monocytes, despite CX3CR1s ubiquitous expression. We aimed to characterize the expression of CX3CR1 on sub-populations of monocytes in early and established RA and to ascertain the functional consequences of the interaction of chemokine and receptor on monocyte biology in RA

Methods: We recruited 83 subjects with early (21), established active (46) or inactive RA (16) and 13 healthy controls as a comparator group. Monocyte subsets (CD14 + CD16- and CD14 + CD16-) were defined by flow cytometry and CX3CR1 surface expression was determined by its Relative Fluorescent Intensity(RFI). Soluble FKN(sFKN) was quantified in peripheral blood (PB) and synovial fluid (SF) by ELISA. The effect of membrane-bound FKN (mbFKN) on osteoclast differentiation of monocyte subsets was assessed in vitro. Serum from subjects with the combination of elevated CD16+ monocytes and increased sFKN were analysed using a multiplex cytokine array and compared with controls.

Results: The percentage of circulating CD16+ monocytes was increased in the active RA groups [early, mean (+/-SEM) 24.22% (3.9) and active RA, 21.99% (2.61] in comparison with inactive disease 12.9% (2.2), $p = 0.04$, and healthy controls 11.1% (0.89), $p = 0.03$. Furthermore, individuals with increased sFKN and elevated CD16+ monocytes had significantly more circulating Il1a,-1b,-2,-10 and TNFα than controls.

Downregulation of CX3CR1 on the osteoclast progenitor CD16- sub-population was restricted to active RA, $p < 0.005$. Additionally, CX3CR1 surface expression was down-regulated on CD16+ monocytes in established RA but not in early arthritis, $p = 0.004$. Serum sFKN was significantly higher in active RA, $p = 0.02$. CX3CR1 down-regulation was replicated in vitro by co-incubation with sFKN. MbFKN significantly enhanced the osteoclastogenesis of the CD16- monocyte subset ($p < 0.0001$) potentially mediated by a decrease in CX3CR1 surface expression.

Conclusions: These findings support the presence of a unique monocyte phenotype in established RA. The downregulation of CX3CR1 on osteoclast precursors is mediated by the interaction with FKN. In addition the pro-osteoclastogenic effect of mbFKN strongly supports that this chemokine partnership is critical to the erosive process in RA.

Disclosure statement: The authors have declared no conflicts of interest.

Cytokines and inflammatory mediators

25. CERTOLIZUMAB PEGOL HAS A DIFFERENT PROFILE FROM THE OTHER ANTI-TNFS, INCLUDING GOLIMUMAB, IN A VARIETY OF IN VITRO ASSAYS

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Background: Activities of the anti-TNFs, certolizumab pegol (CZP), etanercept (ETA), infliximab (IFX) and adalimumab (ADA), have been compared in a range of in vitro assays. CZP is the only licensed PEGylated Fab' anti-TNF; ETA is a fusion protein with an IgG1 Fc, and IFX and ADA are both antibodies with an IgG1 Fc. Golimumab (GLM) is a monoclonal IgG1 TNF inhibitor recently approved for a number of indications; it is thus of interest to assess the in vitro activity of GLM. In vitro assays previously used were neutralisation of TNF in the L929 bioassay, inhibition of LPS-driven cytokine production by monocytes, induction of apoptosis in activated lymphocytes and monocytes, and induction of neutrophil necrosis.

Methods: Neutralisation of human TNF was assessed in the L929 bioassay using a range of concentrations of the anti-TNFs and a fixed concentration of TNF (100 pg/mL). Activity of the anti-TNFs at inhibiting LPS-driven IL-1β secretion by monocytes was assessed by incubating peripheral blood monocytes with various concentrations of the anti-TNF for 1 hour (hr) and then washing the cells. LPS was added for 4 hrs, the supernatants collected and the IL-1β level measured by ELISA. To assess induction of apoptosis, peripheral blood lymphocytes were activated for 2 days with 2 μg/mL CD3/CD28 and monocytes with 300 U/mL IL-4 and GMCSF for 3 days. The effect of the anti-TNFs on apoptosis was assessed by Annexin V staining using flow cytometry 24 hrs later. The effect of the anti-TNFs on neutrophil necrosis was determined by measuring myeloperoxidase release after 12 hrs. An isotype-matched control was used in all assays except the L929 bioassay.

