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Description of Patterns of Active Joint Count Trajectories in Juvenile Idiopathic Arthritis

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Objective: To describe the patterns of longitudinal disease activity (active joint count (tender and swollen joints) in juvenile idiopathic arthritis (JIA) and to examine the association of clinical and laboratory characteristics with these patterns.

Methods: A retrospective cohort study at two Canadian centres was performed. The longitudinal patterns of active joint counts were described using latent variable growth modeling analysis. This method is ideally suited to a population whereby the underlying hypothesis is that the population is comprised of (unobserved) subpopulations. Latent variable growth modeling aims to classify individuals into statistically distinct groups based on individual response patterns so that individuals within a group are more similar than individuals between groups. The trajectory classes are each defined by a longitudinal growth curve. The association of baseline characteristics with class membership was examined using a multinomial logistic regression.

Results: Data were analyzed on 659 children diagnosed with JIA between 1990/03-2009/09. The median age at diagnosis was 10.00 (IQR 3.67-13.39), 61% (402/659) were female and 45% (286/629) were ANA positive. The distribution of the ILAR diagnoses were as follows: systemic (7%), oligoarthritis-persistent (34%), oligoarthritis-extended (6%), polyarthritis (RF negative) (15%), polyarthritis (RF positive) (4%), psoriatic arthritis (8%), enthesitis-related arthritis (22%) and undifferentiated (4%). A maximum of 10 years of follow-up data was included in the longitudinal analysis. The 659 patients were classified into 5 statistically different patterns of longitudinal active joint count (AJC) profiles using growth mixture modeling. 44% of patients were in group 1 characterized by a low initial AJC (mean 0.9) following by a decrease in joint count, 18% in group 2 with minimal to no active joint disease throughout course (mean 0.3), 19% in group 3 with persistent low AJC (mean 2.8), 10% in group 4 with initial mean AJC 4.9 followed by an increase in AJC at 5 years (mean 9.7) and finally 10% in group 5 characterized by an initial mild polyarthritis (mean 12.7) followed by a decline in AJC.

Conclusion: Using a novel longitudinal statistical method we were able to classify patients with JIA based on their pattern of active joint count over time. These results need to be interpreted in light of clinical significance. Examination of the association of baseline characteristics with each trajectory is ongoing. Identification of patterns of disease course is important in working towards the development of an outcome-based classification system in JIA.

Application of High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT) To Diagnose and Quantify Bony Damage in Rheumatoid Arthritis

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Objective: (1) Determine the performance of high-resolution peripheral quantitative computed tomography (HR-pQCT) (isotropic voxel size of 82 μm) in the diagnosis of RA. (2) Provide quantitative assessment of joint space narrowing, erosions and peri-articular morphometric indices.

Methods: PIP and MCP joints of the dominant hand of 15 patients with established RA and their age- and sex-matched control patients were imaged by HR-pQCT (XtremeCT; Scanco Medical, Switzerland). Various models of erosion number and location were tested to determine the optimal diagnostic test performance for HR-pQCT compared to the clinical diagnosis of RA. Quantitative measures of bony damage were calculated from 3D images of the joints, reconstructed by a semi-automated segmentation program that identifies bone mineral based on changes in the gray-scale. The minimum joint space width was calculated by counting the number of voxels between articular surfaces (Image Processing Language). Standard morphometric indices were calculated for a predetermined region of interest for the MCP joints. The number and location of erosions were assessed visually from the two-dimensional images. Reproducibility was assessed by recontouring and segmenting a random sample of images.

Results: The best test performance for the clinical diagnosis of RA was determination of an erosion in MCP2 (sensitivity 76.9%, specificity 93.3%, ROC area 0.851, positive likelihood ratio 11.5 (95%CI 1.7-78.4)). Reproducibility was good for bone density parameters (all root square mean coefficients of variance < 1%), but less so for joint space measurements (17%), perhaps related to difficulties in contouring angulated joints. Joint space narrowing was detected in the MCP joints of RA patients compared to controls (relative difference for the 2nd MCP 131 μm ; 3rd MCP 262 μm ; 4th MCP 106 μm ; 5th MCP 145 μm). There were no significant differences in morphometric indices between patients and controls. The majority of RA erosions occurred at the proximal bone surface, with a mean of 23.6 erosions over the 10 joints. Erosions were detected in some controls, mainly in the IP and PIP joints.

Conclusion: In this pilot study, HR-pQCT demonstrated good performance characteristics for RA diagnosis. Methods to provide quantitative measurements of bony damage in established RA have been developed. Differences in joint space width are most pronounced at the MCP joints. A larger sample size may reveal detectable differences in morphometric indices between subjects with active inflammatory arthritis and those without. Erosions at MCP2 are highly specific for RA, but erosions were detected in controls unrelated to clinical disease.

Disease-free First-degree Relatives of RA Patients have a Serum Cytokine Profile that is Intermediate Between their Affected Relatives and Controls having no Family History of Autoimmunity

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Objective: RA is prevalent in North American Native (NAN) populations, with a high frequency of multi-case families. We have studied the first-degree relatives (FDR) of NAN RA probands and prospectively followed this cohort for the earliest evidence of disease onset. Previous data from studies of pre-clinical RA cohorts suggest that RA autoantibodies and serum cytokines can predict the onset of clinical disease. Thus, we sought to determine whether serum cytokine profiles can predict disease onset in healthy individuals belonging to high risk NAN families.

Methods: We studied NAN RA patients (n=105), their disease-free FDR (n=123), healthy NAN (NC) (n=100) and Caucasian controls (CC) (n=100) with no family history of autoimmune disease. Rheumatoid factors (RF) and anti-citrullinated protein antibodies (ACPA) were assessed using nephelometry and ELISA. We used a cytokine/chemokine 42-plex array to test a range of pro and anti-inflammatory cytokines. Raw cytokine data were normalized and differences between groups were analyzed using ANOVA. Discriminant analysis was used to classify individuals based on 2 canonical functions generated from the transformed cytokine data.

Results: The NAN FDR and NC groups were well matched for age and gender, while the RA and CC groups were older. The prevalence of RF and/or ACPA in the 4 groups was RA= 81%, FDR=33%, NC=1% and CC=1%. Levels of almost all cytokines tested were markedly elevated in the RA patients compared to all other groups; 20/42 (48%) of the cytokines were significantly higher in the FDR compared to NC and CC, in particular IFN α , MCP-1, IL-1b, TNF α . Discriminant analysis showed a remarkable distinction between RA, FDR, and controls based on the canonical function centroids. Centroids from NC and CC were similar. A model based on the functions correctly classified 85% and 96% of the FDR and controls, respectively. Gender, age, and autoantibody status did not add to the model. Longitudinal levels in disease-free RF \pm ACPA positive FDR remained relatively stable. Cytokine profiling in 3 FDR who have developed clinical onset of synovitis demonstrated a sharp rise on most cytokines with disease onset, and subsequent levels reflected disease activity.

Conclusion: Both pro and anti-inflammatory cytokines are elevated in RA. Surprisingly, levels of these biomarkers are also significantly higher in disease-free FDR from autoimmune families compared to individuals from non-autoimmune families. These data suggest that elevated basal cytokine levels, potentially based on genetic or epigenetic factors, may be part of the risk profile for developing of RA in families at risk for autoimmune disease.

Response to Second-Line DMARDs and to Biologics in Seropositive vs. Seronegative Patients in Early and Late RA: Results from the CATCH Cohort of Early RA and a Large Established RA Database

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Objective: To investigate differences in treatment response to second-line DMARDs and to biologics in seropositive versus seronegative rheumatoid arthritis patients. Some treatment responses have been found to be blunted in RF negative RA such as treatment with rituximab. We wanted to determine if this was the case with DMARDs and TNFis in two cohorts.

Methods: Patients from the CATCH ERA Cohort who had failed first line DMARD therapy and continued to second-line therapy were selected. These were defined as those on first-line therapy with DAS28 $>$ 2.6 who added new DMARD(s). Patients treated with DMARDs before inclusion in the CATCH cohort were excluded from the analysis. The proportion achieving DAS $<$ 2.6 in next 6 months after the first addition of DMARD(s) were compared with regards to RF status and anti-CCP status. Similarly, patients with DAS28 $>$ 2.6 adding biologic therapy were selected and the proportion achieving DAS $<$ 2.6 in the next 6 months were compared with regards to RF and anti-CCP status using Pearson Chi-square analyses. In an established RA Cohort from an outpatient rheumatology practice at London, Ontario, RA patients using TNFis were studied by response to treatment by RF status on HAQ-DI and pain change, and proportion of patients still on first TNFi using T tests (two-tailed, equal variances assumed) and Chi-square analyses.

Results: CATCH Cohort: No significant difference was found in second-line DMARD response between RF+ and RF- groups as well as in anti-CCP+ and negative groups. Proportion achieving DAS $<$ 2.6 at follow-up after initiating biologic therapy was significantly higher in anti-CCP - patients (14/22=63.6%) versus Anti-CCP+ patients (11/32=34.4%) $p=0.034$. Established RA Cohort: Mean one year HAQ-DI change was found to be significantly greater in 90 RF+ patients at $\$0.356$ versus 38 RF- patients at $\$0.126$ ($p=0.043$). Mean HAQ-PS change was also found to be significantly greater in 77 RF+ patients at $\$0.725$ versus 32 RF- patients at $\$0.332$ ($p=0.031$).

Conclusion: RF+ patients with established disease may be more responsive to TNFi therapy as measured by changes in HAQ and pain. Perhaps in established RA with DMARD failure, any biologic may have a blunted response in RF negative patients as was previously found with rituximab. However, anti-CCP negative patients may also be more responsive to TNFi therapy in ERA but other datasets may be needed to confirm these results.

The Functional MICA-129 Polymorphism is Associated with Psoriatic Disease Independently of HLA-B and C

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Objective: The major histocompatibility complex chain-related gene A (MICA) is located 47kb centromeric to HLA-B. MICA alleles can be classified into high and low-affinity binders of the natural killer/T-cell receptor NKG2D, based on a functional polymorphism at amino acid 129 (Met/Val). Our aim was to determine whether the high affinity MICA-129 Met allele is increased in psoriatic arthritis patients compared to patients with psoriasis without arthritis and controls.

Methods: 248 unrelated Caucasian psoriatic arthritis patients, 250 psoriasis subjects without arthritis, and 249 healthy controls were allelic typed for MICA using PCR-SSP and for HLA-B and C by PCR-SSO reverse line blot. All psoriatic arthritis patients satisfied CASPAR criteria and psoriasis subjects were examined by a rheumatologist to exclude psoriatic arthritis. MICA-129 Met/Val genotypes were assigned from allelic typing using DNA sequences available from the IMGT/HLA database (release 3.1.0). Univariate logistic regressions and chi squared tests were performed to determine the effect of MICA-129 genotype on group membership. Multivariate logistic regressions were also performed using the Val/Val genotype as the reference category, to adjust for the presence of HLA-B*13, B*27, B*38, B*57, C*01, C*02, C*06, and C*12.

Results: Univariate analyses showed that the presence of a Met allele significantly increased the risk of developing psoriatic disease (OR=1.6, $p=1.5 \times 10^{-3}$), psoriasis without arthritis (OR=1.7, $p=5.3 \times 10^{-3}$), and psoriatic arthritis (OR=1.6, $p=7.7 \times 10^{-3}$). Multivariate analyses showed that after adjustment for significant HLA-B and C alleles, homozygosity for the Met allele (genotype Met/Met) significantly increased risk of psoriatic disease (OR= 3.8, $p= 1.0 \times 10^{-4}$), psoriasis without arthritis (OR = 2.8, $p= 6.1 \times 10^{-3}$), and psoriatic arthritis (OR = 2.4, $p= 2.7 \times 10^{-2}$). Heterozygosity (Met/Val) did not affect risk. There were no significant differences in MICA genotypes between patients with psoriatic arthritis and psoriasis without arthritis.

Conclusion: Individuals with a high-affinity Met residue at MICA-129, particularly those who are homozygous for the Met allele (Met/Met), have an increased risk of developing psoriatic disease, psoriasis without arthritis, and psoriatic arthritis independently of the presence of HLA-B and C risk alleles.

A Longitudinal Trivariate Model of Disease Activity Score, Physical Function and Radiographic Damage: Results from SONORA Study

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Objective: Rheumatoid arthritis (RA) affects approximately 1% of adults in North America. Active disease leads to radiographic damage and poor physical function. There is no literature available on common predictors for these three important aspects, that is, disease activity score (DAS); physical function, which is health assessment questionnaire (HAQ) and radiographic damage (Sharp Score). The purpose of this study is to demonstrate the use of longitudinal trivariate model and address the issue of longitudinally relationship between DAS28, HAQ and Sharp score and identify the significant common predictors for three of them.

Methods: 994 Patients diagnosed as having new onset RA (symptoms ≥ 3 but ≤ 12 months) by a board-certified rheumatologist were recruited from 98 rheumatology practices. Clinical, laboratory, X-ray and health questionnaire data were collected by the enrolling rheumatologist at baseline, year 1 and year 2. A trivariate longitudinal model of DAS28, HAQ and sharp score was constructed and estimated using pooled cross sections for two years period, adjusting the significant predictors from the univariate analysis at the same time allowing for the latent individual-level effect. Different covariance structures were tested for the assumptions among these three outcomes in the model.

Results: The mean age of patients was 53 years (SD, 14.8), with 72% female and 90% Caucasian. The mean RA symptom duration was 170 days (180). The DAS28, HAQ and Sharp score were 4.4(1.32), 1(0.73) and 5.01 (7.28) at baseline, 3.4(1.38), 0.82(0.71) and 6.19(8.73) at year 1, 3.2(1.34), 0.77(0.72) and 6.39(9.25) at year 2, respectively. Partial correlation adjusting for time point showed that DAS, HAQ and Sharp score are significantly correlated (all p-values < 0.001). The longitudinal trivariate model showed that only higher baseline DAS, HAQ or Sharp Score value ($P < 0.0001$), higher 28 swollen joint count ($P < 0.0001$), longer disease duration ($P = 0.002$) and lower house hold income ($P = 0.015$) were significant predictors for these three combined outcomes.

Conclusion: This innovative method identified the significant common predictors for three outcomes which related to the different aspects of RA patients. This method can help us better understand the longitudinally complex relationship between different aspects from a broader view of the disease. These identified factors can help rheumatologists to identify the patients who are at greater risk of worsen disease, physical function and radiographic damage and make treatment decisions for RA patients at the early stage.

The Prevalence of Systemic Autoimmune Rheumatic Diseases in Canadian Pediatric Populations: Administrative Database Estimates

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Objective: Administrative healthcare databases offer interesting possibilities for national disease surveillance in Canada. Our aim was to use provincial administrative data to estimate pediatric-onset systemic autoimmune rheumatic disease (SARD) prevalence in Quebec (1994\$2003), Alberta (1994\$2007), and Manitoba (1995 to 2009).

Methods: We studied all health care beneficiaries aged 18 or younger. Data included all physician billing claims, and hospitalizations where discharge diagnoses indicate a systemic autoimmune rheumatic disease. We used three definitions: the first algorithm defined a case of SARDs on the basis of a hospitalization indicating a discharge diagnosis (primary or non-primary) for any SARD (including systemic lupus, scleroderma, or inflammatory myopathies). The second algorithm, using billing data, required two or more physician visits for these SARDs. (The visits had to occur at least two months apart, but within a two-year span.) In the third algorithm, cases were defined on the basis of one or more relevant billing code contributed by a rheumatologist. A subject was included in our prevalence estimates if they met one or more of these three algorithms, and were aged < 18 as of the end of the study interval in each province. We stratified our results by sex, and using postal code information also stratified by urban residence (defined as a census metropolitan area) versus rural residence.

Results: Pooling the data across provinces, the pediatric SARDs prevalence estimate was 18.9 cases per 100,000 (95% confidence interval, CI, 17.4, 20.6). Stratifying by sex, the SARDs rate was, as expected, higher in females (26.7 cases per 100,000 95% CI 24.0. 29.6) than males (11.5 cases per 100,000, 95% CI 9.8, 13.4). We found similar rates in SARDs in residents of rural areas (17.0 cases per 100,000, 95% CI 14.6, 19.7) and urban areas (20.1 cases per 100,000, 95% CI 18.1, 22.4).

Conclusion: In our work, prevalence estimates had fairly good face validity and potentially provide useful information about potential regional and demographic variations. Our results suggest that surveillance of some rheumatic diseases using administrative data may indeed be feasible.

Pathogenicity of Anti-Citrullinated Protein Antibodies (ACPA) from Unaffected First Degree Relatives (FDRs) of Rheumatoid Arthritis Patients in a Population of North American Natives (NAN)

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Objective: The prevalence of RA in NAN is approximately twice that of Caucasian populations. NAN also have a higher frequency of the Shared Epitope (SE), which is a major risk factor for RA and associated with ACPA. The rate of ACPA-positivity in unaffected FDR of NAN is 17%, much higher than in Caucasians (2%). We have previously reported that ACPA from RA patients injected intra-peritoneally (ip) into Fc γ RIIB-deficient mice induced inflammatory arthritis (IA); whereas, ip injections of IgG devoid of ACPA from the same RA patients did not. The objective of this study is to determine whether transferring ACPA from unaffected siblings of NAN RA patients into Fc γ RIIB-deficient mice induces inflammatory arthritis.

Methods: Patients were self-reported NAN recruited from the University of Manitoba Arthritis Centre Clinics and community health clinics on reserves in Manitoba and Saskatchewan. All patients met ACR criteria for RA and were positive for anti-CCP2. FDRs were deemed unaffected after assessment by a rheumatologist. ACPA was affinity purified using a synthetic citrullinated peptide (JED) and administered ip to Fc γ RIIB-deficient mice. ACPA were measured by ELISA; Rheumatoid Factor (RF) by nephelometry.

Results: Serum was obtained from 5 FDRs. Anti-CCP titres ranged from 7.7 to 138.9 RU/ml (mean 42.7). 2/5 were positive for anti-JED and anti-Modified Citrullinated Vimentin, 5/5 for anti-citrullinated Fibrinogen and 3/5 for RF. Both anti-JED positive FDRs were females (ages 30 and 38), current smokers and positive for SE. During the course of the study, one of these FDRs developed RA. The other FDR remained unaffected despite very high titre of anti-JED. Ip transfer of serum and ACPA from the FDR recently diagnosed with RA induced IA; whereas this subject's IgG devoid of ACPA did not (ankle widths 0.40, 0.39, 0.0625 mm respectively; $p < 0.001$, $p = 0.002$). Interestingly, the serum and ACPA from the unaffected FDR also induced IA (ankle widths 0.40 and 0.37 mm, respectively, vs. 0.005 mm in the IgG devoid of ACPA-injected mice; $p = 0.009$, $p = 0.008$).

Conclusion: Unaffected FDRs of RA patients of NAN ethnicity have a high prevalence of ACPA; although presence of anti-CCP2 does not necessarily correlate with positivity of other ACPA. Transfer of ACPA and sera from both affected and unaffected FDRs induced IA in a mouse model, suggesting a directly pathogenic role of ACPA in RA. Future work will involve recruiting more subjects and studying mechanisms by which unaffected ACPA-positive individuals develop RA.

Pregnancy and Rheumatoid Arthritis (RA): Observations in a Fertile First Nations Population at High Risk for RA Development

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Objective: Previous studies have suggested correlations between RA risk and pregnancy history. First Nations (FN) Canadians have a high risk of RA, develop disease at a younger age, and have a high birth rate. We compared the pregnancy history of FN RA patients and controls to Caucasian(Cau) RA patients and controls.

Methods: We examined pregnancy history and RA risk using results from females enrolled in a study of RA in FN RA patients (n=141) and their unaffected 1st degree relatives (n=197); and FN (n=46) and Cau (n = 120) RA patients and healthy controls (FN=238; Cau=190) enrolled in a study of autoimmunity in FN populations. All participants were interviewed using identical questionnaires detailing reproductive history. RA patients with onset before menarche were excluded. Only those pregnancies occurring prior to the diagnosis of RA were included. Age was defined as age at RA onset for RA patients, and age at study enrolment for controls.

Results: RA patients (n=307) and controls (n=625) were overall similar in age, number of pregnancies and age at first pregnancy, but RA patients had a later age at menarche (13 vs. 12.7 years; p =0.002). Thirty-two percent of RA patients and 28% of controls were smokers. FN participants were younger (36 vs. 42 years; p < =0.001), had a higher number of children (54% \geq 4 births vs. 23%; p< 0.001) a younger age at first birth (62% < age 20 vs. 13%; p< 0.001), were more likely to smoke (49% vs. 21%), and had a similar age at menarche compared to Cau. In regression analysis, after adjusting for ethnicity, age, smoking status and education, odds of RA were less than half for women with \geq 4 births compared to nulliparous women (OR =0.39, 95% CI 0.22\$0.68); and odds of RA were 1/3 (OR =0.32, 95% CI 0.18\$0.58) for women aged \geq 26 years compared to those aged < 20 at the time of first birth, while a later age at menarche significantly increased the odds of RA (OR = 1.2, 95% CI 1.05 -- 1.32).

Conclusion: We found strong correlations between RA risk, an earlier age at menarche, a delayed first pregnancy and greater parity in this study; however any RA-protective mechanism is unclear. Unknown confounders may play a role in the age of menarche as well as age of first pregnancy, while a protective effect of greater parity on the evolution of RA may result from the repeated immunosuppressive effects of multiple pregnancies.

Gene Silencing of ERAP1 and ERAP2 Displays Differential Effects on Intracellular Free Heavy Chain Accumulation and Peptide Presentation in AS-Associated compared to Non-Associated B*27 Subtypes

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Objective: HLA subtypes B*2704 and *2705 are associated with AS while *2706 and *2709 are not. We investigated the interaction of 2 novel AS associated genes ERAP1 and ERAP2 with HLA B*27 subtypes.

Methods: C1R cells stably transfected with the respective B*27 subtypes (B*2704, *2705, *2706 and *2709) were used. For gene silencing, two duplexes each of Stealth RNAi™ for ERAP1 and ERAP2 and a negative control (NC) siRNA were nucleofected. For flow cytometry, ME1, HC10, W6/32 and MARB4 antibodies were used respectively for intact B27, MHC-I free heavy chains (FHC), intact MHC-I and B27 presenting abnormally long peptides (B27_lp). For intracellular FHC (IFHC) HC10 was used after cell permeabilization. The change in MFI was calculated as a ratio of the MFI with specific siRNA to NC for each antibody. Western blot showed more than 80% suppression of ERAP with specific siRNAs but not with NC.

Results: Silencing of ERAP1/2 was associated with a significant increase in IFHC in B*2704 and *2705 cells compared to *2706 and *2709 cells ($p=0.002$). The median (IQR) increase in IFHC (Δ IFHC) in the B*2704 and *2705 cells was 2.5 (1.8, 4.2) compared to 1.3 (1.1, 1.5) in the *2706 and *2709 cells. There was no significant difference in the level of surface FHC, B27 or MHC-I expression. The median Δ B27_lp expression with ERAP1/2 silencing in B*2704 and *2705 cells was 1.2 (1.1, 1.4) and was significantly higher ($p=0.03$) than the median Δ B27_lp of 0.9 (0.8, 1.0) in *2706 and *2709 cells. There was no significant difference in the results whether ERAP1 or ERAP2 was suppressed.

Conclusion: ERAP1/2 silencing causes accumulation of more IFHC and higher B27_lp in AS-associated B*27 subtypes cells compared to non-associated subtypes. This is the first report suggesting that ERAP1/2 could be the missing link in the conundrum of B27 subtype specificity in AS.

Biologic Therapy in Juvenile Idiopathic Arthritis (JIA) at One ReACCH-Out Centre: A Pilot Study

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Objective: To describe the use of biologic medications in Canadian children with JIA and determine factors associated with earlier use.

Methods: We analyzed patients from one centre of the Research on Arthritis in Canadian Children Emphasizing Outcomes (ReACCH-Out) inception cohort to refine methods that can then be applied to the complete cohort. Patients given any biologic medication were described with clinical and laboratory characteristics at study entry and at the visit prior to initiation of biologics. Children receiving early biologics (within 18mo from diagnosis) were compared to controls who did not receive biologics (matched follow-up), and to patients receiving late biologics (after 18mo). Univariate analysis was used to evaluate factors associated with early biologics. Multivariate logistic regression was conducted to explore baseline characteristics that predict early biologic use.

Results: 29/254 Vancouver ReACCh-Out participants (11.4%) used a biologic agent. Median age was 11.3y (1.6S15.6) and 41% male: 48.3% Caucasian, 10.5% Asian, and 17.2% Aboriginal. Thirteen patients (45%) had polyarticular disease, five (17%) ERA, six (21%) systemic-onset, and two (7%) oligoarticular. Two were given biologics for uveitis and two for IBD. Median time from diagnosis to start of biologics was 17.67mo (range 0.2S50). Fourteen children (48%) received early biologics at median 9.5mo (0.2 S17.7). At baseline, they had median 5 active joints (0S32) and baseline physician global VAS 4.4 (0S7.7), compared to 2 (0S35) active joints and VAS 3.2 (0S8.2) for matched controls, and 12 active joints (1S51) and VAS 6.3 (2.8S7.6) for late biologics. At the visit prior to starting biologic, early biologics had a MD global VAS 4.5 (0S8.2) versus 0.35 (0S5.4) for controls and 3.3 (0.6S7.6) for late biologic. They had 12.5 (2S22) active joints versus 0 (0S18) for controls and 6 (0S26) for late biologic. Methotrexate was used by 86% of early biologic, 52% controls, and 100% late biologics. Two or more DMARDs were used before starting biologics by 29% early biologic, 3.7% controls, and 31% late biologic. Predisone was used by 86% of early biologic, 35.8% controls, and 69% late biologic. We are currently exploring the logistic regression models.

Conclusion: Children with systemic-onset and polyarticular disease are prescribed biologics more frequently. Aboriginal children have a high proportion of biologic use, which may reflect more severe disease in this population. The full ReACCh-Out cohort may allow us to predict who will require early biologic so that we can better plan and inform families.

Fracture Risk Assessment and Hip Structural Analysis in Canadian Females Living with Systemic Lupus Erythematosus (SLE)

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Objective: In women with Systemic Lupus Erythematosus (SLE), to determine: 1) prevalence of osteoporosis (OP) and low bone mass (LBM) in women age >50 and < 50 , 2) fracture risk using the Canadian Fracture Risk Assessment Tool (FRAX) in women >40 , 3) bone quality by Hip Structural Analysis (HSA), and 4) correlations between FRAX and HSA with SLE/OP risk factors.

Methods: Demographic data including age, SLE duration, OP risk factors, and medications were collected from 271 participants without prior OP fractures. Bone mineral densities (BMD) at the hip, spine, and femoral neck were determined using DXA. OP was determined using WHO definitions for females >50 (32.8%) and LBM was defined as z-scores < -2 for those < 50 . For those >40 (63.5%), the 10-year probabilities of a major fracture (FRAX-Major) and hip fracture (FRAX-Hip) were calculated. High fracture risk is FRAX-Major $>20\%$ or FRAX-Hip $>3\%$ and low risk is FRAX-Major $< 10\%$ or FRAX-Hip $< 1\%$. HSA was completed in 81 participants and included section modulus (SM, bending strength) and buckling ratio (BR, cortical stability) at the narrow neck of the femur. BR $>10\%$ is considered high fracture risk.

Results: Subjects had a mean (SD) age of 43.8 (13.0) years, SLE duration of 11.6 (10.4) years, 38% were postmenopausal, 13% had a prior non-OP fracture, 24% were on corticosteroids >7.5 mg, and 41% used corticosteroids for >3 months. Calcium and vitamin D were used by 48% and 39%, respectively. Overall, OP and LBM were diagnosed in 14.6% and 8.8%, respectively. Significant but low correlations were found between femoral neck BMD ($r = -0.31$, $p = 0.001$) and hip BMD ($r = -0.41$, $p < 0.01$) with corticosteroid duration. The mean (SD) FRAX-Major was 10.2% (6.3) and FRAX-Hip was 1.9% (3.3). FRAX-Major $>20\%$ was seen in 12 patients with 7 treated. FRAX-Hip $>3\%$ was seen in 27 patients with 18 treated. Treatment was given to 19.4% and 14.6% who had FRAX-Major $< 10\%$ and FRAX-Hip $< 1\%$ respectively. FRAX-Major correlated significantly with: corticosteroid duration ($r = 0.33$, $p = 0.008$) and age ($r = 0.21$, $p = 0.01$). FRAX-Hip correlated significantly with: corticosteroid duration ($r = 0.35$, $p = 0.03$), age ($r = 0.23$, $p = 0.02$), and SLE duration ($r = 0.20$, $p = 0.01$). The mean (SD) BR was 9.5 (2.2). BR $>10\%$ was seen in 43.2%. BR significantly correlated with: FRAX-Major ($r = 0.538$, $p < 0.01$), FRAX-Hip ($r = 0.599$, $p < 0.01$), age ($r = 0.232$, $p = 0.037$), SLE duration ($r = 0.435$, $p < 0.01$), and corticosteroid duration ($r = 0.285$, $p = 0.026$). No associations were found between SM with FRAX or SLE/OP risk factors.

Conclusion: OP and LBM are prevalent in SLE women. FRAX and HSA provide insight to fracture risk by deriving fracture risk probabilities useful for prescribing treatment or assessing bone structure non-invasively.

Access To Care For Arthritis In Three First Nations Communities: Results Of A Mixed-Methods Study

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Objective: Aboriginal people in Canada are believed to have a high prevalence of arthritis, yet limited research has examined access to care. Our objectives were to: 1) evaluate access to healthcare services for arthritis among three First Nations communities and 2) examine the perceptions of First Nations people regarding the arthritis care received and barriers experienced.

Methods: We used a mixed-methods approach. An interview-administered household survey of all adults living in three on-reserve communities was performed to identify people who reported having received an arthritis diagnosis by a health professional, or who reported having chronic pain in the neck, back, or joints, and related functional limitations. All adults identified as such were then asked about their access to arthritis care services and barriers to care. Semi-structured interviews were conducted with a subsample of participants to further explore their perceptions of care received and barriers to care. Interviews were tape recorded for transcription. Descriptive analyses of the household survey and content analysis of interview data were conducted.

Results: Of 536 residents, 402 (75%) completed the household survey. Participants' mean age was 46 years, 52% were female, and 61% were married. Thirty-percent (n=119/402) reported a health professional diagnosis of arthritis (excluding fibromyalgia). In comparison, non-age adjusted prevalence estimates reported in national surveys using the same question was 19% for off-reserve Aboriginal people and 16% for non-Aboriginal people. Chronic joint, neck, or back pain and functional limitations were reported by 41% (166/402). Of these 166 individuals, 140 reported at least one healthcare professional visit for their problem: family doctor=75%; physical therapist=28%; occupational therapist=20%; rheumatologist=16%; and, traditional healer=15%. Only 8% had participated in an arthritis/chronic disease self-management program. Difficulties obtaining care in the past 12 months were reported by 28% (n=47/166), including long wait lists (n=20), difficult access to rheumatologists (n=19), poor transportation availability/high costs (n=16), lack of awareness of health professional to see (n=12), high treatment costs (n=11), and perceived inadequate/culturally inappropriate care (n=10). Subsequent in-depth interviews (n=11) revealed additional barriers to care: the need for flexibility in the time/location of services, culturally sensitive care, and family involvement in care plans

Conclusion: The burden of arthritis was high among the participating First Nations' communities. The prevalence of reporting an arthritis diagnosis exceeded that reported in national surveys for off-reserve Aboriginal and non-Aboriginal people. Culturally specific care challenges included the need for culturally safe care and a desire for greater family involvement in care.

Comparison of Patients with Systemic Lupus Erythematosus with and without Peripheral Nervous System Involvement

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Objective: To determine in SLE patients: 1) the prevalence and the clinical course of peripheral neuropathies (PN), 2) characterize the clinical features and sub-classes of the PN, 3) whether PN was related to SLE or to other comorbid conditions and, 4) whether there is an association between any of the features of SLE and PN.

Methods: Patients who met at least 4 of the ACR classification criteria and the ACR case definition criteria for peripheral neuropsychiatric syndromes in SLE were selected from the University of Toronto Lupus Clinic database registry. PN found as exclusions and associations were analyzed but considered non-SLE related. Demographic data including age, gender, SLE duration, SLE-related clinical and laboratory data and the outcomes were extracted. Health-related quality of life was assessed using the mental (MCS) and physical (PCS) component summary score of the SF-36 questionnaire. In a nested case-control study, SLE patients with PN were matched by SLE duration to SLE patients without PN and were compared. Chart review was performed to confirm clinical findings and determine the contributing factors to PN. Data were analyzed using SAS statistical program.

Results: Out of 1533 patients in the database, 207 (13.5%) with a mean (SD) age of 36.5 (14.9) years and ACR criteria of 5.5 (2.0) met the inclusion criteria. Eighty-two (39.6%) patients were with non SLE-related PN. Polyneuropathy was diagnosed in 55.5%, mononeuritis multiplex in 9.2%, cranial neuropathy in 12.5% and mononeuropathy in 11.1% of patients. Asymmetric presentation was most common (59.3%) and distal weakness occurred in 34.2%. Peroneal nerve (53.9%), sural nerve (55.2%) and median nerve (37.3%) were frequently involved. EMG/NCS indicated axonal neuropathy in 70.3% and signs of demyelination in 20.3% of patients. PN improved in 65.8% of patients with SLE-related PN, with a mean (SD) follow up period of 10.7 \pm 9.6 years. Compared to patients without PN, those with PN had significantly: more CNS involvement (14.2% versus 6.6%, $p=0.02$), higher median SLEDAI (8.0 versus 6.0, $p=0.007$) and lower SF-36-PCS (35.0 ± 11.3 versus 38.3 ± 11.2 ; $p= 0.04$).

Conclusion: PN is relatively prevalent in SLE, may occur at any time after the SLE onset and have different presentations. Many of these patients have also CNS SLE and high SLEDAI. There is a predilection for asymmetric and lower extremities involvement, especially peroneal and sural nerve. This manifestation of the disease has a big impact on the patient's quality of life.

Giant Cell Arteritis and MRI Evaluation of the Cranial Arteries

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Objective: To evaluate whether high field Magnetic Resonance Imaging (MRI) can demonstrate mural edema and inflammation within the superficial temporal artery and other intra- and extracranial arteries and how it compares to Temporal artery biopsy results in patients who meet American College of Rheumatology (ACR) criteria for giant cell arteritis

Methods: 55 patients meeting ACR criteria for GCA, and 9 patients otherwise suspicious of GCA were examined by 3T MRI using a head coil. The MRI protocol matured over the course of the study but, in general, high-resolution Gadolinium enhanced images of the clinically-affected STA were obtained, in addition to larger field of view sequences to visualize the other scalp arteries. The images were graded according to protocols reported in recently published studies. All patients except 1 underwent temporal artery biopsy. Images and biopsy were obtained as soon as possible after initiating corticosteroid therapy.

Results: Overall 30/64 patients had positive scalp artery findings and 10/64 had positive biopsy findings. In patients meeting ACR criteria for GCA, MRI demonstrates inflammation in 46% of patients. This is much higher than the biopsy positivity rate of 17.9%. Of these biopsies 7 reported superior temporal artery inflammation and 1 demonstrated cavernous internal carotid artery inflammation and one demonstrated occipital artery inflammation. One false negative occurred when an inadvertent protocol deviation occurred with suboptimal image resolution obtained for the patient. Sensitivity of MRI compared to biopsy as gold standard was 90%. Negative predictive value was 97%. Other important findings in patients who had negative artery inflammation included 1 case ipsilateral pachymeningitis, 1 cortical infarct, 1 ipsilateral pansinusitis and 1 case of multiple meningiomas requiring neurosurgery referral.

Conclusion: These results support previous studies and suggest that MRI could complement or even replace biopsy as an effective and non-invasive way to diagnose GCA. MRI protocol and image resolution are crucial components in MRI evaluation of scalp artery inflammation. MRI is clearly useful in diagnosing other pathologies that may clinically mimic giant cell arteritis.

Direct Imaging Evidence That Adalimumab Induces Resolution Of Inflammatory Lesions In AS Patients At Sites Of Complete Spinal Ankylosis

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Objective: Post-hoc analysis of clinical trial data has demonstrated that AS patients who have extensive spinal ankylosis on radiographs experience clinical improvement with adalimumab that is similar to patients without extensive ankylosis. This benefit has been documented by patient self-report and not objectively using imaging data. We aimed to assess the impact of treatment in AS patients where both radiographs and MR scans were available to analyze the fate of vertebral corner inflammatory lesions (CIL) that demonstrated syndesmophytes and ankylosis on the baseline radiograph.

Methods: MRI scans were performed at baseline, 12, and 52 weeks while radiographs were done at baseline and 104 weeks in 76 AS patients randomized to receive either adalimumab (ADA) 40 mg every other week or placebo (PBO) for 24 weeks in a, double-blind, Phase III study of active AS with an inadequate response to at least one NSAID or DMARD. After the week 12 assessment, patients not achieving an ASAS20 response were eligible for early escape therapy with ADA and after 24 weeks all patients received ADA. The anterior vertebral corners (VC) of the cervical (C2 lower to T1 upper) and lumbar (T12 lower to S1 upper) spine were examined for syndesmophytes and ankylosis on lateral radiographs of the cervical and lumbar spine by 2 readers scoring independently. Anonymized MR scans were read independently by 2 readers who recorded the presence/absence of both typical CIL (Type A) and complex CIL (dimorphic) at the same anterior VC that were assessed by radiography. The primary analysis was based on concordant radiographic and MRI data. A CIL was defined as being persistent if it was recorded as being present on each MRI scan (baseline, 12, and 52 weeks) and as being completely resolved if either the baseline or 12 week MR scan showed a CIL that was no longer present at the 52 week final MRI examination.

Results: Ankylosis across the disc space was recorded on the baseline radiograph at 248 of 1736 (14.3%) VC that were assessed by both radiography and MRI. A syndesmophyte was recorded in 137 (7.9%) of VC at baseline. A CIL was observed significantly more frequently at VC without either ankylosis or syndesmophytes (212/1351 (15.7%)) as compared to those with ankylosis (13/248 (5.2%), $p < 0.0001$) on baseline radiographs. Over half of CIL at VC with ankylosis at baseline resolved completely (7/13 (53.8%)) as compared to 157/212 (74.1%) of CIL at those VC without syndesmophytes/ankylosis at baseline ($P = NS$). For VC with baseline ankylosis, complete resolution was observed for almost all Type A CIL (5/6) but in only 2/7 dimorphic CIL.

Conclusion: Our data provide objective evidence for ongoing inflammation at sites of complete spinal ankylosis that can resolve completely with adalimumab, and that complete resolution of inflammation is observed more often in those CIL with a typical configuration than in more complex, dimorphic inflammatory lesions.

Neuropsychiatric Lupus: The Prevalence and Autoantibody Associations Depend on the Definition: Results from the 1000 Faces of Lupus Cohort

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Objective: The prevalence of neuropsychiatric systemic lupus erythematosus (NPSLE) varies widely depending on the definition used. We determined the prevalence of NPSLE in 1000 Faces of Lupus, a large multi-centre Canadian cohort.

Methods: Adults who satisfied the ACR classification for SLE were included. NPSLE was defined as: (i) NPSLE by ACR classification criteria (seizures or psychosis), (ii) ACR, SLEDAI (seizure, psychosis organic brain syndrome, cranial nerve disorder, headache and CVA), SLAM (CVA, seizure, cortical dysfunction and headache) and SLICC (cognitive impairment, psychosis seizures, CVA, cranial or peripheral neuropathy and transverse myelitis) with and (iii) without minor nonspecific NPSLE manifestations (including mild depression, mild cognitive impairment and EMG-negative neuropathies, and (iv) by ACR and SLEDAI NP indices alone. Factors associated with NPSLE were explored using regression models.

Results: 1253 were enrolled with mean disease 12 ± 10 years, age 41 ± 16 years and 86% female. Subgroup size was dependent on the specific definition of NPSLE. Prevalence of NPSLE was: 6.4% in Group (i); 38.6% in Group (ii); 28.7% in Group (iii); and 10.2% in Group (iv). In univariate analysis, Aboriginals had increased frequency of NPSLE in all groups (nearly two-fold) with ethnicity being significant in group (i) ($p=0.04$). Education level was not associated with NPSLE ($p=0.32$) and income was only significant in group (i) ($p=0.03$). Anti-Ro was significantly associated in groups (i) and (iv) and antiphospholipid (aPL) was increased groups (i), (ii) and (iii); however, aPL+ lost significance when thromboembolic events were excluded from SLICC, SLEDAI, and SLAM indices. In group (iv) absence of anti-Sm was significant. In multivariate analysis, anti-Ro and aPL (i) and anti-Ro+ and lack of anti Sm (iv) were significant. NPSLE was not increased in those with + anti-DNA, anti-La, or anti-RNP. Total number of ACR criteria, SLAM, age at diagnosis, disease duration and gender were not associated with NPSLE.

Conclusion: The prevalence and factors associated with NPSLE varied depending on the definition used and was highest in the Aboriginals, and may be higher if +anti-Ro or aPL. SLAM and SLICC include mild subjective disease manifestations, which contributed to a 10% higher prevalence of NPSLE compared to a more strict definition. NPSLE may be less in this database than other publications as it may be decreasing, or selection bias of entry into an observational cohort. NPSLE was associated with aPL and often anti-Ro and varied by ethnicity but Aboriginals had higher aPL which was associated with some definitions of NPSLE.

The Pharmacist Initiated Intervention Trial in Osteoarthritis (PhIT-OA):**Clinical Outcomes**

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Objective: Osteoarthritis (OA) is the leading cause of disability in North America. Recent studies have shown that there are care gaps both in identifying knee OA and in delivery of appropriate interventions. Community pharmacists could assist in addressing these gaps. This study determined whether a multidisciplinary intervention initiated by pharmacists could improve the quality of care for OA.

Methods: We used a cluster randomized, controlled trial design, with pharmacies randomized to provide the intervention or usual care. The outcome measures assessed in a multilevel model included the pass-rate on the Arthritis Foundation Quality Indicators (QI) for the Management of OA at six months, the Western Ontario and McMaster Universities Index of Osteoarthritis (WOMAC), Lower Extremity Function Scale (LEF) and the 5 dimensional paper-based adaptive test (PAT-5D).

Results: 32 pharmacies enrolled subjects with confirmed knee OA using ACR criteria in the intervention (N=73) and control arms (N=66). There were no differences in participant characteristics between the arms. The baseline global WOMAC score was 8.5 (95%CI 7.4, 9.7). At 6 months the QI pass rate was significantly higher for those in the intervention versus control arm (diff=45%, 95%CI (34.5, 55.9), $p < 0.0001$). Significant improvements occurred in the intervention arm for the WOMAC total, pain and function scores (all $p < 0.03$), the HUI3 single-attribute pain ($p < 0.05$), the PAT-5D pain and daily activity scores (both $p < 0.05$) and the LEFS ($p = 0.02$ at 6 months) compared to control.

Conclusion: A multidisciplinary intervention initiated by pharmacists improved the quality of care for knee OA over six months. This improvement in care was accompanied by a reduction in participants' pain and improvement in functional ability.

The Pharmacist-initiated Intervention Trial in Osteoarthritis (PhIT-OA): A Cost-Effectiveness Analysis

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Objective: Osteoarthritis (OA) is the leading cause of disability and a cause of intensive health resource use in North America. This study determined the cost-effectiveness of a pharmacist-initiated intervention trial in OA (PhIT-OA).

