), and the induction was mediated through PI3K and mTOR activation. Exogenous IL-1β and TGF-β1, but not IL-6, IL-8 or MCP-1, induced EDA^+ FN by 1.8- and 2.3-fold respectively. Recombinant EDA peptide increased native FN, collagen I, laminin and SNAIL expression, but decreased E-cadherin expression, in PTEC.
Conclusions Our data demonstrated a role of EDA^+ FN in the pathogenesis of tubulo-interstitial disease in lupus nephritis.

209 JOINT DEPOSITED IGG INDUCES ARTHRITIS BUT INHIBITS OSTEOCLASTOGENESIS IN SLE THROUGH SYK

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Background and aims Although arthritis is frequent in patients with systemic lupus erythematosus (SLE), its pathogenesis remains unclear. The aim in our study is to investigate the pathognesis of arthritis in SLE.
Methods We analysed the feature of SLE patients with arthritis and lupus-prone mice with arthritis, investigated the role of joint deposited IgG in the development of lupus arthritis.
Results Arthritis lacking bone erosion is common symptom in most of SLE patients and spontaneously develops in lupus prone mice. Large amount of IgG deposited in joint of lupus prone mice. Similar arthritis to lupus prone mice was induced by intraarticular injection of lupus IgG and was dependent on the dose of lupus IgG. Joint deposited IgG, monocytes/macrophages and TNFa were required in the development of lupus arthritis. Joint deposited lupus IgG inhibited RANKL-induced osteoclastogenesis in dose and time dependent manner. Lacking ITAM containing FcγRIII reduced inhibitory effect of lupus IgG on osteoclastogenesis. Lupus IgG quickly stimulated Syk activation than RANKL through lipid rafts. Lupus IgG-induced Syk activation is related to dsDNA Ab. Blocking of Syk significantly inhibited arthritis induced by lupus IgG and arthritis in lupus prone mice, suppressed Syk activation induced by lupus IgG and osteoclastogenesis induced by RANKL.
Conclusions The joint deposited IgG exerts an important role in the development of lupus arthritis lacking of bone destruction, Syk plays a crucial role in lupus IgG-induced arthritis and inhibited osteoclastogenesis. This finding will promote development of effective therapeutic strategy to arthritis in SLE patients.

210 OESTROGEN PROMOTES SLE SERUM IGG-INDUCED SKIN INFLAMMATION VIA THE OESTROGEN MEMBRANE RECEPTOR GPER1

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Background and aims Skin injury is the second most common clinical manifestation in patients with systemic lupus erythematosus (SLE). Oestrogen may affect the onset and development of SLE. This study was undertaken to elucidate the role of oestrogen in the development of SLE skin injury.
Methods We investigated the role of oestrogen and its membrane receptor GPER1 in SLE-related skin injury in mice treated with SLE serum *in vivo*, and monocytes from mouse spleen *in vitro*.
Results We found that skin injury induced by SLE serum was more severe in female mice and required monocytes. E2