Results: IC_{90} neutralisation activity of the anti-TNFs in the L929 bioassay was 0.3 ng/mL for ETA, 4 ng/mL for GLM, 15 ng/mL for ADA, and 20 ng/mL for IFX, compared with 2.5 ng/mL for CZP. CZP was the most potent inhibitor of LPS-driven IL-1β secretion (IC_{50} ~0.1 ng/mL), followed by GLM (20 ng/mL) and IFX (50 ng/mL). GLM, ADA, IFX and ETA induced apoptosis of monocytes and lymphocytes to a similar degree reaching a level of 23% and ~40% at 100 μg/mL, respectively. CZP caused no increase in apoptosis above the levels seen with the isotype-matched control. In the neutrophil necrosis assay, ADA,IFX and GLM caused ~70% necrosis at 100 μg/mL, and ETA 48%. CZP did not increase the level of necrosis above the level of the control.

Conclusions: Bioactivity of the IgG1 molecules GLM, IFX and ADA in neutralising human TNF was inferior to that of CZP and ETA. CZP, the only PEGylated anti-TNF, had a different profile to the other anti-TNFs as it was the most potent at inhibiting LPS-driven IL-1β production by monocytes, did not induce apoptosis of activated monocytes and lymphocytes, and did not cause neutrophil necrosis. The clinical relevance of these in vitro effects is unknown. Nevertheless, these assays show interesting in vitro differences between the anti-TNFs.

Disclosure statement: G.F. and A.N. are employees of UCB.

26. CHEMOKINE-STIMULATED ENDOTHELIAL MICROVILLI AND THEIR ROLE IN INFLAMMATION

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease in which chemokines have been shown to have an important role. Chemokines are known to be inflammatory mediators and attract leukocytes to sites of inflammation; this is achieved by binding to glycosaminoglycan (GAG) chains on the luminal endothelial cell (EC) surface and presentation to leukocyte chemokine receptors.

Methods: This study investigated the chemokine binding molecules present in RA synovium and found that there were specific sulphated heparan sulphate (HS) structures in situ that may be involved in chemokine binding. CXCL8, an inflammatory chemokine that is known to be angiogenic, was shown to induce the formation of microvilli on ECs however, this was not just specific to CXCL8 since the same effects were observed with CXCL10 (IP-10) and CCL5 (RANTES). In vitro studies revealed colocalisation of CXCL8 and HS on the endothelial microvilli. This suggests that the HS-CXCL8 interaction has an important role in leukocyte transendothelial migration, since removing HS caused a significant decrease in the number of leukocytes undergoing transendothelial migration.

Results: Transmission electron microscopy imaging showed that CXCL8-stimulated microvilli interacted with leukocytes prior to transendothelial migration occurring, this again is suggestive that the microvilli are involved in leukocyte transendothelial migration.

Mass spectrometry analysis of CXCL8-stimulated ECs showed significant changes in cytoskeletal proteins, adhesion and extracellular matrix proteins, and signal transduction proteins. This suggests that CXCL8 binding to receptors on the EC surface causes an alteration in Ras and Ca2+ signalling pathways, a reorganisation of the cytoskeleton and a disruption of the basement membrane, in order for the microvilli to form

Conclusions: Overall, there appears to be an important function for EC-microvilli and future targets of this could be of therapeutic advantage to chronic inflammatory diseases such as RA.

Disclosure statement: The authors have declared no conflicts of interest.