Methods: The incremental cost per quality adjusted life year (QALY) gained was calculated using utility measures (i.e., PAT5D and HUI3) collected in the PhIT-OA trial. Cost-effectiveness analysis was done from the government and societal perspectives by excluding and including patient out-of-pocket expenses, respectively. Incremental cost effectiveness ratios (ICERs) were defined as incremental cost per additional QALY between intervention and usual care.

Uncertainty in costs and effectiveness estimates were modeled by the combination of imputation and non-parametric bootstrapping.

Results: From the government perspective, the average patient in the intervention group generated CAN\$129 in costs compared with \$115 for usual care. From the societal perspective, these costs were \$575 and \$319, respectively. With QALYs calculated using HUI3 utility values, compared with usual care the intervention resulted in ICERs of \$582 per QALY gained from the government perspective and \$11,877 per QALY gained from the societal perspective; using PAT5D values, ICERs were \$629 and \$11,090, respectively.

Conclusion: Using the conventional effectiveness value of \$50 000 per QALY, the multidisciplinary intervention initiated by pharmacists was cost-effective both from the government and societal perspectives. Results from this analysis may inform health service planning using pharmacists for OA care.

Environment and Genetic Contributions to Disease Severity in First Nations with Early Inflammatory Arthritis

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Objective: First Nations (FN) populations present with severe inflammatory arthritis at an early age. We sought to determine the influence of genetic predisposition as reflected by HLA DRB1 alleles and environmental factors such as smoking and socioeconomic status on the development and outcome of early inflammatory arthritis (EIA) in this group.

Methods: Patients with EIA (less than 1 year symptom duration: First Nations (FN) =46 and nonFN=269 (Caucasian =222, Metis =13 others =34) were assessed at baseline clinic visit. One year followup was available for 206 (FN n=26 other n=174). Baseline disease activity (DAS28CRP3), functional status (mHAQ) and environmental exposures including self reported current smoking status, current alcohol use, a history of vaccination, flu-like illness, bacterial infection, travel, or trauma occurring within 6 months of symptom onset and socioeconomic status (years of education) were recorded. HLA-DRB1 alleles were determined by DNA sequencing. One year clinical outcomes included treatment response (EULAR criteria) and remission (DAS28CRP3 < 2.6).

Results: FN were more likely to be current smokers (14/25 (56%) vs 53/216 (25%) $p < 0.001$), less likely to use alcohol (7/18 (38%) vs 127/182 (70%) $p < 0.008$) and had less formal education (7.9 vs 12.7 years $p < 0.0001$). There were no significant differences between FN and non-FN in reported exposure to vaccines (3/12 vs 22/104), flu-like illness (3/12 vs 29/102), bacterial illness (2/12 vs 15/100) travel (2/12 vs 46/105) or trauma (1/11 vs 20/100). FN were more likely to have any SE (30/39 (77%) vs 124/225 (55%) $p < 0.01$) and less likely to have DERA protective alleles (1/39 (3%) vs 40/225 (18%) $p < 0.015$) than non-FN. In linear regression models predicting baseline DAS28CRP3 (included variables: years of school, smoking, any SE and DERA) SE ($B = 0.5$ $p = 0.02$) and years of school ($B = -0.05$ $p = 0.02$) were significant. At one year FN were less likely to be in remission (6/26 (23%) vs 83/174 (48%) $p < 0.02$). In multivariate models including ethnic group, smoking, education, and SE and DERA, DERA were associated with remission (OR 2.4 $p < 0.05$).

Conclusion: In this cohort, environmental factors especially socioeconomic status as reflected by years of education is an important contributor to baseline disease activity. The presence of protective DERA alleles is associated with a better clinical outcome.

Pathogenesis and Prevalence of Anti-Citrullinated Protein Antibodies (ACPA) in Unaffected Siblings of ACPA-Positive Rheumatoid Arthritis Patients

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Objective: We previously reported that ACPA from RA patients injected intra-peritoneally (ip) into Fc γ RIIB-deficient mice induced inflammatory arthritis (IA); whereas, ip injections of IgG devoid of ACPA from the same RA patients did not. ACPA has been shown to be positive in some unaffected first degree relatives of patients with RA. The objective is to determine whether unaffected siblings of ACPA- positive RA probands have RA features and whether their ACPA induces IA experimentally.

Methods: Patients met ACR criteria for RA and had anti-CCP2 >5 ; RA-unaffected siblings were confirmed by a physician. ACPA (affinity purified from patient sera using a synthetic citrullinated peptide (JED)) and sera was administered ip to Fc γ RIIB-deficient mice. ACPA were measured by ELISA, Rheumatoid Factor (RF) by nephelometry. All subjects were tested for the presence of the SE and cytokine levels were determined by Luminex®.

Results: 13 families and 33 unaffected siblings were included; there were three monozygotic twins discordant for RA. All subjects were Caucasian. Mean age of probands was 60, age of disease onset was 44, 85% were smokers, and 85% were in remission. Mean age of siblings was 51 and 50% were smokers ($p=0.024$). The SE was present in 86% of RA patients and 61% of unaffected siblings ($p=0.014$). Of the probands, 85% were positive for IgG anti-JED, 54% IgM anti-JED, 77% anti-citrullinated Fibrinogen(cFib), 100% anti-Modified Citrullinated Vimentin (MCV) and 62% RF. One unaffected sibling was IgG anti-JED, anti-CCP2, anti-cFib and anti-MCV positive, 32% of siblings were IgM anti-JED positive and 21% had low titre anti-MCV. Normals ($n=9$) were negative for ACPA. The monozygotic twins were discordant for the presence of ACPA. Pro-inflammatory cytokines were elevated in RA patients compared to siblings and normals. Siblings compared to normals had significantly lower levels of IL-4, ILS7, ILS17, IFN γ and higher levels of IL-8, ILS10 and MCPS1. Purified ACPA and serum ip mouse transfers from a twin proband induced IA; whereas IgG devoid of ACPA and sera from the ACPA-negative unaffected twin did not.

Conclusion: Siblings of ACPA positive RA probands had an increase in IgM anti-JED, but rarely had IgG anti-JED, IgG anti-CCP2, or anti-cFib and lacked the elevation of pro-inflammatory cytokines characteristic of RA. Monozygotic twins discordant for RA were also discordant for ACPA. Sera from unaffected twins, negative for ACPA did not induce IA in a mouse model. Future work involves determining whether ACPA from unaffected siblings will induce IA in this model.

Validation of the 2010 Criteria to Diagnose RA in a Canadian Multicenter Cohort Of Patients with New Onset Inflammatory Arthritis

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Objective: The 2010 ACR/EULAR criteria for RA identify patients likely to have persistent and/or erosive inflammatory arthritis (IA). They have not been validated in North American patients or shown to identify patients eligible for clinical trials recruiting patients with a DAS28 of ≥ 3.2 . We aimed to determine what proportion of patients with early IA of < 1 year duration the 2010 ACR/EULAR criteria newly identify as having RA and if these newly identified patients would be eligible for clinical trials in early RA.

Methods: Baseline (BL) data collected from patients (n=1146) enrolled into the Canadian Early Arthritis Cohort (CATCH) study, a multi-centre observational prospective “real world” cohort of patients with early IA recruited since July 2007 were analysed for this study. Inclusion Criteria: age >16 , symptom duration ≥ 52 weeks of persistent synovitis, ≥ 2 effused joints or 1 swollen MCP/PIP + ≥ 1 of: + RF, +anti-CCP, AM stiffness >45 minutes, response to NSAIDs, or painful MTP squeeze test. The 2010 criteria were applied to determine what proportion of patients with EIA fulfilled new criteria at BL. Patients were treatment naive or had received a few weeks of DMARDs. Patients newly identified as RA by the new criteria were evaluated for disease activity and the proportion of patients with a DAS28 ≥ 3.2 were considered as potentially being eligible treatment of for an early RA clinical trial.

Results: BL characteristics were: mean age 52 ± 16 years, 73% female, median symptom duration 5.5 months, mean DAS28 ESR 4.9 ± 1.6 ; 27% initially treated with oral glucocorticoids, 50% treated with MTX. 26% (226/874) had erosions at BL. 57% (N=648) of patients were eligible for this analysis. Of the remaining 648 patients, 68% (N=441) met 1987 ACR criteria for RA at BL. 31% (N=201) had undifferentiated IA (UIA). Of these 80% (N=518) had a score of ≥ 6 on the new criteria. Of the 68% of 441 who met old criteria, 87% (N= 384) met new criteria. Of 201 UIA patients remaining, 66% (N= 133) could now be diagnosed with RA using the new criteria. These patients had a mean (DAS28=4.0). 78% of UIA patients now meeting the new criteria had a DAS28 of ≥ 3.2 .

Conclusion: Based on data from a Canadian cohort, revised ACR/EULAR 2010 criteria identify a substantial number of UIA patients as having RA. The majority of patients would be eligible for clinical trials in ERA. Most patients who fulfill the 1987 ACR criteria also fulfill the 2010 criteria.

Prevalence of Risk factors for Rheumatoid Arthritis in a North American Native Community

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Objective: The etiology of RA remains unknown. Gene-environment interactions have been proposed to play a major role in disease susceptibility. Specific alleles of the HLA-DRB1 locus collectively known as shared epitope (SE) alleles are associated with disease risk. Environmental risk factors thought to contribute to RA development include smoking and periodontal disease (PD). We have recently shown that antibodies against the oral pathogen *Porphyromonas gingivalis* (anti-PG) are associated with the presence of anti-citrullinated protein antibodies (ACPA), these being the hallmark of RA autoimmunity. Since North American Native (NAN) have high rates of RA, we tested hypotheses regarding disease risk in a genetically and environmentally homogeneous Northern Manitoba NAN community.

Methods: A random community sample of 172 participants from St Theresa Point with a mean age of 34 years, 53% of whom were females, answered questionnaires regarding joint and periodontal symptoms, as well as oral health related behaviors and smoking. The participants underwent a joint exam by a rheumatologist and were evaluated for periodontitis by a dental hygienist who generated a O_S4 score using a validated instrument, the Periodontal Screening Record (PSR). The participants had their serum tested for rheumatoid factor (RF) and ACPA, as well as anti-PG. HLA DRB1 testing was undertaken using sequence specific primers (n=106).

Results: Four participants with established RA had their data censored. Of the remaining 168 RA-free individuals, 42% reported hand symptoms of pain, stiffness, or swelling, while 10% were found to have joint tenderness or minimal swelling on exam. Current smoking was reported by 87% of subjects. The median PSR score was 3, and 81% had scores of either 3 or 4 (4=most severe). PSR scores correlated strongly with subjective symptoms of bleeding gums. In total, 7% were RF positive, and 2% were ACPA positive, in both cases titers generally being low, while 44% were anti-PG positive based on an arbitrary cutoff level. SE prevalence was 88% and 40% had 2 SE copies. There was no significant association between PSR score, joint symptoms or RA autoantibodies.

Conclusion: There is a high prevalence of both genetic and environmental risk factors for RA development in this Northern Manitoba First Nations community. However, there was no clear association between PD or anti-PG with either non-specific joint symptoms and signs suggestive of early RA or with RA autoantibodies, although the sample size and data distribution may have precluded a demonstration of such an association.

A Population-Based Assessment of Live Births in Women with SLE

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Objective: There is a general notion that live births are not decreased in women with SLE compared to healthy women. However, there is little evidence to support this; in fact, several disease-related factors may limit the number of children borne to women with SLE. Therefore, we calculated live births in women with SLE, and compared this with general population rates.

Methods: We identified women with SLE using Quebec administrative databases (1994/01/01 to 2003/12/31), which cover all health care beneficiaries. Incident SLE cases were women with ≥ 1 hospitalization with either a primary or secondary diagnosis of SLE, or ≥ 2 physicians' claims for SLE within any 2-year period (at least 8 weeks apart), with no prior diagnosis of SLE in the 5 years preceding the interval. Only women aged ≤ 35 on 1994/01/01 were included. We determined the number of live births during the interval, as defined by procedure codes or physicians' claims for delivery. We applied age-specific and relevant calendar-period birth rates to the observed years of follow-up to determine the expected number of live births. We then calculated the standardized incidence ratio (SIR) of observed to expected live births. We also performed multivariate analyses to explore potential predictors of live births in women with SLE.

Results: 1334 women with SLE were identified. Mean age at diagnosis was 28.9 years (standard deviation, 8.0). Most births occurred before or at SLE diagnosis date (respectively 41% and 15%), while 45% were observed after diagnosis. Overall, the number of live births over the interval (559) was below that which would be expected (708) (SIR 0.79; 95% CI 0.73-0.86). Compared with the general population, live births were substantially lower after SLE diagnosis (SIR 0.62; 95% CI 0.55-0.70) compared to before diagnosis (SIR 1.01; 95% CI 0.90-1.13). In multivariate analyses, prior hospitalization for SLE (RR 0.52; 95% CI 0.37-0.73) was associated with markedly decreased live births. There were trends for fewer live births in women with disease duration ≥ 5 years (RR 0.86; 95% CI 0.65-1.14) and in those living in rural regions (RR 0.79; 95% CI 0.60-1.06). We did not definitively establish a decrease in live births independently attributable to antiphospholipid syndrome (RR 0.90; 95% CI 0.65-1.25) or renal disease (RR 0.89; 95% CI 0.33-2.39).

Conclusion: After diagnosis, women with SLE have substantially fewer live births compared with the general population. Prior hospitalization for SLE was the most important predictor of live birth (after diagnosis) in our sample.

Prevalence of Flow Mediated Dilatation and its association with Framingham Risk Score in a population of women with Systemic Lupus Erythematosus

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Objective: In women with SLE, to determine: 1) CVD risk using FRS and FMD, 2) association between FMD and FRS.

Methods: 173 females with >4 ACR criteria for SLE and no previous history of CVD had their 10-years FRS calculated using patient's age, systolic blood pressure (SBP>130mmHg), smoking, total (TC>5.5 mmol/l) and HDL cholesterol (< 1.3 mmol/L). In addition serum triglycerides>1.7 mmol/l, LDL-cholesterol>2.5 mmol/l, homocysteine>15 μ mol/L, hsCRP > 1.0 mg/L and TC/HDL > 4 were considered risk factors for CVD. FMD was assessed using an ultrasound of the brachial artery where 6-15% increase in diameter post-cuff inflation is considered optimal and < 6% increase is considered abnormal. Associations between FMD and FRS were assessed using linear regression analysis.

Results: The mean (SD) age was 43.6 (12.7) years, SLE duration was 8.9 (2.4, 18.6) and 23% were smokers. The mean (SD) serum profile were: triglycerides: 1.2 (0.6) mmol/l, TC: 4.7 (1.1) mmol/l, LDL-cholesterol 2.6 (0.8) mmol/L, HDL-cholesterol: 1.7 (0.6) mmol/L, TC/HDL ratio: 3.0 (1.0), homocysteine: 10.7 (4.3) μ mol/L and hs CRP: 3.2 (6.2) mg/l. Abnormal serum levels were seen in 14.2 % for TG, 21.2% for TC, 50.8% for LDL, 18.4% for HDL, 16.7% for homocysteine and 62.7% for hsCRP. Among patients, 31% had 1, 44 % had 2 -- 4 and 25 % had \geq 5 risk factors for CVD. According to FRS, 44% were at low risk (FRS=1-5%), 24% at intermediate risk (FRS=6-10%), 20% at high risk (FRS=11-20%) and 12% at very high risk (FRS> 20%). Abnormal FMD was seen in 40% of the patients with FRS< 5%. Adjusted linear regression including SLE duration, SLE-Disease-Activity Index, SLICC-damage index, post menopausal status and FRS in the model showed that for each 1% increase in FRS, a 0.24% decrease in FMD cuff change was observed.

Conclusion: FRS explains only a subgroup of patients with abnormal FMD, with approximately 40% of SLE patients with low FRS having abnormal FMD. Assessment of FMD in SLE may identify a subgroup of patients with endothelial dysfunction not identified by FRS. Following these patients prospectively may help to determine their actual CVD risk.

Patterns and Determinants of Leisure-time Physical Activity in Women with Systemic Lupus Erythematosus

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Objective: To describe leisure-time physical activity (LTPA) patterns of women with systemic lupus erythematosus (SLE) and to identify demographic, psychosocial, disease related and physiological factors associated with LTPA levels.

Methods: Two hundred and seventy-eight women completed standardized questionnaires assessing LTPA, psychological distress, self-efficacy and health status. A clinical examination determined lupus disease activity and cumulative damage. Demographics and clinical variables, which include systemic inflammation factors (C-reactive protein (CRP) and homocysteine) were also collected. Sufficient and insufficient patterns of LTPA were identified and the association between these patterns with Health related quality of life (HRQoL) and other determinants were examined.

Results: Fifty percent (n=139) of the participants were meeting recommendations for achieving at least 7.5 metabolic equivalent hours per week (MET-hr/wk) of LTPA, 26.2% (n=73) were insufficiently active (< 7.5 MET-hr/wk of LTPA) and 23.7% (n=66) were sedentary. Walking was the preferred form of LTPA, reported by participants who were sufficiently (82%) and insufficiently active (79.5%). Participants who were sufficiently active scored significantly better in 7 of the 8 HRQoL domains compared to the less active and sedentary groups, including: physical functioning, role limitations due to physical health problems, bodily pain, vitality, and social functioning. Univariate analysis showed overall levels of psychological distress to be lower in sufficiently active individuals when compared to sedentary and insufficiently active patients. Physiological data shows systemic inflammation to be similar between activity groups with a decreasing trend in CRP values in active individuals. Along with similar values in disease activity and disease damage between the activity groups, this suggests exercise does not exacerbate symptoms of SLE. Multivariable logistic regression revealed that being sufficiently active was significantly associated with lower BMI (OR = .69, 95% CI= 0.49\$0.99) and higher physical component summary scores (OR = 1.04, 95% CI= 1.01\$1.08).

Conclusion: Patients with systemic lupus erythematosus who exercised regularly were found to have significantly better HRQoL as well as lower psychological distress. These benefits are present in the absence of exacerbations of the disease. Future studies looking at the effects of exercise on patients with SLE should combine longitudinal monitoring of patients with a comprehensive exercise and lifestyle changing program.

Is There an Advantage for a Lupus Specific Quality of Life Measure over SF-36?

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Objective: We aimed to assess whether the LupusQoL contributed additional information not obtained using the SF-36 and to compare the responsiveness of both questionnaires over time in patients who changed clinically.

Methods: 41 patients seen at a single centre were followed at monthly intervals for 12 months. Both questionnaires were co-administered monthly. Lupus activity was determined by SLEDAI-2K 30 days. We compared the mean scores for the 4 comparable domains in both questionnaires in all patient-visits. For the 4 non-comparable domains of the LupusQoL we determined the correlation between each domain with the Physical Component Score (PCS) and the Mental Component Score (MCS) of the SF-36. The effect size (ES) and the standardized response mean (SRM) were used to compare the responsiveness of both questionnaires in patient-visits with lupus flare (SLEDAI-2K \geq 4), improvement (reduction in SLEDAI-2K $>$ 3) and remission (SLEDAI-2K=0) from previous visit.

Results: The mean age at SLE diagnosis was 30.5 ± 10.3 years. At study visit the mean age was 45.3 ± 13.2 and disease duration 14.8 ± 10.3 years; SLEDAI-2K 2.59 ± 2.41 and SDI 2.12 ± 2.48 . 376 patients-visits were recorded. Quality of life assessed by both questionnaires is low among patients. There was no statistically significant difference between the mean scores of comparable domains; Physical Health/Physical Functioning, Emotional Health/Mental Health, Pain/Bodily Pain and Fatigue/Vitality. For the 4 non-comparable domains of the LupusQoL, there was a correlation between Body Image/MCS-SF-36, Planning/MCS-SF-36, Intimate Relationships/PCS-SF-36, and Burden to Others/MCS-SF-36. Both questionnaires displayed responsiveness as determined by SE and SRM among patients who flared (SF-36: SRM moderate effect 0.64 Role Physical, small effect 0.42 Social Functioning and 0.30 PCS ; LupusQoL: SRM moderate effect 0.67 Fatigue and small effect 0.49 Burden to others) and improved (SF-36: SRM moderate effect 0.60 MCS and small effect 0.43 Mental Health, 0.40 General Health, 0.30 Vitality, 0.30 Role Physical, 0.24 Social Functioning and 0.23 Physical Functioning; LupusQoL: SRM moderate effect 0.73 Pain, 0.53 Fatigue and 0.51 Physical Health, and small effect 0.45 Emotional Health, 0.39 Body Image, 0.37 Burden to others and 0.36 Planning) but not among patients in remission when compared to previous visit. There was no significant difference in the responsiveness of both questionnaires in patients with lupus flare and improvement when compared to previous visit.

Conclusion: There is no superiority of LupusQoL over SF-36 in assessing lupus patient's quality of life. Both questionnaires are responsive instruments of lupus quality of life in patients with flare and improvement.

Differences in Clinical Manifestations between Childhood-Onset Lupus and Adult-Onset Lupus: A Meta-Analysis

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Objective: In SLE, it is known that age at disease onset impacts the clinical course and outcome; however, the precise differences in the prevalence of SLE manifestations are debated. The objective of this study was to conduct a systemic literature review and meta-analysis of all studies comparing childhood-onset to adult-onset lupus and determine which clinical manifestations vary with age at disease onset.

Methods: A search of MEDLINE/PubMed, EMBASE, CINAHL, and SCOPUS databases was conducted to identify relevant articles. Clinical manifestation event rates were extracted. Pooled odds ratios were calculated using the random effects method and heterogeneity and study quality were assessed.

Results: Of the 484 studies identified by the search strategy, 16 were included (905 children, 5993 adults). Mean quality was 16 out of 32 ranging from 8 to 29. Malar rash (OR 1.9), ulcers/mucocutaneous involvement (OR 1.4), renal involvement (1.6), seizures (OR 2.3), thrombocytopenia (OR 1.3), hemolytic anemia (1.9), fever (1.5), and lymphadenopathy(3.7) were more common in childhood-onset SLE (all $P < 0.05$). Raynaud's, pleuritis, and sicca are more common in adult-onset SLE ($P < 0.05$; OR 0.4 to 0.7 comparing children to adults or approximately 50% more common in adults). Autoantibodies including ANA, anti-DNA and ENA had no difference in prevalence in adults vs. children. However, antiphospholipid antibodies were more common in child-onset SLE ($p < 0.05$). Other manifestations were not significantly different in adults vs children such as discoid rash, photosensitivity, alopecia, arthritis, psychosis, stroke, thrombosis, pericarditis, serositis, lung and heart involvement, leucopenia and lymphopenia. Limitations include: biases in case selection, inconsistent definitions of cSLE ranging from less than 13 to 18. The strength is large numbers and data from several continents which improves the generalizability of the results.

Conclusion: Several manifestations of lupus are different in cSLE and aSLE. It is not surprising that lymphadenopathy, fevers and seizures were more common in cSLE as they are more common in children than adults and likewise, Sjogren's seems to increase with age of onset of SLE and sicca is increased in older people. However, despite more antiphospholipid antibodies in children, there was no difference in CVA but other risk factors for stroke increase with age such as hypertension. Children had more renal involvement despite similar autoantibodies (ANA, anti-DNA, ENA) but there could be detection bias in that more severe SLE is detected in children as SLE is rarer in children compared to adults.

Health-related Quality of Life in Children with Primary CNS Vasculitis and Juvenile Spondyloarthritis

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Objective: To identify and compare the characteristic patterns of health-related quality of life (HRQOL) in children with two distinct rheumatic diseases: childhood Primary Angiitis of the Central Nervous System (cPACNS) and Juvenile Spondyloarthritis (JSpA). HRQOL is an important health outcome in children with rheumatic diseases. cPACNS is an inflammatory disease of the brain and spine. Children with cPACNS have neurological deficits which interfere with participation. JSpA is an inflammatory arthritis affecting the lower limbs (joint and entheses) and spine resulting in physical limitation. The physical limitations can equally interfere with the child's ability to ambulate and interact with peers. Systemic manifestations of both the diseases may result in fatigue and sleep disturbances. Currently, there is very little information available on the impact of cPACNS and JSpA on HRQOL.

Methods: A single-center cross-sectional study of children with CNS vasculitis (cPACNS by Calabrese criteria) and JSpA (ILAR criteria for enthesitis-related) was performed. Data collection: clinical assessment, inflammatory markers and imaging. HRQOL was assessed using the PedsQL 4.0, a 23-item questionnaire rated by both parent and child and completed at their child's regularly scheduled clinic visit. Disease activity was determined using Physician Global Assessment scales, BASDAI, BASFI and PSOM. Results were calculated compares using descriptive statistics and compared in parametric and non-parametric tests, when applicable.

Results: Twenty-six children (21 males, 5 females) diagnosed with a JSpA and their parents and 58 cPACNS patients (33 M; 25 F) and their parents participated in this study. Children were aged 4.6-16.5 years (mean 8.0). Mean duration of illness was 19 months in cPACNS and 34 months in JSpA. Overall child-reported HRQOL was higher in JSpA (M=82, SD12) than cPACNS (M = 74, SD17). Patients reported significantly higher HRQOL than parents ($p = 0.004$). Differences were found for all domains: 1) psychosocial: JSpA M=85 (SD13), cPACNS M=60 (SD17), 2) physical: JSpA M=86 (SD16), cPACNS M = 91 (SD17), 3) emotional JSpA M=85 (SD=12); cPACNS M=72 (SD12), 4) social: JSpA M=86, (SD14), cPACNS M=76 (SD15) and 5) school JSpA M=82, (SD17), cPACNS M=71 (SD14).

Conclusion: Childhood rheumatic diseases impact on HRQOL. CNS vasculitis and JSpA affect HRQOL distinctly differently: Children with JSpA had lower physical domain scores. In contrast, CNS vasculitis patients scored significantly lower on psychosocial, emotional and school-related domains. Comprehensive care for children with rheumatic diseases has to target these specific areas of impaired HRQOL.

Uveitis Screening in Juvenile Idiopathic Arthritis (JIA): A Quality Improvement Project

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Objective: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children; uveitis is the most severe extra-articular involvement. JIA accounts for 75% of all pediatric anterior uveitis cases in North America and Europe. A positive anti-nuclear antibody (ANA) increases the risk for uveitis in JIA > three fold. Thresholds for considering a titer positive remain undefined. The aims of the study were: 1) To determine, which ANA titer pediatric rheumatologists consistently consider positive, 2) to explore, how the obtained ANA titer information is translated into clinical practice when applying the Uveitis Screening Guidelines and 3) to determine how satisfied pediatric rheumatologists are with the current guidelines.

Methods: A single center quality improvement project was conducted and included all 23 pediatric rheumatologists (fellows and staff). A case based 14-question electronic survey including four hypothetical case scenarios was constructed using surveymonkey software. It explored the domains of 1) consistency of considering an ANA titer positive, 2) knowledge and application of the 2006 American Academy of Pediatrics (AAP) Uveitis Screening Guidelines, 3) satisfaction with guidelines. Results were summarized and compared using descriptive statistics, case-based knowledge and application of guidelines was compared using paired t-tests.

Results: A total of 20/23 (87%) pediatric rheumatologists completed the survey. ANA was considered an important risk factor for uveitis in JIA by 95%. There was inconsistency in the threshold for ANA positivity: 50% considered a titre of $\geq 1:40$ to be positive, 45% selected $\geq 1:80$, and 5% chose $\geq 1:160$. A total of 85% of responders stated they were familiar with the AAP Uveitis Screening Guidelines; 85% reported to apply them “very frequently” or “all the time.” When provided with two cases with unanimously positive ANA titres, before and after being shown the AAP screening guidelines, only 60% of respondents chose the uveitis screening frequency corresponding to the screening guidelines correctly. The reported satisfaction with the guidelines was low at 60%.

Conclusion: Thresholds for positive ANA titres in JIA amongst pediatric rheumatologists were found to be inconsistent. Knowledge and correct application of the Uveitis Screening Guidelines was limited and satisfaction with the guidelines was low. A data based approach is required to determine the risk of developing uveitis at different ANA titers. It will allow for evidence-based, consistent judgement of test positivity with the goal of decreasing variability and improving standard of care for JIA patients.

Musculoskeletal Examination Skills of Pediatric Residents

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Objective: Good musculoskeletal (MSK) examination skills are crucial for accurate assessment of a child with suspected rheumatic disease. It was our perception that pediatric residents do not demonstrate sufficient skills in this regard. Objective of this study was to assess whether pediatric residents feel confident performing a MSK exam focusing on assessment of the presence of inflammatory changes in joints

Methods: Study group: all pediatric residents attending Academic Half Day at the Children's Hospital of Eastern Ontario. Assessment: A self-assessment questionnaire was handed out to all residents to assess their level of confidence in examining specific joints. Responses were scored using a five-point Likert scale (1=not confident, 5=very confident). After completion of questionnaires, the residents participated in a 2hour teaching module on joint examination techniques with a practical hands-on component. Upon completion of the module, the residents were asked to judge whether they rated their skills appropriately in the self-assessment questionnaire.

Results: The session was attended by 25 out of 41 residents (61%) at our institution. Overall, the residents' confidence in performing a MSK exam was poor with the mean score of 3.1 for PGY1, 2.5 for PGY2, 2.9 for PGY3 and 2.6 for PGY4. Moreover, 22% of residents initially overestimated their skills while only 5% underestimated their skills. The residents felt most comfortable with the knee exam (mean score 3.2), least comfortable with the finger and wrist joints exam (mean score 2.4 and 2.5, resp.).

Conclusion: Pediatric residents did not feel confident performing a focused MSK exam. This study demonstrated a need for more emphasis on teaching the MSK examination during residency.

Intra-rater reliability of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Bath Ankylosing Spondylitis Functional Index (BASFI) in Children with Spondyloarthritis

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Objective: Juvenile spondyloarthritis (JSpA), referred to as enthesitis-related arthritis (ERA) sub-type under the International League of Associations for Rheumatology (ILAR) classification of juvenile idiopathic arthritis (JIA), is characterized by inflammation in the joints and entheses. Several instruments assessing disease activity in ankylosing spondylitis have been validated including the BASDAI and BASFI. At this time, there are no disease activity scores for JSpA or ERA. The objective of this study is to measure the intra-rater reliability of the BASDAI and BASFI in JSpA/ERA.

Methods: Patients diagnosed with ERA (ILAR criteria) and followed at The Hospital for Sick Children Spondyloarthritis Clinic were included in this study. Patients were excluded if they lacked English fluency, were less than 6 years or greater than 18 years of age. Prospective subjects were consecutively enrolled over 12 months and, the patient and/or one parent completed the BASDAI and BASFI at baseline and 2 weeks later (a period during which little change is expected). Intra-class correlation coefficient (ICC) was calculated and values greater than 0.6 were considered indicative of good reliability.

Results: Forty-eight patients (81.2% males) were enrolled. The average age at diagnosis was 12.5 years (range, 7.6 to 16.7 years). 41.7% were HLA-B27 positive and 18.8% had an ankylosing spondylitis family history. 52% had hip involvement and 40% had radiographic evidence of sacroiliitis. Eight patients were excluded due to protocol violation. All 40 subjects reported their overall health as “the same” when compared to their baseline visit. The mean BASDAI at baseline was 1.97 ± 1.90 and at 2 weeks was 1.69 ± 1.80 **S** the reliability was substantial; ICC = 0.74, Bland-Altman limits of agreement (LOA) = 2.4 to **S**2.8. The mean BASFI at baseline was 0.99 ± 1.49 and at 2 weeks was 0.75 ± 1.00 **S** likewise reliability was excellent; ICC = 0.87, Bland-Altman LOA = 1.1 to **S**1.4. When examining individual questions from the BASDAI and BASFI, “How long does your morning stiffness last from the time you wake up?” and “Doing a full day’s activities, whether it be at home or at work” had the highest ICCs (ICC = 0.88), respectively.

Conclusion: Both the BASDAI and BASFI showed excellent intra-rater reliability in a cohort of ERA patients. Next steps will include measuring the construct validity and responsiveness of these tools in JSpA/ERA in order to determine if pediatric rheumatologists can use these as validated disease activity/functional impairment measures in clinical practice and research.

Identification of Anti-TNF Candidates Based on Predicted Response and Remission in Ankylosing Spondylitis

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Objective: To identify sub-populations of Ankylosing Spondylitis (AS) patients that are candidates for anti-TNF based on the predicted response / remission rates.

Methods: The ASSERT and GO-RAISE trial data were analyzed and matrix models developed to predict probability for achieving response or remission after initiating anti-TNF therapy or continuing conventional AS therapy. Univariate analyses identified possible baseline predictors for 50% improvement in BASDAI50 at wk 12 and ASAS partial remission at wk 24. Individual variable associations were explored using Spearman correlation analysis. A stepwise selection procedure using multivariate regression, ROC analysis and Spearman correlation was used to select predictors for the final model. Variables are represented as dichotomous or trichotomous parameters and logistic regression was used to calculate the predicted probability of achieving a BASDAI50 response and ASAS partial remission state respective to combined selected predictors at baseline.

Results: 479 AS patients treated with anti-TNF and 156 patients treated with placebo with continued conventional therapy, with BASDAI and spinal pain assessment ≥ 4 were included. Age (mean 39.5, SD 11.3 yrs), BASFI (mean 5.4; SD 2.2 cm), Berlin enthesitis-score (mean 2.4; SD 2.9), therapy (anti-TNF or conventional), CRP (mean 2.1; SD 2.4 mg/dL) and HLA-B27 genotype [(+) or (-)] were included as predictors. After categorization of age (≤ 40 vs. >40 yrs), enthesitis (score = 0 vs. >0 units), CRP (≤ 0.6 , $>0.6 \leq 2.0$, >2.0 mg/dL) and BASFI (≤ 4.5 , $>4.5 \leq 6.5$, >6.5 cm), the AUC of the combined dataset prediction model was 80% for BASDAI50 response and 77% for ASAS partial remission suggesting a good prediction model according to the academic point system. A matrix model was developed and organized to represent increasing proportion of BASDAI50 response (range 1% to 80%) and ASAS partial remission (range 0% to 55%) respective to the characteristic at baseline. Only 2% of patients who did not have BASDAI50 response at week 12 did have ASAS partial remission at week 24.

Conclusion: The majority of AS patients who have elevated disease activity and back pain respond to anti-TNF therapy while few respond to continued conventional therapy. Younger patients and patients without peripheral enthesitis receiving anti-TNF therapy demonstrate an improved response. CRP, functionality and HLA-B27 measurements can help in assessing which patients will respond and subsequently achieve an improved disease state and who might therefore be a better candidate for anti-TNF therapy.

Response to the First Biologic in Patients with Ankylosing Spondylitis: a Real World Experience

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Objective: Biological therapy has brought a paradigm shift in the care of patients with spondyloarthritis. However, the response to these medications is not uniform and data on predictors of response are available only from controlled conditions like drug trials. We present a real world experience of biologic use and response in patients with ankylosing spondylitis (AS).

Methods: Patients with AS (modified New York criteria) and who have been on at least one anti-TNF agent were selected for the study. Patients who stopped a biologic due to lack of response were considered failures. Patients who continued on the same agent or stopped due to low disease activity state were considered responders. Baseline demographic features including age and gender, HLA B27 status, disease duration, gap between diagnosis and initiation of biologic agent, disease activity measures including BASDAI, CRP and ESR, BASFI, BASG and hemogram were noted. The presence of peripheral arthritis, colitis, psoriasis, iritis and concomitant use of DMARDs were compared between the responders and non-responders. Univariate, followed by multivariate logistic regression analysis was performed. Student T test and Fischer's Exact test were done where relevant.

Results: Out of a total of 230 patients with spondyloarthritis attending the clinic over a total of 654 visits, 193 patients had AS and detailed data on biologic use was available on 185 patients who were included in the study. The mean (\pm SD) age (38.5 ± 13 vs 37.5 ± 12) and disease duration (15 ± 11 vs 16 ± 11) were comparable between the responder and non-responder groups. The age of onset of AS, delay in diagnosis or delay in starting biologic after diagnosis was not different between the two groups. The responders had lower BASDAI at baseline compared to non-responders (5 ± 2.5 vs 5.8 ± 1.8 ; $p=0.03$). None of the other clinical or laboratory parameters were significantly different. More non-responders were on DMARDs compared to responders (88% vs 64%; $p=0.04$). In logistic regression analysis, the only predictor of anti-TNF response was leukocyte count with an OR of 0.83 ($p=0.03$). The area under curve of a model predicting anti-TNF response with leukocyte count alone was 0.668. Adding HLA B27, gender, BASDAI, CRP and other clinical variables did not improve the prediction model.

Conclusion: In a real life setting, prediction of biologic response can be different from a controlled setting like a drug trial. Patients who responded to the first anti-TNF agent had lower disease activity and a lower leukocyte count was predictive of response.

Cocaine-Induced Pseudovasculitis: a Case Series of 8 Patients

Nataliya Milman (University of Ottawa, Ottawa); C. Douglas Smith (The Ottawa Hosp, Ottawa)

Case Report: Over the previous year, eight patients who use cocaine presented to the Ottawa Hospital with features suggesting cutaneous vasculitis. Clinically, all patients had a mixture of cutaneous and oral ulcers of variable depth and size, purpuric and hemorrhagic lesions, and areas of skin necrosis. Most had prominent weight loss, 6 had arthritis, 1 had diffuse reactive lymphadenopathy, and 1 had pleural and pericardial effusions. Two patients had episodes of upper airway obstruction, 1 requiring emergent placement of a tracheostomy tube. One of them had a vocal cord fold with a non-specific pathology, while no structural abnormality was found in the other patient. Distinctive laboratory abnormalities included elevated inflammatory markers and positive p-ANCA in all patients. Seven of the 8 patients (7/8) had anti-MPO antibodies (titers 18 to 400AU/mL). C-ANCA was positive in 5/8, equivocal in 2, and negative in 1; anti-PR3 antibodies were found in 6/8 (titers 8 to 400AU/mL). Six/8 patients had positive ANA (homogenous or speckled pattern), with titers between 1:160 and 1:320; 5/8 patients had positive anti-DNA antibodies, 2 of them with low C3 and C4. Most patients had anti-phospholipid antibodies, including lupus anticoagulant (positive in 3/8 and equivocal in 5/8), anti-cardiolipin antibodies (IgG at low titer in 1/8, IgM at low to medium titer in 6/8), and β 2GPI IgM in 1/8. Cold agglutinins were strongly positive in all of the 6 patients in whom they were measured. Also, all patients had at least 1 cytopenia at some point during observation: 6 had low hemoglobin, 3 had leucopenia, all patients had lymphopenia, and 4 had neutropenia. Biopsy of the skin lesions was performed in 7 patients. It showed leukocytoclastic vasculitis in 1 patient, thrombotic microangiopathy in 3, and neutrophilic dermatosis in 2. One patient had a biopsy showing neutrophilic dermatosis followed by a repeat biopsy 9 months later that showed thrombotic microangiopathy. All 8 patients required at least one hospital admission. At some point in their disease all patients required antibiotics and 4 were treated with oral prednisone. In 7/8 patients who were seen on more than one occasion, the course of disease was chronic, with relative improvement after hospital admissions and then recurrent exacerbations, often temporally related to cocaine use. One patient died due to multi-drug overdose. This report outlines clinical features and a distinctive profile of laboratory investigations that when present in the right clinical setting should prompt consideration of cocaine-induced pseudovasculitis.

Giant Cell Arteritis and Coexisting Inflammatory Arthritis

William Leung (University of Alberta, Edmonton); Todd Chaba (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

Objective: The coexistence of Giant Cell Arteritis (GCA) and other inflammatory arthritis conditions is felt to be unusual. Prior studies have shown up to 15% of GCA patients may have synovitis; however they lacked the ability to test for anti-cyclic citrullinated peptide (CCP). We investigated the number of patients with GCA who were identified with inflammatory arthritis and were CCP positive.

Methods: Pathology records of all positive temporal artery biopsies performed in the Edmonton area over a 4-year period (2006-2010) were obtained. The University of Alberta Rheumatology Division, internal database was also reviewed for patients with GCA.

Results: Twenty-five biopsy-positive patients were identified, and their charts were reviewed for the presence of any inflammatory arthritis, as well as the specialty of the physician managing their temporal arteritis. Two patients with biopsy-confirmed GCA were subsequently diagnosed with inflammatory arthritis; one patient with rheumatoid arthritis (RA) the other with psoriatic arthritis (PsA). The patient with RA was CCP positive; the patient with PsA was CCP negative. Of the 25 patients, only 14 patients (56%) were managed by rheumatology. Of the remainder, 10 (40%) were managed by Ophthalmology alone, and one was followed by family medicine.

Conclusion: We present two patients with biopsy-confirmed GCA who were subsequently diagnosed with inflammatory arthritis, one with rheumatoid arthritis (RA) and one with psoriatic arthritis (PsA). The presence of CCP testing is beneficial in patients who have inflammatory symptoms. A significant number of our patients were managed by non-Rheumatologists (44%). This may lead to an underestimation of the incidence of inflammatory arthritis in this population.

Lower Education as a Proxy for Socioeconomic Status (SES) is not associated with Poor Outcomes in Systemic Sclerosis (SSc): Data from a Large SSc Cohort (CSRG)

Samah Mansour (University of Western Ontario, London); Ashley Bonner (McMaster University, Hamilton); Murray Baron (McGill University and Jewish General Hospital, Montreal); Janet Pope (University of Western Ontario, London)

Objective:

It is unknown what the effect of SES is on outcomes in SSc. SES is often measured by income and education. In SSc, highest education would be attained often decades prior to disease onset whereas current income could be low due to SSc, confounding interpretation of effect of SES on SSc. SES can modify outcomes by altering timing of access to care and adherence. Thus education is a proxy of SES.

Methods: The Canadian Scleroderma Research Group (CSRG) collects detailed data annually on more than 1000 SSc patients. For measuring SES we used education: did not complete high school or completed high school (HS). Linear regressions were used to assess the education effect on disease outcome as measured by severity score, global physician scores and survival (time from onset of scleroderma till death). Logistic regressions were done to detect any effect of education on mortality, presence of Class III pulmonary artery hypertension (PAH), interstitial lung disease (ILD) [total lung capacity (TLC) less or more than 70%], renal failure (serum creatinine level less or more than 150 $\mu\text{mol/L}$). Data were subdivided into limited and diffuse cutaneous SSc.

Results: The study included 1145 with mean of 8 years duration of SSc. Eighty six percent of the patients were females (986 females) with a mean age of 55.4 years. Approximately a quarter did not complete high school. Less than high school education was significantly more common in older age ($p=0.000$), males ($p=0.01$), lower income ($p=0.000$), unemployed ($p=0.000$), higher ESR ($p=0.02$) and those more likely to have died in follow up ($p=0.02$). Linear regressions did not show any statistically significant association between education level and severity score, global physician severity, activity or damage score and survival ($p>0.6$). Moreover, logistic regression did not show any statistically significant association between education level and ILD, PAH, and SRC. Education was not predictive of worse outcomes of scleroderma when usual risk factors (Gender, age, ESR, Hbg, ANA and SCL70) were entered into the model. Although, % deceased was significantly related to education by bivariate analysis, regression after adjusting for significant risk factors was no longer significant.

Conclusion: Unlike SLE in SSc education is not associated with worse outcomes when adjusting for usual risk factors. Education may not affect disease course in those with an aggressive disease.

Clinical Correlates of Oral Health Status in Systemic Sclerosis

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Objective: The manifestations of systemic sclerosis (SSc) are heterogeneous and include orofacial abnormalities. The purpose of our study was to identify the oral and disease-related correlates of oral health-related quality of life (HRQoL) in SSc.