27. EVOLUTION OF ECTOPIC LYMPHOID NEOGENESIS AND IN SITU AUTOANTIBODY PRODUCTION IN AUTOIMMUNE DIABETIC NOD MICE: CELLULAR AND MOLECULAR CHARACTERIZATION OF TERTIARY LYMPHOID STRUCTURES IN PANCREATIC ISLETS

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Background: A pivotal role for tertiary lymphoid structures (TLS) in promoting antigen-specific humoral responses during chronic inflammation is emerging in several autoimmune conditions, including rheumatoid arthritis, Sjogren's syndrome and autoimmune thyroiditis.

However, there is limited evidence on the cellular and molecular mechanisms underlying TLS formation and their contribution to autoimmunity in the pancreas during autoimmune insulitis.
Methods: Here we performed a detailed and comprehensive assessment of the evolution of TLS during autoimmune insulitis in 126 female NOD mice from 4 to 38 weeks of age.
Results: We demonstrated that during progression from peri- to intra-insulitis in early diabetic mice, T and B cell infiltration follows a highly regulated process with the formation of lymphoid aggregates characterised by T/B cell segregation, follicular dendritic cells (FDC) networks and differentiation of germinal center (GC) B cells. This process is preceded by local up-regulation of lymphotoxins(Lt)α/β and lymphoid chemokines (CKs) CXCL13 and CCL19 and is associated with infiltration of B220/ IgD+/CD23+/CD21- follicular B cells expressing CXCR5. Despite a similar incidence of insulitis, late diabetic mice displayed a significantly reduced incidence of fully organized TLS and reduced levels of Lt/CKs. Upon development, TLS were fully functional in supporting in situ autoreactive B cell differentiation, as demonstrated by the expression of activation-induced cytidine deaminase (AID), the enzyme required for Ig affinity maturation and class-switching, and the presence of CD138+ plasmacells displaying anti-insulin reactivity.
Conclusions: Overall, our work provides direct evidence that TLS are of critical relevance in promoting autoimmunity and chronic inflammation during autoimmune insulitis and diabetes in NOD mice.
Disclosure statement: The authors have declared no conflicts of interest.

28. TOLL-LIKE RECEPTOR SIGNALS MODIFY THE ENDOPLASMIC RETICULUM STRESS RESPONSE

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Background: During cellular stress, the decrease in protein translation caused by eIF2α phosphorylation reduces protein load in the endoplasmic reticulum (ER) which allows the cell a window of time to instigate a program of gene expression known as the unfolded protein response (UPR). To allow the recovery of protein translation, GADD34 is activated in a negative feedback loop which dephosphorylates eIF2α and enables more efficient protein translation and recovery from cellular stress. We have previously shown that ER stress signals are induced following bacterial infection and that these signals synergise with Toll-like -receptor (TLR) signals to enhance the expression of cytokines such as IL-23. The aim of this study was to determine if TLR signals have a reciprocal activity and modify the ER stress response and in particular the expression of GADD34, the molecule involved in translation recovery from ER stress.
Methods: Monocyte derived dendritic cells (mDC) were subjected to ER stress using thapsigargin (TP) or tunicamycin (TM) in the presence or absence of different pattern recognition receptor (PRR) agonists. mDC were also infected with the obligate intracellular bacterium, *Chlamydia trachomatis* (CT). The expression of GADD34 was analysed by real time qPCR and immunoblotting. To determine which TLR signalling pathways were involved in the upregulation of GADD34 we manipulated TLR signalling pathways in THP-1 cells by the expression of shRNA that targeted MyD88 expression.
Results: The expression of GADD34 mRNA and protein was induced by the ER stress stimuli, tunicamycin but was significantly enhanced by stimulation with LPS (TLR4), Curdlan (dectin 1) or peptidoglycan (TLR2 and NOD2) agonists. Substantial upregulation of GADD34 expression was detected in mDC and THP-1 following infection with CT. The upregulation of GADD34 induced by PRR agonists or CT infection was reduced in THP-1 cells expressing MyD88 shRNA. Using specific inhibitors for defined signalling pathways we identified that upregulation of GADD34 was dependent on the activity of p38Map kinase.
Conclusions: These data suggest that GADD34 upregulation is a common feature of PRR responses when ER stress signals are present. Furthermore intracellular bacterial infection is a potent signal for GADD34 expression and that Myd88 dependent signals are required for these responses.