Methods: In a cross-sectional study, SSc patients from the Canadian Scleroderma Research Group Registry were randomly recruited from 7 centers. Oral HRQoL was assessed with the Oral Health Impact Profile (OHIP), a validated self-reported measure of dysfunction, discomfort and disability attributed to oral conditions. The OHIP is composed of 7 subscales (functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap). Each subscale is scored separately from 0 to 40 (with 0 representing better and 40 representing worse oral HRQoL). An overall score can also be computed using a detailed algorithm. Predictor variables were chosen to represent the spectrum of common oral and disease-related manifestations that could potentially influence oral HRQoL in SSc. Oral findings of interest included interincisor distance, subjective feeling of oral dryness (feeling of dry mouth, difficulty swallowing dry food or swollen salivary glands), salivary flow per minute, and presence of full dentures. Disease-related manifestations included severity of Raynaud's phenomenon, severity of finger ulcers, hand contractures, gastroesophageal reflux and global measures of disease activity and damage. The relationship between the OHIP and each oral and disease-related variable was investigated in separate multivariate models, adjusting for age, gender, education, current smoking and disease duration.

Results: There were 151 patients in the study: mean age 56.5 years, 90.1% female, 52.1% with more than high school education, 9.7% current smokers and mean disease duration 13.8 years. Interincisor distance was 37.6 mm, 63% reported a subjective feeling of oral dryness, mean saliva production per minute was 1.47 gm, and 11.3% had full dentures. The mean OHIP score was 8.67. Objective and subjective measures of oral dryness and full dentures were independent predictors of several OHIP subscales as well as the overall OHIP ($p < 0.05$). Interincisor distance was an independent predictor of functional subscales of the OHIP, but not of the OHIP overall. No other disease-related manifestation tested was an independent predictor of the OHIP.

Conclusion: This is the first study to systematically assess the full spectrum of SSc-related manifestations on oral HRQoL. Oral dryness and reduced mouth opening are independent predictors of oral HRQoL. These findings should help researchers to plan further prevention and intervention studies to improve oral HRQoL in SSc patients.

Joint Space Narrowing has a Stronger Impact on Physical Function Than Joint Erosion: Results From 8-year Longitudinal Analyses

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Objective: Structural damage, assessed by the modified Total Sharp Score (mTSS), has been shown to be related to physical function. Thus far, it remains unclear to what extent the individual components of the mTSS contribute to long-term physical function. The objective of this analysis was to characterize the longitudinal relationship between physical function and Joint Space Narrowing (JSN) or Joint Erosion (JE) in patients with advanced RA.

Methods: DE019 was a 52-week, phase 3, randomized, placebo-controlled trial for the treatment of moderate to severe advanced RA, in which patients with an inadequate response to methotrexate (MTX) were randomized to weekly placebo, weekly adalimumab (ADA) 20 mg, or ADA 40 mg every other week (eow), alongside concomitant MTX therapy. Patients completing the double-blind study were eligible to receive open-label ADA 40 mg eow + MTX for an additional 7 years. This post hoc analysis evaluated the 8-year completers cohort with radiographs available at baseline and years 5, 6, and 8. 28-joint Disease Activity Score (DAS28) was used to assess clinical levels of disease activity. Physical function was assessed through the Health Assessment Questionnaire (HAQ). Radiographic damage was assessed using the modified Total Sharp Score (mTSS). Longitudinal generalized linear modeling was used to characterize the dependence of the HAQ on concurrent DAS28, total mTSS, JSN, and JE values, following adjustment for baseline age and gender and for concurrent CRP.

Results: Over time, DAS28 was linearly associated with the HAQ ($P < 0.001$). Similarly, the mTSS was significantly associated with the HAQ throughout treatment duration ($P < 0.001$). A 1 unit increase in DAS28 and a 20 unit increase in mTSS were associated with 0.22 and 0.044 increases in the HAQ, respectively. A breakdown of mTSS into the individual components revealed that JSN more strongly impacted the HAQ over time than JE, although both were significant determinants ($P < 0.001$ for both). A 20 unit increase in JSN and JE were associated with 0.1 and 0.06 increases in the HAQ, respectively. Interestingly, negative changes in mTSS trended towards lower HAQ values over time.

Conclusion: For patients with advanced disease, long-term physical functioning is associated with both the level of disease activity (DAS28) and the extent of radiographic damage (mTSS). Of the contributors to the mTSS, JSN had a greater impact on the HAQ over time than JE, suggesting that therapies with high potency for inhibiting both the progression of JSN and JE should be considered.

Defining the Smallest Detectable Change for the SPARCC Spine and Sacroiliac Joint MRI Index for Ankylosing Spondylitis

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Objective: The Spondyloarthritis Research Consortium of Canada (SPARCC) magnetic resonance imaging (MRI) index is a scoring method for spinal and sacroiliac joint (SIJ) inflammation in ankylosing spondylitis (AS). The objective of this analysis was to define the cut-off for the smallest detectable change (SDC) on the SIJ and spine SPARCC MRI index.

Methods: Spine and SIJ MRIs were performed at baseline (BL), Week 12, and Week 52 in AS patients randomized to adalimumab 40 mg every other week (eow) or placebo for a 24-week double-blind period, followed by an 80-week open-label period (adalimumab 40 mg eow). Two independent, blinded readers scored the MRIs using the SPARCC index and a global evaluation of change (much worse, worse, no change, better, or much better) for visit comparisons. Change categories were pooled. Mean change in absolute SPARCC scores and 95% confidence intervals (95% CIs) were determined. Receiver operating characteristic (ROC) curves and Youden indices were generated, and sensitivity and specificity of the category change reported as functions of absolute change in SPARCC score.

Results: A total of 82 patients were enrolled. Reader agreement on the evaluation of change was 77%~~S~~83% for the SIJ and 66%~~S~~74% for the spine. For the global evaluation category of change and no change, the 95% CIs of absolute change in SPARCC scores showed comparability between treatments and visit comparisons. Therefore, all cases were combined across treatment groups and visit comparisons. The ROC curves demonstrate that absolute change in SPARCC score is significantly associated with global evaluation of change (area under the curves: 0.960, SI joints; 0.839, spine). The Youden index reached maximum, separating change from no change at 2.0 for SI joints and 4.0 for the spine.

Conclusion: We propose that changes of 2.0 and 4.0 for the SIJ and spine, respectively, define the numerical cut-off for SDC on the SPARCC MRI index for AS.

Articular Tophus Burden by Dual Energy Computed Tomography and Health-Related Quality of Life

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Objective: Dual Energy Computed Tomography (DECT) provides specific colour-coded differential displays between uric acid and other materials, and is a potentially useful tool to diagnose and determine the articular burden of uric acid deposition (tophi) associated with gout. The specific objective of this study was to examine whether associations exist among the number of bodily regions with tophi and both the physical (PCS) and mental (MCS) health components of the Medical Outcomes Study Short-36 Version 2 (SF-36v2) as these data would help to establish the clinical validity of DECT outcomes.

Methods: Our study sample consisted of 20 monosodium urate crystal-proven gout patients recruited from rheumatology offices in the Vancouver area, who prospectively underwent DECT scans at the Vancouver General Hospital and completed the SF-36v2. DECT scans were performed on all peripheral joints (hands/wrists, elbows, knees, feet/ankles) using a color-coding protocol that specifically assessed the chemical composition of the material (i.e. uric acid coloured in red, calcium coloured in blue). We examined the age- and BMI-adjusted relationships among the number of sites with tophi and the SF-36v2 component scores using linear regression analyses.

Results: The study sample was predominantly male (90%). The mean age of the study participants was 65.05 (SD=4.28) years. The average number of tophi sites per participant was 7.3 (range=0-25, median=8.0). The mean PCS score was 41.66 (SD=11.59), and mean MCS score was 49.62 (SD=11.23). The number of sites showing tophi correlated well with the physical component of SF-36v2 (Pearson's $r=0.56$, $p=0.02$). Age- and BMI-adjusted linear regression showed that for every additional site with presence of tophi, the PCS increased by 0.95 ($p=0.02$). There was no correlation observed with the MCS scores. When we limited our analyses to men only, our results did not change materially.

Conclusion: The number of sites with tophi detected on DECT correlates well with the physical component of SF-36v2 among patients with crystal-proven gout. These data help to establish the clinical validity of DECT outcomes, which is of interest to practicing rheumatologists, investigators, and patients with gout and hyperuricemia.

LMP2 and ERAP1 Variants are Associated With Radiographic Severity in Ankylosing Spondylitis in the SPARCC Cohort

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Objective: Endoplasmic reticulum aminopeptidase 1 (ERAP1) and LMP2 polymorphisms are associated with AS. However it is not known if they influence radiographic severity in AS. As part of a SPARCC initiative, we investigated the influence of genetic variants in components of the antigen processing pathway on radiographic progression in AS.

Methods: Caucasian AS patients from Edmonton and Toronto, diagnosed by the modified New York criteria, and having at least two sets of x-rays for scoring severity (mSASSS) were included in the study. All AS patients in the SPARCC registry are followed annually with a standardized protocol. Patients with a baseline mSASSS score of 65 or higher were excluded from the study. Progressors were identified as those patients who had an increase of at least 1 mSASSS unit per year. DNA was prepared from the peripheral blood of AS patients and genotyped for a panel of 13 coding-region SNPs in the ERAP1, LMP2, LMP7, TAP2 and TAP7 genes. Only SNPs with a minimum of 5% patients who were homozygous for the minor allele were included in the final analysis (4 SNPs in ERAP1 and 1 SNP each in LMP2 and TAP2). Regression analysis was done to identify predictors of baseline radiographic severity as well as progressors on follow up.

Results: A total of 241 patients (81% males and 82% HLA B27-positive) were followed up for a mean (\pm SD) duration of 2.4 (\pm 0.8) years. Baseline mSASSS scores were associated with gender, age, the ERAP1 SNP rs30187 and the LMP2 SNP rs17587. Patients with the major allele of the ERAP1 SNP rs30187 (CC/CT) and those homozygous for the minor allele of the LMP2 SNP rs17587 (AA) had significantly higher mSASSS at baseline. In multivariate analysis with the forward conditional method, adjusted for duration of disease and gender, the LMP2 SNP rs17587 were significantly ($B=14.3$; $p=0.04$) associated with the baseline mSASSS. In multivariate analysis of progressors, baseline mSASSS and the ERAP1 SNP rs27044 were significant predictors. This model correctly identified progressors and non-progressors in 75% of cases. After controlling for all variables included in the analysis, patients homozygous for the minor allele of rs27044 (GG) were more likely to progress compared to those with the minor allele, with an OR of 8.2 (CI: 1.8 to 38.5; $p < 1 \times 10^{-2}$).

Conclusion: Genetic variants of ERAP1 and LMP2 are associated with radiographic severity in AS.

Development and Validation of a Pruritus Measure in Patients with Systemic Sclerosis

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Objective: Systemic sclerosis (SSc) is an autoimmune connective tissue disease characterized by abnormal fibrotic processes that can affect multiple organ systems and cause immune dysfunction and vascular injury. Pruritus is reported by patients to be an important problem, but there are only two published studies in SSc. In SSc, pruritus is experienced by about 45% of patients (Razykov et al., 2009) and associated with reduced quality of life (El-Baalbaki et al., 2010). One possible reason why pruritus has been infrequently studied in SSc is that there are no validated, feasibly administered and scored self-report measures. The ItchyQoL (Desai et al., 2008) is a recently piloted 22-item measure, face-valid self-report pruritus questionnaire that is feasibly administered and scored. The objective of this study was to derive a shorter version of the ItchyQoL and compare its validity in SSc to that of the original ItchyQoL

Methods: A total of 487 patients with SSc were recruited from 15 Canadian Scleroderma Research Group Registry centers across Canada. To be in the Registry, patients must have a diagnosis of SSc, be \geq age 18, fluent in English or French, and not have any disorder that compromises ability to give informed consent. Adjusted item-total correlations were computed for each of the 22 items of the original scale. Factor analysis was performed. An expert rheumatologist was consulted to ascertain the relative importance of items, and item severity thresholds were examined to select items that best discriminated among patients across the range of pruritus severity. Convergent validity was tested with bivariate correlations with the CES-D and SF-36 (Mental and Physical Composite scores).

Results: Factor analysis supported a single-factor model for the ItchyQoL and short version of the ItchyQoL. Four items were chosen for the revised ItchyQoL-4. Internal consistency reliability was in the good-to-excellent range (Cronbach's $\alpha=0.82$). Correlation between the full ItchyQoL and the ItchyQoL-4 was 0.94. There was no statistically significant differences between the ItchyQoL and ItchyQoL-4 in regard to measures of convergent validity (ItchyQoL, CES-D $r = 0.37$, SF-36 PCS $r = 0.36$, MCS $r = 0.27$; ItchyQoL-4, CES-D $r = 0.35$, SF-36 PCS $r = 0.38$, MCS $r = 0.22$)

Conclusion: The short ItchyQoL-4 is a feasible, reliable and valid assessment instrument for pruritus in SSc that will improve the study of pruritus in this patient population. The ItchyQoL-4 should be tested against a single-item pruritus visual analog scale in future research.

Experience with Accelerated Rituximab Infusion for Rheumatoid Arthritis in a Single Community Practice

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Objective: Background: Rituximab, a chimeric monoclonal anti-CD20 antibody for treatment of NHL, CLL and RA, is administered as a slow infusion (255 minutes [4.25 hours]), due to the potential for infusion reactions, which is greatest with the initial infusion. However, the long infusion duration is resource intensive. Recently, short-infusion protocols (60 & 90 min) have been shown to be well tolerated in the oncology setting. Little data are available on short infusions in rheumatology. Objectives: To evaluate the practicality, safety and tolerability of a rapid-infusion rituximab protocol in RA patients.

Methods: RA patients meeting the criteria for rituximab treatment were recruited to participate in evaluation of the rapid-infusion protocol. Each treatment course consisted of 2 rituximab 1000-mg infusions, 2 weeks apart. The first infusion followed the recommended schedule (255 min). Second and subsequent infusions were administered over 120 min (2 hr) as follows: 0S30 min: 100 mg; 30S60 min: 200 mg; 60S90 min: 300 mg; 90S120 min: 400 mg. Premedication for all infusions consisted of acetaminophen 1000 mg, diphenhydramine 50 mg, and methylprednisolone 100 mg. Vital signs were recorded at baseline and at 15, 30, 60, 90 and 120 min.

Results: To date, 10 patients have been recruited and 36 infusions administered; of the 36 infusions, 26 followed the rapid-infusion protocol. All patients had failed or did not tolerate at least 1 TNF- α inhibitor. Patients range in age from 28 to 65 (mean 50.6) years, with RA diagnosed for < 2 to >23 (mean 11.4) years. The mean DAS was 5.9 at the first rituximab infusion. The average duration between rituximab infusion courses was 9.2 months. The rapid infusion was safe and well tolerated by all patients. One patient experienced a minor infusion reaction (headache, chest tightness, and shortness of breath), which resolved during the infusion. No infections were reported.

Conclusion: An accelerated rituximab infusion is safe and well tolerated in the community setting. The accelerated protocol optimizes patient, nurse and physician time, and all patients were satisfied with the short infusion duration. Rapid rituximab infusion is a practical option in a community setting.

A Canadian Survey Regarding Musculoskeletal Imaging for Rheumatology Residents

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Objective: Rheumatology residents must be proficient at interpreting musculoskeletal radiographs as stipulated by the Royal College of Physicians and Surgeons of Canada. It is unclear if, or how these skills are acquired. The purpose of this study was to survey Rheumatology program directors (PD) and residents (RR) regarding their perceived educational needs in radiology, types of training received, perceived adequacy of training, as well as acceptability of an on-line module.

Methods: All Canadian PD and RR were invited to participate in a voluntary online survey. The survey consisted of a total of 14 questions exploring the perceived importance of MSK radiology reading skills, present resident skill level, teaching methods, effectiveness, suggestions for improvement, need for web-based teaching tool and questions regarding its content. Results were reported as percentage of applicants selecting a response or the mean of applicant responses on a 5-point Likert scale.

Results: Completion rates were 12/14 (85.7%) for PD and 20/28 (71.4%) for RR. Over 85% of PD and RR felt that the ability to read plain MSK films was extremely important. The types of films that residents should be able to interpret (1 = no, 3=neutral, 5= yes) included plain film (5.0 PD and RR), CT scan (3.58 PD, 3.59 RR), MRI (3.25 PD, 3.7 RR), bone scan (3.25 PD, 3.35 RR) and ultrasound (3.08 PD, 3.89 RR). About half the PD (58.3%) and RR (50%) reported the confidence of residents as “a little confident” in their present ability to read films. The following percentage of those surveyed reported that present skill acquisition involved: formal didactic sessions (50% RR, 75% PD), learning by reviewing patient’s films (85% RR, 100% PD) and web-based material (10% RR, 16.7% PD). Very few reported the present system of instruction as effective (16.7% PD and 25% RR) and none considered it extremely effective. All PD and 85% of RR felt a web-based teaching module would be valuable.

Conclusion: Program directors and residents agree that the interpretation of musculoskeletal plain films is an essential skill for Rheumatologists. Present instructional modalities include primarily learning through patient care, didactic sessions, and electives in radiology. These are perceived as minimally effective which provides support for a more formal curriculum, which could include a web-based training tool specifically tailored for Rheumatology trainees.

Can Body Mass Index Be Considered a Differentiating Factor when Diagnosing Systemic Sclerosis?

Steven Katz (University of Alberta, Edmonton); Alex Yan (University of Alberta, Edmonton); Muneeb Ilyas (University of Alberta, Edmonton)

Objective: We previously reported Body Mass Index was lower in a retrospective cohort of long standing scleroderma patients compared to the overall population. It remains unknown if BMI could be a useful clue to diagnose a prospective cohort of rheumatology patients referred for initial assessment of possible systemic sclerosis.

Methods: In this single rheumatologic practice prospective study, we examined all patients referred for assessment of scleroderma over 5 years between 2005 and 2010 and who had a weight and height recorded from their first physician visit. Gender, final diagnosis, and BMI were recorded. Patients were then stratified and compared based on final diagnosis.

Results: 47 patients were referred for possible scleroderma, with 10 excluded as no BMI was recorded and 4 excluded without a final diagnosis recorded. Of the remaining 33, 20 were diagnosed with scleroderma (Scl+), 19 Females, with an average age of 51. Diagnoses of the other 13 (Median age: 60, 10 Female) included: 6 primary Raynaud's disease, 2 rheumatoid arthritis, 1 systemic lupus, 1 mechanical back pain, 1 rotator cuff tendinopathy, 1 diabetes, and 1 atherosclerosis. The average BMI was 23.7 kg/m² for the Scl+ group and 28.01 kg/m² for the Scl- group (p=0.038). Only 1 Scl+ patient had a BMI greater than 30, compared to 5/13 in the Scl- group (p=0.0248).

Conclusion: For the rheumatologist who is presented with a first time patient with a question of scleroderma, a higher BMI may be a useful differentiating factor. Further study is necessary with a larger cohort and more physician experience.

Sex Differences in Pain Level and Location in Inflammatory Arthritis: A Systematic Review and Meta-Analysis

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Objective: Patient sex may influence the disease experience for patients with inflammatory arthritis (rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and spondyloarthropathy (SpA)), with implications for treatment expectations and predicted response. Our objective was to determine if there are differences in pain level or location reported by females and males in inflammatory arthritis studies.

Methods: A search of PubMed (1950 to April 2010) and EMBASE (1980 to April 2010) was supplemented by manual searches of conference abstracts. We identified studies reporting sex-stratified pain measures (visual analogue scale (VAS), bodily pain component of the 36-item Short Form Health Survey (SF-36BP)) or pain location, in biologic naïve populations. Effects analyzed were a) standardized mean difference (SMD) for pain measures (cross-sectional analyses), b) percentage improvement in pain measure (longitudinal analyses), and c) proportion reporting pain at a particular location. The systematic review for pain measures includes 26 cohorts and 1 randomized controlled trial (23 in RA, 1 inflammatory polyarthritis, 1 AS and 1 PsA), and for pain location includes 12 publications (9 in AS, 2 PsA and 1 SpA). The meta-analysis for pain measures includes 16 cohorts reporting pain by VAS and 3 cohorts reporting pain by SF-36BP (all RA).

Results: Meta-analysis revealed a significant difference in the SMD in pain levels measured by VAS in RA (SMD 0.21 (95%CI 0.16S0.26), $p < 0.001$), likely of modest clinical significance. This difference held when stratified by disease duration at measurement (RA < 1 year SMD 0.30 (95%CI 0.15S0.45), established RA SMD 0.20 (95%CI 0.14S0.25)). The SMD for SF-36BP was not significant (SMD S0.14 (95%CI S0.49, 0.20), $p=0.411$). In longitudinal studies, pain levels in females with RA improved to a greater degree than in males, but were still higher at any time point. In AS, PsA and SpA, males experienced more inflammatory back pain at any time point during their disease (66% vs 51%) and females experienced more pain due to peripheral arthritis (69% vs 51%).

Conclusion: Females with RA experience overall higher pain levels than males, but do have a greater degree of improvement with treatment. Although this analysis does not explore confounding factors to explain this, clinicians should be aware of sex differences in pain when managing inflammatory arthritis. In AS, PsA and SpA, females will develop peripheral arthritis more frequently, with fewer manifestations of inflammatory back pain. This may have diagnostic implications in the clinical setting.

Patient Sex Does Not Influence Pain Levels in Early Inflammatory Arthritis

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Objective: Pain levels in established RA are on average higher in women than men. We sought to determine if patient sex influences pain levels in a prospective multinational cohort of early inflammatory arthritis patients treated to remission.

Methods: As of May 2010, 819 females and 307 males were recruited to the Canadian Arthritis CoHort (CATCH). Patients enrolled are over the age of 16 with ≥ 2 swollen joints or 1 swollen MCP or PIP, with symptom duration of 6 weeks to 12 months, and ≥ 1 of: positive RF, anti-CCP, morning stiffness, response to NSAID or painful MTP squeeze test. Patients are treated at the discretion of their rheumatologists. Sex-stratified analysis of pain measures recorded in CATCH, including the Visual Analogue Scale (VAS), Patient Global Assessment (PGA) and pain components of the Rheumatoid Arthritis Disease Activity Index (RADAI), was performed to identify differences in pain levels between females and males.

Results: The cohort includes patients with a mean disease duration of 6 months at first visit, with a mean (SD) baseline DAS28 of 4.85 (1.50) in females and 4.97 (1.80) in males. Females and males had similar levels of disease activity by DAS28 and RADAI at all assessments, and a similar proportion achieved DAS28 remission. No significant differences were found in pain measures between females and males at baseline, year 1 or year 2 assessments. The mean (SD) VAS at baseline for females and males respectively was 5.40 (2.79) vs 5.49 (2.93); year 1: 2.81 (2.57) vs 2.87 (2.67); and year 2: 2.64 (2.64) vs 2.58 (2.66). The mean (SD) PGA at baseline for females and males respectively was 5.80 (2.90) vs 5.54 (3.08); year 1: 2.85 (2.66) vs 2.93 (2.83); and year 2: 2.73 (2.71) vs 2.26 (2.45). The mean (SD) total joint score of the RADAI at baseline for females and males respectively was 2.58 (1.91) vs 2.78 (1.99); year 1: 1.30 (1.42) vs 1.27 (1.34); and year 2: 1.16 (1.47) vs 1.19 (1.58).

Conclusion: Sex does not influence pain perception in this multinational cohort of early inflammatory arthritis patients. This suggests that differences seen in established RA in other studies may have been influenced by disease duration and other factors.

Seasonal Variation in Vitamin D Levels in Patients with Psoriatic Arthritis from Northern and Southern Latitudes and its Association with Clinical Outcomes

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Objective: We aimed to determine the prevalence of vitamin D deficiency/insufficiency in patients with psoriatic arthritis (PsA), its seasonal and geographic variation, association with demographic and lifestyle characteristics, and with disease activity.

Methods: This study was conducted in a center in a northern geographic area (North) and a center in a subtropical region (South), from March 2009 to August 2009. Most subjects were assessed in both winter and summer. Patients completed a vitamin D questionnaire developed to assess lifestyle determinants of vitamin D levels. Demographic, clinical data, skin type (Fitzpatrick classification), serum 25(OH) vitamin D, creatinine, calcium, phosphorus and liver enzymes were determined. Vitamin D levels were categorized as deficient < 30, insufficient 30-74 and adequate >75 ng/ml. A multivariate linear mixed model that included demographic/lifestyle and clinical variables, latitude, season as covariates, was used to assess the relationship with vitamin D levels.

Results: 302 PsA patients were enrolled: 258 winter (201 in North/57 in South), 214 summer (140 North/74 South). Vitamin D levels (winter/summer) were adequate (North: 41.3/41.4%; South: 42.1/35.1%), insufficient (North: 55.7/58.6%; South: 50.9/62.2%) and deficient (North: 3/0%; South: 3.8/0.9%) among patients. Multivariate regression showed that subjects who had suntanned and received phototherapy, in the past three months, has significantly higher vitamin D levels ($p=0.012$ and $p=0.030$ respectively). Taking multivitamins increased vitamin D levels ($p=0.014$) and vitamin D supplementation was independently associated with higher vitamin D levels $p< 0.001$. Fish oil supplementation was also associated with higher levels of vitamin D ($p=0.036$). Males were more likely to have lower vitamin D levels $p=0.02$. There was no association between vitamin D levels, geographic and seasonal interaction, race, employment status and skin type, and disease activity as measured by PASI score for psoriasis and active joint count, dactylitis and inflammatory spinal pain for PsA in both seasons. No association between disease activity in summer and vitamin D levels in winter could be found.

Conclusion: A high prevalence of vitamin D insufficiency among PsA patients was found. There is no seasonal variation in vitamin D level among PsA patients in the southern and northern sites. No association could be established between disease activity and vitamin D level. However, lifestyle and demographic determinants such as having a suntan and intake of vitamin D supplements did have an effect on vitamin D level.

Unaffected First-Degree Relatives of RA Patients Exhibit a High Prevalence of Joint Symptoms That Is Not Explained by the Presence of RA Autoantibodies: Studies in a Predisposed North American Native

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Objective: We have shown that in a North American Native (NAN) population in Central Canada, the prevalence of RA is 253 times higher than that seen in most other populations, with a high frequency of familial disease. There is also a high prevalence of anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) in the first-degree relatives (FDR) of RA patients. We sought to get a better understanding of the relationship between joint symptoms and RA autoantibodies in disease-free FDR who may be at risk for developing future RA.

Methods: The prevalence of joint symptoms was compared in three distinct groups: 1) FDR of NAN RA patients (n=306), 2) NAN controls (NC, n=330), and 3) Caucasian controls (CC, n=293). The two control groups had no family history of RA or related autoimmune diseases. Study subjects completed a questionnaire which included demographic data, health related habits, family health history, and six questions probing into whether they experience pain, swelling, or stiffness of the hands or of other joints. Anti-CCP2 antibodies were tested by ELISA and RF by nephelometry.

Results: The mean age of FDR= 35 ± 13 , NC= 33 ± 11 , CC= 42 ± 13 , $p < 0.0001$. The percentage of females was FDR=69%, NC=63%, and CC=63%, $p = \text{ns}$. In all groups, females reported more symptoms (OR=1.6, $p < 0.01$). Compared to both control groups, FDR were more likely to report joint symptoms in the hands: pain (54%, 35%, 18%); swelling (36%, 16%, 7%); stiffness (40%, 23%, 14%; for FDR, NC, CC, respectively; all comparisons $p < 0.0001$). Similar findings were reported for other joint areas. Compared to CC, NC had more joint symptoms, and more joint symptoms in FDR living in urban vs. rural locations (79% vs. 60%, $P < 0.0001$). The prevalence of anti-CCP2 was: FDR = 8.3%, NC = 1%, and CC = 1%, $p < 0.0001$, and RF was: FDR = 4.5%, NC = 1%, and CC = 1%, $p < 0.05$. Logistic regression demonstrated that age and FDR status were strong independent predictors of joint symptoms ($p < 0.0001$ for both), while gender, RF, and ACPA status were not.

Conclusion: RA-like joint symptoms are more common in the FDR of NAN RA patients than they are in either NAN or Caucasian controls having no family history of RA. This finding is not explained by a higher prevalence of ACPA and RF in FDR. These data suggest that pre-clinical joint symptoms, based on biological or psychosocial factors, may be part of the risk profile for developing future disease in high risk individuals.

Expert Agreement of EULAR / EUSTAR Recommendations for the Management of Systemic Sclerosis

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Objective: Recently, guidelines in the management of systemic sclerosis (SSc) by EULAR were published. This study was done to determine and compare agreement with these guidelines by SSc experts and identify differences in agreement between North American and European SSc experts.

Methods: A survey was generated using Survey Monkey, which included the 14 EULAR/EUSTAR recommendations. Members of the Scleroderma Clinical Trials Consortium (SCTC) and Canadian Scleroderma Research Group (CSRG) were asked to indicate how little or strongly they agreed with each recommendation on a 10-point scale, from 0 (not at all) to 9 (completely agree). The survey was sent to 117 participants three times.

Results: The response rate was 66 (56%). Mean North American agreement ranged from 5.2 to 8.9, with a range of 41% to 100% (as measured by the % with agreement of 7, 8 or 9). Mean European agreement ranged from 5.5 to 8.8 with a range of 39% to 100%. Agreement was highest with: ACEi use in SRC, monitoring BP for SSc patients using steroids, and PPI use for GERD in SSc. Lowest agreement was with methotrexate for treatment of SSc skin, and bosentan and iloprost for digital vasculopathy. Experts from North America and Europe were significantly different in the strength of agreement with guidelines for digital vasculopathy and PAH. Europeans agreed 83% vs 58% of NA with iloprost for digital ulcers ($p=0.001$). North Americans agreed 95% vs 63% with intravenous epoprostenol for severe SSc PAH ($p=0.006$).

Conclusion: Mostly there was good agreement with the guidelines by experts. Perhaps agreement was low overall with some recommendations due to small treatment effect such as with Mtx treatment for SSc skin. However, agreement for digital vasculopathy may have differed due to variability in access to medications; as iloprost is not available in North America and bosentan is not approved for digital ulcer prevention in North America. Also some treatments for PAH are covered differently in various countries; which may have affected the European vs North American agreement with guidelines.

Progression Patterns of Radiographic Damage: Results from SONORA Study

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Objective: Identifying progression patterns and its characteristics for radiographic damage is important to understand early rheumatoid arthritis (RA). Data from SONORA (study of new-onset rheumatoid arthritis) was analyzed to explore patterns of radiographic progression in early RA patients.

Methods: A total of 529 patients diagnosed as early RA (symptoms ≥ 3 and ≤ 12 months) and had hand radiographs at baseline, year 1 and 2 were included in this study. The radiographs were scored according to original Sharp method (range 0 to 280) in random order per patient. Radiographic progression was defined by a change of at least 3.5 in total Sharp score within a year. Four patterns of radiographic progression were identified; never progressed, progressed at year 1 only, progressed at year 2 only and progressed at both year 1 and year 2. Demographic and clinical characteristics were compared across these four patterns using ANOVA for continuous outcomes and Chi-square test for categorical outcomes.

Results: Among these four patterns, 86% subjects never had radiographic progression, 3.4% progressed in the first year only, 7.6% progressed in the second year only and 2.6% progressed in both year 1 and year 2. There were significant differences between the patterns, for swollen joint count, baseline HAQ score, sharp score, CRP and anti-CCP positive. Subjects who had no radiographic progression in two years were those who are younger, had less swollen joint counts, lower DAS score, lower sharp score, lower CRP, anti-CCP negative and RF negative at baseline.

Conclusion: Majority of the early RA subjects do not have radiographic progression within first two years of the disease. Very few subjects continuously progressed within 2-year period. Baseline sharp score is the best indicator of whether the subject will progress or not. Then it is baseline anti-CCP positive, CRP and swollen joint count. These identified indicators can help clinicians to identify the subjects who are at high risk of continuous radiographic progression.

Scleroderma prevalence in Alberta: A population-based assessment.

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Objective: To estimate the prevalence of systemic sclerosis (SSc) using population-based administrative data, and to compare First Nation (FN) versus non-FN prevalence rates.

Methods: We ascertained SSc cases from provincial physician billing and hospitalization databases in Alberta (covering over 3.7 million individuals). Three case definitions were used; >1 billing codes by a rheumatologist; or >2 billing codes by any physician, >8 weeks apart but within 2 years; or a hospitalization diagnosis. The Alberta Health and Wellness registry file was used to determine FN status, as well as rural and urban residence (by postal code). To account for imperfect case ascertainment, we employed a hierarchical Bayesian latent class regression model that accounted for possible between-test dependence conditional on disease status, and potential differences in case ascertainment sensitivity and specificity based on patient characteristics (age, sex, and rural-versus-urban residence). Cases were ascertained from 1994-2007, and prevalence estimates based on those who were still alive as of 2007.

Results: Accounting for error inherent in both the billing and the hospitalization data, the estimated overall SSc prevalence in Alberta as of 2007, is 57.7 cases per 100,000 females (95% credible interval, CrI 51.3-65.3) and 9.8 cases per 100,000 males (95% CrI 7.2-13.6). Prevalence was higher for individuals aged >45, particularly in rural women (140.2 cases per 100,000, 95% CrI 118.7-166.3). Although the overall prevalence of SSc in FN was similar to that of non-FN, interesting trends were seen for a higher prevalence of SSc in women of FN status (64.6 cases per 100,000; 95% CrI 43.4-94.0) compared to non-FN women (57.2 cases per 100,000; 95% CrI 50.4-65.3). This was particularly marked for females aged >45 living in rural areas, where the prevalence was 264.8 cases per 100,000 in FN (95% CrI 157.0-422.9) and 135.8 in non-FN (95% CrI 113.6-164.4). For females aged >45 living in urban areas, the prevalence was 207.3 cases per 100,000 in FN (95% CrI 95.0-391.7) and 124.6 in non-FN (95% CrI 106.8-146.0). The prevalence of SSc in subjects aged < 45 were similar in FN and non-FN groups, in both rural and urban areas.

Conclusion: We demonstrated differences in SSc prevalence according to age, sex, and region. Though the over-all prevalence of SSc in Alberta was similar for FN and non-FN, we saw a trend towards more cases in FN females aged >45.

Sleep Evaluation Before and After Initiation of Anti-Tumour Necrosis Factor Therapy in Rheumatoid Arthritis

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Objective: To evaluate sleep before and after anti-TNF- α (tumor necrosis factor) therapy initiation in rheumatoid arthritis (RA) patients.

Methods: This was a prospective evaluation of RA patients with poor sleep (abnormal Epworth Sleepiness Scale (ESS) and/or Pittsburgh Sleep Quality Index (PSQI) score) who were to initiate anti-TNF- α therapy. This study utilized overnight polysomnography (PSG) and questionnaire data including: pain, fatigue, global function, modified Health Assessment Questionnaire (mHAQ), depression, stress, SF-36 scores, Rheumatoid Arthritis Disease Activity Index (RADAI), ESS, PSQI, Berlin score for obstructive sleep apnea, and International Restless Legs Syndrome Study Group (IRLSSG) diagnostic criteria. Study patients underwent two PSGs and questionnaires; prior to starting anti-TNF- α therapy and again after initiation. A referent group of RA patients with normal ESS and PSQI scores participated in the baseline evaluation.

Results: Twelve RA patients met inclusion criteria, of which ten initiated anti-TNF- α therapy and underwent repeat PSG and questionnaire studies. Following anti-TNF- α therapy initiation improvements were apparent in the pain, fatigue, mHAQ, RADAI scores. No change in ESS, PSQI, Berlin scores were evident. A trend towards improvement was observed for sleep efficiency ($p = 0.031$), sleep latency ($p > 0.05$), and 'awakening after sleep onset' time ($p = 0.048$).

Conclusion: Improvement in sleep efficiency, sleep latency and 'awakening after sleep onset' time were observed following initiation of anti-TNF- α therapy.

Detecting Latent Tuberculosis Infection during Anti-Tumour Necrosis Factor Therapy

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Objective: To evaluate the reliability of repeat tuberculin skin tests (TSTs) and Interferon Gamma Release Assays (IGRAs) in detecting latent tuberculosis infection (LTBI) in people on anti-Tumor Necrosis Factor (TNF) medication.

Methods: We conducted a prospective, observational study of patients referred to the Saskatoon Tuberculosis (TB) clinic prior to starting anti-TNF medication. A chest x-ray (CXR), 2-step TST and IGRA were performed at baseline. Those patients with a positive TST > 5 mm and/or a positive IGRA were followed with a clinic visit, CXR, TST and IGRA at 3 and 6 months after starting anti-TNF medication.

Results: Of 106 potential patients, 91 consented to participate. Twenty-eight patients had a positive TST or IGRA at baseline. Twelve patients started and stayed on anti-TNF medication during the 6-month follow-up and had all testing done. The baseline mean TST measurement for the 12 participants was 13.92 mm (SD 11.35), this increased to a mean of 16.83 mm (SD 9.32) post-booster. At 3 months post-anti-TNF initiation, there was an overall decrease in TST measurement (mean=10.00 mm; SD 9.32; $p=0.013$). By the 6-month TST, a response recovery was observed with a mean TST measurement of 14.50 mm (SD: 7.65). The IGRA was unchanged throughout the study period in all patients. The overall agreement between TST and IGRA was poor (kappa coefficient = 0.160, $p = 0.033$).

Conclusion: We demonstrated a transient but significant decrease in TST response in the first six months of anti-TNF therapy.

Efficacy and Safety of Febuxostat and Allopurinol in Women with Gout, An Older Subset With Increased Comorbidity

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Objective: Literature confirms that women with gout have a later onset than men (averaging a decade or more after menopause) and suggests that the frequent comorbidities (renal impairment, cardiovascular disease, metabolic syndrome components, diuretic use) accompanying hyperuricemia/gout in men may be more common in women. We report on the efficacy and safety of febuxostat and allopurinol in the subset of women from 3 randomized controlled trials.

Methods: 4101 subjects (3875 men/226 women) participated in the 12-month FACT or the 6-month APEX or CONFIRMS trials. This post-hoc subset analysis focuses on women with gout and baseline serum urate levels (sUA) ≥ 8.0 mg/dL who were randomized to daily placebo (n=11), febuxostat (n=139), or allopurinol (n=76). Baseline renal status was assessed by eCLcr using the Cockcroft-Gault formula. Urate-lowering efficacy (sUA < 6.0 mg/dL) is reported by drug and dose and stratified by baseline renal function.

Results: Women had a mean age of 62 years (vs 52 years for men), and 74% had BMI ≥ 30 kg/m² (62% men). Comorbid history (women vs men) was significant for hypertension (81% vs 48%), diabetes (26% vs 10%), hyperlipidemia (46% vs 37%), and renal impairment (64% eCLcr < 60 mL/min vs 13%). Gout history: 19% of women and 21% of men had tophi; 86% and 85%, respectively, had experienced a gout flare in the prior year, and mean disease duration was 8 years for women and 12 years for men. Mean sUA at baseline was 9.7 mg/dL for both. In women with the most severe renal impairment (eCLcr 17-59 mL/min), sUA < 6.0 was achieved with: placebo (0%), febuxostat 40 mg (44%), febuxostat 80 mg (83%), febuxostat 120 mg (80%), febuxostat 240 mg (100%), and allopurinol ≤ 300 mg (44%). The most frequently reported AEs among women were: URI (16%), diarrhea (11%), and musculoskeletal/connective tissue disorders (11%). The majority of AEs were transient and resolved while on treatment. The most common serious AEs were cardiac disorders: febuxostat (all doses 2%) and allopurinol (4%).

Conclusion: Women with gout are a group with significant comorbidities (including advanced renal impairment) exceeding those of gouty men. In women with gout, urate-lowering to sUA to < 6.0 mg/dL with febuxostat 80 mg was superior to that of allopurinol at recommended renally adjusted doses ($p < 0.05$) and was well tolerated.

Time to and Level of Initial DAS28 Change With Certolizumab Pegol Predicts the Likelihood of Having Low Disease Activity at Years 1 and 2 in Patients With Rheumatoid Arthritis

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Objective: To investigate the predictability of the time to and level of DAS28 response on the likelihood of achieving low disease activity (LDA) at both Years 1 and 2 in rheumatoid arthritis (RA) patients treated with certolizumab pegol (CZP) + methotrexate (MTX).

Methods: Patients treated with every other week CZP 200 or 400 mg + MTX in RAPID 1 were combined for analysis (N=783). The proportion of patients who achieved DAS28 LDA (DAS28 \leq 3.2) at Years 1 and 2 (during the open-label extension [OLE]) were assessed according to the level of DAS28 response (i.e., DAS28 decrease from baseline [BL] < 0.3, 0.6, 0.9, 1.2, 1.5 and 1.8 units) by various time points (Weeks 1, 2, 4, 6, 8, 10 or 12). Last observation carried forward (LOCF) imputation was used for patients who did not re-consent to enter the OLE, received rescue medication or who withdrew from the OLE.

Results: Of the 783 patients randomized to CZP + MTX, 670 patients entered the OLE; of these, 96 patients withdrew and 574 remained in the OLE at Year 2. 98% of randomized patients had DAS28 >5.1 at BL (mean BL DAS28 was 6.9). 86.0% of patients had a 1.2 DAS28 response by Week 12 . LDA was achieved by 35.2% of the original CZP ITT population at Year 2. Failure to achieve LDA at both Years 1 and 2 was dependent on the level of DAS28 change up to Week 12. Patients with DAS28 changes < 0.3 by Week 4, < 0.9 by Week 6, < 1.2 by Week 10 or < 1.8 by Week 12 had a < 5% chance of having LDA at both Years 1 and 2. For any given change in DAS28, failure to respond by Week 12 was more predictive of failure to achieve LDA at both Years 1 and 2 compared with failure to respond by earlier time points.

Conclusion: The majority of patients responded to treatment with CZP by Week 12. These data stress the importance of significant early response by Week 12, in order to achieve long term low disease activity and help the clinician in the treatment decision process.

Efficacy and Safety of Certolizumab Pegol Plus Methotrexate in Patients With Rheumatoid Arthritis: 3-Year Data From the RAPID 2 Study

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Objective: To evaluate the sustainability of improvements in rheumatoid arthritis (RA), inhibition of joint damage progression and tolerability of CZP + MTX over 3 years in patients who completed 24 weeks of double-blind treatment with CZP 200 mg or 400 mg EOW + MTX (completers) in RAPID 2 and entered an open-label extension (OLE) of CZP 400 mg EOW + MTX.

Methods: ACR responses, DAS28(ESR), HAQ-DI, pain VAS (0-100-mm scale) are shown over 3 years (148 weeks) from the RAPID 2 baseline (BL) for CZP completers who entered the OLE; modified Total Sharp Scores (mTSS) are shown over 2.5 years (128 weeks). Patients who withdrew from the OLE for any reason or took rescue medication in the OLE had data imputed from that time point onwards. For mTSS, linear extrapolation (Lin ext) was used. For DAS28, HAQ-DI and pain VAS, last observation carried forward (LOCF) was used for any missing data. For ACR responses, both non-responder imputation (NRI) and observed data are reported. AEs were assessed at each visit (after first study drug administration) from the RAPID 2 BL. Safety analyses were based on the ITT population. AEs and serious AEs (SAEs)/100 patient-years are presented for all pts who received ≥ 1 CZP dose.

Results: Of 494 patients treated with CZP + MTX, 355 completed RAPID 2; of these, 342 (96%) entered the OLE. Completers entering the OLE had high disease activity at the RAPID 2 BL (mean: DAS28: 6.8; HAQ-DI: 1.6; pain VAS: 60.7); mean mTSS at the RAPID 2 BL was 33.6. After 3 years, 79% of CZP completers continued to receive OL CZP; only 2 patients withdrew due to lack of efficacy. ACR responses and improvements in DAS28, HAQ-DI and pain from BL were sustained in the OLE to 3 years in CZP completers. Inhibition of progression of structural damage observed during the placebo-controlled phase was sustained up to the last X-ray evaluation at 2.5 years. The incidence of AEs by Week 148 was 108.17/100 patient-years, and SAEs 13.35/100 patient-years. Most AEs were mild to moderate.