These data show that the regulation of protein translation has not only the potential to be modulated via ER stress but also via the stimulation of PRR pathways. This may have significant implications for the expression of pro-inflammatory or regulatory cytokines. We hypothesize that changes in GADD34 expression induced by TLRs will contribute significantly to the ability of myeloid cells to secrete pro-inflammatory cytokines in response to bacterial infection.
Disclosure statement: The authors have declared no conflicts of interest.

29. HUMAN (H161R) IL-17F MUTANT IS A DUAL ANTAGONIST OF IL-17A AND IL-17F

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Background: The proinflammatory cytokine IL-17A and its closely related isoform IL-17F play a key role in the pathogenesis of rheumatoid arthritis (RA). IL-17A and IL-17F induce the secretion of mediators of inflammation and growth factors such as TNF-alpha, IL-1, IL-6, IL-8, matrix metalloproteases, GRO-alpha, MCP-1, PGE2 and NO; inhibit cartilage synthesis and promote destruction of cartilage and bone. In animal models of arthritis, administration of exogenous IL-17A and IL-17F exacerbated arthritis while blockade of IL-17A ameliorated the disease. In patients with RA, the levels of IL-17A and IL-17F are increased in the synovium and the synovial fluid. Recent phase I and II trials of neutralisation of IL-17A in RA using IL-17 monoclonal antibody have reported significant clinical improvement and no notable side-effects.

A natural variant of IL-17F, (H161R) IL-17F mutant, resulting from substitution of Histidine at amino acid position 161 by Arginine was reported to be an antagonist of IL-17F [1]. Individuals having homozygous alleles for this mutant are protected from asthma. In in vitro studies, the mutant was unable to activate downstream signaling pathways in bronchial epithelial cells (BEC). Further, it competitively inhibited the induction of IL-8 secretion by the wild-type IL-17F in BEC. Hypothesis: IL-17A and IL-17F genes share 55% sequence homology, the proteins bind to the same hetero-receptor IL-17R A/C and have overlapping biological functions. The striking structural and functional similarities between the two isoforms of IL-17 point towards a strong possibility that in addition to IL-17F, the (H161R) IL-17F mutant is also an inhibitor of IL-17A.
Methods: Human IL-17A and IL-17F were cloned into the expression plasmid vector pcDNA3 at BamH1 and Xba1 sites. To create (H161R) IL-17F mutant, the carboxy terminal end of IL-17F at BSPM and Xba1 sites was substituted by custom-ordered oligonucleotide that contained the mutated base pair and cloned into the pcDNA3. The constructs were expressed by transient transfection of 293T cells. The expressed proteins were immunoprecipiated and shown to have the expected molecular weight of 17.5 kDa by Western blotting.

Biological activities of human IL-17A and IL-17F were assessed by measuring IL-17-induced production of IL-6 in HeLa cells by ELISA. Competitive inhibition assays were carried out to determine the degree of inhibition of IL-17A and IL-17F-induced secretion of IL-6 in HeLa cells by addition of equal concentrations of the IL-17F mutant.
Results: IL-17F mutant competitively inhibited IL-17A- and IL-17F-induced secretion of IL-6 in HeLa cells by 76% and 59%, respectively as measured by ELISA.
Conclusions: Results of the study reveal for the first time that(H161R) IL-17F mutant is an antagonist of both IL-17A and IL-17F.
Disclosure statement: Y.C., R.M. and G.M. have received research grants from Barts and The London Charity and Arthritis Research UK.