Conclusion: Addition of CZP provides clinical improvements that are sustained over 3 years, inhibits joint damage progression and is well tolerated.

Efficacy Sustained After Dose De-escalation of Certolizumab Pegol in Rheumatoid Arthritis Patients: Post-hoc Analysis of the RAPID 2 Open-label Extension

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Objective: To investigate the impact of certolizumab pegol (CZP) dose decrease on efficacy in rheumatoid arthritis (RA) patients.

Methods: This analysis includes all RAPID 2 CZP 200 and 400 mg completers who received CZP 400 mg EOW + MTX in the OLE and who subsequently had the CZP dose decreased to 200 mg EOW by the 3-year data cut. CZP dose decrease was mandatory after ≥ 6 months in the OLE. As the dose decrease occurred at different times, data are shown up to 48 weeks of CZP exposure following dose decrease, with Week 0 (for this analysis) set as the last efficacy assessment visit prior to dose decrease; CZP dose decrease occurred between Weeks 0 and 10. Week 12 is therefore the first visit after dose decrease. Analyses include mean DAS28 (ESR) and HAQ-DI scores (last observation carried forward [LOCF]) and ACR responses (non-responder imputation). Data are shown by treatment originally received in RAPID 2 (200 or 400 mg EOW + MTX).

Results: Of 342 RAPID 2 completers who received OL CZP 400 mg + MTX, the CZP dose was decreased in 287 (139 CZP 200 mg and 148 CZP 400 mg completers) by the 3-year data cut. All 287 patients received OL CZP 400 mg for ≥ 1 year prior to dose decrease, with 126 and 132 CZP 200 and 400 mg completers, respectively, having reached up to 48 weeks exposure following dose decrease (Week 48 of this analysis). Mean DAS28 scores were 3.77 (SD: 1.22) and 3.54 (1.08) in CZP 200 and 400 mg completers at Week 0 and remained similar after dose decrease to Week 48. Mean HAQ-DI scores were 0.91 (0.61) and 0.90 (0.56) in CZP 200 mg and 400 mg completers, respectively, at Week 0 and were similar to Week 48 (0.87 [0.59] and 0.84 [0.56], respectively). The ACR50 response rates at Week 48 after dose decrease were 47% and 42% for CZP 200 mg and 400 mg completers, respectively; the ACR70 response rates were 24% and 22%, respectively.

Conclusion: In RA pts who had an initial response to CZP, efficacy was maintained in the OLE after CZP dose decrease from 400 mg to 200 mg EOW + MTX.

Number Needed to Treat to Achieve Broad Relief From the Burden of Rheumatoid Arthritis (RA) in Patients Treated With Certolizumab Pegol Plus Methotrexate

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Objective: To determine the number needed to treat (NNT) to achieve minimum clinically important differences (MCIDs) in multiple patient reported outcomes (PROs) following treatment with certolizumab pegol (CZP) 200 mg + MTX compared with placebo (PBO) + MTX in the RAPID 1 and RAPID 2 trials.

Methods: The proportion of patients reporting improvements \geq MCID in RAPID 1 (Weeks 24 and 52) and RAPID 2 (Week 24) was determined for the following PROs: arthritis pain (0S100-mm visual analogue scale [VAS], MCID \geq 10 mm), fatigue (Fatigue Assessment Scale, 0S10 numeric rating scale, MCID \geq 1 point), physical function (Health Assessment Questionnaire-Disability Index, MCID \geq 0.22 points), patient's global assessment of disease activity (PtGA, 0S100-mm VAS, MCID \geq 10 mm), and HRQoL (SF-36 Physical and Mental Component summaries [PCS, MCS], MCID \geq 2.5 points). NNT and benefit ratios (BR, % responders in active treatment/% responders in PBO) to achieve improvements \geq MCID in at least 1, 2, 3, 4, 5 or 6 out of the 6 considered PROs were calculated.

Results: The NNT to achieve clinically meaningful improvements in up to 5 of 6 PROs following treatment with CZP 200 mg + MTX was 2S3 additional patients after 24 weeks (RAPID 1 and RAPID 2) and remained similar at 52 weeks (RAPID 1); the NNT for improvements in all 6 PROs was 5 patients. Patients having achieved MCIDs in at least 5 of 6 PROs by Week 52 were more likely to be reported in pain, fatigue, physical function and PtGA than SF-36 PCS and MCS. Of the patients who reported improvements \geq MCID in 5 of 6 PROs, 29% and 46% of patients did not report changes \geq MCID in SF-36 PCS and MCS at Week 52, respectively. In contrast, 2S12% of patients did not report changes \geq MCID in the other PROs. Compared with PBO + MTX, CZP 200 mg + MTX patients were 4S6 times more likely to achieve improvements in 5 of 6 PROs, and 6S7 times more likely to report improvements in all 6 PROs.

Conclusion: Low NNTs indicate relatively few patients need to be treated with CZP + MTX to achieve RA relief.

A Comparison of Sleep Quality in Rheumatoid Arthritis and Osteoarthritis Patients

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Objective: To evaluate and compare aspects of sleep quality in Rheumatoid Arthritis (RA) and Osteoarthritis (OA) patient populations.

Methods: Consecutive RA and OA clinic patients were invited to participate in a self-administered questionnaire study which included the multi-domain Pittsburgh Sleep Quality Index (PSQI).

Results: The study population included 145 RA and 78 OA patients. No significant differences in PSQI global or domain scores were observed between diagnostic groups. PSQI global scores were abnormal in 62% of RA and 67% of OA patients. Increased abnormalities in subjective sleep assessment, sleep latency, sleep duration, sleep efficiency, daytime dysfunction and increased sleep aid medication use were observed in both populations. The most common abnormality reported by both RA and OA patients was increased sleep fragmentation with frequent disturbances.

Conclusion: A high prevalence of abnormal sleep quality in both RA and OA patient populations was observed. The most common abnormality was sleep fragmentation with an increased sleep disturbance score.

Development, Evaluation and Implementation of a Successful Interprofessional Education Program for Adults with Inflammatory Arthritis

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Objective: Arthritis is a chronic, debilitating disorder characterized by inflammation, pain and joint destruction. Effective patient education about arthritis and its treatment is an important component of patient care, complementing medical treatment by teaching people to self-manage their disease. This evaluation was designed to assess the feasibility of a one-day, interprofessional, inflammatory arthritis education program and to explore the effect of the program on arthritis self-efficacy, arthritis knowledge and other outcomes. This presentation examines the knowledge translation and adaptive strategies that made the evaluation, implementation and integration of the program possible at an urban teaching hospital.

Methods: A patient-based needs assessment and ongoing patient feedback prior to and during recruitment guided program development. An interprofessional arthritis care team, adult educators, clinical researchers and an arthritis consumer were involved in determining and refining program format, duration and content. The interprofessional team was involved in developing and delivering program content and adapting the program to patient needs following the completion of the present study. Patients attended a single day (6 hours) education session which combined didactic, small group and large group modalities. This was a non-randomized, wait-listed control (with cross-over) trial of patients with inflammatory arthritis. Data was collected at baseline, following intervention (I), at 6 months [cross-over: control group (C) receives I], following cross-over and at 1 year. Self-report measures included: demographics, disorder-related, arthritis self-efficacy, arthritis knowledge, coping efficacy, illness intrusiveness. Outcomes assessed using reliable and valid measures. Analysis included: baseline comparison (I vs C), Standardized Effect Size (SES) at 6 months, Generalized Estimating Equations (GEE) analysis to evaluate repeated measures.

Results: Patient interest was very high. The one-day program format combined with the non-randomized study design made participation and attendance feasible for patients. Program and study modifications based on patient input made recruitment possible. 42 persons participated (I n=23; C n=19) with 93% follow-up at 1 year. No significant baseline differences between groups. Comparison of change at 6 months (I vs C) showed moderate effect sizes (SES ranging from 0.5 to 0.7). GEE analysis showed significant main effect, pre to post RxEd, in both groups across outcomes.

Conclusion: Program feasibility was dependent on patient feedback and program adaptations. This study provides evidence that the RxEd program is feasible, improves arthritis self-efficacy, arthritis knowledge and other outcomes. The program is now successfully being implemented as part of usual care, supported by ongoing program evaluation.

Low Rates of Infliximab Dose Titration and Discontinuation Are Observed in Rheumatoid Arthritis (RA) Patients in a Real-life Canadian Cohort

Bill Bensen (McMaster University, Hamilton); Rafat Faraawi (N/A, Kitchener); Hayssam Khalil (Merck Canada Inc, Montreal)

Objective: The recommended dose of infliximab (IFX) in RA is 3 mg/kg given as an IV infusion followed by additional 3 mg/kg doses at 2 and 6 weeks after the first infusion then every 8 weeks thereafter. For patients who have an incomplete response, consideration may be given to adjusting the dose up to 10 mg/kg and/or treating as often as every 4 weeks. The aim of this analysis is to evaluate the dose changing patterns and related therapeutic response observed in RA patients treated with IFX in Canada.

Methods: The data for this analysis were obtained from an observational study of adult RA patients initiated on treatment with IFX and followed prospectively as per routine care since 2002. Patients enrolled were biologic naïve or had initiated treatment with a biologic less than six months prior to enrolment.

Results: A cohort of 385 patients, who were enrolled up to May 31st 2006 and thus had the potential of treatment for at least 48 months, and who had at least one follow-up visit, were included in this analysis. At baseline, mean (SD) age was 56.4 (13.5) years and mean disease duration was 11.2 (10.3) years. During 48 months of follow up, 2075 infusions were recorded and the mean dose of IFX used was 3.46 (0.59) mg/kg. A similar value was obtained for patients (n=81) who ended their participation (median time to discontinuation was 38.2 months) due to lack or loss of response, disease progression or an adverse event (mean of 3.52 mg/kg (0.61) for a total of 337 infusions). Among patients discontinued due to lack/loss of response or disease progression (n=67), only 11 (16.4%) had an increased dose and/or frequency of IFX compared to their baseline levels (3 patients had an increased dose and 8 an increased frequency), while none of the patients who were discontinued due to an adverse event (n=14) was dose-optimized. For 17% of patients the initial dose of IFX was < 3 mg/Kg. After 48 months of treatment, 83.1% of patients remained on a stable dose and frequency of IFX (n=320).

Conclusion: The results of this real-life observational study demonstrate that a low rate of IFX dose optimization and a low rate of discontinuation are observed in Canadian RA patients treated with IFX. Additionally, the data from this cohort suggest that very few patients are dose optimized before discontinuing treatment due to lack or loss of response or disease progression.

Long-term Safety, Under Routine Care, of Infliximab in Patients With Rheumatoid Arthritis in a Large Canadian Cohort

Bill Bensen (McMaster University, Hamilton); Denis Choquette (Hôpital Notre-Dame, Montreal); Niall Jones (University of Alberta, Edmonton); Dalton Sholter (124 Street Medical Group, Edmonton); Alex Yan (University of Alberta, Edmonton); Rafat Faraawi (N/A, Kitchener); Heidi Imhoff (Merck Canada Inc, Kirkland)

Objective: The efficacy and safety of Infliximab (IFX) in Rheumatoid Arthritis (RA) has been demonstrated in several controlled clinical trials. Assessment of long-term safety under real-life conditions is necessary for the population based benefit-risk evaluation. This analysis describes for the first time the long-term safety profile of IFX in a routine care cohort of Canadian patients with RA.

Methods: The data for this analysis were obtained from an observational study of adult RA patients initiated on treatment with IFX and followed prospectively as per routine care since 2002. Patients enrolled were biologic naïve or had initiated treatment with a biologic less than six months prior to enrolment. All adverse events were reported using preferred term and high-level System Organ Class codes, using the most severe intensity for that event.

Results: 765 patients were recruited with a mean (SD) age of 55.9 (13.4) years and mean (SD) duration of disease at baseline of 10.3 (9.9) years. After a mean follow up of 17.8 (16.9) months, 76 out of 765 patients (9.9%) reported 121 serious adverse events (SAEs). Among these, serious infections were reported by 23 patients (3.0% or 2.2 serious infections / 100 pt-yrs). Non serious AEs (NSAEs) were reported by 36.2% of patients, including 92 patients (12.0%) experiencing an infection. Malignancies were reported in 6 patients (0.8%) and 33 out of the 765 patients (4.3%) had infusion-related reactions, 85% of which were mild to moderate in severity. There was one case of disseminated tuberculosis reported 25.4 months after baseline, which resulted in death. A newly acquired infection seems likely as the patient's TB screening at baseline was negative and the patient had traveled to India four months prior to TB onset. One additional death was possibly related to the study treatment (atherosclerosis of coronary artery), while 3 deaths were judged unrelated.

Conclusion: In the Canadian routine care setting IFX was well tolerated for the management of RA.

The Efficacy of Non-biologic Disease-modifying Antirheumatic Drugs (DMARDs) in the Treatment of Pain in Early Versus Late Inflammatory Joint Disease (IJD): a Systematic Literature Review

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Objective: Non-biologic DMARDs have been used in the management of IJD for decades. In recent years, the importance of prompt initiation of such treatment to prevent the development of joint erosions and resultant damage has become apparent, especially in the treatment of rheumatoid arthritis (RA). Another clinically important outcome is that of pain control. In this systematic literature review, we investigated the effect of commonly prescribed non-biologic DMARDs on pain in early and late IJD. Biologic DMARDs were not studied.

Methods: A systematic literature search was performed with Medline, Embase, Cochrane Central and Cochrane Database of Systematic Reviews, and abstracts from the 2008/2009 annual congress of the American College of Rheumatology. A manual search of the citation lists of retrieved publications was performed. Only randomized controlled trials were included in the analysis. Their quality was assessed with the Risk of Bias tool; those fulfilling a minimum of 3/5 criteria were included. Descriptive statistics were used in the metaanalysis.

Results: Of 9,860 articles identified, 29 (8 for ankylosing spondylitis (AS), 6 for psoriatic arthritis (PsA), 8 for early rheumatoid arthritis (ERA) and 7 for RA) were included for analysis (some had >1 DMARD arm). For each of AS and PsA, only one study reported average disease duration < 5 years; the remainder studied established disease. In AS, 4 studies revealed VAS-pain improvement with sulfasalazine, while 4 studies revealed no VAS-pain improvement with DMARDs (2 studied sulfasalazine, 1 leflunomide, 1 methotrexate). In PsA, 5 studies (3 sulfasalazine, 2 gold) reported VAS-pain improvement, whereas 3 studies (1 each of methotrexate, methotrexate + cyclosporine, and gold) did not. In ERA and RA, use of all DMARDs and combinations thereof resulted in significant VAS-pain improvement excepting two studies of gold salts. Although there was heterogeneity, for studies that could be analyzed, the DMARD-associated mean VAS-pain decrement in ERA, RA, PsA and AS (using a 100 mm scale) was 29.3, 20.6, 16.9, and 12.8 (median 28.4, 21.4, 13.5 and 11.5), respectively. There was no difference in mean disease duration between studies reporting efficacy and those that did not in any disease category.

Conclusion: Sulfasalazine may be beneficial in improving pain in AS and PsA. All DMARDs appear to improve pain in early and established RA. The greatest VAS-pain decrement was in ERA patients, and the least in AS patients. Relative efficacy of DMARDs in pain control in early versus late IJD could not be addressed.

Assessing the Efficacy of Early Optimal Parenteral Methotrexate in an ERA Cohort, Single-site Experience

David Rowe (Saba University School of Medicine, Stouffville); Carter Thorne (Southlake Regional Health Care, The Arthritis Program, Newmarket); CATCH Scientific Advisory Committee (Canadian Arthritis Cohort, Toronto)

Objective: We have previously used the CATCH cohort to investigate the efficacy of treatment of rheumatoid arthritis with early optimal dosing of parenteral methotrexate (pMTX) (≥ 20 mg/week). **S** initial results suggested increased remission rates. As a follow-up study we examined a single site (with an established treatment strategy that uses early optimal pMTX) in an attempt to develop more robust data. Outcomes were: Proportion of single-site patients treated with early optimal pMTX achieving DAS28-defined remission ($\text{DAS28} < 2.6$) and low disease activity (LDAS; $\text{DAS28} < 3.2$) by 3, 6 and 12 months.

Methods: A chart audit was conducted for a Newmarket, ON community Rheumatology practice. Patients previously eligible for the CATCH cohort were selected for review. Baseline clinical data was recorded from first visit so as to capture evidence of disease activity prior to treatment. Clinical indicators of disease activity were assessed at baseline, 3, 6 and 12 months **S** including swollen joint count, tender joint count, ESR/CRP, DAS28 and HAQ score. Rheumatoid factor (RF) and anti-CCP positivity as well as radiographic evidence of erosive change were also recorded if available.

Results: One hundred and nineteen ($n=119$) patient charts were eligible for review at time of submission. At this site 76% of patients with Early Rheumatoid Arthritis were started on early optimal doses of pMTX. Of these, 81% also received initial corticosteroid injections or short course oral prednisone. At 12 months 67% of patients started on early optimal pMTX had achieved DAS28-defined remission; 86% had achieved low disease activity (LDAS). 52% of patients were RF positive.

Conclusion: Remission rates in patients treated with early optimal pMTX at this particular site appear to be higher than previously reported results within the cohort. Potential confounders include patient enrolment in a local arthritis program, concurrent treatment with corticosteroids and, in fewer cases, other DMARDs, and the possibility of more self-limiting disease in those patients who are RF negative. At time of conference, further review of updated clinical visits and data will be available to strengthen initial results.

Correlation of CDAI and SDAI with DAS in a Large, Real-life Cohort of RA Patients Treated With Infliximab

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Objective: In recent years, the efficacy of anti-TNF-alpha in the management of RA has been demonstrated in numerous controlled clinical trials. The Clinical Disease Activity Index (CDAI) and Simplified Disease Activity Index (SDAI) have been recently designed as simplified disease activity scores. The purpose of this analysis is to evaluate the correlation between these simplified disease activity scores and routine clinical practice scores.

Methods: The data for this analysis were obtained from an observational study of adult RA patients initiated on treatment with infliximab and followed prospectively as per routine care since 2002. Patients enrolled were biologic naïve or had initiated treatment with a biologic less than six months prior to enrolment.

Results: A total of 440 patients, who were enrolled up to 31 May 2006 for RA and thus had the potential of treatment for 48 months, were included in this analysis. Mean (SD) age was 56.4 (13.6) years and mean (SD) disease duration at baseline was 11.0 (10.2) years. Mean (SD) SDAI at month 0, 6, 12, 24, 36 and 48 were 44.0 (16.5), 18.8 (13.9), 16.5 (13.1), 13.5 (12.0), 13.4 (11.9) and 10.6 (9.8), respectively. Mean (SD) CDAI at months 0, 6, 12, 24, 36 and 48 were 41.6 (15.9), 17.5 (13.4), 15.0 (11.9), 12.3 (11.7), 11.5 (11.6) and 8.7 (9.7), respectively. Mean (SD) DAS28-4 CRP at month 0, 6, 12, 24, 36 and 48 were 5.0 (1.1), 3.3 (1.2), 3.2 (1.2), 3.0 (1.1), 2.9 (1.2), and 2.6 (1.0), respectively. HAQ scores at month 0, 6, 12, 24, 36 and 48 were 1.8 (0.7), 1.3 (0.8), 1.2 (0.8), 1.2 (0.8), 1.1 (0.8) and 1.0 (0.8), respectively. These results show that by 6 months of treatment significant changes ($P < 0.05$) were observed using all scores. Further slight improvement in between 6 months and 48 months were observed with all analyzed scores.

Conclusion: The results of this real-life observational study demonstrate that over four years of treatment infliximab is effective in reducing symptom severity and improving outcomes in patients with Rheumatoid Arthritis using different scores. Also, the data from this registry confirmed the validity of the SDAI and CDAI as disease activity measures in a real-life RA cohort.

Profile of Patients with Rheumatoid Arthritis Treated With Infliximab in Canada-Trends Toward Less DMARD Use Prior to a Biologic, Earlier Use of Infliximab and Differences in Baseline Disease

Bill Bensen (McMaster University, Hamilton); Christopher Atkins (University of Victoria, Victoria); Maqbool Sheriff (Nanaimo Regional General Hospital, Nanaimo); John Kelsall (Mary Pack Arthritis Center and St Paul's Hospital, Vancouver); Hayssam Khalil (Merck Canada Inc, Montreal)

Objective: The efficacy of Infliximab (IFX) in Rheumatoid Arthritis (RA) is well established. Patient profiles and use of biologics have reportedly changed since their introduction. The aim of this analysis is to describe Canadian patient profiles at the time of initiation of IFX and treatment outcomes in the years 2002 until 2009.

Methods: The data for this analysis were obtained from an observational study of adult RA patients initiated on treatment with IFX and followed prospectively as per routine care since 2002. Patients enrolled were biologic naïve or had initiated treatment with a biologic less than six months prior to enrolment. Patients were analyzed by the year of their enrolment.

Results: A total of 757 patients were enrolled between 2002 and December 31st, 2009. A tendency was observed across years towards earlier IFX initiation upon disease diagnosis as indicated by the decrease in disease duration (12.4 years in 2002 vs 7.8 years in 2009) and treatment of patients with fewer DMARDs prior to study enrollment, as indicated by the decrease in proportion of patients who had received >4 DMARDs prior to initiation of IFX (25% in 2002 vs 5% in 2009). Furthermore, patients' profile at baseline (BL) changed significantly across years towards less severe disease: mean DAS28-CRP 5.9 in 2002 vs 4.6 in 2009; mean HAQ 1.8 in 2002 vs 1.4 in 2009; mean SJC 13.9 in 2002 vs 7.4 in 2009; mean TJC 16.1 in 2002 vs 10.1 in 2009; mean PGA 7.2 in 2002 vs 5.9 in 2009; mean SGA 63.4 in 2002 vs 54.9 in 2009; and mean pain (VAS) 60.1 in 2002 vs 50.6 in 2009. Interestingly, patients with provincial coverage (n=380) had higher DAS28 [5.5 (1.1) vs. 5.0 (1.3)], HAQ [1.9 (0.6) vs. 1.5 (0.7)], SJC [12.9 (7.0) vs. 10.8 (6.9)], TJC [15.0 (7.9) vs. 12.9 (7.7)], PGA [7.0 (1.8) vs. 6.1 (2.3)], SGA [64.8 (22.2) vs. 57.2 (26.0)], Patient Pain [62.4 (22.6) vs. 52.6 (25.4)] and AM stiffness [75.2 (43.4) vs. 67.2 (43.9)] compared to patients with private coverage (n=270).

Conclusion: The results of this study show a significant change in several clinical and patient outcomes towards lower disease activity at initiation of IFX treatment between 2002 and 2009. Patient management has also changed, with a trend to initiate IFX treatment after failure of fewer DMARDs. Finally, patients with public coverage appear to have a more severe disease profile at baseline compared to patients on private coverage.

Disconnect Between Disease Activity and Joint Space Narrowing for Patients with Early RA Treated with Adalimumab plus Methotrexate but not Methotrexate Alone: Case for Anti-Tnf Cartilage Protection

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Objective: Joint space narrowing (JSN) is inhibited by treatment with the combination of adalimumab (ADA) and methotrexate (MTX). Importantly, it is not known whether ADA+MTX treatment exerts these protective effects solely by controlling inflammation or also by a specific effect on cartilage as has been shown for joint erosions. The objective of this analysis was to compare the relationship between disease activity (DAS28) and progression of JSN in patients with early rheumatoid arthritis (RA) treated with ADA+MTX vs. MTX.

Methods: Two-year data of the PREMIER study (a randomized controlled trial comparing MTX with ADA+MTX in patients with early RA) were used to perform this analysis. Data were from patients (n=525) randomized to MTX or ADA+MTX. DAS28 was time-averaged (TASDAS28) over 3 intervals from baseline: 26, 52, and 104 weeks, and multivariate analyses were performed to assess the impact of treatment and TASDAS28 on change in JSN after 26, 52, and 104 weeks of treatment. To control for continuous between-group variations in DAS28, we compared groups by TASDAS28 quartile.

Results: All results are changes in JSN expressed by quartile (range) of TASDAS28. In the MTX group, JSN increased as TASDAS28 increased [Week 26 (observed): Q1 (< 3.6): 0.38; Q2 (3.6 ≤ 4.4): 0.39; Q3 (4.4 ≤ 5.1): 0.64; Q4 (≥ 5.1): 2.43. Week 52 (observed): Q1 (< 3.2): 0.60; Q2 (3.2 ≤ 4.0): 1.05; Q3 (4.0 ≤ 4.8): 1.38; Q4 (≥ 4.8): 3.97. Week 104 (linear imputation): Q1 (< 3.3): 0.82; Q2 (3.3 ≤ 4.2): 2.11; Q3 (4.2 ≤ 5.1): 2.98; Q4 (≥ 5.1): 8.14]. However, this relationship was not apparent in the ADA+MTX group [Week 26: Q1 (< 3.6): 0.15; Q2 (3.6 ≤ 4.4): 0.17; Q3 (4.4 ≤ 5.1): 0.06; Q4 (≥ 5.1): 0.63. Week 52: Q1 (< 3.2): 0.52; Q2 (3.2 ≤ 4.0): 0.43; Q3 (4.0 ≤ 4.8): 0.55; Q4 (≥ 4.8): 0.53. Week 104: Q1 (< 3.3): 0.56; Q2 (3.3 ≤ 4.2): 0.90; Q3 (4.2 ≤ 5.1): 1.02; Q4 (≥ 5.1): 1.60]. Week 104 results were similar using either observed data or linear imputation.

Conclusion: The typical relationship between TA-DAS28 and progression of JSN was observed in patients treated with MTX; however, this relationship was not apparent in patients treated with ADA+MTX. These results suggest that ADA+MTX may have direct protective effects on cartilage that are beyond its ability to control for disease activity, potentially through the inhibition of catabolytic activities in chondrocytes.

Safety of Infliximab Treatment in a Real-World Clinical Setting: Description and Evaluation of Infusion Reactions

John Kelsall (University of British Columbia, Vancouver); Mary De Vera (Arthritis Research Centre of Canada, Vancouver); Pamela Rogers (Arthritis Research Centre, Vancouver); Griselda Galindo (Arthritis Research Centre, Vancouver); Alice Klinkhoff (Mary Pack Arthritis Program, Vancouver)

Objective: Our objective was to describe acute and delayed infusion reactions in a large cohort of patients treated with infliximab (IFX).

Methods: We conducted a retrospective chart review of patients treated with IFX at the Mary Pack Arthritis Centre between 2000 and 2008. Primary outcome was the occurrence of acute infusion reactions occurring during or up to 2 hours after each infusion and secondary outcome was the occurrence of delayed infusion reactions occurring between 1 to 14 days after an infusion. Descriptive statistics were used to characterize demographics, clinical histories, and acute and delayed infusion reactions. Rates of acute and delayed reactions were calculated as the number of reaction episodes divided by the number of INF infusions during the follow-up. Analyses were conducted for all patients and for patients with rheumatoid arthritis (RA) separately, who represented the largest proportion of patients in the cohort.

Results: Overall, we report on 200 patients: 135 (67%) patients had RA, 23 (12%) psoriatic arthritis, 22 (11%) ankylosing spondylitis, 6 (3%) ocular inflammatory disease, and 14 (7%) other inflammatory arthritis. Mean disease duration at first infusion for all patients and RA patients were 15.8 ± 10.9 and 16.7 ± 11.2 years, respectively. Altogether, patients received 4,399 IFX infusions over mean 140 ± 132 weeks of follow-up. Of these, 135 were patients with RA who received 2,977 IFX infusions over mean follow-up of 138 ± 132 weeks. 258 episodes of acute reactions were observed for an overall acute reaction rate of 5.9% (5.2% for RA patients). Acute reactions were mostly mild (42.6%) and moderate (43.8%) in presentation and the most commonly affected sites were head and neck (31.5%) and skin (21.1%). 37 delayed reaction episodes were observed (0.84% for all patients; 0.81% for RA patients) and were also mostly mild (16.2%) and moderate (64.9%) in presentation.

Conclusion: This study provides a description of acute and delayed infusion reactions in 200 patients treated for rheumatologic conditions in a real world clinical setting. Overall, data demonstrate that acute and delayed infusion reactions occur infrequently and when they do occur, are mostly mild to moderate in severity.

A Description of Surgical Procedures Among Patients with Rheumatoid Arthritis on Infliximab Treatment

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Objective: Despite the growing use of biologics in rheumatoid arthritis (RA), there is limited information on the characteristics of patients undergoing surgeries during treatment courses with these agents. Our objective was to characterize RA patients undergoing surgeries during treatment on infliximab (IFX) in a real world clinical setting.

Methods: We conducted a retrospective chart review of RA patients treated with IFX at the Mary Pack Arthritis Centre between 2000 and 2008. Extracted clinical data included demographic information, RA disease characteristics, comorbidities, medication history, and information over all infusions performed. A detailed history of all surgical procedures occurring after a first IFX infusion was collected. Surgeries were classified according to specialty (i.e., orthopedic, cardiothoracic) as well as type (i.e., athroplasty, bypass procedure). For each surgery, we calculated the elapsed period from a prior and subsequent IFX infusion. Descriptive statistics were used to present the data. To compare characteristics of RA patients who received surgery with those who did not, we used independent samples t-tests for continuous variables and chi-square tests for categorical variables.

Results: A total of 135 RA patients (79% female) received 2,977 IFX infusions over mean follow-up of 138 ± 132 weeks. At baseline (1st IFX infusion), mean age was 54 years and RA duration was 16.7 ± 11.2 years. Overall, 39 RA patients (29%) underwent at least one surgical procedure during treatment with IFX. RA patients who underwent surgery did not differ from RA patients who did not undergo surgery across baseline disease characteristics. Among the 39 surgical patients, a total of 78 procedures were recorded during treatment with IFX (24 patients underwent 1 surgery, 6 patients underwent 2 surgeries, 4 patients underwent 3 surgeries, 1 patient underwent 4 surgeries, 2 patients underwent 5 surgeries, 1 patient underwent 7 surgeries, and 1 patient underwent 8 surgeries). The most frequent type of surgery was orthopedic 58% (n=45) of these 47% were joint prostheses; 10% (n=8) were cardiothoracic surgeries; 9% (n=7) were nodule excisions and tendon repairs, 8% (n=6) involved abdominal procedures such as colostomies; 4 were dental procedures, 4 were genitourinary procedures and 4 miscellaneous, including ophthalmological procedures.

Conclusion: This study provides a description of surgical procedures in RA patients undergoing IFX treatment in a real world clinical setting. Overall, data demonstrate that surgical patients did not differ from non-surgical patients at baseline disease and that orthopedic procedures represent the most common surgeries in these patients.

A Comparison of Methotrexate Use Amongst Dermatologists and Rheumatologists in Canada

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Objective: Methotrexate (MTX) is commonly used by both dermatologists in the treatment of psoriasis and rheumatologists for psoriatic arthritis (PsA) and rheumatoid arthritis (RA). Treatment guidelines on use of MTX have recently been published in both specialties but current use patterns are largely unknown. This study set out to explore and compare the current preferences of MTX use amongst Canadian dermatologists and rheumatologists.

Methods: An online survey was made available to 414 Canadian dermatologists and 415 Canadian rheumatologists during a two-week period in September 2010. The 50 question survey explored MTX use in the treatment of psoriasis, PsA, and RA with topics ranging from administration route to biologics use. Influencing factors were also explored.

Results: 27.2% of rheumatologists and 16.4% of dermatologists responded to the survey. Psoriasis 80.0% of rheumatologists and 96.8% of dermatologists who treated psoriasis used oral tablets to initiate MTX therapy. When needed, 95.7% of rheumatologists and 49.2% of dermatologists would switch to parenteral MTX. When they switched, 98.0% of rheumatologists and 62.5% of dermatologists switched to subcutaneous (SC) injections. When using biologics with MTX, 75.6% of rheumatologists did not change the MTX dose, while 81.1% of dermatologists discontinued MTX. Psoriatic Arthritis 82.0% of rheumatologists and 100% of dermatologists who treated PsA initiated MTX therapy with oral tablets. When needed, 100% of rheumatologists versus 68.8% of dermatologists would switch to parenteral MTX, specifically to SC injections (98.0% of rheumatologists, 81.8% of dermatologists). When using biologics, 70.4% of rheumatologists did not change MTX dose while 43.8% of dermatologists discontinued MTX.

Conclusion: The survey had an overall response rate of 21.8% (95% CI: 15.8% to 27.8%) so the results should be interpreted with this in mind. In treatment of psoriasis and PsA both specialties initiated MTX treatment with oral tablets. However, rheumatologists were more likely to switch to a parenteral route and use SC injections. While both specialties used biologics, they differed in how they bridged it from MTX. Rheumatologists would often not change the MTX dose after initiating a biologic whereas dermatologists would discontinue MTX, either immediately or through a taper. Rheumatologist's use of MTX was largely similar for RA and PsA. Overall, this study showed that in the treatment of psoriasis and PsA, rheumatologists and dermatologists do not differ in their initial use of MTX. However, the specialties showed a notable difference in their preferences for how they proceed with MTX use.

Patient-physician discordance of global disease assessment in psoriatic arthritis patients

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Objective: The visual analog scale (VAS- using a standard 0S10 range) is a common measure for global disease severity used by both patients and physicians. We assessed the concordance of psoriatic arthritis (PsA) patient scores compared with physician scores.

Methods: In our longitudinal study, 10 patients with active PsA completed the VAS assessing their global disease activity approximately every 4 weeks for up to 4 years. A physician's VAS was completed for every patient VAS completed. In addition, a count of both swollen and tender joints was completed for each visit, representing a standard scale of severity.

Results: Overall 237 assessments were analyzed, which showed VAS scoring for global disease by patients differed from the physician significantly; patients gave a higher level of severity than the physician (mean for patients = 2.70, mean for physician =1.97, paired t-test = 3E-9). More specifically, 7 of the 10 patients gave values that were significantly higher than the physician's values. The physician's VAS values correlated more strongly with the swollen joint count than the patient's VAS values (physician vs. swollen $r = 0.74$, patient vs. swollen $r = 0.36$).

Conclusion: This study demonstrates a significant discordance of the VAS scores for global assessment for patients with PsA between the patients and their physician. The physician's VAS score values correlated more strongly with the swollen joint count than did the patients. For patients, it would appear there are other factors beyond their swollen joints contributing to their global disease measurement.

Clinical and Radiographic Implications of Time to Treatment Response in Patients With Early Rheumatoid Arthritis

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Objective: Recent publications advocate treatment adjustment at 12 weeks (wks) for patients with rheumatoid arthritis (RA); still, data support the possibility of later responses to therapy. Our objective was to evaluate the association of early (12 weeks) and delayed (24 weeks) clinical responses with rates of clinical remission, low-disease activity (LDAS), and rapid radiographic progression (RRP) at 52 weeks in patients with early RA treated with MTX monotherapy or adalimumab (ADA) + MTX combination therapy in the PREMIER trial.

Methods: PREMIER was a 104-week, phase 3, randomized, placebo-controlled trial in a MTX-naïve population with early RA. In this post hoc analysis, observed data comparing MTX with ADA + MTX therapy are presented. Clinical outcome measures included the 28-joint Disease Activity Score (DAS28) and mean change from baseline in modified Total Sharp Score (Δ mTSS) at 52 weeks. Patients were categorized on the basis of clinical response (DAS28 improvement >1.2 or 20/50/70% improvement in ACR score) at 12 and 24 weeks: “early responders” achieved the clinical target at week 12 and maintained the response at week 24; “delayed responders” did not meet the clinical target until week 24. The percentages of patients at 52 weeks with LDAS (DAS28 < 3.2), clinical remission (DAS28 < 2.6), and RRP (Δ mTSS >3 units/year) in each group were determined.

Results: In both treatment groups, early clinical responses were associated with better long-term outcomes than delayed responses. Achieving early or delayed ACR70 responses did not result in treatment group differences in the proportion of patients achieving LDAS or clinical remission at week 52. However, delayed responses to MTX resulted in a high proportion of patients with RRP. Indeed, delayed ACR70 responses were associated with an RRP prevalence of 40%. In addition, even an early improvement of DAS28 >1.2 with MTX was insufficient to slow radiographic progression (41% RRP). In contrast, early or delayed clinical responses to ADA + MTX resulted in low proportions of RRP at 52 weeks, even for patients with a delayed ACR20 response (11% RRP). Of note, ADA + MTX delayed responders had less RRP than MTX-treated early responders.

Conclusion: MTX-treated patients with early RA who fail to achieve an ACR70 within 12 wks of treatment are at risk for RRP and should be considered for treatment adjustment. In contrast, ADA + MTX treatment is associated with better clinical outcomes and less severe radiographic progression at 52 wks, even among patients with a delayed clinical response.

The Relationship Between Oral Health and Psychosocial Outcomes in Systemic Sclerosis

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Objective: Orofacial manifestations of systemic sclerosis (SSc) are common and SSc is known to be strongly associated with worse psychosocial outcomes, including depression, health-related quality of life (HRQoL), function and fatigue. The purpose of our study was to evaluate the association between oral health and psychosocial outcomes in SSc patients.

Methods: In a cross-sectional study, SSc patients from the Canadian Scleroderma Research Group Registry, were randomly recruited from 7 centers. Oral health was assessed using the Oral Health Impact Profile (OHIP), a validated self-reported measure of dysfunction, discomfort and disability attributed to oral conditions. The OHIP is composed of 7 subscales (functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap). Each subscale is scored separately from 0 to 40 (with 0 representing better and 40 representing worse quality of life). An overall score, ranging from 0 to 40, can also be computed using a detailed algorithm. In this study, psychosocial outcomes of interest included: depression (measured using the Center for Epidemiologic Studies Depression questionnaire, range 0-60), HRQoL (measured using the Medical Outcome Trust Short Form 36 Physical and Mental summary scores, SF-36 PCS and MCS, range 0-100, mean = 50, standard deviation = 10), function (measured using the Health Assessment Questionnaire, HAQ, range 0-3) and fatigue (measured using the Vitality subscale of the SF-36). The associations of the OHIP and the outcomes of interest were estimated using hierarchical regression analyses, adjusting for age, gender, education, current smoking and disease duration.

Results: There were 151 patients in the study: mean age 56.5 years, 90.1% female, 52.1% with more than high school education, 9.7% current smokers and mean disease duration 13.8 years. Mean OHIP score was 8.67. Mean SF-36 PCS and MCS scores were 37 and 50, respectively, HAQ was 0.79, depression was 14 and fatigue was 45. In multivariate analyses controlling for sociodemographic variables and disease duration, the OHIP was an independent predictor of the SF-36 PCS ($p \approx 0.001$), SF-36 MCS ($p < 0.001$), HAQ ($p < 0.001$), depression ($p < 0.001$), and fatigue ($p < 0.001$). The OHIP contributed 7 to 13% of the variance in the outcomes of interest.

Conclusion: This study demonstrates the significant impact of oral health on psychosocial outcomes in SSc. We recommend more attention and research on oral health in SSc patients.

Exploring the Needs of People with Rheumatoid Arthritis

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Objective: Comprehensive effective treatments for Rheumatoid Arthritis (RA) require patient-centered approaches that identify and address patients' needs and encourage patients to work in partnership with their health care providers. The goal of this study was to evaluate the extent to which medical, psychological, and social needs of people with RA are being met. Findings will be used to tailor interventions to optimize treatment and self-management.

Methods: Participants were recruited from the general rheumatology clinics at a major urban university hospital. Two focus groups of RA patients were held in August 2010 to elicit discussion about patient experiences and preferences. Sessions were audio-taped, transcribed, and analyzed using grounded theory methodology.

Results: Nine women and 2 men participated with a mean (SD) age of 53.6 (18.3), disease duration of 17.8 (13.3) yrs, and HAQ of 1.6 (0.8). Patients reported an average of 23.6 (22.7) minutes of morning stiffness, pain of 33.6 (28.4) and patient global function score of 42.1 (35.0). Nearly half (46%) were on DMARDS and/or biologics. Almost all endorsed a need for more information about their disease, RA medications, ways to effectively maneuver the health care system for prompt care, self-management and complementary/alternative treatments (CAM), along with ways to identify and access credible resources. Uncertainty related to RA (disease course, medications, disability, prognosis) increased patients' need for emotional support from family, friends, employers, health care providers, and the community at large. Current community-based services were seen as infrequent and inadequate to meet emotional and information needs, particularly with respect to self-management. Patients expressed a strong desire to partner with providers through ongoing communication and active participation in treatment decisions. Most described creating effective partnerships with providers by being assertive and taking initiative. Continued care with patient-centered multi-disciplinary providers was highly valued. Referral and access to specialists knowledgeable about the needs of RA patients and coordination of services is suboptimal.

Conclusion: While new therapies and treatment paradigms have changed RA outcomes, many daily challenges remain under-recognized and unaddressed. Timely, reliable information in an accessible format is needed about disease process, as well as conventional and CAM therapies. Support to remain active in family, work and community roles, creation of multi-disciplinary treatment teams and emphasis on creating and sustaining patient-centered partnerships offer important opportunities to improve quality of life. Evidenced-based methods to address unmet needs (e.g. information toolkits, support groups, patient-provider communication skills training) warrant investigation.

Demyelinating events in Seniors with Rheumatoid Arthritis (RA): A Population-based Study

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Objective: Up until recently, demyelinating syndromes were reported only rarely in RA. However, since the introduction of RA therapies targeting tumour necrosis factor (TNF), numerous case reports have arisen in the literature. Currently there are very few cohort-based assessments of the incidence of demyelinating events in RA, and/or the possible influence of drug exposures. The Ontario Biologics Research Initiative (OBRI) is an innovative undertaking to promote real-world rheumatic drug surveillance. Using Ontario's administrative healthcare databases we were able to assess the risk for developing demyelinating events in seniors with RA, and explore for potential drug effects in this sample.

Methods: We studied a population-based RA cohort using physician billing and hospitalization data (1992S2008) for patients aged > 65. RA diagnosis was based on > 2 billings with a diagnosis code of RA >2 months apart but < 5 years and >1 prescription for an oral glucocorticoid, DMARD or biologic. Cohort entry was defined by the first RA billing code; we excluded any individuals with a diagnosis of a demyelinating event, prior to their entry into the RA cohort. Our primary outcome was assessed over 1998S2008. Our case definition of a demyelinating event was based on >1 hospitalization diagnoses, or >2 billing claims diagnoses (> 8 weeks apart, but < 2 years). Cases were matched (on age, sex, and date of cohort entry) to up to 5 controls from the same RA cohort. We calculated the incidence rate of demyelinating events in seniors, and described medication use in relationship to these events.

Results: In 85,458 seniors with RA (over 614,915.5 person-years), 51 demyelinating events occurred. This provides an event rate of 8.3 events/100,000 person-years. Biologic exposures were rare in our cohort, and none of the cases of demyelinating events in our RA cohort had been exposed to an anti-TNF agent at the time of the event, or within the 12 months preceding the event. In both cases and controls, the most common medication exposures were NSAIDs/COXIBs, glucocorticosteroids, hydroxychloroquine, and methotrexate.

Conclusion: We provide novel data on the incidence of demyelinating events in a cohort of seniors with RA. The incidence rate is comparable to recent rates for Canadian seniors in the general population. None of these events appeared to have been triggered by anti-TNF drug exposures. Estimating the risk for demyelinating events due to these agents was problematic in our sample, given relatively low drug exposure rates.

The Incidence of Herpes Zoster in Seniors with Rheumatoid Arthritis: A Population-Based Study

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Objective: Herpes zoster (HZ) is a painful cutaneous eruption caused by varicella-zoster reactivation. It results in substantial morbidity, particularly in elderly and/or immunocompromised patients. Recent literature suggests that patients with rheumatoid arthritis (RA) are at particular risk for HZ. The Ontario Biologics Research Initiative (OBRI) conducts real-world surveillance through administrative database linkage with primary data collection, based in Canada's largest province (population > 13 million).

Methods: An RA cohort was assembled from Ontario billing, hospitalization and prescription data, 1992-2008. Analyses were limited to subjects aged >65 who filled >1 prescription for a disease-modifying agent (DMARD), oral corticosteroid, or biologic. We studied cases of HZ identified from physician billing and hospitalization diagnoses over 1998-2009. RA controls (age, sex and time matched) were randomly selected by risk-set sampling. Multivariate conditional logistic regression assessed the independent effects of concomitant drug treatments on HZ, adjusted for demographics, co-morbidity, and markers of RA severity (rheumatology visits, extra-articular RA features, joint replacement).

Results: A total of 3,999 cases of HZ were recorded among 85,458 seniors with RA during 614,915 person-years (6.5 events/1000 person-years). Comparing these HZ cases to 19,995 RA controls, 21.9% of cases versus 10.8% of controls were exposed to prednisone at the time of infection. Multivariate models demonstrated that risk of HZ was higher among current and previous users of current and past use of all DMARD groups. There was a notable increasing trend for higher risk of HZ with increasing steroid doses. Due to low rates of biologic drug exposures in our sample, the estimated effects of these agents were imprecise, but also consistent with a higher risk.

Conclusion: Our estimates emphasize an association of anti-rheumatic therapies with the occurrence of HZ. However, potential limitations of our study include the possibility of incomplete ascertainment of biologic exposures, disease activity and 'channelling bias' (where persons at highest risk for infections may not be prescribed biologics).

Treating Rheumatoid Arthritis to Target: A Canadian Physician Survey

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Objective: To assess agreement and application of T2T recommendations in Canadian practice.

Methods: A nationwide, web-based survey was conducted. Agreement with each recommendation was measured on a 10 point Likert scale (1= fully disagree, 10 = fully agree). A 4 point Likert scale (never, not very often, very often, always) assessed application of each recommendation in current practice. Responders who answered “never” or “not very often” were asked whether they were willing to change their practice according to the particular recommendation.

Results: 78 physicians (approximately 26% of the Canadian rheumatology community) responded. The mean number of participants’ years in practice was 18 and the average number of patients seen per month was 98. Average agreement scores ranged from 6.92 for recommendation #5 (Measures of disease activity must be obtained and documented regularly, as frequently as monthly for patients with high/moderate disease activity or less frequently [such as every 3 to 6 months] for patients in sustained low disease activity or remission) to 9.1 for recommendation #10 (The patient has to be appropriately informed about the treatment target and the strategy planned to reach this target under the supervision of the rheumatologist). A majority of participants indicated that they apply T2T recommendations in their practice. However, recommendations #4 (Until the desired treatment target is reached, drug therapy should be adjusted at least every 3 months), #5, and #6 (The use of validated composite measures of disease activity, which include joint assessments, is needed in routine clinical practice to guide treatment decisions) received the highest number of “never” or “not very often” responses (15.38%, 33.33%, and 32.05% for recommendations #4, #5, and #6, respectively). In addition 92%, 73%, and 17% of participants who were not applying recommendations #4, #5, and #6, respectively, in their practice indicated that they were not willing to change their practice according to these recommendations. Busy practice and disagreement with inclusion of composite outcome measures in treatment decisions were the main reasons for objections.

Conclusion: Although a majority of Canadian rheumatologists agreed with and supported T2T recommendations, there was also resistance toward specific aspects of these recommendations. Efforts are needed to better understand reasons behind identified disagreements, upon which action plans to re-enforce application of T2T recommendations in Canada should be developed.

Disease Activity in Patients Prescribed Biologics in Ontario: Results from the OBRI

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Objective: The goals of the Ontario Biologics Research Initiative (OBRI) are to determine the long term effectiveness and safety of Biologics in actual practice and to develop and evaluate a range of strategies to facilitate best practice implementation. To describe the disease characteristics of RA patients being prescribed a new biologic, in Ontario.

Methods: Patients registered in the OBRI, and prescribed a new biologic at the time of their enrollment, were included in the analysis. Two groups were identified; patients receiving their first biologic prescription (i.e., biologic naïve, n = 73) versus patients who had previously used a biologic (i.e., not biologic naïve, n = 77). Rheumatologist reported data at the time of enrollment included patient demographics and measures of disease activity. t-tests of the means were used to compare the two groups.

Results: A total of 150 (25%) of the 579 patients registered in the OBRI study were prescribed a new biologic at the time of enrollment. Their mean age was 53.2 years (SD of 12.9), and 85% were females. The mean RA duration was 12.9 years (10.7), physician global 5.9 (2.1), patient global 5.8 (2.5), mean ESR 33.1 mm/hr (23.1), and CRP 14.5 mg/l (19.6). Erosions on X-rays were reported in 80% of patients and 77% of patients were positive for Rheumatoid Factor. Two or more co-morbidities were reported in 60% of patients. Mean tender joint count was 9.3 (6.7), swollen joint count 9.0 (5.8), mean DAS 28 was 5.5 (1.2), SDAI was 33.5 (14.2), and CDAI was 30.4 (14.1). The majority of these patients were on concurrent Methotrexate treatment at the time of the new biologic prescription (69%). Enbrel was the most commonly prescribed biologic (33% of patients), followed by Humira (28%), and Rituxan (9.3%). When the biologic naïve patients were compared to those patients who had previously used a biologic, there were no statistically significant differences in any of the above measures.

Conclusion: While the biologic naïve patients were found to have higher DAS 28, SDAI, CDAI and patient and physician global scores, when compared to patients who had previously used a biologic, these differences were not found to be statistically significant.

A Conceptual Framework for the Design of Real-Time Systems for Clinical Monitoring and Research in Rheumatology

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Objective: The use of computers in rheumatology clinical practice is increasing with many clinicians developing their own databases, the use of institutional e-charts and the NIH Patient-Reported Outcomes Measurement Information System. This topic is of particular importance in rheumatology as current guidelines recommend tight monitoring of patient outcomes as a component of optimal care. Our objective was to develop a conceptual framework for the design of real-time systems for clinical monitoring and research in rheumatology.

Methods: Phased feasibility pilot to develop and evaluate technical prototypes combined with a scoping study which included a review of the literature and key informant interviews with experts within the fields of rheumatology, health informatics, ethics, privacy and security, patients and rheumatologists.

Results: We found that few of the established initiatives address the complex dynamics of a clinical research environment and issues related to ethics, privacy and data security. The E-Rheum infrastructure was developed through a series of phased feasibility studies funded by the CIHR. Phase one included key informant interviews with a range of stakeholders; testing of various types of devices and technologies for data entry; and the development of a prototype patient data capture interface that allowed patients with rheumatoid arthritis to complete validated measures and to summarize these data in a cumulative report available at the point-of-care. Phase two explored the feasibility of having the electronic data-capture and reporting system available on-line and continued to evaluate ease of use and satisfaction. Phase three involved multi-site deployment and real- life implementation to determine the organizational and technical requirements to integrate the application into usual care. Challenges related to ethics, privacy and data security were identified during each phase. In 2009, investigators received funding to develop the system for full implementation and deployment. Data from the feasibility pilot and scoping study informed the development of a conceptual framework for system development.

Conclusion: While there is an increasing body of literature to address issues of standardization, parsing, classification, etc. within health informatics, we could not find a conceptual framework through which we could communicate with our information technology experts to build user and system requirements that can respond to evolving ethics and privacy legislation. By including ethics and privacy experts as a part of the investigative team we were able to create a conceptual framework that takes into account the dynamic nature of the electronic clinical research environment.

Psychometric Properties of Self-Administered Early Inflammatory Arthritis Detection Tool

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Objective: To evaluate the discriminant validity, comprehensibility, test-retest reliability and internal consistency of an Early Inflammatory Arthritis (EIA) Detection Tool self-administered questionnaire.

Methods: A total of 166 adult English-literate outpatients attending Sunnybrook Health Sciences Centre and Mt. Sinai Hospital have participated in one of four study groups: 1.EIA (n=37): A rheumatologist's assessment of, or established diagnosis of either AS, PsA, RA, ReA, other SpA or undifferentiated IA with a symptom duration of six to 52 weeks; 2.Established Inflammatory Arthritis (IA) (n=41): A rheumatologist's assessment of established IA with more than 52 weeks of symptom duration; 3.Musculoskeletal (MSK)/non-IA (n=50): A rheumatologist's established diagnosis of osteoarthritis, osteoporosis, fibromyalgia, arthralgia, bursitis, tendonitis, or other rheumatologist-determined and documented, established non-inflammatory MSK condition; and 4.Non-IA/non-MSK (n=38): Hospital outpatients without bone or joint complaints and no history of arthritis, willing to consult with a study rheumatologist. Discriminant validity is reported using a Kruskal-Wallis test for nonparametric differences in total questionnaire Yes responses (Score) between groups including Mean (\pm SD), and Median (+ range). Comprehensibility is defined as the percentage of patients who agree or strongly agree with the comprehension of the tool. The EIA Detection Tool is delivered a second time (T2), at one to 2 weeks after the first time (T1) to ascertain Test-Retest reliability, ($Kappa \pm$ SD). Patients who report a change in symptoms will be omitted from the assessment of reliability. To measure Internal Consistency, one question is repeated within the tool, (Kuder-Richardson-20, binary equivalent to Cronbach Alpha). Study participants will be blinded to the specific purpose of the study.

Results: Discriminant Validity for Group 1.EIA: Mean score 6.7 ± 2.8 Median 7 (0S11); 2.Established IA: Mean score 5.2 ± 2.3 Median 5 (2S10); 3.MSK/non-IA: Mean score 5.0 ± 2.9 Median 5 (0S11); 4. Non-IA/non-MSK: Mean score 2.7 ± 3.1 Median 2 (0S9) $p=0.006$. Over all groups Comprehensibility ranged from 94.6% S97.1%, while within Group 1.EIA, Comprehensibility ranged from 91.3% S100.0%. $Kappa = 0.85 \pm 0.08$ across all questions for Test-Retest reliability. Finally, Internal Consistency had a value of $KR-20=0.990$ at T1 and $KR-20=0.985$ at T2.

Conclusion: The EIA Detection Tool shows very good discriminate validity between the four study groups, and excellent Comprehensibility, Test-Retest reliability and Internal Consistency. Further analyses will be conducted to determine if weighting scales and/or decision rules may be imposed on the EIA Detection Tool to improve its discriminative properties.

Incidence of Post-operative Complications following Orthopaedic Procedures in Patients with Rheumatoid Arthritis treated with TNF- α Inhibitor Therapy

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Objective: TNF- α inhibitor therapies (TNFi) have improved the management of rheumatoid arthritis (RA). The therapies are however associated with an increased risk of infection and delayed wound healing. This observation raises concerns particularly in patients who are having surgical procedures. Although complications following orthopaedic procedures are commonly reported in RA patients there are limited data regarding RA patients being treated with TNFi. In this study, we examined the incidence of post-operative complications following orthopaedic surgery in such patients and sought to identify other potential risk factors for complications.

Methods: We identified all TNFi-treated RA patients who underwent an orthopaedic procedure between January 1st 2005 and December 31st 2009 in the Calgary Health Region. Data on these patients is included in our Pharmacovigilance database. Demographic and clinical data, which included the type of orthopaedic procedure, disease duration, co-morbidities and current therapies, were recorded for each patient. Patients were followed for a minimum of one year and post-operative complications were recorded. The complication rates were compared between surgery types, and with the rates recorded in the literature.

Results: Between January 1st 2005 and December 31st 2009, a total of 57 patients on TNFi therapy underwent 90 orthopaedic procedures. A total of 16 complications occurred (17.7%) which was higher than the 6% complication rate reported for orthopaedic procedures in RA patients. The complications were stratified into post-operative wound infections (11/90, 12.2%) and other types of complications (5/90, 5.5%). No independent predictors for post-operative complications were identified in this group.

Conclusion: TNFi therapy in RA patients appears to confer an increased risk of post-operative complications. Larger scale studies are required to elucidate how best to manage RA patients who are receiving TNFi therapies when they are to undergo orthopaedic surgical interventions.

Prevalence of Metabolic Syndrome in Psoriasis and Psoriatic Arthritis

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Objective: Psoriasis (Ps) is an immune-mediated skin disease affecting 25.3% of the population, of whom about 30% develop Psoriatic Arthritis (PsA), an inflammatory arthritis. The metabolic syndrome (MetS) is a cluster of cardiometabolic risk factors that includes abdominal obesity, dyslipidemia, hyperglycemia and hypertension. It is known that Ps and PsA patients have an increased prevalence of cardiovascular disease. However, the prevalence of MetS in PsA and the differential cardiovascular risk between Ps and PsA are not established. The objective of this study was to determine if PsA patients have a higher prevalence of MetS compared to Ps patients because of higher inflammatory burden.

Methods: Patients with PsA are followed prospectively in the Toronto Western Hospital PsA clinic. Patients with Ps without arthritis have been included in an observational cohort since 2006. All patients undergo a clinical examination according to a standard protocol which includes assessment of the components of MetS. Descriptive statistics are used to describe the patients. Univariate analysis including t-tests for continuous variables and chi-squared tests for dichotomous variables was performed to compare MetS in Ps and PsA. Multivariate analysis using a stepwise logistic regression model was used to identify associations between potentially related variables and MetS.

Results: 167 patients with PsA (42.5% F/ 57.5 % M, mean age 51.1 yrs, mean Ps duration 25.3 yrs, mean PsA duration 15.6 yrs, mean number of actively inflamed joints 8.6, mean PASI (psoriasis skin severity score) 4.1) and 98 Ps patients (43.9% F/56.1% M, mean age 50.3 yrs, mean Ps duration 18.4 yrs, mean PASI 5.8) were included. Prevalence of MetS was 36.5% in PsA, and 25.5% in Ps ($p=0.0773$). Multivariate analysis revealed that age, use of anti-TNF agents, and psoriasis skin severity scores (PASI) are associated with MetS, with odds ratios of 1.063 ($p< 0.0001$), 2.455 ($p=0.055$), and 1.049 ($p=0.033$) respectively.

Conclusion: Our interim results provide the first report of the prevalence of MetS in PsA. Our results further show that MetS is not more prevalent among patients with PsA compared to Ps. However, a larger sample size may be necessary to detect a significant difference. It is notable that markers of severe disease activity, such as use of anti-TNF agents and high PASI scores, are associated with increased the development of MetS in patients with Ps with or without arthritis.

Predictors of Radiographic Progression in Adalimumab-Treated Patients with Ankylosing Spondylitis

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Objective: To identify factors contributing to radiographic progression in Ankylosing Spondylitis (AS) patients treated with adalimumab (ADA).

Methods: The ATLAS trial randomized AS patients to treatment with ADA or placebo for a 24-week double-blind period, followed by an open-label extension with ADA. Two independent blinded readers scored X-rays obtained at baseline and year 2 using the mSASSS method. Dependent variables were: 1) change in mSASSS ≥ 2 and ≥ 4 , and 2) development of new syndesmophytes. Independent variables were age, disease duration, baseline spinal mobility, baseline ASDAS, baseline mSASSS, and 2-year area under the curve (AUC) for CRP and ASDAS. Categorical variables included: HLA-B27, sex, peripheral synovitis at baseline (SJC>0), peripheral enthesitis at baseline (MASES>0), presence of baseline syndesmophytes, and history of uveitis. Associations were tested univariately; significantly associated variables were entered as explanatory variables in a multivariate analysis.

Results: This analysis includes 275 subjects with 2 years of exposure to ADA; at baseline, subjects had mean disease duration of 10.8 years, mean ASDAS of 3.7, and mean mSASSS of 20.3; syndesmophytes were present in 85% of patients at baseline. Radiographic progression (Δ mSASSS ≥ 2) was found in 61 subjects (22%), and severe radiographic progression (Δ mSASSS ≥ 4) was observed in 22 subjects (8%). New syndesmophytes were found by either reader in 106 subjects (39%). Univariate analysis identified significant associations of age, mobility, and baseline bone damage with radiographic progression. For example, odds ratios (95% confidence intervals) for Δ mSASSS ≥ 2 were: age, 1.04 (1.009, 1.062); baseline syndesmophytes, 3.87 (1.126, 13.301); baseline mSASSS, 1.03 (1.011, 1.039); and baseline cervical rotation, 0.98 (0.968, 0.995). Linear regression revealed similar findings. Sex, HLA-B27, uveitis, peripheral synovitis or enthesitis, disease duration, baseline ASDAS, and CRP levels were not predictive in any analysis. In multivariate analysis, only baseline mSASSS was consistently identified as a significant contributor to radiographic progression (Δ mSASSS ≥ 2 and ≥ 4 , OR [95% CI]: 1.02 [1.005, 1.036] and 1.02 [1.001, 1.046]) and only baseline syndesmophytes were predictive of the development of new syndesmophytes (OR [95% CI]: 7.63 [2.381, 24.476]).

Conclusion: Clinical measures of disease activity were not related to radiographic progression. Only the presence of radiographic damage at initiation of therapy was consistently associated with the formation of new syndesmophytes in adalimumab-treated AS patients. These results support previous studies demonstrating a disconnect between disease activity and bone formation in patients with long-standing AS, and suggest treatment initiation prior to syndesmophyte formation might be advantageous for decreasing structural damage.

Psoriatic arthritis (PsA) in Canadian Clinical Practice: the PsA Assessment in Rheumatology (PAIR)

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Objective: We aimed to determine disease severity and treatment of patients with PsA followed in rheumatology practice in Canada.

Methods: Rheumatologists were invited to participate in the Assessment in Rheumatology (AIR) PsA program through the Canadian Rheumatology Association. Rheumatologists were asked to complete a form for each patient addressing demographic questions, CASPAR criteria, medication use, current status including joint counts, presence of dactylitis, enthesitis, back involvement, patient (PGA) and physician (MDGA) global assessment, acute phase reactant, assessment of prognosis and plans for change of medication. Descriptive statistics are provided.

Results: From across Canada 22 rheumatologists, from 5 provinces submitted 233 consecutive PsA patients 145 males (62.2%), 88 females (37.8%), mean age of 53.2 (12.7) years, 88.4% having disease for >2 years. 80.7% fulfilled CASPAR criteria (95% entered on peripheral arthritis, 15.9% on spondylitis and 34% on enthesitis). The majority fulfilled current psoriasis, 50 (21.7%) did not have current psoriasis but had previous psoriasis or a family history of psoriasis. 38% had nail lesions, 80% were rheumatoid factor negative, 48% had dactylitis, and 16% had fluffy periostitis. 30% had taken no DMARDs. Current (past) medications included 6.9% (22.9%) oral steroids, 7.3% intra-articular injections, 58% (25%) methotrexate, 12.0% (25.8%) sulfasalazine, 3.9% (10.3%) leflunomide, 6% (17.5%) antimalarials, and 2.6% (6.9%) on gold/auranofin. 67 patients were taking biologics, the majority receiving etanercept. At the time of the visit, patients averaged 3 swollen joints, 4 tender joints, PGA 2.3, MDGA 1.9. 16% had dactylitis at the time of the visit with equal distribution in hands and feet. 11% of the patients had enthesitis, mainly at the Achilles tendon or both Achilles and plantar fascia. Spinal involvement was documented in 13% of the patients. Most rheumatologists did not measure spinal metrics. Clinical joint damage was documented in 60% of the patients, active skin disease in 70% and nail lesions in 32%. Only 22% were rated as moderate to high disease activity while 52% were rated as low disease activity and 26% were deemed in remission. The decision was based on joint counts, PGA, MDGA and acute phase reactants. 27% of the patients were to have their medications changed based on the current visit, the majority for inadequate response to medications.

Conclusion: PsA patients seen in regular rheumatology practice fulfill CASPAR criteria, have active disease, and more than half have clinical damage. The majority have low activity or remission.

Clinical Trials in Canada 5 A Review of Study Design and Selection Criteria in Rheumatoid Arthritis (RA) Trials

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Objective: Current clinical trial design for pharmacologic interventions in rheumatoid arthritis (RA) do not reflect the innovations in RA diagnosis, treatment and care in Western countries over the past decade. The objective of this project was to develop evidence-informed entry criteria and to make recommendations about additional study design requirements that best meet the Canadian RA population characteristics and current best practices for usual care in Canada.

Methods: Initial recommendations were developed by an expert panel of rheumatology trialists and other experts affiliated with the Canadian Rheumatology Research Consortium. A scoping review methodology was then used to examine the evidence available to support or refute each initial recommendation. Scoping reviews can include a literature review and a key informant consultation phase. Research considered in this project included very recent diagnosis and treatment guidelines, systematic reviews and meta-analyses, and primary research data. Recent critical reviews and narrative reviews by experts in the field were also considered.

Recommendations were finalized using a consensus process.

Results: Recommendations for clinical trial inclusion and exclusion criteria addressed measures of disease activity [use of the Disease Activity Score (DAS) with 28 joint count, tender and swollen joint count, acute phase reactants, functional classification criteria] and disease duration; concurrent conditions [prior infection, laboratory abnormalities and tuberculosis screening prior to starting biologics]; and previous and concomitant RA treatments [stability and duration of Methotrexate and other DMARDs at optimal dosing for add-on trials, stability, dosing and duration of oral corticosteroids, minimum washout requirements, and use of prior biologics and DMARDs]. Additional recommendations regarding study design addressed rescue strategies, the use of intra-articular corticosteroid injections for rescue, long-term extension and timing of visits.

Conclusion: Over the past two decades, clinical trials in rheumatology have become increasingly complicated. Early aggressive treatment and tight monitoring means that rescue is an important component of trial design. Most pharmacologic treatment evidence collected to date has been in moderate to severe RA populations. There has been a recent movement to the globalization of trials which impacts the generalizability of research results. Less severe disease in high income countries impacts rescue strategies and rules for concomitant medications in trials. There is an urgent need to modify trial inclusion and exclusion criteria to better reflect the current characteristics of people living with RA in the countries where the new agents will be used.

Primary anti-TNF Failures Experience Better Clinical Responses but Similar Health Care Utilization to a Second anti-TNF Agent than Secondary Failures: Analysis of the Alberta Rheumatoid Arthritis Biologics Registry

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Objective: Meta-analysis of anti-TNF switching data from observational cohorts has concluded that responses are inferior in those switching due to primary as compared to secondary anti-TNF failures but limitations include small sample size of individual studies, failure to define response, and selection bias. We assessed the impact of switching anti-TNF agents at different time points in the Alberta Biologics Registry, an observational cohort of RA patients starting anti-TNF therapy in 2004, where collection of outcome data on all patients is requested by the Provincial pharmaceutical formulary.

Methods: The Alberta Biologics Registry collects clinical, employment, and health economic data at baseline, 3 months, and every 6 months thereafter. Health-related quality of life is measured with the EQ-5D and self reported health care utilization is measured for the six months prior to each visit. We analyzed responses according to time of switch (3 month versus subsequent time points) and according to specific anti-TNF agent switches.

Results: From 1,222 patients in the registry, 649 patients had 27 month follow up assessment and 498 (76.7%) of these remained on the first anti-TNF during the study period. There were 28 (4.3%) primary failures and 123 (19%) secondary failures who switched a median of 15 months from baseline. The response rate to the second anti-TNF was somewhat better in the primary versus the secondary failures ($p=NS$) at 3 months after initiation of the second anti-TNF for HAQ, DAS, EQ-5D. By 27 months, switchers due to primary failures had attained comparable reductions in outcomes to non-switchers while changes in secondary failures were from 50% (HAQ) to 68% (EQ-5D) lower compared to non-switchers ($p < 0.05$). Health care utilization was significantly reduced in four measured parameters over 27 months: number of rheumatologist visits ($\$0.31$ visits, $p < 0.001$), family physician visits ($\$0.95$, $p < 0.001$), % having ≥ 1 outpatient visit ($\$0.22$, $p < 0.001$), and % having day surgery ($\$0.026$, $p < 0.001$). This reduction was comparable between switching groups and non-switchers.

Conclusion: The results from this mandatory registry show that primary failures to anti-TNF show similar responses to patients responding to their first anti-TNF agent. Clinical responses in secondary failures are less optimal. Despite this, there is no significant difference between primary and secondary failures in the significant reduction in the health care utilization while receiving their second anti-TNF agent over the course of the 27 month follow up period.

Oral Health Related Quality of Life and Clinical Features in Systemic Sclerosis

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Objective: Orofacial manifestations of systemic sclerosis (SSc), as well as xerostomia and caries, are thought to occur commonly. Nevertheless, few studies have systematically assessed their prevalence and impact on oral health related quality of life (OHRQoL). The purpose of this study was to describe the orofacial abnormalities, caries and the impairment of OHRQoL in SSc compared to controls.

Methods: All SSc patients were randomly recruited from 7 sites of the Canadian Scleroderma Research Group (CSRG) registry. Controls were non-SSc rheumatology patients from the same clinics. Patients and controls underwent a standardized dental examination that included a Diseased/Missing/Filled Teeth (DMFT) scoring, interincisal and oral aperture measurements and the Saxon test for saliva production. The OHRQoL was measured using the Oral Health Impact Profile-49 (OHIP-49) questionnaire, which consists of 7 domains. Orofacial abnormalities and OHRQoL were compared in a multivariate regression analysis between SSc patients and controls, adjusting for demographic characteristics, partial and full dentures, and study center.

Results: There were 151 SSc patients and 150 controls included in the study. SSc patients and controls were similar: mean age 56.5 and 57.9 years, 90.1% and 91.2% female, 52.1% and 61.7% with more than high school education and 9.7% and 13.4% current smokers, respectively. On average, oral aperture and interincisal distance in SSc patients were 18.7 mm (95%CI = 14.2-23.9) and 7.0 mm (95%CI = 5.2-8.8) smaller than controls, respectively. They had an average of 0.19 g (95%CI = 0.01-0.39) less saliva production per minute. SSc patients had more missing and filled teeth than controls, mainly in the maxillary and mandibular posterior quadrants ($P < 0.05$). The OHIP-49 total score was significantly higher in SSc patients than controls (mean increase: 1.88, $P < 0.001$), indicating worse OHRQoL. OHIP-49 domains showing the greatest impairment were functional limitation, psychological discomfort and physical disability ($P < 0.002$).

Conclusion: This study demonstrated that SSc patients have a significantly smaller oral opening and interincisal distance than controls, and there was a strong trend towards greater xerostomia. The OHIP-49 indicates that SSc patients have significantly worse OHRQoL than controls. The results of this research will facilitate the development of future projects related to the prevention and treatment of orofacial manifestations of SSc, with the aim of reducing its impact on quality of life.

Information Needs And Information-Seeking By People With Rheumatoid Arthritis: A Qualitative Study

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Objective: To assess educational needs of people with rheumatoid arthritis (RA); specifically, to investigate the topics of information that they consider most important, where people go to look for that information, and how they evaluate the information they find

Methods: We performed a qualitative study using focus groups with people with RA.

Participants were recruited from people having attended multidisciplinary outpatient arthritis services for rheumatoid arthritis in the preceding 2 years or having attended the Learning Centre at the Mary Pack Arthritis Centre in Vancouver. Eligible participants had to be older than 18 years, English-speaking, live in the Greater Vancouver region and have a physician-confirmed diagnosis of rheumatoid arthritis. Each focus group included 6 to 8 participants and was moderated by an experienced facilitator who used predefined open-ended questions and probes to stimulate group discussion. The sessions were audio-taped, transcribed, and analyzed using content analysis to identify key concepts emerging from the data.

Results: To date, one out of the 5 expected focus groups has been conducted ($n = 7$, median age 57 years, 6 women). Preliminary analysis revealed that the three most important topics of information about RA to them were emotional and psychological well-being, RA medications, and current research findings. A diverse range of sources were used by the participants in their search for information on these topics. Participants placed great importance on emotional and psychological well-being, yet these areas were greatly lacking in resources. For medications and other information related to their disease management, people often sought and found information from secondary health care providers, rather than from their physician. In evaluating the information that they found by themselves, people reported authenticity of the source and the presence of red flags as important in determining the credibility of the information. General characteristics of useful resources for RA were discussed, including that it should be realistic, at an appropriate level of detail, and easily accessible.

Conclusion: While there is an abundance of general information available about RA, the most important topics of information to people with RA are not being addressed adequately. People were dissatisfied with the paucity of resources dealing with the emotional and psychological issues around RA. By understanding how people evaluate the information they find, as well as what characteristics people with RA find useful in a resource, effective educational interventions can be created to address topics of information most relevant to people with RA.

Efficacy of Tocilizumab (TCZ) in Rheumatoid Arthritis (RA) Patients (pts) with No Prior Exposure to or No Prior Failure of Methotrexate (MTX): Long-Term Extension Study (Up to 3 Years of Treatment)

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Objective: To evaluate the long-term efficacy and safety of TCZ as monotherapy or in combination with DMARDs/MTX in pts with active RA who had never been exposed to or had never failed MTX therapy (AMBITION study pts). Data from the ongoing long-term extension (LTE) study were used.

Methods: Pts included in the analysis received ≥ 1 dose of TCZ (8 mg/kg every 4 wks) in the AMBITION or LTE studies. Pts who showed a reduction of $< 50\%$ from baseline in tender joint count (TJC) and swollen joint count (SJC) during the AMBITION study were eligible to receive MTX or other permitted DMARDs during LTE. A separately evaluated subgroup of pts received TCZ 8mg/kg as monotherapy for the duration of their treatment. Assessment of efficacy parameters was performed every 12 weeks (wks) from initial TCZ exposure. Efficacy data were analyzed from the time of initial TCZ exposure through February 6, 2009. Results included pts who had assessments at each visit and no imputation was performed for missing data.

Results: 618 pts received TCZ 8 mg/kg either as monotherapy or in combination with MTX/DMARDs, 2.4% of whom withdrew due to insufficient therapeutic response. There was a continuous increase in ACR 20, 50 and 70 response rates over time. The proportions and absolute numbers of pts who achieved low disease activity (LDAS; $\text{DAS28} \leq 3.2$) and/or DAS28 remission ($\text{DAS28} \leq 2.6$) were sustained through wk 60 of TCZ treatment; proportions of pts were maintained through wk 156. By wk 96, 25%, 40%, and 23% of pts had zero TJC, zero SJC, and achieved HAQ-DI scores of zero, respectively. The TCZ monotherapy subgroup amounted to 234 pts. Efficacy in this subgroup was demonstrated by sustained improvements in ACR 20, 50 and 70 and DAS remission rates.

Conclusion: Response rates to TCZ, as monotherapy or in combination with DMARDs, were maintained with up to 3 years of treatment. As the results of this analysis indicate, the benefits of TCZ treatment for RA pts who had never been exposed to or had never failed MTX continued beyond 24 wks.

Tocilizumab (TCZ) Long-Term Efficacy in Rheumatoid Arthritis (RA) Patients (pts) Treated up to 3.7 Years

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Objective: To assess TCZ long-term efficacy in RA pts treated with TCZ and DMARDs/methotrexate (MTX).

Methods: Two populations from ongoing long-term extensions (GROWTH95, GROWTH96, open-label phase of LITHE) of phase 3 trials were analyzed: 1) pts who previously had inadequate response to DMARDs (DMARD-IR: OPTION, TOWARD, LITHE) 2) pts with no previous failure or exposure to MTX (AMBITION). Besides pts from the AMBITION study who received TCZ monotherapy, pts received ≥ 1 dose of TCZ + DMARDs/MTX in the phase 3 or extension trials. Pts from AMBITION with $< 50\%$ reduction from baseline in tender and swollen joint counts (TJC, SJC) were eligible for DMARDs/MTX in the extension. In the original studies and in the extensions, outcomes were assessed every 4 wks and every 8 (LITHE) or 12 (GROWTH95/96) wks from initial TCZ exposure to Aug 28, 2009, respectively. For pooling, data were assigned to the nearest 12 wk point. Due to withdrawal or failure to reach later assessments, the number of pts with assessments decreased over time. Results included pts who had assessments at each visit, with no imputation for missing data. Data were included until $< 10\%$ of the baseline pts was reached.

Results: 2904 DMARD-IR pts and 618 never exposed/failed MTX pts were analyzed. 27.7% of DMARD-IR and 24.6% of never exposed/failed MTX pts withdrew by the cutoff date. The absolute numbers of DMARD-IR pts reaching ACR50, LDA (DAS28 3.2), and DAS28 remission (DAS28 2.6) through wk 96 and ACR70 through wk 120 continuously increased. The absolute numbers of never exposed/failed MTX pts achieving ACR50/70, LDA, and DAS28 remission to wk 96 were sustained. The proportion of pts achieving ACR50/70, LDA, and DAS28 remission was maintained to wks 168 and 192, with lower absolute numbers reaching these visits. By wk 24, 20% and 27% of assessed DMARD-IR and never exposed/failed MTX pts, respectively, had achieved the major clinical response of ACR70 maintained for 24 consecutive wks. At wk 120, 52.3% and 38.4% of assessed DMARD-IR pts and 59.5% and 38.3% of assessed never exposed/failed MTX pts, respectively had 1 SJC and 1TJC. 38.4% and 48.4% of DMARD-IR and never exposed/failed MTX pts had HAQ-DA scores of 0.5.

Conclusion: Increasing and sustained numbers and/or proportions of pts achieving ACR50/70, LDAD, and DAS28 remission support TCZ as an effective, long-term treatment for RA pts.

Safety Analysis of Tocilizumab (TCZ) in Rheumatoid Arthritis (RA) Patients (pts): Long-Term Extension Studies (Median of 3.1 Years of Treatment)

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Objective: To assess the longer-term safety of TCZ in RA pts using pooled data from long-term extension studies.

Methods: The analysis included pts who received ≥ 1 dose of TCZ in the 24-week (wk) phase III clinical trials (OPTION, AMBITION, RADIATE, TOWARD), in the 2-year phase III clinical trial (LITHE), in a phase I study, or in the ongoing, open-label extension studies (GROWTH95, GROWTH96). Safety data from the all-exposed population were pooled and analyzed from the time of initial exposure to TCZ to the cutoff date of August 28, 2009.

Results: A total of 4,009 pts received TCZ, with a total TCZ exposure of 10,011 pt-yrs (PY) and a total duration of observation of 10,994 PY. The median treatment duration was 3.1 years (mean of 2.7 years). Withdrawal rate due to adverse events (AEs) was 5.4/100 PY. The overall serious AEs (SAEs) rate was 14.6 /100 PY and the overall rate of serious infections was 4.5/100 PY. The overall rate of malignancies, including non-melanoma skin cancers, was 1.1/100 PY. Myocardial infarction and stroke occurred at an overall rate of 0.27 and 0.16/100 PY, respectively. Both rates remained stable with continued exposure to TCZ. There was an increase from baseline to wk 6 in mean total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglyceride levels, which then stabilized. 313 pts (7.8%) initiated lipid-lowering therapy during TCZ treatment and generally responded to treatment without complications. ALT/AST elevation $>3x$ upper limit of normal occurred in 7.8% of pts during the first 12 months of treatment, with no rate increase over time. Dose reductions and/or interruptions were used to manage transaminase elevations, which were not associated with clinically apparent hepatitis or hepatic dysfunction.

Conclusion: Results from this analysis indicate that no new safety signals have emerged with prolonged exposure to TCZ, which supports a favourable benefit/risk ratio for the use of TCZ in pts with moderate-to-severe RA. During longer-term TCZ treatment, AE and SAE rates were stable over time, and transaminase elevations could be effectively managed with no clinically significant sequelae detected.

Treatment to Target: Retreatment with Rituximab (RTX) Provides Better Disease Control than Treatment as Needed in Patients with Rheumatoid Arthritis (RA)

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Objective: Assessing differences in efficacy and safety profiles of the two treatment approaches employed in RTX RA clinical trials may help in determining an optimal treatment regimen.

Methods: RA patients (pts) who were inadequate responders to methotrexate (MTX) were recruited into Phase II or III studies (MIRROR, SERENE, Phase IIa and DANCER). Pts received open-label RTX 2 x 1000mg, IV 2 weeks apart + MTX based on two retreatment strategies: a) Treatment to target (TT), with pts assessed and retreated 24 weeks (wks) after each course, if and when not in remission ($\text{DAS} \geq 2.6$); b) Treatment as needed (PRN), with pts retreated at the physician's discretion after ≥ 16 wks if both swollen and tender joints were ≥ 8 . In both approaches, study visits were performed at least every 8 wks. Pooled data were analyzed according to treatment group. Clinical outcomes, including ACRn, DAS28-ESR and HAQ-DI, and safety data were assessed over time.

Results: Compared to baseline, responses were maintained or improved over multiple courses of RTX in both treatment strategies. Compared with PRN, TT resulted in greater improvements in DAS28-ESR, lower HAQ-DI and higher ACRn, reflecting tighter control of disease activity. PRN resulted in recurrence of disease symptoms as indicated by DAS28-ESR scores returning close to pre-RTX treatment levels and higher rates of withdrawals from the trial due to RA flare. Compared with PRN, TT resulted in more pts achieving major clinical response (ACR70 at 6 months; 12.3% vs 5.1%). TT led to more frequent retreatment with a median time between courses of approximately 25 wks compared with approximately 62 wks for PRN. Comparable safety profiles were obtained for the two regimens. However, compared with PRN, TT had a numerically reduced rate of serious infections (2.2 vs 3.5 per 100 pt-yrs) and serious adverse events (12.0 vs 16.2 per 100 pt-yrs). There were no clinically relevant differences in the proportion of pts with Ig levels below the lower limit of normal across the two treatment groups.

Conclusion: Repeat treatment to a target of DAS28 remission with RTX led to tighter control of disease activity compared with PRN treatment.

The Role of the Patient Ambassador in Support of the Identified Theme of Hope in the Needs of Patients Attending an Inflammatory Arthritis Education Program at The Arthritis Program (TAP).

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Objective: Patient Ambassador Pilot Project **S** to determine the response and success of the pilot patient ambassador role within the inflammatory arthritis education program. QA Project **S** to trend the monthly identified individual goals of patients attending the inflammatory arthritis education program to determine if these goals were being met by attendance and completion of the program.

Methods: Patient Ambassador Pilot: Patients who had attained self management and empowerment over their disease process and who were seen as dynamic and good orators were identified by TAP. They were asked to consider participating in group speaking engagements within the inflammatory arthritis education program. Some predetermined guidelines were given for use in the talks to groups. QA Project: patients participating in the QA project were asked questions by the TAP team social worker about their educational needs and the goals they hoped to achieve as a result of attending the two-week inflammatory arthritis education program.

Results: Sample patients that attended the inflammatory arthritis education program identified the need to hear hopeful information on treatment options and disease prognosis. The majority of patients in the sample described a “hopeful” outlook as a result of attending TAP’s inflammatory arthritis education program. This finding was in support of our pilot initiative of developing the role of the patient ambassador within the inflammatory arthritis program. Identifying patient ambassadors to express their own experiences may be a way to improve the outlook of other patients.

Conclusion: Based on the results gathered, the patient ambassador role is now being considered for pilot in other education programs within TAP and the Chronic Disease Management Portfolio

Assessing the Rate of Serious Infections in Rheumatoid Arthritis (RA) Patients who Receive Other Biologic Therapies after Discontinuing Rituximab (RTX)

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Objective: To describe the rate of serious infection events (SIEs) in RA patients (pts) treated with RTX and who subsequently received another biologic disease-modifying antirheumatic drug (BDMARD) while being potentially peripherally B-cell depleted as a result of RTX selectively targeting CD20+ B-cells.

Methods: Pts included in the study had moderately-to-severely active RA and received RTX + methotrexate (MTX) within an international trial program. After completion or withdrawal from their studies, pts entered a safety follow-up (SFU) during which peripheral B-cell counts were monitored at regular intervals for 48 weeks (wks) and BDMARDs could be received. All SIEs, defined as adverse events and/or infections that required IV antibiotics, were collected.

Results: As of September 2009, 3,189 RA pts had received at least 1 course of RTX, yielding a total follow-up number of 9,365.03 pt-yrs. 283 pts who entered SFU subsequently received another biologic (median time of 8.5 months (mo) after last RTX infusion). Of these 283 pts, 30.7% received their biologic within 6 mo of their last RTX infusion. The largest group (n=230 pts) received a TNF-inhibitor (TNFi) after RTX. The median follow-up time post-reception of the subsequent biologic was 11 mo. 83% of patients had peripheral B-cell counts below the lower limit of normal (< 80 cells/ μ L) at the time of receiving further BDMARD treatment. For this group of 283 pts, 6.01 SIEs per 100 pt-yrs were reported during treatment with RTX and prior to receiving the biologic. Following BDMARD treatment initiation, the rate fell to 4.97 SIEs per 100 pt-yrs. The median time to SIE after initiation of BDMARD treatment was 11 mo. In 43 pts who received abatacept (ABA) as their initial BDMARD, 1 SIE before and 1 SIE after receiving ABA were reported (97.7 total pt-yrs). Overall, the infections were variable and typical for RA pts. No opportunistic or fatal infections were reported.

Conclusion: As indicated by this updated analysis, subsequent biologic therapies after RTX discontinuation were not associated with an increased rate of serious infections in pts who received biologics or in the subgroup who received TNFi. The SIE rate was consistent with rates observed in long-term safety data.

Results from the RESET Study: Rituximab Response Based on Reasons for TNFi-Discontinuation and Rheumatoid Factor Status

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Objective: To analyze the response to rituximab (RTX) based on the reasons for discontinuing a TNF-inhibitor (TNFi) as well as baseline characteristics that can be used as predictor of response.

Methods: RA patients (pts) receiving background methotrexate (MTX) (10-25 mg/week) received 1000 mg of RTX on Days 1 and 15, as per approved label. Key inclusion criteria comprised pts with moderate/severe RA with swollen joint count ≥ 6 and tender joint count ≥ 6 at baseline and treatment history with only one prior TNFi. Efficacy was assessed at weeks 4, 12, 24, 36 and 48. Between Week 24 and 48, pts having achieved a clinically relevant response to the first course of RTX were eligible for one retreatment course of RTX. Efficacy assessments for the retreatment group were performed at week 12 and 24.

Results: The baseline characteristics (mean \pm SD) of the cohort were: age: 55.6 (\pm 10.2); disease duration: 13.9 (\pm 9.8) years; disease activity (DAS 28): 6.4 (\pm 1.1), HAQ-DI: 1.7 (\pm 0.6). 73% of the population was rheumatoid factor (RF) positive and 73% of the population was female. Improvements in ACR 20, 50 and 70 were achieved after the first course of treatment in 58.0%, 27.0% and 7.0% of the population and in 63.0%, 32.0% and 8.0% of RF positive pts at week 24, respectively. Changes in DAS were observed as early as week 4 (-1.1 vs. baseline) and had decreased by -2.0 (-2.2 in RF positive pts) by week 24. ACR 20, 50 and 70 for pts who had discontinued treatment with their previous TNFi for the following reasons were: lack of initial response: 55, 24, 10; loss of response: 59, 26, 4; tolerability concerns: 67, 33, 8, respectively. After the second course of treatment, ACR 20, 50 and 70 improved in 57.1%, 30.0% and 10.4% of pts at week 24 and in 60.7%, 34.0% and 11% of RF positive pts, respectively. Changes in DAS had decreased by -2.2 (-2.4 RA positive pts) by week 24. ACR 20, 50 and 70 were 48, 19, 5 for lack of initial response; 65, 31, 10 for loss of response and 80, 80, 20 for tolerability concerns, respectively.