Reference:

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30. CANAKINUMAB PROVIDES RAPID IMPROVEMENT WITH SUSTAINED CLINICAL AND INFLAMMATORY REMISSION IN CRYOPYRIN-ASSOCIATED PERIODIC SYNDROME PATIENTS ACROSS ALL SEVERITY PHENOTYPES

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Background: Cryopyrin-associated periodic syndrome (CAPS) is a spectrum of hereditary fever diseases including, familial cold auto-inflammatory syndrome [FCAS]; Muckle-Wells syndrome [MWS]; neonatal-onset multisystem inflammatory disease/chronic infantile neurological cutaneous and articular syndrome/ [NOMID/CINCA]) associated with mutations in NLRP3 causing overproduction of interleukin-1β (IL-1β). Effect of selective and prolonged IL-1β blockade with canakinumab, a fully human mAb, was evaluated in the largest cohort of CAPS patients studied to date.
Methods: Canakinumab-naïve or pretreated patients from earlier studies received canakinumab s.c. 150 mg or 2 mg/kg (≤40 kg) every 8 weeks for up to 2 years. Primary objective was to assess the long-term safety and tolerability of canakinumab in CAPS patients. Key assessments included complete response (CR, for naïve patients), response maintenance, and percentage of patients requiring dose adjustments. CR was defined as physician's global assessment of disease activity (PGDA) and skin assessment≤minimal and normal CRP and/or SAA values (<10 mg/L). Relapse was defined for patients with complete response as serum CRP and/or SAA levels>30 mg/L and PGDA> minimal or PGDA=minimal plus skin assessment>minimal.
Results: This phase III, open-label study enrolled 166 (47 paediatric) patients aged 3-91 years (30 FCAS; 103 MWS; 32 MWS/NOMID [14 NOMID/CINCA]; one child without CAPS discontinued [protocol violator]). 109 patients were canakinumab-naïve and 57 were pre-treated with canakinumab. 151 (91%) patients completed the study and 15 patients discontinued (3 due to adverse events [AEs]). Median treatment duration was 414 days (range 29-687 days) and the mean number of injections/patient was 7.2. CR was achieved in 85/109 (78%) canakinumab-naïve patients (79 achieved CR within 8 days, and others later within 21 days). Of the 141 patients with relapse assessment, 127 (90%) had no relapse, 14 (10%) relapsed and 23 incomplete responders later had improvement of disease symptoms. Dose/dosing frequency adjustments were needed in 40 (24.1%) patients (19.3% adults vs 36.2% children). In canakinumab-naïve patients median CRP/SAA levels normalized by Day 8 [2.5/4.9 mg/L (at baseline 19.9/35.6 mg/L, respectively] and were maintained through 2-years in the entire cohort. Predominant AEs were infections (65%) of mostly mild to moderate severity. Most frequent AEs were nasopharyngitis, headache and rhinitis. Serious AEs were reported in 18 (11%) patients, mainly infections responsive to standard treatment. Injection-site reactions were absent in 92% of patients and 8% reported mild to moderate reactions.
Conclusions: Canakinumab 150 mg s.c. every 8 weeks provided rapid improvement of symptoms and sustained remission in a large cohort of CAPS patients across different severity phenotypes. Safety profile supported the earlier data, reassuring good tolerability and safety of canakinumab.
Disclosure statement: R.C. has received consultancy fees from Novartis Pharmaceuticals Corporation, and is/has been a member of speakers' bureaus for GlaxoSmithKline, Sanofi-Aventis, Pfizer, Inc. and UCB, Inc. M.G. is/has been a member of a speakers' bureau for Novartis Pharmaceuticals Corporation. A.G. has received consultancy fees from Novartis Pharmaceuticals Corporation, Pfizer, Inc. and UCB, Inc. E.H., P.H. and I.K. have received consultancy fees from Novartis Pharmaceuticals Corporation. J.K. has received a research grant and consultancy fees from Novartis Pharmaceuticals Corporation. H.L. has received a research grant from the EU framework, and consultancy fees from Novartis Pharmaceuticals Corporation. N.P. and R.P. are shareholders and employees of Novartis Pharmaceuticals Corporation. P.Q. has received a research grant and consultancy fees from Novartis Pharmaceuticals Corporation. A.W. is a shareholder and employee of Novartis Pharma AG. All other authors have declared no conflicts of interest.