Conclusion: Treatment with RTX resulted in clinically significant improvements in disease activity. Compared with the overall population, RF positive pts appear to have an enhanced response. RTX efficacy was not affected based on the TNFi-discontinuation reasons.

Management of Rheumatoid Arthritis in the Peri-operative Period: A Look at the Literature and Local Practices

Michael Zawadowski (University of Saskatchewan, Saskatoon); Regina Taylor-Gjevre (University of Saskatchewan, Saskatoon)

Objective: There is a paucity of data looking at optimal rheumatoid arthritis therapy in the periarthroplasty period. The objective of this study was to review the literature for guidelines and to review local practice.

Methods: A literature review was conducted to ascertain current guidelines and recommendations of pharmacotherapy perioperatively in the RA patient. Additionally, chart reviews were performed on RA patients undergoing elective joint replacement surgery.

Results: A review of current literature suggests that biologic therapies be discontinued one week or two half lives prior to arthroplasty. Studies on the safety of methotrexate periarthroplasty suggest that it can be continued, except in patients with specific comorbidity profiles. Other sources make suggestions for DMARD management perioperatively on the basis of pharmacokinetics. We reviewed 49 charts of RA patients who had TKR or THR between January 2006 and March 2010. We collected demographic, anti-rheumatoid medications, surgical risk factor and complication data. We deemed anti-rheumatoid management appropriate if it did not conflict with current guidelines or with what current literature suggested was appropriate management. 41 were deemed eligible for the study, 6 were excluded for lack of anti-rheumatoid treatment, and 2 were excluded for unclear management. 21 (51%) patients had appropriate anti-rheumatoid management, while 20 (49%) had inappropriate. Of the 15 patients on biologic therapy, 9 (60%) were treated appropriately, 6 (40%) inappropriately. Of 9 patients on leflunomide, none were managed appropriately.

Conclusion: In conclusion, just over half of patient's management of rheumatoid arthritis received "appropriate" care. We recommend that further studies be done to evaluate the appropriate care for RA patients around the time of arthroplasty to strengthen current guidelines. We also recommend introducing a standard pre-arthroplasty form for perioperative management including recommendations on care.

Baseline Characteristics and Effectiveness of Treatment With Infliximab in Canadian Patients With Rheumatoid Arthritis: Comparison of an Individual Practice With the BioTRAC Registry

Rafat Faraawi (N/A, Kitchener); Susan Ottawa (Merck Canada Inc, Kirkland)

Objective: The efficacy of Infliximab (IFX) in Rheumatoid Arthritis (RA) has been well established in controlled clinical trials. Small area variations with respect to patient profile and outcomes may affect global assessment of real-life effectiveness. The aim of the current analysis is to compare the patient profile and outcomes of an Individual Rheumatology Practice cohort in Ontario to that of the entire Ontario and Canadian RA cohorts.

Methods: The data for this analysis were obtained from BioTRAC, an observational prospective registry of adult RA patients initiated on IFX since 2002 and managed as per routine care.

Results: A total of 70 RA patients were enrolled in the Individual Rheumatology Practice (IRP) between 2002 and 2010 while 695 patients comprised the total registry (Canadian) and 291 patients the Ontario cohort (ON). Patient baseline characteristics differed between the 3 cohorts with patients in the IRP cohort having significantly lower mean age (50.1 vs. 56.4 and 57 years in the IRP, Canadian and ON cohorts, respectively), disease duration (5.7 vs. 11.1 and 9.4 years, respectively), ESR (25.5 vs. 33.8 and 37.1 mm/hr, respectively) HAQ (1.5 vs. 1.7 and 1.7, respectively), pain (50.9 vs. 58.8 and 59.1, respectively), Physician's Global Assessment of Disease Activity (PGA) (4.5 vs. 6.8 and 7.0, respectively), swollen joint count (SJC) (7.9 vs. 12.2 and 12.4, respectively) and DAS28 (4.8 vs. 5.3 and 5.4, respectively) compared to the Canadian and ON cohorts. Regression analysis over time showed that morning (AM) stiffness, Patient's Global Assessment of Disease Activity (SGA), HAQ, tender joint count (TJC), SJC, and DAS28-CRP improved significantly in all cohorts without significant between-group differences. However, median time to discontinuation due to treatment failure (adverse event, disease progression, lack or loss of response) was significantly longer in this IRP cohort vs. Canadian (P=0.004) or ON (P=0.011) cohorts. After mean follow-up of 12.8, 13.0 and 13.3 months for the IRP, Canadian and Ontario cohorts ACR20/50/70 response rates were 54%/52%/52%, 49%/46%/43% and 40%/38%/33%, respectively.

Conclusion: The results of this real-life observational study demonstrate that significant variation in patient baseline characteristics in individual rheumatology practices may exist within the BioTRAC registry. This may impact individual physician experience with respect to median time to discontinuation due to treatment failure. Nevertheless, treatment with IFX for up to 4 years is effective in reducing symptom severity and improving outcomes in patients with RA in this Individual Rheumatology Practice, Canadian and ON cohorts within the BioTRAC registry.

Regional Variation of the Profile of Patients With Rheumatoid Arthritis Treated With Infliximab in Quebec and Ontario

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Objective: The efficacy of Infliximab (IFX) in Rheumatoid Arthritis (RA) is well established. The aim of the current analysis is to describe regional differences in the patient characteristics at initiation of IFX treatment and their effect on response to IFX treatment after 6 and 12 months.

Methods: The data for this analysis were obtained from an observational study of adult RA patients initiated on treatment with IFX and followed prospectively as per routine care since 2002. Patients enrolled were biologic naïve or had initiated treatment with a biologic less than six months prior to enrolment.

Results: A total of 514 RA patients were enrolled between 2002 and 2010, whereof 156 (30.4%) were from Québec (QC) and 358 (69.6%) from Ontario (ON). Patient baseline (BL) characteristics differed between the two provinces with patients from ON having a significantly higher ESR (34.9 mm/hr vs. 28.2 mm/hr) ($P = 0.004$) and a significantly higher number of prior disease-modifying antirheumatic drugs (DMARDs) (58% of QC patients treated with 1 DMARD vs. 39.6% of ON; $P = 0.007$) despite the comparable disease duration (8.6 years in ON vs. 9.5 years in QC; $P = 0.413$). The vast majority of patients starting IFX in both provinces had a high disease activity ($\text{DAS28} > 5.1$). Treatment with IFX resulted in statistically ($P < 0.001$) and clinically significant reductions in the DAS28 (DAS28ON: $\$1.4$ and $\$1.7$, DAS28QC: $\$1.9$ and $\$2.2$ at 6 and 12 months, respectively) and HAQ (HAQON: $\$0.3$ and $\$0.4$, HAQQC: $\$0.5$ and $\$0.6$ at 6 and 12 months, respectively). However, significantly lower DAS28 and HAQ values were achieved by 6 and 12 months in patients from QC compared to ON ($P < 0.001$). Similarly, lower disease activity was achieved in patients from QC compared to ON as indicated by the EULAR definition of response ($P_{6\text{mo}} = 0.006$ and $P_{12\text{mo}} = 0.003$) and DAS28 categories ($P_{6\text{mo}} = 0.008$ and $P_{12\text{mo}} = 0.019$). Regression analysis over time showed that all parameters observed (CRP, ESR, AM stiffness, HAQ, pain, patient and physician global assessment, tender and swollen joint count and DAS28-CRP) improved significantly. The only difference between provinces was a stronger decrease in CRP in ON.

Conclusion: The results of this study have shown a significant regional variation in Canadian RA patients with patients from ON having higher ESR and having been treated with more DMARDs before initiation of IFX. All patients showed a significant response to IFX treatment with patients from QC reaching lower disease activity.

Age Differences in the Prescription of Biologics versus DMARDs

Charmaine Navis (University of Alberta, Edmonton); Paul Davis (University of Alberta, Edmonton); Walter Maksymowych (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

Objective: The treatment of patients with Rheumatoid Arthritis (RA) has reported to have age bias in elderly patients. We investigated whether a similar bias occurred in our database of patients on biologics versus leflunomide.

Methods: We performed an analysis of our RA Clinical Registry patients to determine whether an age difference existed between initiation with a biologic versus leflunomide. Data was collected from the RAPPORT database (Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics). Information collected included date of birth, dates of visit, HAQ (Health Assessment Questionnaire) and DAS (Disease Activity Score).

Results: Data of 1271 patients with RA were analyzed. A modest age difference of patients initiated on biologics were younger by 3.83 years. Disease severity was higher in elderly patients initiating biologics in analysis of both the HAQ and DAS.

Conclusion: In this cohort of patients with RA, we detected a modest age bias in the use of biologics compared to leflunomide. Several confounding factors may include: incomplete data on all patients treated with leflunomide; and younger patients with better insurance coverage. Clinical measures identified that the elderly patients had more severe disease compared to the younger patients, identifying a need for treatment. Treatment disparities are a serious concern, and elderly patients must have access to medications when appropriate.

The Relationship between Function and Disease Activity as Measured by HAQ DI and DAS Varies by Rheumatoid Factor Status in ERA. Results from the CATCH cohort.

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Objective: Older publications have compared the relationship between function and disease activity over the course of RA. Some have found HAQ correlated significantly with DAS scores in the earlier phases of RA while others have found a strong correlation throughout the disease course. Our goal was to investigate the relationship between disease activity and functional capacity in the early stages of inflammatory arthritis using data collected in the CATCH cohort and to determine if the correlations changed; and whether they were similar when studying the effects of age and RF status.

Methods: Data from patients (n=1145) enrolled were collected from the Canadian Early Arthritis Cohort (CATCH); a multi-site observational cohort of early inflammatory arthritis. The HAQ and DAS28 were assessed at each visit. Correlations were done between HAQ and DAS every 3 months for the first year and then at 18 and 24 months. Data were then stratified by age (< 65 vs. ≥65), and RF status (positive versus negative).

Results: Mean HAQ and DAS scores were highest at first visit. All correlations between HAQ and DAS were significant at all time points ($p < 0.01$). At baseline, there was a good correlation between HAQ and DAS ($r = 0.49$) whereas at 6, 9, and 12 months the correlation was weaker ($r=0.39$, $r=0.29$, and $r=0.38$, respectively). However, correlations between HAQ and DAS were strongest at 18 months ($r = 0.52$) and 24 months ($r = 0.53$). Age did not change the association between HAQ and DAS {< 65 years old ($r=0.50$, $N=868$) vs. ≥65 ($r=0.48$, $N=254$)}. The correlation between HAQ and DAS was stronger with RF+ patients ($r=0.63$, $N=636$) than RF negative ($r=0.47$, $N=477$).

Conclusion: Through comparison of correlations of HAQ and DAS at different time points in early RA, we were able to determine how strongly these measures were associated in a population with a relatively short duration of symptoms; most of whom had not yet experienced significant joint damage which would lead to irreversible functional impairment. Functional capacity was strongly influenced by disease activity in early RA. Although associated, the scores are measuring different aspects of RA and both are necessary to determine activity and function in ERA.

Treatment of Vascular Involvement in Systemic Sclerosis (SSc): What to Use When First-line Treatment Fails - a Consensus of SSc Experts.

Kyle Walker (Trinity College, Dublin, Dublin, Ireland, London); The CSRG and SCTC (University of Western Ontario, London); Janet Pope (University of Western Ontario, London)

Objective: Most published treatment in SSc is in first-line therapy such as ACE inhibitors (ACEi) for scleroderma renal crisis (SRC). There is a need for standardization in SSc management, particularly for treatment after failure of first-line therapy. We attempted to gain consensus among SSc experts for treatment and management of specific organ systems.

Methods: Members of the Scleroderma Clinical Trials Consortium (SCTC) and Canadian Scleroderma Research Group (CSRG) (n=117) were sent electronic surveys. The surveys asked both open-ended and multiple-choice type questions pertaining to various treatments, management and testing for the manifestations of SSc including vascular complications such SRC, Raynaud's phenomenon (RP) and digital ulcers (DU). Each survey was sent 3 times. Those who responded to the first survey were invited to continue in the study for a total of 3 surveys. Results are in % who responded with each treatment option and only common choices are reported.

Results: SRC **S** Forty-seven % would routinely hospitalize a patient with mild SRC and 93% in more severe SRC. Regardless of severity, first-line therapy for SRC is an ACEi (97%). For mild SRC, second-line is either adding a calcium channel blocker (CCB) (37%) or angiotensin receptor blocker (ARB) (35%), third-line is a CCB (35%) and fourth-line an alpha-blocker (27%). For more severe SRC, second-line is adding a CCB (27%), third-line is either a CCB (28%) or ARB (27%) and fourth-line an alpha-blocker (20%). RP **S** For mild RP, first-line treatment is a CCB (92%), second-line a phosphodiesterase inhibitor (PDEi) (35%), third-line an ARB (32%) and fourth-line iloprost (23%). For more severe RP, second-line is either a PDEi (45%) or iloprost (32%), third-line is either a PDEi (45%) or iloprost (27%) and fourth-line is to try another CCB (32%). DU **S** For DU prevention (depending on previous DU history **S** mild or severe), first line is a CCB (73%), second line a PDEi (57% mild, 43% severe), third-line an endothelin receptor antagonist (ERA) (47% mild, 47% severe) and fourth-line iloprost (38% mild, 40% severe).

Conclusion: Physicians managing SSc are relatively comfortable with choosing a first-line treatment for the various manifestations of SSc. Discrepancies and variation in drug choice differ after failure or incomplete response to first-line treatment. However, many SSc experts chose similar treatment but some considered a specific drug to be a second choice and others a third choice. This study can help clinicians decide how to treat more complicated vascular events in SSc.

Prevalence of and Predictive Factors for Sustained Remission in Early RA: Results from SONORA Study

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Objective: Remission constitutes the best achievable state in patients with rheumatoid arthritis (RA). Current measures of Disease Activity - such as the DAS28 - define the patient's remission status at a given point in time. While, for the patient, sustained remission over time is the ultimate goal. The purpose of this study is to assess the frequency and predictors of sustained remission in a large cohort of early RA patients in regular clinical practice.

Methods: A total of 994 patients diagnosed as early RA (symptoms ≥ 3 and ≤ 12 months) by a board-certified rheumatologist across North America were recruited in this study. We analyzed remission and sustained remission in 851 patients who had two-year complete follow up information. Remission was defined as less than 2.6 for DAS28 and sustained remission was defined as consecutive remission at year 1 and year 2. Univariate logistic regressions were used to explore the predictors for sustained remission and multivariate logistic regression were used to estimate the remission probabilities controlling for significant factors.

Results: The mean age of patients was 53 years (SD, 14.8), with 72% female and 90% Caucasian. The mean RA symptom duration was 170 days (180), 61% were seropositive for rheumatoid factor and 43% anti-CCP positive (>20 unit/ml) at baseline. Seventy-four percent of patients had received DMARDs at baseline compared to 90% at year 1 and, 87% at 2. Two percent of the subjects were on Biologics at baseline compared to 15%, 23% at year 1 and 2. Remissions at any one of the two visits were seen in 238 (28%) patients. Among them, 68 (8%) patients achieved sustained remission. The univariate logistic regression showed that low baseline DAS28 score, HAQ score, disease duration and CRP are significant predictors for sustained remission. The multivariate logistic regression showed that HAQ was no longer significant when other factors (low baseline DAS28, low CRP and short disease duration) were included in the model. Therefore it was excluded. In this final multivariate analysis the low baseline DAS 28 (OR 0.66, 95% CI= 0.54-0.81; $p < 0.0001$), disease duration (months) (0.88, 0.8-0.97; $p = 0.0091$) and baseline CRP (0.83, 0.72-0.96; $p = 0.013$) remained significant.

Conclusion: Low sustained remission rates were observed in this early RA cohort recruited before the wide use of biologics. The multivariate model predicts the probability of sustained remission using easily accessible clinical and laboratory variables. These identified factors can help guide rheumatologists in making treatment decisions for early RA patients.

Demographics of Seniors Attending a Rheumatology Clinic

Paul Davis (University of Alberta, Edmonton); Angela Juby (University of Alberta, Edmonton)

Objective: An increasingly aging population is impacting healthcare delivery in subspecialty areas of medicine outside of geriatrics including rheumatology. Geriatric patients can be challenging due to comorbidities and polypharmacy. This study was undertaken to assess the impact and demographics of seniors attending a rheumatology clinic and data compared to a younger cohort.

Methods: A retrospective chart review was undertaken on all patients attending a subspecialty rheumatology clinic in 2008. All patients were prescreened and triaged for inflammatory arthritis or multisystem connective tissue diseases before attending the clinic. Patients with degenerative peripheral or axial disease and those with chronic pain syndromes were excluded where possible. Charts were reviewed for demographics including age, sex, diagnosis and comorbidities the data obtained from those >65 were compared to the younger cohort.

Results: 295 patients were seen in a 1 year period. 78 patients (26%) were >65. Their mean age was 73 (range 65-90) compared to the mean age of the < 65 group which was 53 (range 16-65). The gender ratio in the >65 group was 1.25:1, compared to the < 65 group of 2.06:1. Rheumatoid arthritis and other inflammatory arthropathies was the predominant diagnosis in both groups of patients (48% v 53%). Other connective tissue diseases were equally represented (12% v 14%). Osteoarthritis (usually inflammatory) was twice as common in the >65 group (17% v 8%). Polymyalgia rheumatica was diagnosed in 12% of seniors. Fibromyalgia was observed in 6% of the < 65 group. Co-morbidities were a prominent feature of the >65 group. Hypertension (31%), osteoporosis (27%), diabetes (15%), hypothyroidism (11%) and coronary artery disease (9%) were the most prevalent. Only 1 patient had cognitive impairment. Given the high number of comorbidities, polypharmacy and potential drug/drug interaction with anti rheumatic therapy was often encountered.

Conclusion: Seniors comprise a significant proportion of patients attending a speciality rheumatology clinic. Inflammatory arthritis, polymyalgia rheumatica, osteoarthritis were the commonest diagnoses. Osteoporosis was commonly observed as a comorbidity. Other comorbidities and polypharmacy posed a significant challenge in many. This study highlights the need for reciprocal knowledge by both rheumatologists and geriatricians alike to optimize care for seniors with rheumatic diseases.

Prognostic Factors for Survival in Systemic Lupus Erythematosus Associated Pulmonary Arterial Hypertension

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Objective: Pulmonary hypertension (PH) is a rare but severe manifestation of systemic lupus erythematosus (SLE) that can ultimately result in death. The identification of factors that prognosticate survival in SLE-PH is necessary for appropriate monitoring, timing of therapeutics and lung transplantation. The primary objective of this study was to identify prognostic factors for survival in SLE-PH through review of the literature. We also evaluated the methodological quality of the prognostic studies.

Methods: A systematic review of the literature was performed to identify studies evaluating prognostic factors for survival in SLE-PH. Medline, EMBASE, CINAHL, and Cochrane Central Registry of Controlled Trials (inception **S** week 2 2010) were searched. A standardized abstraction form was used to extract prognostic factors by 2 independent reviewers. Methodologic quality was evaluated using a validated quality index.

Results: Twenty-three studies (retrospective cohort studies and case reports) from 375 citations were evaluated. Elevated mean pulmonary artery pressure, Raynaud's phenomenon, thrombocytopenia, plexiform lesion, infection, thrombosis, pregnancy, pulmonary vasculitis and anti-cardiolipin antibodies were associated with decreased survival. Lupus disease activity, nephritis and CNS disease were not associated with survival. The sample sizes were small and methodological quality of the studies was variable.

Conclusion: Our study summarizes factors that may be associated with decreased survival in SLE-PH. The small sample sizes and variable methodological quality preclude definitive conclusions. This study provides the groundwork for further research using large cohorts.

GAVE Unmasked by Alprostadil for Digital Ulceration in a Scleroderma Patient

Mohammed Omair (Mount Sinai Hospital, Toronto); Sindhu Johnson (University of Toronto, Toronto)

Objective. Prostaglandins are commonly used in the treatment of systemic sclerosis (SSc)-associated digital ulceration. Similarly, gastro-intestinal (GI) bleeding secondary to vasculopathic lesions in the GI tract is a recognized complication in SSc. We highlight an infrequent but clinically important occurrence in a common practice **S** gastric antral vascular ectasia (GAVE) unmasked by alprostadil therapy for severe digital ulceration.

Case Report: A 54 year old female with limited SSc based on sclerodactyly, calcinosis, telangiectasia, esophageal dysmotility, Raynaud's phenomenon and anti-centromere antibody presented with a refractory ulcer in the right 3rd digit. She was treated with nifedipine, losartan, topical nitroglycerin, aspirin and pentoxifylline with inadequate response. She was admitted to hospital for intravenous (IV) alprostadil. The ulcer size and pain improved. On day 3 of the infusion, she developed hematemesis and a significant decline in hemoglobin. Endoscopy revealed severe esophagitis, esophageal ulceration and appearance of the stomach consistent with GAVE. A previous endoscopy in February 2008 did not show any of these findings. She was treated with blood transfusion, pantoprazole and discontinuation of alprostadil. The bleeding stopped and her hemoglobin stabilized.

Discussion: Prostaglandins produce inhibition of platelet aggregation, vasodilatation and smooth muscle proliferation through a G-protein coupled receptor linked to adenylate cyclase; and promote fibrinolysis by reducing plasma concentrations of tissue-type plasminogen activator and plasminogen activator inhibitor¹. Long-term therapy reduces the level of factor VIII and Von Willebrand factor causing further inhibition of the coagulation cascade. GAVE is a rare but important cause of anemia in SSc patients with a prevalence of 2%⁵5.7%. The endoscopic pattern of GAVE is classically described as erythematous streaks on the longitudinal rugal folds traversing the antrum and converging on the pylorus. As these streaks resemble the stripes on the outside rind of a watermelon, this condition is also known as "watermelon stomach." Biopsy specimens demonstrate mucosal dilated capillaries containing fibrin thrombi, reactive epithelial changes, and fibromuscular hyperplasia of the lamina propria. The time of presentation is usually variable, presenting early in the diffuse and late in the limited subtypes; and may be affected by other factors like use of non-steroidal anti-inflammatories, steroids and proton pump inhibitors.

Conclusion: Alprostadil may precipitate bleeding from high-risk vascular lesions in the GI tract of SSc patients through its vasodilatory effects, inhibition of platelet aggregation, and promotion of fibrinolysis. Identification of high risk patients, close monitoring for occult blood loss and early intervention is recommended.

Arthritis In Celiac Disease Patients Does Not Respond Significantly To Gluten Free Diet Celiac Disease Arthropathy StudyS A Single Centre Canadian Perspective

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Objective: The purpose of our study was to determine the prevalence of arthritis in a Canadian population of Celiac disease patients and to ascertain whether a gluten free diet improves the symptoms of arthritis associated with Celiac disease.

Methods: This prospective, questionnaire based, cross-sectional cohort study was designed to evaluate the presence or absence of arthritis (primary outcome) simultaneously in both Celiac and non-Celiac disease cohorts. 1770 questionnaires in a ratio of 1:2 were sent to patients with Celiac disease and healthy age and sex matched volunteer non-Celiac disease controls respectively.

Results: 356/590 (60.33%) patients with celiac disease responded to the invitation to participate in this study. 443 (75%) responders (median age 58 years) were female; 60.5% with Celiac disease and 39.5% with non-Celiac disease. Celiac disease diagnosis (median duration 7 years) was endoscopically confirmed in 78.6% patients Overall, a doctor diagnosed arthritis in 223 (37.8%) patients; (65.5% GP & 22.9% rheumatologists). 131 cases of arthritis were reported in Celiac disease patients and 92 in non-Celiac disease patients. Osteoarthritis (89 vs. 59, $p=0.93$) was the most common diagnosis reported by Celiac disease patients, while rheumatoid arthritis (23 vs. 16, $p=0.017$) and psoriatic arthritis (5 vs. 1, $p=0.60$) were more commonly reported in non-Celiac disease patients. 4 patients with Celiac disease had Sacroiliitis and 2 patients had Ankylosing Spondylitis. Celiac disease group patients with diarrhea (66%) and anemia (53%) improved on gluten free diet. Only 51 (14.5%) patients with Celiac disease reported improvement in arthritis symptoms with gluten free diet compared to 121 (34%) patients reported no improvement. Univariate logistic regression analysis showed \leq high school education (OR 4.13, $p=0.003$), age \geq 60 yrs (OR 4.6, $p<0.001$), and osteoporosis (OR 2.78, $p<0.001$) to be significantly associated with report of arthritis in celiac disease patients, the latter two being still significant on multivariate logistic regression analysis. Being on gluten free diet and smoking did not significantly reduce or increase the incidence of arthritis in Celiac disease patients respectively. Autoimmune thyroiditis (10.6% vs. 0.4%), insulin dependent diabetes mellitus (2.2% vs. 1.7%), SLE (1.1% vs. 0), and psoriasis (12.9% vs. 5.5%) occurred more frequently in celiac disease patients.

Conclusion: There was no increase in inflammatory arthritis (Rheumatoid arthritis and Psoriatic arthritis) in Celiac disease patients. Being on gluten free diet did not result in significant improvement in arthritis symptoms, compared to improvement in anemia and diarrhea in celiac disease patients.

Telemedicine as a Tool Assisting Therapists to Deliver Arthritis Care in Remote/Rural Communities

Sydney Lineker (The Arthritis Society, Toronto); Mary Ellen Marcon (The Arthritis Society, Sault Ste. Marie); Jocelyne Murdock (The Arthritis Society, Sudbury); Sue MacQueen (The Arthritis Society, Kitchener); Diane McGall (The Arthritis Society, Owen Sound); Barbara Brown (The Arthritis Society, Kenora); Julie Herrington (The Arthritis Society, Burlington)

Objective: Telemedicine technology is in widespread use and therapists working in rural and remote communities are in a position to improve access to arthritis care through the use of this technology. This presentation will describe how therapists use telemedicine to enhance the integration of arthritis care in remote/rural communities.

Methods: Physical and occupational therapists working for a community rehabilitation program 1) developed a training protocol and trained telemedicine coordinators and nurse practitioners to be the 'hands' of the therapists and assess patients with arthritis remotely.

Results: Therapists reported that they have been able to expand the number of communities and patients they served, at a reduced cost in terms of travel time and mileage expense. They reported other benefits including less stress with winter driving, less wear on their vehicles, more efficient use of time, and fewer patient 'no shows'. They also identified potential benefits for patients including more timely access to care, less client travel and reduced costs of receiving care. Challenges were also identified including difficulties with scheduling and the need for extra people to assist with the technology.

Conclusion: Telemedicine technology was free, efficient and easy to use, offering benefits to therapists delivering arthritis care in remote and rural locations. The potential benefits to patients, other health professionals, rheumatologists and the health care system need to be assessed further.

Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K) Responder Index (SRI)-50: a Valid Index for Measuring Improvement in Disease Activity

Zahi Touma (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto); Dominique Ibanez (University of Toronto, Toronto); Murray Urowitz (University of Toronto, Toronto)

Objective: SRI-50 describes partial improvement, $\geq 50\%$, in disease activity between visits in lupus patients. We aim to determine whether SRI-50 would capture patients who have improved by $\geq 50\%$ as determined by physician global assessment (PGA), construct validity of SRI-50 for assessing improvement in disease activity in SLE.

Methods: All patients attending the Lupus Clinic from September 2009 to December 2009 were enrolled in a prospective longitudinal study. Of the 298 patients enrolled 141 had a follow-up visit and were studied further. SLEDAI-2K and SRI-50 scores were determined initially and on a follow-up visit at 153 months. During the first visit a PGA was determined on a visual analog scale (VAS) line of 100 mm, with anchors of 0 “no disease activity” and 10 for very active disease”. During the follow-up visit a PGA was determined on a 7-point Likert VAS; 7 much, 6 moderately, and 5 slightly improved, 4 unchanged, 3 slightly, 2 moderately, and 1 much worse. We defined a 50% improvement as $PGA \geq 6$. An external clinician evaluated patients’ records and grouped them on follow-up visit into: improved, same and worse using standardized predefined definitions. The external construct was the Likert VAS. We hypothesized that patients who had $\geq 50\%$ improvement ($PGA \geq 6$) would be captured by SRI-50 and the change in their SRI-50 scores would meet the definition of improvement by SLEDAI-2K (decrease ≥ 4).

Results: 126 females and 15 males were enrolled. 58% were Caucasian, 16% Black, 10% Asian and 16% others. Age at diagnosis 29.1 ± 11.4 , age at the visit 29.1 ± 11.4 , disease duration 15.3 ± 11.2 years and time between baseline and follow-up visits 3.2 ± 1.4 months. Patients were assessed as: worse 14, same 65 and improved 62. SRI-50 scores did not decrease below their presenting SLEDAI-2K score in patients who remained stable or worsened. In patients who improved, the SRI-50 score decreased by a mean of -2.40 ± 3.11 while SLEDAI-2K scores did not decrease. SRI-50 scores decreased more in patients with $PGA \geq 6$ compared to $PGA 4-5$ with a decrease of ≥ 4 ($r=0.52$; $p=0.0001$). The decrease in SRI-50 scores compared to the decrease in SLEDAI-2K scores were statistically and clinically more significant in patients with $PGA \geq 6$ ($p < 0.0001$) compared to those with $PGA 4-5$ ($p=0.003$).

Conclusion: These results show that the SRI-50 has construct validity. SRI-50 is able to demonstrate incomplete improvement which would not have been discerned using SLEDAI-2K.

Smoking Significantly Increases Disease Activity in Systemic Lupus Erythematosus (SLE): Results from the 1000 Faces of Lupus Cohort

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Objective: Smoking has been shown to increase SLE disease activity. However, smoking is also strongly associated with sociodemographic variables such as ethnicity, education and income, all of which also impact on SLE disease activity. We examined the relationship between smoking, sociodemographic variables, and disease activity in SLE patients.

Methods: Adult SLE prevalent and incident cases were enrolled in a prospective, multi-centre cohort. Sociodemographic variables, and data on health-related habits, diagnostic criteria, disease activity, autoantibodies, treatment, and damage were collected annually using standardized tools, and results were compared between smokers and non-smokers. Disease activity was evaluated using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). We analyzed annual follow-up data over a 3 year period, testing for differences in disease activity between smokers and non-smokers in univariate analyses; significant variables from univariate analyses were included in multivariate regression models examining predictors of disease activity.

Results: A total of 1380 adult participants were enrolled from July 2005-May 2009. Two hundred forty-one (17%) were current smokers and 1139 were non-smokers (83%). There were no significant differences between smokers and non-smokers with respect to age (44 ± 0.9 years vs. 45 ± 0.9 years), gender (88% vs 91% female), disease duration (11 ± 0.6 years vs. 12 ± 0.3 years), age at diagnosis (31 ± 0.9 years vs. 31 ± 0.4 years), ACR classification criteria met (5.9 ± 0.1 vs. 6.0 ± 0.1), and SLICC/ACR damage index (SDI) (1.5 ± 0.1 vs. 1.6 ± 0.1). A higher proportion of Caucasians (19%) and Aborigines (44%) were smokers compared to Asians (6%), and Afro-Caribbeans (9%), ($p < 0.001$). Thirty-seven percent of smokers had annual incomes $> \$50000$ compared to 47% of non-smokers, and 25% of smokers had annual incomes $< \$15000$ compared to 12% of non-smokers; $p=0.002$. Smokers (76%) were less likely to have completed high school compared to non-smokers (87%), $p < 0.001$. SLEDAI scores did not differ between smokers and non-smokers in univariate analysis over the 3 years (5.53 in smokers compared to 4.95 in non-smokers at first visit) but in multivariate analysis smoking status was the only significant predictor of SLEDAI, (parameter estimate=1.2, 95% CI .17S2.3, model R²=55%) other than current treatment with prednisone, when income, education, ethnicity, ACR criteria, and age were included.

Conclusion: Smoking contributes to higher disease activity in SLE, and accounts for some of the differences in disease activity seen between ethnic and socioeconomic groups.

Quality Assurance: Pharmacist Feedback on a Cost Effective Solution for Rheumatology Electronic Prescription Software

Steven Katz (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

Objective: Hand written physician prescriptions are fraught with potential medical errors. With improving patient safety in mind, electronic health records and electronic prescription programs are becoming more common, but they remain cost-prohibitive and can be technically difficult to implement. We previously presented a cost effective (free) design and implementation of an e-prescription program specifically for the rheumatologist. Pharmacist feedback was now sought to determine if this new program is perceived to be an improvement on handwritten prescriptions and equal to other potentially more costly e-prescription programs.

Methods: Between May and August 2010, consecutive rheumatology patients receiving a printed copy of their prescription from the electronic prescription software were asked to submit a 1 page survey to their pharmacist when filling the prescription. 100 surveys were to be distributed. A pre-stamped envelope was provided for return of the survey. The survey asked pharmacists to rank the legibility, clarity and overall effectiveness of the printed prescription on a scale of 1(worse) to 6 (better) compared to a hand-written prescription as well as other electronic prescriptions. Space was provided for comments. The survey was anonymous. Ethics approval was received from the University of Alberta Health Ethics Research Board.

Results: 100 surveys were distributed, with 61 returned. Compared to hand written prescriptions, the electronic prescription software was highly rated, with an average of 5.84 for legibility, 5.64 for clarity and 5.69 overall. Interestingly, the electronic prescription program was also rated higher than other electronic software available, rated 5.03 for legibility, 4.95 for clarity and 5.02 overall. 36 comments were received, the majority considered positive. Recurring comments included appreciation for developing the software, soliciting pharmacist feedback, and the simplicity of the prescription print out itself compared to other prescriptions.

Conclusion: This cost-effective rheumatology specific prescription program was well received by pharmacists and was identified as a superior option compared to other available software. Future work to consider includes wider adoption in the rheumatology community and identifying areas to further reduce prescription error.

Treating Osteoporosis After A Fragility Fracture: The Family Physician As The Hub

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Objective: To describe the implication of Family Physicians (FPs) in the management of osteoporosis revealed by a fragility fracture.

Methods: The impact and costs of fractures is straining the health system. A better collaboration between specialists and FPs should improve the evaluation and treatment of affected patients. Since January 2007, the OPTIMUS initiative is an attempt to reach that objective in the Estrie area of the Province of Québec. With OPTIMUS, rates of appropriate treatment of osteoporosis at one year in previously untreated patients more than double (53% vs 20%). In OPTIMUS, FPs remain responsible for investigation and treatment of their patients after identification of a bone fragility fracture. A coordinator based in orthopaedists' outpatient clinics identifies fragility fractures in patients older than 50 y.o. , informs them about bone fragility and its link to osteoporosis, and spurs them to contact their FPs to get treated; the importance of persistence on treatment is reinforced during phone follow ups. Initially and when patients remain untreated upon follow up, the coordinator sends a letter to the patient's FP about the occurrence of the fracture, its predictive value for future fractures, and the need for investigation and treatment. This represents a personalized form of continuous medical education for FPs, in the hope that FPs become leaders in the prevention of fragility fractures. To evaluate the perception of FPs about OPTIMUS, we performed a mail survey targeting FPs reached at least once by OPTIMUS.

Results: The survey was sent to a total of 212 FPs. One hundred and nine (51.4%) answered. Of these, 97 (89%) agreed that a fragility fracture is an indication for treatment of osteoporosis; 56 (51%) agreed that OPTIMUS had helped them take charge of osteoporosis; and 105 (96.3%) were Satisfied or Very Satisfied of the OPTIMUS initiative.

Conclusion: Because of this high level of acceptance, we propose to put into place a more elaborate intervention including a fall prevention program that will be managed by nurse coordinators in 16 FP Groups (GMF); these 16 Groups include 178 of the 360 FPs of the area. The FPs practicing in GMF are also involved in teaching to colleagues, residents and medical students; we expect an exponential effect on the practice of FPs over the years. We believe this enhanced intervention will improve the quality of life and autonomy of the patients while decreasing their rate of fractures.

Efficacy and Safety of Cannabinoids for Pain in Musculoskeletal Diseases: a Systematic Review and Meta-analysis.

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Objective: To evaluate the efficacy and safety of Cannabinoids compared to placebo in adults with musculoskeletal disease.

Methods: We performed a systematic review comparing cannabinoids to placebo for the treatment of pain in patients with musculoskeletal (MSK) diseases. Trials were identified in MEDLINE, EMBASE, the Cochrane Library and ACR/EULAR meeting abstracts for 2008-2009. The primary outcome for efficacy was the mean difference in comparable numerical pain outcomes: pain Visual Analogue Scale (VAS) and Numerical Rating Scales (NRS). Primary outcomes for toxicity were serious adverse events (SAEs) and withdrawals due to adverse events. Secondary outcomes for toxicity were 3 specified adverse events (AEs): drowsiness, confusion or euphoria.

Results: A total of 4 randomized trials (218 patients) from 2450 citations investigated use of cannabinoids vs. placebo in MSK diseases. Although a much broader definition of MSK disease was entertained, only trials in rheumatoid arthritis (RA), back pain and fibromyalgia (FM) were retrieved. Where comparable data were not available, authors were contacted to obtain original data. For efficacy, the mean difference (10-pt scale) favoured cannabinoid treatment for pain over placebo (mean difference \$1.47, 95% C.I. \$2.01, \$0.94) which is above the minimal important difference. There was no statistically significant difference in the risk of SAEs (Odds Ratio: OR 0.61, 95% C.I. 0.10, 3.68, Power=0.08), withdrawals due to adverse events (OR 1.32, 95% C.I. 0.43, 4.01, Power=0.08) or risk of euphoria (OR 4.05, 95% C.I. 0.24, 67.39, Power=0.16). Side effects were rare with no between group differences but analyses were underpowered. With respect to the secondary outcomes, AEs were statistically significantly different and more common in cannabinoids as compared to placebo for drowsiness (OR 4.05, 95% C.I. 1.82, 9.00) and confusion (OR 5.48, 95% C.I. 1.91, 15.73), translating to numbers needed to harm (NNH) of 4 and 9 respectively.

Conclusion: Cannabinoids appear to be efficacious for treatment of pain in the musculoskeletal diseases RA, FM and back pain. The statistically significant improvement in pain scores corresponded to a modest clinical difference in these few studies (only one in RA) against placebo. Information is still lacking with respect to the most important toxicity outcomes designated as SAEs and those leading to withdrawal of medication. However, substantial numbers of patients may experience bothersome adverse events such as confusion and drowsiness. Given preliminary efficacy data but incomplete data on toxicity, further studies with cannabinoids in MSK disease are warranted, particularly against active comparators.

SLEDAI-2K Responder Index (SRI)-50: A Reliable Index for Measuring Improvement in Disease Activity

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Objective: To test the inter-rater and intra-rater reliability of the SRI-50, an index designed to measure $\geq 50\%$ improvement in disease activity between visits in lupus patients.

Methods: This is a multicenter, cross-sectional study with raters from Canada, United Kingdom and Argentina. Patient profile scenarios were derived from “real” adult patients. Ten rheumatologists, from university and community hospitals, and postdoctoral rheumatology fellows participated. An SRI-50 data retrieval form was used. Rheumatologist scored SLEDAI-2K at the baseline visit and SRI-50 on follow-up visit, for the same patients on two occasions 2 weeks apart. Physician Global Assessment (PGA) was determined on a numerical scale at baseline visit and Likert Scale (LS) on follow-up visit. Inter-rater and intra-rater reliability was assessed using intraclass correlation coefficient (ICC) and kappa statistics whenever applicable.

Results: Forty patient profiles were created. 55% were Caucasian, 22% black, 5% Asian and 18% others. Age at diagnosis 30.4 ± 12.7 , age at the visit 38.0 ± 13.5 years, disease duration 7.6 ± 8.1 years and SDI 1.05 ± 1.45 . All 24 descriptors of SLEDAI-2K were represented. The ICC performed on 80 patient profiles for inter-rater ranged from 1.00 for SLEDAI-2K and SRI-50 to 0.96 for PGA. The ICC for SLEDAI-2K, SRI-50 and PGA ranged from 1.00 to 0.86. Substantial agreement was determined for inter-rater LS with a kappa statistics of 0.57.

Conclusion: The SRI-50 is reliable to assess $\geq 50\%$ improvement in lupus disease activity. The use of the SRI-50 data retrieval form is essential to ensure the optimal performance of SRI-50. SRI-50 can be used by both rheumatologists and trainees and performs equally well in trained as well as untrained rheumatologists.

SLEDAI-2K Responder Index-50 Enhances the Ability to Identify Responders in Clinical Trials

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Objective: The 3 component SLE Responder Index (SRI) was able to demonstrate clinically significant improvement in recent trials of a new therapeutic agent in SLE. The purpose of our study was to evaluate the performance of SRI when SLEDAI-2K is substituted by SRI-50. To determine if SRI-50 will enhance the ability of SRI in detecting improvement in disease activity.

Methods: This is a cross-sectional study conducted on patients who attended the Lupus Clinic from September 2009 to July 2010, who had active lupus on baseline visit (SLEDAI-2K ≥ 4) and had one follow up visit. SRI incorporates SLEDAI-2K, BILAG and Physician Global Assessment (PGA). SLEDAI-2K, SRI-50, BILAG and PGA were determined initially and at follow-up. Patients who showed worsening in disease activity on follow-up visit (increase in SLEDAI-2K score) were excluded from the analysis. SRI response is defined as 1) a ≥ 4 point reduction in SLEDAI-2K score, 2) no new BILAG A or no more than 1 new BILAG B domain score, and 3) no deterioration from baseline in the PGA by ≥ 0.3 points. SRI was determined at follow-up visit according to the original definition using SLEDAI-2K score. SRI was further evaluated in the same group of patients but this time substituting SLEDAI-2K with SRI-50.

Results: 107 patients, 97 females and 10 males with SLEDAI-2K score ≥ 4 at baseline were further studied. The length of time between both visits was 2.9 ± 1.0 months. The mean change of SLEDAI-2K (SLEDAI-2K Follow-up - SLEDAI-2K Baseline) was $\$1.85 \pm 3.27$ and the mean change in SRI-50 (SRI-50 Follow-up - SLEDAI-2K Baseline) was $\$2.59 \pm 3.41$. Although patients had only one follow-up visit over a 3 months period, 30 patients (31%) met the original definition of SRI and 37 patients (35%) met the definition of SRI when SLEDAI-2K was substituted with SRI-50 score. The use of SRI-50 definitions allowed us to determine a clinically significant improvement in 7 additional patients. This improvement could not be discerned with the use of SLEDAI-2K as a component of SRI.

Conclusion: These results show that SRI-50 enhances the ability of SRI to capture patients with clinically significant improvement in disease activity. Although the period of follow-up was very short, SRI-50 was superior to SLEDAI-2K in detecting partial clinical improvement, $\geq 50\%$, between visits. SRI-50 should be used as the response measure of disease activity improvement in current trials of new treatments for lupus.

Comparison of Lupus Quality of Life and SF-36 Questionnaires in Lupus Patients with Moderate Disease Activity-a Cross-sectional Study

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Objective: We aimed to evaluate whether the LupusQoL contributed additional information not obtained using the SF-36 in Lupus patients and moderate disease activity.

Methods: 35 patients with moderate disease activity (SLEDAI-2K 30days ≥ 6) seen at a single centre over 3 months were enrolled. Both questionnaires were co-administered at the same visit. Cumulative damage was determined by Systemic Lupus International Collaborating Clinics/ACR Damage Index (SDI). We performed a descriptive analysis of the mean scores for all domains and compared comparable domains in both questionnaires. For the 4 non-comparable domains of the LupusQoL we determined the correlation between each domain with the Physical Component Score (PCS) and the Mental Component Score (MCS) of the SF-36. We determined the correlations between LupusQoL and SF-36 with SLEDAI-2K and SDI scores. We compared LupusQoL and SF-36 scores in patients with and without damage.

Results: Among the 35 patients (female 29 /male 6), 40% were Caucasian, 31% Black, 1% Asian, and 17% other. The mean age at SLE diagnosis was 25.0 ± 10.9 years. At study visit the mean age was 35.1 ± 10.7 and disease duration 10.1 ± 6.4 years, SLEDAI-2K 10.31 ± 5.36 and SDI 1.06 ± 1.20 . Both questionnaires assessed quality of life as low among patients. There was no statistically significant difference between comparable domains of both questionnaires. For the 4 non-comparable domains of the LupusQoL, there was a correlation between Body Image and MCS-SF-36 $r=0.73$, Planning and MCS-SF-36 $r=0.63$, Intimate Relationships and PCS-SF-36 $r=0.59$, and Burden to Others and MCS-SF-36 $r=0.34$ (all p were significant). Neither questionnaire correlated with disease activity nor with cumulative damage. When comparing the domains in patients with damage to patients without damage, there was a statistically significant difference with some of the SF-36 scores (Physical Functioning $p=0.03$ and PCS $p=0.046$) but not LupusQoL scores. In both cases, the scores were lower in patients with damage. No relationship could be identified between LupusQoL and fibromyalgia since there were only 2 patients with fibromyalgia.

Conclusion: Quality of life as determined by LupusQoL and SF-36 questionnaires is significantly compromised in lupus patients with moderate disease activity, but does not correlate with disease activity or damage. These findings confirm that the quality of life is an independent outcome measure in the assessment of lupus. There is no superiority of LupusQoL over SF-36 in assessing lupus patients' quality of life. The responsiveness of LupusQoL needs to be evaluated in patients with moderate to severe disease activity.

Prolonged Serologically Active Clinically Quiescent (SACQ) Systemic Lupus Erythematosus (SLE): Novel Predictors of Flare?

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Objective: Anti-double stranded DNA antibodies (anti-dsDNA) and complement levels can predict SLE flare. Some patients, however, are clinically quiescent despite persistent serologic activity (i.e., elevated anti-dsDNA and/or hypocomplementemia). Past studies reveal that 60% of such SACQ patients flare, but do so only after average 182 weeks. In these patients changes in anti-dsDNA and/or C3/C4 levels measured at routine clinic visits did not predict disease flare. Some studies suggest that anti-chromatin (-nucleosome) antibodies are more sensitive than anti-dsDNA to detect active SLE, and that time to first flare after a SACQ period significantly correlates with their presence. We investigated whether levels of anti-dsDNA and -chromatin isotypes, measured during a prolonged SACQ period, differed in patients who remained SACQ versus those who flared.

Methods: Archived serum samples of patients with a prolonged SACQ period, stored at 80°C , were retrieved and divided by disease activity (during SACQ period vs during flare). Serum levels of IgM, IgA, total IgG, and IgG1-4 anti-dsDNA and anti-chromatin antibodies were measured by ELISA. H1-stripped chromatin was prepared from the human cell line, MOLT4. ELISA plates were coated overnight with dsDNA (40 ug/ml) and chromatin (8 ug/ml) diluted in PBS at 4°C . Serum was diluted 1/100 for IgM, IgA, and IgG, or 1/50 for IgG1-4. SACQ was defined as at least a two year sustained period with SLEDAI-2K of 2 or 4 from serologic activity only, during which patients could be taking antimalarials, but not steroids or immunosuppressives. Flare was defined as any clinical disease activity. Non-parametric statistics were used.

Results: Thirty-eight samples corresponding to a prolonged SACQ period (from 23 patients) were analyzed. 15/38 (39%) samples corresponded to patients who flared. Anti-chromatin total IgG levels were lower in SACQ patients who flared than in those who remained SACQ (0.361 ± 0.277 vs 0.835 ± 0.700 , $p=0.007$; normal < 0.147), however there was no difference between these groups when IgG was broken down by subtype.; IgM and IgA were comparable between groups. Anti-dsDNA IgA (but not IgM or IgG) was lower in patients who flared compared to those who remained SACQ (0.028 ± 0.025 vs 0.081 ± 0.095 , $p=0.018$). When only the most recent sample from each SACQ patient was analyzed (9/23 (39%) of whom flared), there was no difference between anti-chromatin or anti-dsDNA isotype levels between patients who flared and those who remained SACQ.

Conclusion: In this pilot study neither anti-chromatin nor anti-dsDNA antibodies predicted flare in patients with a prolonged SACQ period. Alternate biomarkers must be sought.

The Prevalence of Systemic Lupus in Alberta: A Population-based Assessment

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Objective: To estimate the prevalence of SLE using population-based administrative data, and to compare prevalence rates between First Nation (FN) and non-FN persons.

Methods: Three case definitions were used to ascertain SLE cases from Alberta physician billing claims and hospitalization databases (covering over 3.7 million individuals): >1 billing codes by a rheumatologist; or >2 billing codes by any physician, >8 weeks apart but within 2 years; or a hospitalization diagnosis. The Alberta Health and Wellness registry file was used to determine FN status, and rural or urban residence by postal code. To account for imperfect case ascertainment, we employed a hierarchical Bayesian latent class regression model that accounted for possible between-test dependence conditional on disease status and potential differences in case ascertainment sensitivity and specificity based on patient characteristics (age, sex, and rural-versus-urban residence). Cases were ascertained from 1994-2007, and prevalence estimates based on those alive as of 2007.

Results: Accounting for error inherent in both data sources, the estimated overall SLE prevalence in Alberta is 27.3 cases per 10,000 females (95% credible interval, CrI 25.9-28.8) and 3.2 cases per 10,000 males (95% CrI 2.6-3.8). Prevalence was higher for individuals aged >45, particularly in urban women (51.2 per 10,000; 95% CrI 47.5-55.3). Although the overall prevalence in FN was similar to that of non-FN, interesting trends were seen with higher rates in FN women (30.2 per 10,000; 95% CrI 24.5-37.4) compared to non-FN women (27.1 per 10,000; 95% CrI 25.7-28.6). This was particularly marked for females aged >45, with an urban FN prevalence of 100.8 per 10,000 (95% CrI 66.5-147.4) versus non-FN 50.6 per 10,000 (95% CrI 46.9-54.7); and rural FN prevalence of 86.7 per 10,000 (95% CrI 61.2-127.3) versus non-FN 44.3 per 10,000 (95% CrI 40.0-49.2). Prevalence rates tended to be higher in FN females aged < 45 compared to non-FN of that age group, but with overlapping 95% CrI. Point estimates in FN men were lower than in non-FN men, but the 95% CrI were wide and overlapping.

Conclusion: We demonstrated differences in SLE prevalence according to age, sex, and region. The administrative data suggest a 2-fold increase in SLE cases among FN females aged >45, compared to non-FN females of this age group. This may reflect a true predominance of SLE among FN women, but alternate explanations may be that patterns of health care use and/or billing codes may differ across demographic groups, creating biased estimates. An additional limitation is imprecision in some sub-group estimates.

Treatment of Hypertension and Hypercholesterolemia is not Successful in the Majority of Patients with Systemic Lupus Erythematosus

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Objective: Patients with SLE demonstrate accelerated atherosclerosis and are at an increased risk of coronary artery disease. Previous quality improvement studies have demonstrated that increasing numbers of patients are being treated for hypertension and hypercholesterolemia. The objective of this study was to determine whether the initiation of treatment with antihypertensive or lipid lowering medications led to successful control of these risk factors.

Methods: Patients from a large lupus cohort presenting within 1 year of SLE diagnosis and who received treatment with anti-hypertensive medications since 1985 and/or lipid lowering medications since 1995 were included. Success was defined as having met target blood pressure (BP), systolic BP ≤ 140 and diastolic BP ≤ 90 mmHg, serum total cholesterol (TC), TC ≤ 5.2 mmol/L or serum LDL, LDL ≤ 3.2 mmol/L during at least 90% of follow-up).

Results: 70% and 29% of patients with documented hypertension or hypercholesterolemia respectively were initiated on appropriate therapy. 107 patients were treated for hypertension (86% female, mean \pm SD age at treatment was 43.3 \pm 15.4, mean \pm SD disease duration at treatment was 2.6 \pm 4.2years) and 49 were treated for hypercholesterolemia (82% female, mean \pm SD age at treatment was 42.9 \pm 13.3, mean \pm SD disease duration at treatment was 3.2 \pm 3.6 years). Overall the adjusted mean systolic pressure decreased from 147.00 \pm 18.71 mmHg to 131.49 \pm 14.32 mmHg following treatment and the adjusted mean diastolic pressure decreased from 90.37 \pm 12.05 mmHg to 80.39 \pm 14.32 mmHg. However, only 36 of 104 patients (35%) met our criteria for successful treatment of hypertension. The adjusted mean total serum cholesterol and LDL decreased from 6.29 \pm 1.48 mmol/L to 4.76 \pm 1.01 mmol/L and 3.65 \pm 1.29 to 2.56 \pm 0.81 respectively. However, only 19 of 48 patients (40%) attained target total cholesterol levels while 25/40 (63%) attained target LDL levels during over 90% of follow-up.

Conclusion: Treatment of hypertension and hypercholesterolemia does not necessarily result in successful control of these risk factors in the majority of SLE patients. Further analysis will be important to discern the reasons for unsuccessful treatment and to compare CAD outcomes in patients who were successfully treated and those who were not.

Examination of Steroid Dose and Steroid-related Damage in an International Inception Cohort of Systemic Lupus Erythematosus Patients

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Objective: Corticosteroids (CS) remain the mainstay in the treatment of Systemic Lupus Erythematosus (SLE). It is known that cumulative CS dose is associated with damage; however the role of mean dose over time is not known. The purpose of this study is to determine the effect of dose dependent factors in the accrual of steroid related damage in SLE patients.

Methods: Patients with SLE from the multicentre SLICC-RAS inception cohort were followed prospectively for 5 years. Annual data collection includes clinical and laboratory features of SLE, past and current therapy, and the SLICC/ACR damage index (SDI). The occurrence of permanent damage, as measured by the SDI, was categorized as definitely related, possibly related, or independent of CS. Steroid courses over this period were captured and used to calculate accumulated dose and average daily dose. Multivariable stepwise logistic regression and Mantel-Haenszel chi-square tests were performed to identify significant associations between dose dependent variables and steroid-related permanent damage.

Results: Of the 342 patients in our analysis (295 female, mean(\pm std) age of 35 ± 13 years at enrolment), the median cumulative steroid dose increased from 0.49g to 13.2g from enrolment to 5 years follow-up. During the same period, the mean damage (SDI) increased from 0.15 ± 0.50 to 0.97 ± 1.33 , of which 0.24 ± 0.60 (25%) was definitely related to steroids. Damage associated with cumulative dosages are as follows: at 0 g total SDI was 0.50 ± 0.84 of which 0.11 ± 0.34 (19.4%) was definitely related CS, and at ≥ 40 g the total SDI was 1.77 ± 1.74 of which 1.00 ± 1.15 (50%) was definitely related to CS. Damage associated with average daily dosages are as follows: total SDI at 0 mg/day was 0.50 ± 0.84 of which 0.11 ± 0.34 (19.4%) was definitely related to CS, and at ≥ 20 mg/day the total SDI was 1.64 ± 1.75 of which 0.54 ± 0.96 (28.9%) was definitely related to CS.

Conclusion: SLE patients receiving CS therapy accrue damage due to disease and other therapy factors, as well as due to CS over time; however the relative contribution of damage due to CS remains the same over a five year period. Additional research is required to better determine the susceptibility of SLE patients to steroid damage due to dose over an increased duration of corticosteroid use.

Adverse Obstetrical and Neonatal Outcomes in RA and SLE

Cheryl Barnabe (University of Calgary, Calgary); Peter Faris (Alberta Bone and Joint Institute, Calgary); Hude Quan (University of Calgary, Calgary)

Objective: Adverse obstetrical and neonatal outcomes have historically been documented in women with rheumatic disease. These outcomes may be improved in recent times where better rheumatic disease and prenatal management is available.

Methods: An administrative database (years 1998/9 to 2008/9) provided obstetrical hospitalization details for women with RA and SLE, and each identified case was matched with 4 controls based on maternal age and year of delivery. Conditional logistic regression was used to calculate the odds ratio (OR), with adjustments made for known confounders, for the following outcomes in patients compared to controls: pregnancy-related hypertension, cesarean section, premature births and neonates meeting criteria for small for gestational age (SGA). We also compared the hospital length of stay and proportion of neonates requiring special care unit admission.

Results: There were 38 singleton pregnancies in women with RA and 95 in women with SLE during the study period. The adjusted OR (aOR) for pregnancy-related hypertension in RA was 2.9 (95%CI 1.0\$8.3; p=0.051) and in SLE 2.2 (95%CI 1.2\$4.3; p=0.017). The aOR for cesarean section in RA was 2.3 (95%CI 0.9\$6.3; p=0.097) and in SLE 2.8 (95%CI 1.5\$5.1; p=0.01). The aOR for prematurity in RA was 2.7 (95%CI 1.0\$7.0; p=0.043) and in SLE 6.6 (95%CI 3.5\$12.3; p< 0.001). The aOR for SGA in RA was 3.0 (95%CI 1.2\$7.2; p=0.017) and in SLE 2.8 (95%CI 1.5\$4.9; p=0.001). Additionally, more women with SLE experienced postpartum infections compared to their controls (6.3% vs 1.3%, p=0.004). The maternal length of stay was longer for women with rheumatic disease (mean difference for RA 0.9 days (95%CI 0.4\$1.3; p=0.003), for SLE 1.8 days (95%CI 1.1\$2.6; p< 0.001). More neonates born to mothers with RA or SLE required admission to the special care unit (RA 29% vs 11%; p=0.006; SLE 36% vs 13%; p< 0.001).

Conclusion: Women with RA and SLE have increased odds of developing pregnancy-related hypertension, and a large proportion deliver by cesarean section. Neonates of women with rheumatic disease are more likely to be premature, and small for gestational age. These findings are in keeping with the historical literature, and do not appear to have improved over time. Additionally, women with SLE demonstrate a trend to an increased risk of postpartum infections, which has not been previously identified. Increased collaboration between rheumatologists and obstetrical care providers is suggested to identify modifiable risk factors for these adverse outcomes.

A 50 Year Old Woman with Fever, Hemoptysis and Rash

Zorheh Sabbagh (University of Saskatchewan, Saskatoon); Regina Taylor-Gjevre (University of Saskatchewan, Saskatoon)

Case Report:

BACKGROUND: Churg Strauss Syndrome (CSS) is an eosinophil-associated small vessel vasculitis. Its incidence is 2.4/4 per million which makes it one of the rarest of the systemic vasculitides. ANCA, both PR3 and MPO, have been detected with variable frequencies in patients with CSS and is more associated with cutaneous, neurological, and pulmonary involvement. **CASE:** We present a 50 year-old woman with a history of asthma and rhinitis who was admitted because of fever, hemoptysis, recurrent ear infections, sinusitis, weight loss, and purpuric rash. She reported swelling in her elbows and knees as well as tingling and numbness in her feet. In addition, leukocytosis, eosinophilia, elevation of CRP and ESR were observed. She developed rapid renal failure with serum creatinine of 189, proteinuria of 0.7 gr /day and RBC casts. Moreover, ANCA/PR3 was positive. Chest radiograph and computed tomography showed patchy air-space consolidation in both lung fields. Echocardiogram was normal. Skin biopsy depicted lymphocytic vasculitis with eosinophils. Given the clinical picture, laboratory data and pathologic findings, our patient fulfilled the ACR criteria for diagnosis of CSS. Following the skin biopsies, therapy with methylprednisolone and cyclophosphamide was initiated. Eosinophilia, fever, hemoptysis, and weakness improved dramatically in the first 24 hr. **CONCLUSION:** Our patient is a rare ANCA/ PR3 positive CSS with involvement of the lung, skin, kidney, and nervous system. The presence of ANCA/PR3 may contribute in severity of her renal impairment. These manifestations in a patient with asthma and eosinophilia should alert the clinician to the possibility of CSS. Immunosuppressive therapy with steroids and cyclophosphamide is beneficial.

Relapsing Polychondritis Associated with Hepatitis C Virus Infection

Iman Hemmati (Department of Medicine, UBC, Vancouver); Eric Yoshida (Division of Gastroenterology, UBC, Vancouver); Kam Shojania (University of British Columbia, Vancouver)

Case Report:

Objective: Review of relapsing polychondritis (RP) and its association to hepatitis C virus (HCV) infection. **Method Used:** A case of RP associated with HCV infection in a 59-year-old male is reported. The English medical literature was reviewed for RP and its association with HCV infection. **Results Obtained:** RP is a rare autoimmune and multisystem disorder of unknown etiology in which the cartilaginous and related tissues are the primary targets of inflammation. HCV infection is a more common systemic illness with known hepatic and extra-hepatic manifestations. Although RP is associated with other diseases in about 35% of cases, only one case of RP, HCV and mixed cryoglobulinemia has been reported. We report a case of RP associated with HCV infection. Treatment with pegylated interferon and ribavirin resulted in sustained virologic response and remission of treatment resistant RP with azathioprine. **Brief Conclusion:** We report a case of RP and associated HCV infection. Although treatment of HCV infection resulted in remission of RP, It is unknown if there is a causal relationship between HCV infection and RP.

Perceptions of Advanced Clinician Practitioner in Arthritis Care (ACPAC) Program-trained Practitioners: Roles and Role Utilization within the Ontario Healthcare System

Kelly Warmington (St. Michael's Hospital, Toronto); Carol Kennedy (St. Michael's Hospital, Toronto); Katie Lundon (St Michael's Hospital, Toronto); Linda Rozmovits (Linda Rozmovits Qualitative Research, Toronto); Sydney Lineker (The Arthritis Society, Toronto); Rachel Shupak (St Michael's Hospital, Toronto); Rayfel Schneider (The Hospital for Sick Children, University of Toronto, Toronto)

Objective: To capture practitioner and stakeholder satisfaction with the roles of Advanced Clinician Practitioner in Arthritis Care (ACPAC) program-trained physical therapists (PTs) and occupational therapists (OTs).

Methods: ACPAC program graduates and their colleagues were recruited from 15 institutions across the province of Ontario. Participants included program graduates, nurse practitioners, physicians, unit managers and program directors. Patients' perspectives have been captured in a separate study. Program graduates participated in focus groups and their clinical colleagues and administrators participated in individual interviews. Interviews and focus groups were digitally audio-recorded for verbatim transcription. Transcripts were verified and entered into HyperResearch software for textual data analysis. Transcripts were coded for anticipated and emergent themes using the method of constant comparison including searches for disconfirming evidence. Focus groups, interviews and analyses were conducted by a qualitative researcher.

Results: Graduates (n=20) valued their ACPAC training and the advent of their extended practice roles (where achieved), seeing them as positive opportunities for career advancement. Those enjoying extended practice roles felt they were improving communication and continuity of care, improving access to care in under-served communities, providing timely and appropriate referrals and earlier recognition of potentially serious problems. Barriers to role utilization included lack of dedicated funding and administrative recognition through title, remuneration and medical directives and the unwillingness of others to understand or accommodate extended practice roles within their practice structure. Colleagues of ACPAC graduates (n=18) generally highly valued graduates' roles. They felt that graduates were innovative, communicative, provided enhanced provision of care in under-served areas, allowed physicians to see more patients and greatly enhanced education for patients regarding their disease process, treatment and recovery. Administrators expressed concern about the cost-effectiveness and sustainability of extended practice roles for graduates within the current system. A lack of hands-on therapists if graduates move into extended practice roles was also a concern. At the system-level, it was felt that ACPAC graduates could reduce patient wait times, improve access to rheumatologists, reduce long-term disability, and provide a better approach to chronic disease management for an aging population.

Conclusion: Administrators, clinical colleagues and program graduates themselves value their capabilities and perceive that they improve patient care on many levels; however, barriers to role utilization at the team, institution and system levels pose challenges for the sustainability of extended practice roles. Future work needs to focus on ways to break down these barriers and maximize role utilization for the benefit of patients with arthritis.

Advanced Clinician Practitioner in Arthritis Care (ACPAC) Program-Trained Therapists in Ontario: Impact on System Integration and Change

Carol Kennedy (St. Michael's Hospital, Toronto); Kelly Warmington (St. Michael's Hospital, Toronto); Leslie Soever (Mount Sinai Hospital, Toronto); Laura Passalent (St Michael's Hospital, Toronto); Sydney Lineker (The Arthritis Society, Toronto); Ryan Thomas (St Michael's Hospital, Toronto); Katie Lundon (St Michael's Hospital, Toronto); Rachel Shupak (St Michael's Hospital, Toronto); Rayfel Schneider (The Hospital for Sick Children, University of Toronto, Toronto)

Objective: The Advanced Clinician Practitioner in Arthritis Care (ACPAC) program is an innovative, clinical and academic, interprofessional education program for licensed physical and occupational therapists. The program focuses on assessment, diagnosis, triage and independent management of selected musculoskeletal and arthritis-related disorders. This study aimed to evaluate the performance of ACPAC program-trained extended role practitioners with respect to health care delivery using System Integration and Change (SIC) indicators. The research objectives were to measure: 1) the role utilization of the ACPAC program-trained practitioner, 2) access to ACPAC program-trained practitioners in Ontario, and 3) integration with internal/external services and other services/resources.

Methods: ACPAC program-trained practitioners (n=30) were recruited from 15 healthcare institutions across the province of Ontario. These included urban, rural, academic, non-academic, adult and paediatric settings. ACPAC program-trained practitioners completed a longitudinal survey at the end of each fiscal quarter in 2009. Data were collected using SurveyMonkey®. SIC indicators and related questionnaire items were developed by: teleconference brainstorming, ranking and pilot testing with ACPAC program graduates; input from stakeholders (healthcare administrators and patients of these extended role practitioners). Descriptive statistics were used to summarize the data.

Results: The response rate varied from 83% to 93% over the fiscal quarters. Most respondents were working in an extended practice role (range 84% to 93%). The mean wait time to see an ACPAC program-trained practitioner varied from 14 to 22 days. These practitioners provided a wide range of services to patients in the 2009 fiscal year: referring 3946 patients to internal or external services, 1867 patients to medical doctors (general practitioners or specialists), and 3262 patients to educational resources. Most ACPAC graduates (75%) reported acting under the auspices of medical directives to support their extended practice role. Most respondents ordered X-rays (82%), lab tests (64%) and diagnostic ultrasounds (54%). 70% reported recommending medication/dosage changes and 4% made these changes independently. 89% reported recommending joint injections and 8% were performing them.

Conclusion: ACPAC program-trained practitioners were working in extended practice roles performing tasks that have the potential to improve access to care for patients with arthritis. Future evaluations will monitor the evolution of these new roles and assess their impact on patient outcomes. This new human health resource may be an effective strategy to address the declining number of arthritis care specialists which has resulted in inappropriate wait times for care and the need for an interprofessional approach to managing patients with musculoskeletal disorders more efficiently.

A Simulation Model of Medication Use and Impact among Persons with Osteoarthritis in Canada

Jacek Kopec (University of British Columbia, Vancouver); Eric Sayre (Arthritis Research Centre of Canada, Vancouver); M Mushfiqur Rahman (Arthritis Research Centre of Canada, Vancouver); Weiqun Kang (Arthritis Research Centre of Canada, Vancouver); Philippe Finès (Statistics Canada, Montreal); William Flanagan (Statistics Canada, Ottawa); Jolanda Cibere (University of British Columbia, Vancouver); Nicholas Bansback (Centre of Clinical Epidemiology and Evaluation, Vancouver); Aslam Anis (University of British Columbia, Vancouver); Elizabeth Badley (University of Toronto, Toronto)

Objective: The objective of this research was to build a drug treatment module for POHEM-OA, a population-based computer model of osteoarthritis (OA). POHEM-OA is a microsimulation model in which aggregate results for the adult population of Canada are obtained by simulating “life histories” of about 25 millions individuals, one at a time.

Methods: Model parameters have been derived from analyses of administrative data in BC (prescription drug use), national population surveys (over-the-counter use), and a comprehensive review of the literature (benefits and adverse effects of medication). POHEM-OA simulates the use of 4 types of medication (acetaminophen, NSAIDs, COX-2 inhibitors and opioids) as a function of age, sex, OA, and health level, measured by the Health Utilities Index 3 (HUI3). HUI3 is an 8-domain health index that includes pain. The model also simulates the benefits of medication in terms of its positive impact on HUI3 (estimated from data on pain reduction), as well as adverse effects of drugs and their negative impact on HUI3 and survival.

Results: Probabilities of use for each type of medication have been estimated for 390 subgroups defined by age, sex, OA diagnosis, OA duration, surgical treatment, and HUI3 category. These probabilities ranged from 0.01 to 0.77 for acetaminophen, 0.03–0.93 for NSAIDs, 0.001–0.28 for Coxibs, and 0.0002–0.67 for opioids. For example, the highest users of coxibs were men, < 50 years of age, < 2 years after joint replacement surgery. HUI3 levels had a strong effect on the use of opioids and coxibs and moderate-to-weak effect on the use of acetaminophen and NSAIDs. Average relative pain reductions (0–100 scale) ranged from 28% for acetaminophen to 38% for NSAIDs and coxibs and 40% for opioids. Excess risks of adverse effects in NSAIDs/coxibs users were 7.4/1.1 per 1000 person-years for serious gastrointestinal complications, 3.7/4.5 for cardiovascular disease and 1.4/2.4 for stroke. Dyspepsia was most common with opioids (118 per 1000 p-y) followed by NSAIDs (57 per 1000 p-y). We also estimated the average impact of the side effects on HUI3 and the risk of death. These parameters have been implemented in POHEM-OA.

Conclusion: POHEM-OA synthesizes quantitative knowledge about the use and effects of medication in OA. Applications of the model include projections of the future use of drugs by persons with OA in Canada and evaluations of the health impact of changes in the pattern of drug utilization in the population.

MU2SCLES online: MUsculoskeletal MUlti-professional Simulated Collaborative Learning E-nitiativeS online

Jodie Jeffery (University of Saskatchewan, Saskatoon); Regina Taylor-Gjevre (University of Saskatchewan, Saskatoon); Liz Harrison (University of Saskatchewan, Saskatoon); Anne Dzus (University of Saskatchewan, Saskatoon); Rob Woods (University of Saskatchewan, Saskatoon); Jordan Buchko (University of Saskatchewan, Saskatoon); Katie Rooks (University of Saskatchewan, Saskatoon); Michael Katz (University of Saskatchewan, Saskatoon); Sathish Rajasekaran (University of Saskatchewan, Saskatoon)

Objective: Musculoskeletal (MSK) medicine exemplifies the benefits of collaborative interprofessional care. By incorporating an interprofessional approach into the foundation years of medical education, one can predict that it will not only encourage more collaborative patient care but that it will be established as 'standard of care'. Currently, the allocation of teaching time in medical school devoted to MSK-related conditions is disproportionate to the burden of disease in society. As such, there is a need for creative, persistent and standardized MSK educational resources in the undergraduate curriculum.

Methods: A dynamic, self-study MSK learning resource was developed with the aid of various medical disciplines and allied health care professionals in Saskatoon. Actual patient cases are selected in accordance to both commonality of the problem in Saskatchewan and urgency of management to identify a minimum level of competency for managing patients with musculoskeletal problems. With the aid of the Bone Joint Decade Undergraduate Curriculum Group (BJDUCG) recommendations and Medical Council of Canada (MCC) objectives, all possible knowledge, skills, and attitudes that may be relevant to MSK conditions are prioritized. Integration of a Saskatchewan-developed pharmaceutical resource, RxFiles, and online discussion boards are additional features. Pre and post-case quizzes are integrated to reinforce key learning issues.

Results: "MU2SCLES online" complements the lecture component of the University of Saskatchewan undergraduate MSK curriculum. By providing evidence-based teaching, optimal learning can occur while developing an appreciation for the fundamental role of intra and interprofessional collaboration. The pre-clinical learner will gain a greater understanding of the diagnosis and management of MSK conditions through simulated cases, across a variety of clinical settings. Students have the opportunity to familiarize themselves with the clinical use of the evidence-based drug therapy guide RxFiles. Links to external resources encourage self-directed learning and optimal utilization of established, validated online resources.

Conclusion: "MU2SCLES online" provides a standardized, interactive learning experience to a large number of students over a wide geographical area. The flexibility of this resource allows students to gain experience across the various disciplines involved in MSK medicine, ensuring the opportunity for equal exposure to all students. As a relatively low-cost educational tool, e-learning fits in with the distributed nature of today's learning society. By using an intra and interprofessional, case-based approach, "MU2SCLES online" enhances the learning of musculoskeletal medicine and promotes professional collaboration. Future partnerships through the Canadian Healthcare Education Commons (CHEC) enable sharing of this unique Saskatchewan resource.

Amyloidosis and GCA/PMR: Case Report of a Rare Association

Kimberly Legault (McMaster University, Hamilton); Anjali Shroff (McMaster University, Hamilton); Mark Crowther (St. Joseph's Healthcare Hamilton, Hamilton); Nader Khalidi (McMaster University, Hamilton)

Case Report:

Objective: AA amyloidosis is caused by extracellular deposition of fibrils that are composed of fragments of the acute-phase reactant serum amyloid A (SAA) protein. It is associated with several rheumatological conditions, most notably rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, and systemic lupus erythematosus. GCA and/or PMR have not been commonly associated, with only nine cases previously reported in the literature. We present a case of secondary amyloidosis presenting as nephrotic syndrome that developed in a patient who was previously diagnosed with GCA/PMR. In contrast to the majority of the cases previously reported, our patient did not have clinical evidence of uncontrolled rheumatologic disease activity at the time of presentation with amyloidosis, with the exception of persistently elevated ESR. To further clarify this complex clinical area we elected to survey the published literature with respect to the association between amyloidosis and GCA/PMR. **Methods:** We systematically reviewed the published literature and summarized previous cases of AA amyloidosis in GCA/PMR, including treatment options. **Results:** We identified a total of 9 cases in 7 reports. All except one of the patients reported presented with the nephrotic syndrome and renal dysfunction leading to a diagnosis of amyloidosis. Most of the patients died as a result of progressive renal insufficiency. However two patients were treated with colchicine with subsequent stabilization of creatinine and proteinuria. In our patient, treatment with colchicine was initiated with subsequent evidence of stabilization of renal disease. **Conclusion:** Our case highlights the need for consideration for the development of amyloidosis in patients with GCA/PMR presenting with renal insufficiency even if their rheumatologic disease is quiescent. Although evidence is limited our results suggest a course of colchicine may be beneficial in ameliorating renal insufficiency.

Optimal Therapy for Osteoporosis in Respiratory Patients: A Systematic Review

Ganesh Subramanian (University of Alberta, Edmonton); Tripti Papneja (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

Objective: Osteoporosis is a common problem in patients with chronic respiratory failure of various origins. The purpose of this review is to assemble the currently available high-quality treatment data for treatment of osteoporosis in patients with respiratory illnesses such as cystic fibrosis(CF), chronic obstructive pulmonary disease(COPD) on chronic steroid therapy, and post-lung transplant.

Methods: MEDLINE, EMBASE, and Cochrane trials registers were systematically searched to identify randomized controlled trials comparing drug therapy for osteoporosis in patients with CF, COPD on chronic steroid therapy, and post-lung transplant. In addition, reference lists were searched by hand. The articles were screened on title, abstract and full-text. Selected studies were scored using the Jadad score. The primary outcome was bone mineral density (BMD) changes. Data extraction was carried out by first reviewer and verified by a second reviewer.

Results: Four studies in patients with CF, eleven studies in patients on chronic steroid therapy and three studies in patients with lung transplant were included. There are no clinical trials evaluating effects of treatment of osteoporosis in samples consisting of COPD patients exclusively. Efficacy of oral and intravenous bisphosphonates in increasing BMD has been demonstrated in patients with CF, chronic steroid therapy, and post-organ transplant. Risedronate was shown to decrease vertebral fracture risk in patients on chronic steroid therapy in one study. Teriparatide has been shown to improve BMD and decrease vertebral fracture incidence in patients with osteoporosis on chronic steroid therapy compared to alendronate.

Conclusion: Current evidence supports the use of oral and intravenous bisphosphonates in patients with CF, chronic steroid therapy and post-lung transplant. Teriparatide can be used for patients with osteoporosis on chronic steroid therapy who have failed bisphosphonates. These studies have not been powered to look at fractures as an end-point, so treatment recommendations are based on the effects on the surrogate end-points. Multicenter RCTs with long follow-up periods and larger sample sizes are needed in these patient populations to guide osteoporosis clinical care for them.

Community-based Rheumatologists Practice Audit during Electronic Medical Record Implementation

Manoji Pereira (Sherbrooke University, Mississauga); Matthew Got (Credit Valley Rheumatology, Mississauga); Andrew Chow (Credit Valley Rheumatology, Mississauga); Elaine Soucy (Credit Valley Rheumatology, Mississauga)

Objective: The purpose of this study is to illustrate that practice audit can be easily preformed during implementation of an electronic medical record.

Methods: Patient's profile including demographics and current medications were inputted and updated during each patient's visit. PS Suite by PS Solutions Software Inc. was used to create the EMRs, with the following fields entered manually: patient problem list, current medications, personal traits, risk factors, allergies, past health history problems, known allergies, and DMARD history. Patients with a diagnosis of RA were identified by either the presence of ICD-9 code 714.0 or the text "rheumatoid arthritis" contained in the patient's problem list. The list of patients with RA was further refined to include only those over the age of eighteen. The data in these selected records was then examined and the practise profile was obtained. As patients with inflammatory arthritis were reassessed every three to four months, a practise audit was performed four months after implementations of the EMR, most of the regular patients have been updated.

Results: From a total of 2987 EMRs, 896 was diagnosed with RA according to the search parameters specified above. 642 currently on Methotrexate, 344 (38.3%) on biologics agent, and the break downs are: 125 on Etanercept, 41 on Infliximab, 39 on Adalimumab, 14 on Abatacept, 10 on Tocilizumab, 8 on Golimumab, 6 on Rituximab, and 1 on Certolizumab

Conclusion: In a community based rheumatology practice with two rheumatologists, once EMRs are implemented, many taks that would have been very time consuming using traditional paper based charts can be accomplished quickly. This is an example of practise audit for biologics use in RA patients in the practice. If the database is set up properly, further analysis can be done on drug survival and identification of active patient that needs to have their medications adjusted.

Characteristics of Hospitalizations of Patients with Systemic Lupus Erythematosus: A retrospective study from London, Ontario

June Lee (University of Western Ontario, London); Janet Pope (St Joseph Health Care, London)

Objective: Hospitalization is an important cause of patient morbidity and health care burden in systemic lupus erythematosus (SLE). The aim of our study was to explore the causes of hospitalization and predictors of poor outcomes of patients with SLE admitted to hospitals in London, Ontario.

Methods: A retrospective chart review of all patients admitted to University Hospital, Victoria Hospital, and St. Joseph's Hospital in London, Ontario with SLE between January 2006 and June 2009. These patients were identified by a discharge diagnosis M32, which refers to SLE as per the ICD Version 10 (International Statistical Classification of Diseases and Related Health Problems).

Results: There were 160 hospitalizations for 102 individuals with SLE over the three and a half year period. The most common reasons for hospitalization were disease flare (20.0%), infection (15.6%), adverse drug reaction (8.1%) and labour and delivery (6.9%). Acute coronary syndrome accounted for 2.5% of hospitalizations, while venous thromboembolic event and ischemic stroke comprised 1.9% and 0.6%, respectively. The most frequent manifestations of disease flare were renal and hematologic flares. There were 22 hospitalizations (13.8%) resulting in an ICU admission and the mean length of hospital stay was 8.5 days. The in-hospital mortality rate was 5.6%. There was no significant difference in ICU requirement, length of hospitalization, or incidence of death between those who were hospitalized primarily for an SLE flare and those who were not. Patients who died in-hospital were older than those who did not ($p=0.03$). There was no association of in-hospital mortality with disease duration, Charlson co-morbidity score, presence of anti-dsDNA or antiphospholipid antibody, or specific SLE medications.

Conclusion: Disease flare remains a major cause of hospitalization of SLE patients, specifically renal and hematologic flare. The morbidity of patients hospitalized secondary to SLE flare was not significantly different than those hospitalized for other reasons. Major predictor for in-hospital mortality in our cohort includes age.

A Systematic Review to Evaluate the Quality and Reporting of Administrative Database Validation Studies for Rheumatic Diseases

Jessica Widdifield (University of Toronto, Toronto); Jeremy Labrecque (McGill University Health Centre (MUHC), Montreal); Lisa Lix (University of Saskatchewan, Saskatoon)

Objective: To systematically investigate the quality and reporting of studies about the validity of administrative claims databases for ascertaining diagnoses of rheumatic diseases (RD).

Methods: A comprehensive search strategy was applied to MEDLINE and EMBASE to capture validation studies published between 1990 and 2010. All studies that adopted medical records or patient self-report measures as the gold standard to validate administrative data were selected for inclusion. Data were abstracted using modified versions of the STARD and QUADAS tools.

Two reviewers evaluated all studies. Results are reported using frequencies.

Results: A total of 21 validation studies were identified. Two-thirds used US administrative data, 19.0% used UK/European data, and the remaining 14.3% used Canadian data. The most common diagnosis was Rheumatoid Arthritis (57.1%). Osteoarthritis, Spondyloarthropathies, Gout, SLE, fibromyalgia, and unspecified arthritis were less commonly investigated. 85.7% validated linked databases (inpatient, outpatient and/or pharmacy data). Diagnostic codes were most frequently validated using medical records (81.0%). Gold standard definitions included clinical classification criteria, diagnoses documented in medical records and patient-reported data. Most studies (74%) sampled patients by identifying diagnostic codes prior to data collection. The most common sampling strategy involved sampling all patients (57.1%), followed by systematic sampling (38.1%). All studies described inclusion criteria and three-quarters reported using an a priori data collection tool. However, only 19.0% of studies performed an a priori sample size calculation. Excluding the four studies that used patient self-reported diagnosis as the gold standard, 29.4% of studies reported readers of the gold standard to be blinded to the results of the classification by administrative data. Most studies (76.2%) reported clinical/demographic characteristics of the study population, but only 38.1% described misclassified patients. While 81.0% of studies reported methods for calculating diagnostic accuracy, only 28.6% reported four or more estimates of diagnostic accuracy. Only 52.4% of studies reported the prevalence of disease in the target population.

Conclusion: Considering the diversity of administrative databases worldwide, the number of published validation studies is small. The quality of the studies and completeness of the reporting of study details varied considerably. Studies to evaluate the validity of administrative database ascertainment of RD in Canada are needed.

Which Coping Strategies do Women Living with Systemic Lupus Erythematosus Utilize?

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Objective: The Coping with Health, Injuries, and Problems (CHIP) Scale is a multidimensional self-report measure designed to assess four basic coping styles characteristically utilized by persons living with health problems. The coping dimensions measured include: distraction (a form of avoidance with actions and cognitions aimed at avoiding preoccupation with the health problem), palliative (self-help strategies to reduce the unpleasantness of the situation - making oneself comfortable, getting rest etc.), instrumental (active task-oriented strategies, such as seeking help and trying to learn more about the illness), and emotional preoccupation (focusing on the emotional impact of the health problem). The objective of this study was to assess the coping strategies used by women living with Systemic Lupus Erythematosus (SLE).

Methods: Demographics and SLE-Disease Activity Index (SLEDAI) were obtained from SLE females with no history of osteoporosis and cardiovascular disease enrolled in the Health Improvement and Prevention Program (HIPPP) study. Coping strategies were assessed using the CHIP scale consisting of 32-items (8 items per subscale; range 8-40 for each subscale). Distraction, palliative and instrumental coping are considered "task-oriented" and emotional preoccupation is considered an emotional strategy. Participants used a 5-point Likert scale (1=not at all to 5=very much) to indicate how much they engaged in a specific activity when encountering their particular health problem.

Results: The sample was composed of 269 female, 54.3% were Caucasians, 53.9% were married and 90.2% graduated from high school among which 60% had some post-secondary education. The average (SD) age of the sample was 44.4 (13.1) years and the SLE duration was 11.5 (10.2) years. Patients had low SLEDAI score of 4.4 (4.5) at enrollment. The mean (SD) for each coping strategy were as follows: Distraction: 25.0(6.4); Palliative coping 23.0(4.8); Instrumental coping 29.1(5.7) and Emotional preoccupation: 19.7 (7.5). Emotional preoccupation and the use of distraction focused coping strategies were higher than the reported means for the general population (distraction: 19.2 ± 6.1 ; emotional preoccupation: 16.3 ± 6.2). There were weak correlations between emotional- preoccupation coping and: age ($r = -0.140$; $p = 0.02$), SLE duration ($r = -0.173$; $P < 0.004$) and SLEDAI ($r = 0.193$, $p = 0.003$).

Conclusion: Women with SLE in this study used various forms of coping strategies despite a relatively low disease activity and a number of co-morbid conditions. This instrument would be useful for Rheumatologists and allied health professional (i.e. nurses, psychologists) involved in lupus care to better understand the specific ways by which patients cope with their disease.

Multiple Pulmonary Nodules Suspicious for Pulmonary Metastases: a Diagnosis Unmasked by Diffuse Alveolar Hemorrhage

Jodie Jeffery (University of Saskatchewan, Saskatoon); Chris Hergott (University of Saskatchewan, Saskatoon); John Gjevre (University of Saskatchewan, Saskatoon)

Case Report:

While Wegener's granulomatosis is a rare cause of thoracic pathology, it is important to be aware of the various clinical and radiographic manifestations. We describe a case of Wegener's granulomatosis initially manifesting as multiple pulmonary nodules presumed to be metastases. A 58-year-old female was seen in the outpatient respiratory clinic at the University of Saskatchewan for the workup of multiple pulmonary nodules recently found on a chest CT performed to evaluate dyspnea. Prior to visiting the clinic she was notified of the CT findings and their potential for pulmonary metastases. A chest x-ray (CXR) and pulmonary function tests (PFTs) were completed the morning of her appointment and available to the physician at the time of initial consultation. A striking result found among normal pulmonary flows and volumes was a DLCO (diffusing capacity of the lung for carbon monoxide) of 136%, suspicious for alveolar blood. The CXR revealed a large area of airspace consolidation within the right mid lung field; a striking change from a CXR done a month prior. Consultation revealed a four-day history of moderate hemoptysis, fatigue, generalized joint discomfort and a ten-pound weight loss with a low-grade fever over the preceding month. Blood work showed a twelve-point reduction in hemoglobin and urinalysis was positive for blood with few dysmorphic red cells and moderate protein. The patient was admitted to the pulmonary service for the work-up of a pulmonary-renal syndrome. Bronchoscopy with bronchoalveolar lavage was consistent with diffuse alveolar hemorrhage (DAH) and was negative for organisms and malignant cells. Investigations revealed a positive p-ANCA with a high titre MPO-ANCA. Toxicity and medication-induced etiology was ruled out and she was started on methyl-prednisolone. Limited findings on renal biopsy and a consistently normal creatinine ruled out significant renal involvement. The patient was diagnosed with Wegener's granulomatosis and treated with daily, oral cyclophosphamide and prednisone. Her DAH drastically improved over a week and her hemoglobin stabilized and gradually improved. Six months following the diagnosis, the patient is clinically in remission on oral cyclophosphamide and prednisone. Physicians are taught to consider uncommon manifestations of common diseases over common manifestations of uncommon diseases. Wegener's granulomatosis presents a diagnostic challenge to the physician due to its rarity and diverse clinical manifestations. Pulmonary nodules are common CT findings, thus physicians should have a broad differential while interpreting clinical data.

Case Based Learning in Pediatric Rheumatology - An Effective Method for Teaching the Medical Expert Role

Roman Jurecak (Children's Hospital of Eastern Ontario, Ottawa); Johannes Roth (Children's Hospital of Eastern Ontario, Ottawa)

Objective: To design, implement and evaluate a Case-based Learning (CBL) module focused on rheumatic disorders.