31. IRF5 PROMOTES INFLAMMATORY MACROPHAGE POLARIZATION AND TH1/TH17 RESPONSE

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Background: Genetic polymorphisms in the interferon regulatory factor 5 (IRF5) gene, leading to expression of several unique isoforms of IRF5 or increased expression of IRF5 mRNA, are associated with a number of autoimmune diseases, including rheumatoid arthritis (RA), systemic lupus erythematosis (SLE), Sjogren's syndrome and atherosclerosis. The remarkable consistency of IRF5 detection in genome-wide association studies of autoimmune diseases is likely to relate to their common inflammatory origin. Many autoimmune diseases are characterised by the predominant presence of Th1/Th17 cells as well as macrophages. It has become increasingly clear that macrophages are dynamic and heterogeneous cells that can be divided into specific, although overlapping, subsets according to their polarization requirements, phenotype and function. Based on Th1/Th2 polarisation concept they are now referred to as pro-inflammatory classical M1 (IL-12high, IL-23high, TNFhigh, IL-10low) macrophages and anti-inflammatory M2 (IL-12low, IL-23low, TNFlow, IL-10high) macrophages. However, in contrast to T cell subsets, characterised by the expression of master regulator transcription factors, e.g. FOXP3, RORgammaT etc, the transcription factor(s) underlying macrophage polarization remain largely unknown.
Methods: Enriched populations of human monocytes were obtained from the blood of healthy donors and differentiated into M1 and M2 macrophages. Cytokine production (IL-12, IL-23, TNF, IL-1beta, IL-17, IL-10) was measured by ELISA and RT-PCR. Mixed lymphocyte reactions were performed to examine the effect of IRF5 expressing macrophages on lymphocyte proliferation, fate and activation state. Micro array analysis was used to define the IRF5-induced expression profile on a genome-wide level. ChIP was used to investigate the recruitment of IRF5 to specific target genes. The involvement of IRF5 in macrophage polarization was also investigated in vivo by performing a mouse model of M1 polarizing inflammation in wild-type and IRF5 knock-out mice.
Results: IRF5 directs transcriptional activation of the majority of M1-specific cytokines (IL-12, IL-23, TNF), chemokines (RANTES) and co-stimulatory molecules (CD40, CD86). It promotes T lymphocyte proliferation, the development of Th1/Th17 lineages and plays a major role in the plasticity of macrophages, from inflammatory to those that mediate resolution of inflammation. Furthermore, IRF5 controls macrophage plasticity by acting as a transcriptional repressor of IL-10 and other selected M2-specific molecules.
Conclusions: Here we define IRF5 as the first major transcriptional regulator of importance for the dichotomy between pro-inflammatory M1 and anti-inflammatory M2 macrophages. The identification of such a master regulator of macrophage phenotype and function has ramifications for all inflammatory diseases characterised by excessive type 1 cytokines and provides a potential new target for immune intervention.
Disclosure statement: The authors have declared no conflicts of interest.

32. 25-HYDROXYVITAMIN D_3 CONVERSION BY DENDRITIC CELLS AND T CELLS DRIVES 1,25-DIHYDROXYVITAMIN D_3-MEDIATED ANTI-INFLAMMATORY $CD4^+$ T CELL RESPONSES

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Background: Low vitamin D status is associated with an increased risk of autoimmune diseases, including rheumatoid arthritis. Thus, understanding how vitamin D modifies immune reactions holds therapeutic potential. We have shown that $1,25(OH)_2D_3$, the active form of vitamin D, acts directly upon human $CD4^+$ T cells, suppressing inflammatory cytokines (IL-17, IL-21, IFNγ and IL-22) whilst enhancing regulatory-markers (CTLA-4, CD25, FoxP3 and IL-10). However, the short half-life of $1,25(OH)_2D_3$ and its low serum level imply that local conversion of $25(OH)D_3$, the major circulating form of vitamin D, by 1α-hydroxylase (CYP27B1), is necessary for immune regulation in-vivo. Thus, we have studied the effect of $25(OH)D_3$ upon T cell responses. In view of the critical role of CTLA-4 in immune-regulation and its strong sensitivity to $1,25(OH)_2D_3$, we have also investigated CTLA-4 function in vitamin D-modified immune responses. Lastly, in considering a use for vitamin D in inflammatory arthritis treatment, we analysed its effects upon T cells from synovitis patients.
Methods: $CD4^+CD25^-$ T cells were purified from human peripheral blood (PB) and stimulated with LPS-matured allogenic dendritic cells

(DCs) plus antiCD3 or with antiCD3/CD28 beads in the presence and absence of $25(OH)D_3$. FoxP3, CTLA-4 and cytokines were measured by flow cytometry and CYP27B1 by qPCR. In function assays, CTLA-4 was blocked with antiCTLA-4 and T cell division monitored by CFSE. DC expression of CD80 and CD86 was assessed by flow cytometry. Synovitis patients were recruited from Birmingham City Hospital. Their PB and synovial fluid (SF) mononuclear cells were stimulated with antiCD3 in the presence and absence of $1,25(OH)_2D_3$ and cytokines examined by flow cytometry.
Results: Stimulation of T cells by DCs in the presence of $25(OH)D_3$ led to strong suppression of IL-17 and IFNγ but up-regulation of CTLA-4 and CTLA-4^+FoxP3^+ frequencies. By contrast, in the absence of DCs, $25(OH)D_3$ caused modest CTLA-4 induction and IFNγ suppression ($P < 0.05$ for all). These differences corresponded with CYP27B1 levels, as maturation induced much higher CYP27B1 in DCs than arose in T cells ($P < 0.05$). CTLA-4 blockade overcame $1,25(OH)_2D_3$-mediated suppression of T cell division in DC stimulations and prevented down-regulation of co-stimulatory CD80 and CD86 on DCs. PB T cells from synovitis patients responded normally to $1,25(OH)_2D_3$ with suppressed IL-17 and IFNγ ($P < 0.0001$). $1,25(OH)_2D_3$ also reduced SF IL-17 ($P < 0.05$) but not IFNγ.
Conclusions: We have shown that DCs can efficiently convert $25(OH)D_3$ to drive $1,25(OH)_2D_3$-modified T cell responses and that up-regulation of CTLA-4 is mechanistically important in immune suppression by vitamin D. Thus, $25(OH)D_3$ supplement could be useful in the treatment of conditions such as RA. This is supported by our finding that T cells from synovitis patients can respond to $1,25(OH)_2D_3$.
Disclosure statement: The authors have declared no conflicts of interest.

Education research

33. EVALUATION OF THE FIRST BSR ULTRASOUND ANATOMY TRAINING COURSE

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Background: The expansion of US availability has allowed increasing numbers of rheumatologists to perform MSKUS in clinic. As yet there is no formalized program of ultrasound learning or competency assesment for rheumatologists. Detailed understanding of 3D ultrasound anatomy is recommended by European authors but very few UK rheumatologists have recieved any formal anatomy training since medical school.
Methods: The aim was to deliver a short anatomy training course in an anatomy laboratory for rheumatologists tailored to the published BSR ultrasound competency outcomes. The course was intended to be learner centred, clinically meaningful and as recommended in current anatomy teaching guidance the course would use a variety of learning techniques in small groups including dissected prosections, ultrasound demonstrations on living models, radiological images and 3D interactive software. This new course took place at Newcastle University Anatomy Laboratory with 15 delegates in October 2010.
Results: In a specific questionaire survey of the 15 delegates (Likert scale 1-5, not agree at all-very much agree), the aims and objectives of the course were considered to have been acheived. AIMS: to help understanding and interpretation of the human anatomy encountered using US (4.5), facilitate progression through levels of US competency (3.7). OBJECTIVES: identification of the relevant anatomical structures using regional cadaveric anatomy (4), increase confidence in identifying anatomical structures using USS (3.5), and identification of surface anatomy of regional anatomical structures (3.9). The course methods recieved high scores - learner centred (4.3), clinically meaningful (4.6), and the tutors were considered to be experts in their field (4.8). In qualitative feedback, 3D anatomy skills were self reported ''seriously deficient'' prior to the course and opportunity to handle prosections was ''highly valued''. There was some support for course attendance counting towards a formal postgraduate certificate in US, but limited interest among respondees in a formal anatomy assessment within the course (2.5). This one day course allowed very limited time for US practice which was a percieved deficiency (2.54).
Conclusions: A coordinated approach is needed to ensure US competency among rheumatologists, and this short anatomy training course with expert tutors (radiologists, anatomists and rheumatologists with US skills) acheived specific aims and objectives including increased confidence in identifying anatomical structures using US, though it is not known if the course improved anatomy skills and knowledge.
Disclosure statement: The authors have declared no conflicts of interest.

34. WHAT DO PEOPLE WITH PRIMARY SYSTEMIC VASCULITIS WANT TO KNOW ABOUT THEIR ILLNESS?

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Background: The primary systemic vasculitides; Wegener's granulomatosis (WG),Churg Strauss syndrome (CSS), Microscopic polyangiitis (MPA) and Polyarteritis Nodosa (PAN) are a group of rare conditions. Modern therapy has converted these diseases from ones with a very poor outcome to chronic diseases, which relapse and remit. Very little is known about the educational needs of this group of people.
Methods: A postal questionnaire survey of the membership of the Stuart Strange Trust (a national UK vasculitis support group). Respondents were asked to rank using a 5-point scale (1= not important to 5 = extremely important) the importance of providing accurate information using the following categories: disease, medication and side effects, disease management, investigations and tests, psychosocial care, and the preferred method of educational delivery. Data was collected on who provided information at diagnosis
Results: 1000 questionnaires were distributed, 397 returned, 63 excluded not PSV, 40 returned not known at the address. 329 responses were available for analysis. Diagnosis WG 255, CSS 46, PAN 15, MPA 13. 65% of respondents were male, median age 63 years (interquartile range 52-70), median disease duration 5 years (interquartile range 4-6y). Only 41% of people received information at diagnosis. Of these, the majority of information was provided by a doctor 71%, other 18.5%, relative 5.7% and a nurse 4.8%. Respondents ranked information on diagnosis, prognosis, results of tests, treatments and side effects of medication as extremely important. Lifestyle issues were very important. Surprisingly information on patient support groups and psychosocial care was viewed as less important. There were no real differences in information needs between the sexes and disease duration. Individuals preferred to be told by a doctor that they had vasculitis and for this to be supported with an information leaflet about their particular disease
Conclusions: This study highlighted that people with PSV required a significant amount of information concerning their disease, treatment regimes and side effects and the results of investigations and tests. Individuals preferred to receive this information from a doctor. However a significant number of people did not receive any information. These individuals should be treated like other chronic illnesses where patient education is a fundamental part of patient care. Education programmes for PSV should be developed to empower patients to become active partners in the management of their condition.
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35. ADHERENCE TO TREATMENT OF THE ELDERLY PATIENTS WITH INFLAMMATORY ARTHRITIS AT THE RHEUMATOLOGY UNIT

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Background: For optimal health recovery, adherence to medication is very important [1]. According to dherence to treatment is the behaviour of how an individual takes his medication [2]. Adherence or compliance can be used simultaneously. Salzman (1995) [3], estimated that non-compliance in the elderly can vary from 40% to as much as 75%. There can be three forms of non-compliance: overuse and abuse, forgetfulness and changing of doses and schedules.
Methods: This was a quantitative study of a sample population of 50 patients aged over 60 years. These patients were assessed at the outpatient rheumatology clinic in mater dei hospital in Malta. The aim of the study was to assess adherence to medication in the elderly population over the age of 60 who suffer from an inflammatory arthritis and who are on treatment. Patients could be on one drug or double or triple therapy. A validated questionnaire was used to assess the patient's adherence to their prescribed medication. The questionnaire was used before and one month after the counselling on increasing