Methods: Course structure: 4 weekly sessions, each of 30minutes duration, were implemented into each 4-week rheumatology rotation of pediatric residents. Course participants: pediatric residents. Case database: A case-scenario database was established from which cases were chosen to reflect the spectrum of clinical problems encountered by the resident in the past seven days. All cases are open-ended and allow for discussion, modification and adjustment of the clinical scenario as necessary. Each case was emailed to the residents several days in advance to allow for adequate preparation. Evaluation: Each resident completed an anonymous detailed evaluation questionnaire of the teaching module at the end of their rotation. The questionnaire consisted of 5-point Likert scale questions (1=strongly disagree, 5=strongly agree) as well as open ended questions.

Results: 24 CBL sessions were evaluated by 6 residents (each attended 4 sessions). The course was highly valued among the residents and consistently rated as very beneficial for thought organization, application of knowledge and learning organization (mean Likert scale score=5). The residents felt the course improved their clinical reasoning skills as well as problem solving skills (mean Likert scale score 5 for each domain). The trainees appreciated the extra time and space specifically dedicated to this teaching unit as well as the opportunity to study each case in advance.

Conclusion: Our study illustrates the usefulness of CBL in teaching of pediatric rheumatology. In our experience, CBL greatly contributes to resident's understanding of complex rheumatic disorders in pediatric population such as systemic lupus erythematosus, inflammatory myopathies and vasculitides which ultimately leads to improvement of residents' analytic skills in a clinical setting and their role as Medical Expert.

Moving From Patient-Centred To Family-Centred Care? A Systematic Review Of Psycho-Educational Programs For People And Partners Affected By Arthritis

Allen Lehman (Arthritis Research Centre of Canada, Vancouver); Sennait Yohannes (Arthritis Research Centre, Vancouver); Cynthia MacDonald (Arthritis Research Centre, Vancouver)

Objective: Coping with arthritis takes place in a social context among family and friends. A small but increasing number of interventions involve both people living with arthritis and family/friends to promote coping and overall health. Our objective was to review the effectiveness of psycho-educational interventions targeted at people living with arthritis and a family member in order to improve health outcomes and/or arthritis management.

Methods: We conducted a systematic review of controlled studies evaluating the effectiveness of psycho-educational interventions targeted at both people living with arthritis and a partner (i.e., spouse, other family member, friend) aimed at improving health outcomes and/or arthritis management. We conducted an extensive electronic literature search using Medline, PsychInfo, EMBASE, and CINAHL for English language publications from time of database inception through September 2010. Two independent reviewers screened the titles and abstracts and did secondary in-depth reviews of the included articles. Eligible articles were categorized by 1) type of intervention, 2) inclusion of partner-specific skills-training, and, 3) effectiveness at improving health outcomes.

Results: The search yielded 10 articles that met the inclusion criteria (including one that was a long-term follow-up of an included study). The intervention studies focused on OA of the knee/lower extremity (n=6), rheumatoid arthritis (n=3), and systemic lupus erythematosus (n=1). Interventions used a variety of techniques including cognitive behavioural therapy; disease self-management or skills training in social support, communication, problem solving, and/or pain coping; and educational information. The duration of interventions varied from one session with monthly telephone counselling for 6 months (n=1) to weekly meetings for six to 12 weeks (n=9). Overall, there is mixed evidence for the short- and long-term effectiveness for interventions incorporating psycho-educational techniques on variables such as self-efficacy, arthritis self-management, psychological well-being, social support, couples' communication, and physical function. All six interventions with positive health outcomes for the person with arthritis included skills-training specifically targeted to a partner, whereas two of the four interventions with no positive effects did not offer skills-training to partners. A number of limitations were identified, such as small sample sizes, limited long-term follow-up, and self-selection bias (e.g., satisfied couples in long-term relationships).

Conclusion: This systematic review has highlighted the potential role for family or partner-based psycho-educational interventions to promote health outcomes and/or the management of arthritis. More research is required to determine if specific couples might benefit more from inclusion in psycho-educational programs and if, and under what conditions, long-term positive effects are maintained

Identifying Patients who are Arthroplasty Candidates within a Medically based Osteoarthritis Education and Treatment Program

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Objective: To identify patients who are enrolled in an osteoarthritis education and treatment program for medical management who currently meet criteria and are good candidates for arthroplasty surgery

Methods: To determine the current tools through literature review and expert consultation to assist with paper triage process To develop a pilot paper and clinical algorithm for triage and identification To support additional options for those patients who are triaged as arthroplasty candidates but don't meet surgical criteria To evaluate the pilot project (clinical outcomes, metrics and patient education) in order to determine next steps for future recommendations

Results: •Environmental scan showed that currently there was no clear cut paper algorithm readily available in the arthritis literature to identify patients who were candidates for an arthroplasty procedure. New tools were in the works but not ready for threshold to be identified. A TAP paper algorithm was developed for testing that included the WOMAC ©, PASS©, HOOS/HOOS-PS ©, KOOS/KOOS-PS ©, VAS, ICOAP©. An individual TAP physical assessment process was developed to triage patients to determine if criteria were met for a surgical consult. Pilot process was successful in identifying patients enrolled in a medical education and treatment program who were arthroplasty candidates. Those triaged, who did not meet inclusion criteria for surgery had other musculo skeletal issues that were brought to the forefront due to the triage process

Conclusion: Patients referred to OA program are for the most part appropriate for these classes. A proportion of patients improved by the end of the classes, others on their way to improvement. Some patients had barriers to improvement in OA program because of other musculo skeletal issues that needed to be addressed on an individual basis. Many patients had appointments for consultation with orthopods and were being followed even though they did not have dates for arthroplasty. Further piloting is needed on a larger scale to confirm and consolidate the algorithm developed.

Effect of Odanacatib on Bone Density and Bone Turnover Markers in Postmenopausal Women with Low Bone Mineral Density: Year 4 Results

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Objective: The selective cathepsin K inhibitor odanacatib (ODN) reduced bone resorption markers and progressively increased bone mineral density (BMD) during 3 years of treatment in a Phase 2b study. This study was extended for 2 additional years to further assess ODN efficacy and long-term safety.

Methods: In the 2-year base study, postmenopausal women with BMD T-scores between S2.0 and S3.5 at the lumbar spine, femoral neck, trochanter or total hip received placebo or ODN at 3, 10, 25 or 50 mg weekly. In Year 3, participants were re-randomized to ODN 50 mg weekly or placebo. In Years 4/5, women who received placebo or 3 mg ODN in Years 1/2 and placebo in Year 3 were switched to 50 mg ODN for Years 4/5; all others continued with their Year 3 regimen. 141 women entered the extension, and 133 completed 4 years. Endpoints were BMD at the lumbar spine (primary), total hip and hip subregions, and 1/3 radius; levels of biochemical bone turnover markers; and assessments of safety.

Results: Overall, 100 women received 50 mg ODN during Year 4 and 41 received placebo. Continuous treatment with 50 mg ODN for 4 years induced significant BMD increases from baseline at the spine (10.7%), total hip (8.3%), femoral neck (8.9%), and trochanter (10.3%) and maintained BMD (S0.1%) at the 1/3 radius; BMD changes from Year 3 were 2.8% (spine), 2.5% (total hip), 3.9% (femoral neck), and 2.9% (trochanter). Serum CTx remained low at Year 4 (S41%), whereas BSAP was relatively unchanged (S2%) from baseline. Women who received active treatment for 2 years and switched to placebo for 2 years experienced bone loss, with BMD near baseline for most sites and decreased by 4.5% at the 1/3 radius at the end of Year 4. Levels of bone turnover markers in women who discontinued active treatment after 2 years rose in the first month off-treatment, but all levels returned to baseline by the end of Year 4. ODN was generally well tolerated.

Conclusion: 4 years of ODN treatment increased lumbar spine and hip BMD and was generally well-tolerated in postmenopausal women with low bone mass. Bone formation markers remained relatively unaffected. Discontinuation of ODN after 2 years of treatment was promptly followed by resolution of effects on bone turnover and density such that BMD and bone biomarker levels at Year 4 were at or near baseline.

Rheumatology Learning Needs Among Physicians in Kenya

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Objective: The goal of this project was to identify the rheumatological learning needs of primary care physicians and internists in East Africa. Data will be used to inform the development of educational programs to enhance skills to recognize, diagnose and treat patients with musculoskeletal conditions in this region.

Methods: A survey was conducted among physicians attending the Kenya Association of Physicians 2010 Annual Scientific Conference. Areas queried included age, gender, specialty, number of years of practice, weekly patient load, former rheumatology education and duration, most common rheumatic conditions encountered, confidence performing a MSK exam and arthrocentesis, relevance of improving MSK skills and ways to do so.

Results: Participants included 36 (52%) community practicing physicians (CPP) and 33 (48%) residents from 6 cities in Kenya. Most (97%) were GPs or internists. CPPs were mostly male (71%) with a mean age of 45.1 ± 9.2 yrs; 52% of residents were male, with a mean age of 30.9 ± 2.5 yrs. CPP and residents reported seeing a median of 80 patients per week. Among CPP, 64% reported that one every ten patients they see has a MSK complaint, compared with 24% of residents ($p=.007$). Back pain was ranked as the most common condition encountered (64%), followed by OA (47%), RA (19%), gout (11%) and septic arthritis (8%). Almost all physicians (97%) reported receiving some training in rheumatology; however, most (67%) received a total of < 2 weeks of instruction. Almost all (91%) reported greater confidence conducting a cardiovascular vs. MSK exam. 34% of CPP vs. 6% of residents reported injecting joints at least 1/month; 11% of CPP and 30% of residents reported not doing injections ($p = .001$). Only 20% of CPP (but 0% of residents) “always felt confident” injecting joints ($p=.01$), though notably only in knees. Nearly all (88%) agreed it is “very relevant” to improve their skills in the evaluation and treatment of rheumatic conditions. To improve skills, 82% indicated a preference for face-to-face courses, followed by online tutorials (9%) and printed materials (6%).

Conclusion: Access to rheumatologists is severely limited in Eastern Africa. While internists see many patients with MSK complaints, their training in rheumatological evaluation, diagnosis and treatment remains minimal. Training CPP specific skills to identify and treat patients with musculoskeletal disorders can help improve health and reduce disparities in East African Countries.

Does Age Influence Choice of Pharmacotherapy for Rheumatoid Arthritis?

Paul Davis (University of Alberta, Edmonton); Angela Juby (University of Alberta, Edmonton)

Objective: Seniors (>65 age) constitute 26% of patients seen in our practice with rheumatoid arthritis being the most prevalent diagnosis. Ageism in medicine is of increasing interest with evidence to suggest that aging may be not only a barrier to access of care but also to choice of therapeutic options. Recent studies have suggested that this may also be the case in rheumatology. The objective of this study was to review therapeutic choices in the management of rheumatoid arthritis and compare them in a cohort of seniors with a younger group.

Methods: An audit of the charts of 295 patients referred to a specialty rheumatology clinic were reviewed. 78 (26%) were seniors, mean age 73 (range 65-90), M:F ratio 1.25/1. 37 were diagnosed with RA. Of the 217 younger patients 69 had RA. Current therapy for RA was extracted from the charts. Previous therapies were not recorded. The usage of antirheumatic drugs between the 2 groups was compared.

Results: Drug utilisation was documented under the following categories---NSAIDs/COXIBs, hydroxychloroquine, methotrexate, other DMARDs, leflunamide, prednisone, and biologics. Most patients were receiving >1 drug in a variety of combinations. All but 2 patients were receiving a DMARD. The usage of NSAIDs were similar in both groups (31% v 37%). Hydroxychloroquine therapy was greater in the < 65 group (22% v 37%). The use of all DMARDs was somewhat higher in the < 65 group (61% v 82%) with methotrexate being the most widely prescribed in both groups. Leflunamide usage was similar in both groups. Prednisone usage (< 15mg po daily) was slightly higher in the seniors group (19% v 11%). The only major difference between the 2 groups was the use of biologic agents which was twice as high in the younger cohort than the seniors (11% v 23%). An incidental, disturbing observation was that only 40% of patients on prednisone were receiving anti resorptive therapy for osteoporosis.

Conclusion: This study demonstrates that in this small cohort of patients the pharmacotherapy for RA was not significantly different based on age. This limited experience suggests that seniors with RA can be just as effectively treated with the full spectrum of antirheumatic drugs as younger patients. We encountered no obvious issues relating to added toxicity in our senior patients. Minor differences in some drug utilisation might be explicable on the basis of disease presentation in the different groups (eg palindromic onset in the younger group v polymyalgic onset in the elder group).

Outcomes of SLE Patients Cared for by Rheumatology or Nephrology

Serena Cheung (University of Alberta, Edmonton); Erik Beuker (University of Alberta, Edmonton); Steven Katz (University of Alberta, Edmonton); Neesh Pannu (University of Alberta, Edmonton); Dwight Harley (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

Objective: To assess the outcome and management of lupus nephritis (LN) patients under the care of both rheumatologists and nephrologists (R+N), rheumatologists only (R), and nephrologists only (N).

Methods: LN patients (n=66), who met the ACR criteria or had a positive kidney biopsy for systemic lupus erythematosus (SLE), were studied. Clinical and laboratory data, as well as past and current medications and/or other treatments were assessed. Disease damage and disease activity were scored using the Systemic Lupus International Collaborating Clinics Damage Index (SLICC)/American College of Rheumatology (ACR) Damage Index (SDI) and SLE Disease Activity Index (SLEDAI), respectively. Focus was placed on the comparison between the R+N and the N group, as the assumption was made that these patients had similar renal manifestations.

Results: Of the 66 patients studied, 48 were R+N patients, 8 were R patients, and 10 were N patients. The mean SDI score of the R+N, R, and N groups were $1.96(\pm 1.81)$, $2.25(\pm 3.14)$, and $1.89(\pm 2.93)$, respectively. The mean SLEDAI of all 3 groups in the same order were $4.55(\pm 4.06)$, $2.75(\pm 1.58)$, and $5.44(\pm 5.08)$. The differences in the SDI and SLEDAI between all 3 groups were not found to be significant. Forty-two out of forty-eight R+N patients (87.5%) compared to 50% of N patients were on hydroxychloroquine (HCQ). Using the Fisher's-Exact test, the differences in these two groups is significant (p value = 0.0153). All patients seen only by rheumatologists were on HCQ. Thirty-seven out of forty-eight R+N patients (77.1%) compared to 90% of N patients were on ACE inhibitors and/or angiotensin receptor blockers (ARB) (p value = 0.6700). The difference was not significant according to the Fisher's-Exact test.

Conclusion: There is no difference in disease damage and disease activity among patients seen by both rheumatologists and nephrologists versus those seen by only one or the other subspecialist. However, the use of HCQ is more frequent in LN patients under the care of a rheumatologist in conjunction with a nephrologist. This has implications on the management and care of LN patients. Whether or not HCQ should become part of the standard of care of LN still requires more research. More studies need to be done to evaluate the effect of HCQ on renal outcomes, morbidity, and mortality. Education of both Rheumatologists in the use of ACE-i and ARB's, and Nephrologists in the use of HCQ should be a priority.

Evaluation of Patient Satisfaction at the Sunnybrook Health Sciences Centre Rheumatology Outpatient Clinic

Jenny Shu (University of Western Ontario, Toronto); Paula Veinot (Sunnybrook Health Sciences Centre, Toronto); Ruben Tavares (McMaster University, Hamilton); Jennifer Boyle (The Arthritis Society, Toronto); Mary Bell (Sunnybrook Health Sciences Centre, Toronto)

Objective: The purpose of this study was to evaluate and quantify overall patient satisfaction at the Sunnybrook Health Sciences Centre (SHSC) rheumatology outpatient clinic using the Leeds Satisfaction Questionnaire (LSQ), a validated and reliable tool designed specifically for a study of the follow-up of rheumatology patients. Differences in satisfaction scores between various aspects of care and amongst the four rheumatologists participating in this study were also assessed.

Methods: 329 LSQ questionnaires were collected July 2007 to June 2008. All patients attending a follow-up rheumatology appointment who were capable, over 18 years, and able to comprehend English were given the voluntary option of completing a LSQ anonymously. A total of 321 questionnaires were included in the study. Data was exported from a Microsoft Access 7 database to SAS for statistical analysis. Descriptive statistics (i.e. mean, median, standard deviation) were used to analyze the scores of the patient satisfaction questionnaires while the Kruskal-Wallis and one-way ANOVA tests were used to compare scores between rheumatologists.

Results: The satisfaction of patients at the SHSC with the care they received was generally positive and comparable with previous studies using the LSQ. The mean score across all providers was 4.08 on a Likert scale of 1 to 5 (SD = 0.49). There were statistically significant differences between the overall satisfaction of the 4 rheumatologists participating in this study ($p < 0.05$). Patients identified technical quality and competence as the area they were most satisfied with (4.44, SD = 0.47), whereas access to service and continuity of care received the lowest satisfaction score (3.77, SD = 0.68).

Conclusion: Patient satisfaction has been previously found to influence whether one seeks medical advice, treatment compliance, and the longitudinal relationship with a practitioner. Hence, in order to improve future delivery of care to patients with rheumatic disease, patient satisfaction with current care should be assessed to identify specific aspects of care that could potentially serve as target areas for reflection and improvement. This study is a pioneer example of evaluating patient satisfaction in a Canadian rheumatology outpatient setting and presents other rheumatologists with a potential tool to assess patient satisfaction in their practices. Furthermore, patient satisfaction with access to and continuity of care were found to be weaknesses in this study, which may suggest a future area of quality improvement.

Clinical Significance Of Renal Vascular Lesions (RVL) On Renal Biopsy In Lupus Nephritis.

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Objective: To determine the clinical significance of Renal Vascular Lesions (RVL) detected in renal biopsies of patients with systemic lupus erythematosus (SLE).

Methods: Renal biopsies were scored according to the ISN/RPS revised 2004 criteria for Lupus Nephritis (LN). RVL were defined as: 1) thrombotic microangiopathy (TMA), 2) arterial fibrinoid necrosis (AFN), 3) lupus vasculopathy (LV), and 4) arterial sclerosis (AS).

Demographic, renal, vascular outcomes, overall mortality, disease activity measured by SLE-disease activity index-2000 (SLEDAI-2K) and organ damage assessed by SLICC damage index (SDI) were evaluated.

Results: 207 biopsies from 164 patients were examined. TMA was seen in 13 patients (7.9%), 15 had LV (9.1%), 3 patients had TMA and LV, 93 (56.7%) had only AS, 0 patients had AFN and 40 patients with LN and no RVL (24.4%) were used as controls. Baseline demographics including age at SLE diagnosis, gender and ethnicity were similar between groups. At time of renal biopsy the mean arterial pressure and the percentage of patients with an SDI score ≥ 1 was higher in the TMA (MAP 110.6 ± 20.7 mmHg, $P < 0.001$; SDI: 55.6%, $P = 0.018$), LV (MAP 108.3 ± 14.3 mmHg, $P < 0.001$; SDI: 43.8%, $P = 0.033$), and AS patients (MAP 101.9 ± 13.9 mmHg, $P < 0.001$; SDI: 45.4%, $P = 0.001$) compared to controls (MAP 91.6 ± 10.9 mmHg, SDI: 14.3%). Only patients with LV had higher SLEDAI at the time of biopsy compared to controls (16.9 ± 8.5 vs 10.5 ± 6.2 , $P = 0.003$). Grade of LN, activity indices and proteinuria were similar between groups; however, chronicity indices on biopsy were significantly higher in all RVL subgroups compared to controls. GFR by MDRD was lower in LV (60.7 ± 33.0 mL/min/1.73m², $P < 0.001$), and AS patients (70.5 ± 33.3 mL/min/1.73m², $P = 0.03$) compared to controls (84.5 ± 26.6 mL/min/1.73m²). A subset of 133 patients with similar duration of follow-up was then evaluated for associations between RVL and outcomes such as thrombotic events (TE), end-stage renal disease (ESRD), chronic kidney disease (CKD) and death. On univariate analysis, presence of RVL was significantly associated with TE ($P = 0.009$). However, RVL was not independently predictive of the outcomes of interest on multivariate analysis.

Conclusion: RVL are common in SLE patients with LN and may be associated with thrombotic events but the presence of RVL on initial renal biopsy was not independently associated with increased TE, ESRD or mortality.

Bone Health in Patients with Interstitial Lung Disease

Ganesh Subramanian (University of Alberta, Edmonton); Tripti Papneja (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

Objective: Osteoporosis is a common condition in patients with end-stage lung disease, but little attention has been given to bone disease in patients with interstitial lung disease (ILD). The purpose of this study is to perform a systematic review of the literature to determine: (1) the prevalence of low bone mineral density (BMD) in patients with ILD, (2) identify correlates of osteoporosis/osteopenia in this special group of patients, (3) effects of treatment of low BMD in patients with ILD.

Methods: We reviewed the literature for all English language publications from 1950-September 2010 in Pubmed, EMBASE, MEDLINE, and Cochrane database of systematic reviews. The articles were screened on title, abstract and full-text. In addition, reference lists were searched by hand. Trials evaluating prevalence, predictors and treatment of osteopenia/osteoporosis in patients with ILD were included. Data extraction was carried out by first reviewer and verified by a second reviewer.

Results: The prevalence of low bone mineral density varied 62-70% with 5-43% ILD patients having osteoporosis. Only one study compared the observed prevalence of osteoporosis and osteopenia in ILD patients to the expected prevalence in a normal population matched for age, gender, and race. ILD patients had similar observed rates of low BMD as the matched healthy controls, with the exception of a higher proportion of ILD men with lower BMD at the lumbar spine. Correlate of osteoporosis in ILD is mainly body mass index, although causality has not been proven. Effects of treatment of osteoporosis have not been investigated in ILD patients specifically.

Conclusion: There is lack of high-quality data evaluating the prevalence and predictors of osteoporosis in ILD patients exclusively. In addition, prospective comparative studies assessing the effects of treatment of osteoporosis in ILD patients only are warranted.

Panniculitis/Fasciitis due to a Drug-Induced Neutrophilic Dermatosi s: A case report

Nathaniel Dostrovsky (McMaster University, Hamilton); Srinivasan Harish (McMaster, Hamilton); Madeleine Verhovsek (McMaster, Hamilton); Samih Salama (McMaster, Hamilton); Nader Khalidi (Mc Master University, Hamilton)

Case Report: Objectives: 1. To describe a case of a neutrophilic dermatosis presenting with panniculitis/fasciitis of the feet 2. To review the musculoskeletal manifestations of neutrophilic dermatoses A 56 year old man presented for evaluation with a one year history of progressive pain and swelling in his feet. The pain and swelling began after he started granulocyte-colony stimulating factor (G-CSF) for idiopathic neutropenia. Other symptoms included fatigue, hoarseness of voice and recurrent bullous skin lesions. On examination, there was diffuse swelling and tenderness over the plantar aspects of both feet. Laboratory investigations were significant for elevated ESR (96mm/hr) and CRP (49.7mg/L). C3 and C4, ANA, p and c ANCA, RF and anti-CCP were all negative. Ultrasound and MRI of his feet showed swelling and hyperemia consistent with panniculitis as well as some fasciitis, but there was no evidence of synovitis, myositis or abscesses. Ultrasound-guided percutaneous biopsy of the inflamed plantar fat was performed. This demonstrated heavy inflammatory infiltration of the tissue including with neutrophils in keeping with a panniculitis/fasciitis. The patient was started on 30mg/day of prednisone and the pain and swelling in his feet dramatically improved. His hoarseness of voice, fatigue and skin lesions also resolved. Additionally, his neutropenia improved and he no longer requires G-CSF. Musculoskeletal involvement, notably arthritis and arthralgia, is a relatively common manifestation of neutrophilic dermatoses such as Sweet's syndrome. However, this case is unusual in that the primary presenting feature was panniculitis and fasciitis. This case exemplifies the contributions of clinical, radiological and histological assessments in making the appropriate diagnosis and guiding further management.

Focus Group to Review a Pilot Education Program for Inflammatory Myositis

Anita Dey (University of Alberta, Edmonton); Lois Flakstad (University of Alberta, Edmonton); Kathy Cotton (University of Alberta, Edmonton); Stephanie Keeling (University of Alberta, Edmonton)

Objective: The main objective of this study was to review a pilot education program for patients with inflammatory myositis through the use of a patient focus group. The hypothesis was that an education program for inflammatory myositis would improve patient understanding of their condition, efficacy and quality of life.

Methods: Edmonton area rheumatologists were invited to refer their inflammatory myositis patients to participate in a pilot education program and a follow-up focus group. Inclusion criteria included a rheumatologist's diagnosis of either "polymyositis" or "dermatomyositis" and age over 17 years. The main exclusion criteria included inability to speak English and severe disease that would limit participation. Of the nine patients referred to the program, six attended the education program and five agreed to participate in the focus group. The focus group was conducted over 2 hours and was recorded by video camera. A list of pre-specified questions to review the education program was created after conducting a literature search to identify optimal focus group methodology. The rheumatologist (SOK), physiotherapist (LF), and occupational therapist (KC) did not attend the focus group session that was arranged and conducted by the medical student (AD) in order to avoid influencing the responses.

Results: Three main areas of interest emerged from this focus group. (1) Patients felt that disease information provided by this program would serve them better if delivered closer to the time of diagnosis. (2) The patients felt that instruction on how to exercise more effectively was extremely valuable. (3) Continued contact between patients in a support group format after the program was finished ranked highly. Areas for program improvement included: i) increased use of electronic resources such as a website; ii) the inclusion of information on nutrition; and iii) the individualization of exercise programs. Further discussion of the impact of disease on "return to work" was also requested by participants.

Conclusion: The focus group reviewing a pilot education program for inflammatory myositis revealed that such programs are extremely important in improving patient quality of life. This work suggests that education enhances disease management strategies over standard-of-care and may have long-term impact on patient outcomes. Patients were assessed one month prior to the program for objective measures of disease activity and quality of life measures and follow-up data will be available upon reassessment of these patients in November 2010.

Quality of Life Before and After Joint Replacement Surgery

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Objective: The purpose of this study was to describe the level of health-related quality of life (HRQL) among persons with osteoarthritis prior to and following joint replacement surgery (JRS).

Methods: We used administrative data from the British Columbia Linked Health Database (BCLHD) 1986-2007 linked by a unique identifier to the BC component of the Canadian Community Health Survey (CCHS, 2001, 2003, and 2005). The BCLHD includes diagnostic codes for all visits to doctors and hospital admissions and procedure codes for patients undergoing surgery. Health-related quality of life was measured in all cycles of the CCHS using the Health Utilities Index 3 (HUI3). We compared the median and mean HUI3 levels for persons grouped according to the time between the date of the CCHS interview and the date of JRS.

Results: There were 25,658 individuals in the linked dataset. Of those, 223 patients with OA had a date of JRS after the date of the CCHS interview. The median HUI3 was 0.78 (mean=0.71, SD=0.27, min=0.12, max=1.0). When patients were grouped according to time from HUI3 assessment to JRS, the median (mean) HUI3 were as follows: time >4 years (N=49), median HUI3=0.91 (mean=0.82); time 3-4 years (N=35), 0.86 (0.79); time 2-3 years (N=21), 0.91 (0.71); time 1-2 years (N=48), 0.67 (0.67); time < 1 year (N=70), 0.66 (0.62). We have identified 340 cases assessed in the CCHS after their JRS. When they were grouped according to time between their JRS and CCHS interview, the median (mean) HUI3 were as follows: time < 1 year (N=50) median HUI3=0.73 (mean=0.67); time 1-2 years (N=32), 0.74 (0.71); time 2-3 years (N=42), 0.74 (0.66); time 3-4 years (N=23); 0.84 (0.68); time 4-5 years (N=42), 0.71 (0.59); time 5-7 years (N=41), 0.71 (0.64); time 7-10 years (N=54), 0.73 (0.68); time 10-15 years (N=42), 0.80 (0.69); time >15 years (N=22), 0.47 (0.53). Adjusting for age did not change the results significantly.

Conclusion: Linking administrative and survey data provides an alternative method for assessing the long-term trajectory of HRQL before and after JRS. These data suggest a strong decline in average quality of life starting about 2-3 years before surgery. HUI3 after JRS is higher than < 2 years prior to surgery and stable for up to 15 years, but does not achieve levels comparable to those 4-5 years before surgery. Individual variation in HUI3 in these patients is very large.

Results of a Needs Assessment for Canadian Systemic Lupus Erythematosus Guidelines: A New CANIOS Initiative

Stephanie Keeling (University of Alberta, Edmonton)

Objective: The Canadian Network for Improved Outcomes in Systemic Lupus Erythematosus (CANIOS) is planning on developing Canadian Guidelines for the diagnosis and/or management of systemic lupus erythematosus (SLE). These guidelines would (1) have a Canadian-based focus on SLE treatment to help governing bodies approve future agents and (2) provide Canadian Rheumatologists with the best-evidence in the management of these complicated patients to improve standard-of-care. The main objective of this study was to conduct a needs assessment of Canadian rheumatologists to identify the utility of such guidelines in the diagnosis and/or management of SLE.

Methods: A systematic review of the literature was conducted in order to identify existing guidelines and review their content. A draft survey monkey questionnaire was devised to determine the level of interest and need of the Canadian rheumatology community for such guidelines. The draft questionnaire was reviewed by 2 CaNIOs subcommittees and co-chair of the CRA Therapeutics Subcommittee. The final 10-question survey was sent by email to the CRA membership and responses collected over a 2.5 week period at the end of September/early October 2010.

Results: Of the 133 CRA members who responded to the questionnaire, 88.6% (n=117) were adult and 11.4% (n=15) were pediatric rheumatologists, while 66.4% (n=87) had academic/university practices compared to 33.6% (n=44) with community practices. The majority of respondents saw a total of “153 SLE patients” per week (38.6% (n=51)) and “153 new SLE patients” per month (40.9% (n=54)). The most common SLE manifestations seen in clinic included arthritis (54.7% (n=70)) and cutaneous (38.5% (n=50)) followed by nephritis (31.6% (n=36)). 84 respondents (63.2%) felt that the guidelines would be helpful to their practice, with the “management of lupus nephritis” ranked highest followed by the “management of pregnancy in SLE” and “existing therapeutics in SLE”.

Conclusion: In Canada, SLE patients constitute a significant percentage of adult and pediatric rheumatology practice. A need does exist for the development of SLE guidelines, with specific interest in lupus nephritis and pregnancy. Distinction between adult and pediatric SLE populations will be important. Future directions include focusing the goals of SLE guidelines and establishing a working-group to pursue this task.

An Evaluation of Autoimmune Antibody Testing Patterns in a Canadian Health Region and an Evaluation of a Laboratory Algorithm Aimed at Reducing Unnecessary Testing

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Objective: ANA, ENA, and anti-dsDNA antibodies are being requested at increasing rates in the Vancouver Coastal Health (VCH) region. We attempted to identify areas for improvement in the utilization of these tests by examining ordering patterns retrospectively at the VCH laboratories. We also measured the potential cost benefit of establishing a new laboratory algorithm aimed at reducing unnecessary testing.

Methods: Laboratory data for ANA, ENA, and anti-dsDNA test requests received at VCH laboratories over a three year period (January 2007-December 2009) were reviewed and the following data were extracted: number of tests, dates, results, and ordering physician specialties. Based on the evaluation of this data and a relevant literature review, a laboratory algorithm was constructed and applied retrospectively to laboratory data from inpatients at Vancouver General Hospital from January to December 2009. An analysis of potential cost reduction was performed limited to evaluating costs of laboratory tests.

Results: 18,475 ANA, 10,656 ENA, and 5,170 anti-dsDNA tests were performed over the three year period. 8.5% of the ANA tests were repeats within the VCH laboratories, and of these, 1198/1551 (77%) were ordered after a previously negative result. Of the repeated ANA tests, 1.5% changed from $< 1:80$ to $\geq 1:160$ over the three year period. Over half of the ENA and anti-dsDNA tests were ordered simultaneously with ANA, indicating their possible use as screening tests. 15%, 16.8% and 13.3% of ANA, ENA and anti-dsDNA tests, respectively, were positive. A laboratory algorithm was constructed where ENA and anti-dsDNA tests would be automatically cancelled if ANA was negative in the same sample, and automatically added if it was positive (using $\geq 1:80$ cut-off). ANA tests repeated within a one year period would also be cancelled but the prior result would be provided. Hypothetical application of the algorithm showed a 27% reduction in laboratory testing costs for these tests over 1 year.

Conclusion: Autoantibody tests for rheumatic diseases are being ordered in excess of what is clinically useful. Education is needed to reduce the frequency of ANA tests and to encourage more efficient use of ENA and anti-dsDNA tests. Our proposed laboratory algorithm would reduce laboratory test costs. To effectively impact ordering practices without negative impact on patient care, implementation of the algorithm should be accompanied by appropriate educational information for ordering physicians.

Long-Term Safety of Rituximab (RTX): Rheumatoid Arthritis (RA) Clinical Trials and Retreatment Population

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Objective: To assess the long-term safety of RTX in RA patients (pts) in clinical trials.

Methods: Safety data from a global clinical trial program were pooled and analyzed to evaluate safety in pts treated with RTX + methotrexate (MTX). RTX retreatment was offered to all pts based on physician's decision of clinical need, including assessment of active disease. Pts receiving placebo during placebo-controlled study periods were pooled to provide a placebo population.

Results: As of September 2009, 3189 pts had been treated with RTX, for a total exposure of 9342 pt-years (yrs). The analysis contained >9 yrs of follow-up with up to 15 courses of RTX. Over 1500 pts were followed for >3 yrs and 587 pts for >5 yrs, with 1724, 1392, 1036 and 656 pts receiving ≥ 3 , ≥ 4 , ≥ 5 and ≥ 6 courses, respectively. The safety profile of RTX was comparable to the placebo population or general RA populations, with the exception of infusion-related reactions (IRR). The most frequent adverse event (AE) in RTX patients was IRR; most were CTC grade 1 or 2 and occurred after the first infusion of the first course (23%), with 0.5% considered serious (over all courses). Generally, rates of serious AEs and infections remained stable over time and over multiple RTX courses, and in pts in long-term follow-up (≥ 5 yrs). Similar overall rates of serious infection were observed between RTX and placebo populations [4.35 (3.19 in >5 yrs follow-up) vs. 4.29 events/100 pt-yrs, respectively]. Lower respiratory tract infections were the most frequent serious infections, with pneumonia being predominant (2%). Serious opportunistic infections were rare, with a rate comparable to the placebo population (0.04 vs. 0.01/100 pt-yrs, respectively). Myocardial infarction and stroke rates in the RTX group (0.49 and 0.25 events/100 pt-yrs, respectively) were consistent with rates in the general RA population (0.34-0.59 and 0.11-0.76 events/100 pt-yrs, respectively).

Conclusion: Data from long-term follow-up of RA pts treated with RTX in clinical trials indicate that RTX continued to be well tolerated over time and over multiple courses, with safety profiles similar to that of the placebo population and consistent with published data on pts with moderate-to-severe RA. No new safety signals were observed in both the all-exposed population and the >5 yrs exposure group.

Risk of developing Myocardial Infarction among Uveitis patients.

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Objective: To find an association between uveitis and myocardial infarction.

Methods: Based on the understanding of an association between systemic inflammation and increased risk of myocardial infarction, we considered that there may also be an association between uveitis and myocardial infarction. We conducted a prospective cohort study using information from Population Data BC, a pan-provincial population health data service in British Columbia. Hospital admissions and office visits covered by the Medical Services Plan of BC for calendar years 1991 to 2006 were analyzed. Incident uveitis cases were determined by tracking diagnostic code descriptions (ICD9 code 364) between April 1, 1996, and March 31, 2004. The case definition was a subject 20 years of age or older with two or more ophthalmologist visits anytime during the study period separated by seven days, based on the corresponding ICD9 code. Cases were included if they did not have a diagnosis of ischemic heart disease (IHD) prior to the diagnosis of uveitis. Cases were excluded if uveitis was initially diagnosed from 1991 to 1996 to ensure that the diagnosis of uveitis in our subjects was new. For each uveitis case, five controls were selected after matching for age, sex and year of diagnosis. None of the controls had a diagnosis of IHD prior to the index date. A Cox proportional hazard regression model was used to estimate the relative risks. The process was repeated with a second case definition of two ophthalmologist visits within one year separated by seven days with the corresponding uveitis ICD9 code.

Results: We found 9,386 uveitis cases between 1996 and 2004, of which 52 percent were women. The incidence rate of uveitis was three cases per 100,000 person-years. The mean age was 51 years with a standard deviation of 16.7 years. After adjusting for age and gender, the relative risk (RR) of myocardial infarction was 1.11 (95% confidence interval (CI) 0.93 - 1.33). Using the second case definition, we found 7,941 uveitis cases. For this case the RR was 1.15 (95% CI, 0.96 - 1.39).

Conclusion: From this prospective cohort study, no statistically significant correlation between uveitis and myocardial infarction was obtained. A further study with a different database is needed to support this argument.

Postal Survey of Pregnancy in Rheumatoid Arthritis and Systemic Lupus Erythematosus Patients

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Objective: Pregnancy in women with rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE) is heterogeneous, with variable effects of disease on pregnancy and pregnancy on disease. Pre-conception counselling will help limit disease flares, avoid medication-related teratogenicity and help towards a healthy pregnancy. The objective of this study was to describe the impact of RA and SLE on pregnancy and whether it affected future pregnancies.

Methods: A group of female RA and SLE patients under the age of 70 were identified during a chart review for another study of nine academic rheumatologists. A self-report questionnaire was created to review all pregnancies (including miscarriages and terminations) in SLE and RA patients and quantify disease activity and medication use during pregnancy. The questionnaire was mailed to 180 RA and 40 SLE patients with a postage-paid return envelope.

Results: Of 220 mailed questionnaires (180 RA, 40 SLE patients), 43 (24%) RA and 12 (30%) SLE patients returned their completed questionnaires. Thirty-eight (88%) RA and 10 (83%) SLE patients had been pregnant, where 15 (39%) RA and 5 (50%) SLE patients developed their disease prior to pregnancy. The number of miscarriages in RA patients and SLE patients during the first, second and third trimesters respectively was: 16 (17%), 2 (2%), 0 and 4 (14%), 3 (10%) and 0. Eight (53%) RA and 1 (20%) SLE patient reported active disease during pregnancy. Eleven (73%) RA patients continued DMARD therapy, including 1 (2.6%) on methotrexate, 2 (5.3%) on sulfasalazine, 5 (13%) on anti-malarials, and 5 (67%) took prednisone during their pregnancy. None of the 5 SLE patients continued their medications or took prednisone during their pregnancy. Four (27%) RA patients decided to not pursue further pregnancies as a result of increased disease activity during pregnancy and/or postpartum. One SLE patient aborted her last pregnancy because of increased past disease activity and 1 SLE patient had a tubal ligation. Four (9%) RA and 1 (8%) SLE patient reported difficulties with becoming pregnant.

Conclusion: In this descriptive study, many RA and SLE patients had pregnancies predating their disease onset. SLE patients appeared more reluctant to continue therapy compared with RA patients. Despite literature supporting improved RA disease activity in pregnancy, half of the pregnant RA patients reported continued activity during pregnancy. The impact of SLE or RA disease activity on future pregnancies could not be reliably assessed due to low numbers. Comprehensive preconception discussions and close monitoring peripartum are required.

Comorbidity is Commonly Reported in Early Inflammatory Arthritis

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Objective: To determine the prevalence of co-morbid medical conditions in patients with recent onset inflammatory arthritis.

Methods: Patients in CATCH are age >16 years old, have symptoms for ≥ 6 weeks but < 12 months, have ≥ 2 swollen joints or 1 swollen metacarpophalangeal or proximal interphalangeal and ≥ 1 of: positive rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP), morning stiffness > 45 minutes, response to non-steroidal anti-inflammatory drug or painful metatarsophalangeal squeeze test. Comorbid medical conditions are self reported at baseline and new diagnoses identified at each visit. Patients in the CC cohort have inflammatory arthritis involving at least 2 joints of less than 1 year duration; comorbidity is assessed annually by patient self report (SR) and physician reported Charlson comorbidity index (CCI).

Results: Baseline comorbidity data was available for 803 CATCH subjects (74% female; 81% Caucasian, mean age 53; mean symptom duration 5.5(3.2) months; mean DAS28(3)CRP 4.34 (1.31)). 539(67%) reported at least one comorbid medical condition (median 1, range 0-8). The following non-rheumatic conditions were reported at baseline: hypertension (213(27%), hypercholesterolemia (112(14%), diabetes (DM) 65(8%), thyroid disease (101(13%), CVD (angina, other heart disease, stroke) 89(11%), neurologic disease(73(9%), respiratory (107(13%), hematologic (56(7%), gastrointestinal 94(12%) and cancer (51(6%). CATCH subjects reporting at least one comorbid condition had higher baseline DAS28(3)CRP (4.44 vs 4.13 $p=0.003$) and higher baseline HAQ scores (1.05 vs 0.85 $p<0.0001$). In the CC cohort (75% female, mean age 49 years, DAS28(3)CRP 3.74 (1.37)); self report comorbidity data was available at baseline ($n=291$), and at one year ($n=143$). At least one non-rheumatic comorbid condition was reported by 239(82%)(median 3 range 0-14); hypertension 55(19%), DM 24(8%), CVD (any cardiac and stroke) 26(9%), neurologic (neurologic conditions, any headache)123(42%), any respiratory 73(25%), hematologic 36(12%), gastrointestinal 76 (26%), and cancer 9(3%). The physician reported baseline CCI was median 0 range 0-5;MI (2%), cerebrovascular disease (0.4%), ulcer (3.2%), diabetes (4.4%), diabetes with complications (1.2%), end stage renal disease (0.4%), tumor (1.6%), leukemia (0.4%). Paired baseline and one year CCI were available for 101 subjects and were similar. New diagnoses (SR or CCI) at one year included: hypertension (6) heart disease (2), diabetes (1), cancer (3), respiratory (7), gastrointestinal(7).

Conclusion: Comorbid medical conditions are common in early arthritis and may be associated with more active disease. Further longitudinal followup is needed to determine the extent of comorbidity accrual in early disease

Does Moderate or Severe Knee Strain Affect the Progression of Radiographic Osteoarthritis?

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Objective: Knee injuries increase progression of radiographic osteoarthritis (ROA). Such injuries include knee ligament, patella or meniscal trauma ("specific" injuries). Less physiologically quantifiable injuries can be called "strain". The purpose of this study is to understand the effect of moderate and severe knee strain on ROA progression.

Methods: We recruited a population-based sample with knee pain "on most days of the month at any time in the past and any pain in the past 12 months", aged 40 to 79 (weighted mean=57.6), stratified by age and sex, from Vancouver, Canada. Baseline was between 2002 and 2005, follow-up 2.5 to 5.6 years later (mean=3.3) (N=163). 54% were female. Average BMI was 26.1 (18.1-34.2). Study knee was the more painful knee. Radiographs were taken using fixed-flexion anteroposterior view and skyline view. X-rays were graded using the Kellgren Lawrence (KL) scale (0-4). Grades 0 and 1 were collapsed and progression was an increase in grade. Specific knee injury was self-reported cruciate ligament tear, collateral ligament tear, meniscal tear or patellar injury. Other knee injuries were considered strain. Injury severity was either severe (requiring a walking aid for at least 1 week) or moderate. Logistic regression was used to model ROA progression. The model included the 3-level variables specific knee injury and strain (levels none/moderate/severe). An additional model collapsed them into two levels (yes/no). Both models were controlled for baseline age, sex, BMI and follow-up time.

Results: 39.4% had baseline ROA. Specific injury/strain history was absent, moderate (7.8/24.4%) or severe (11.0/10.8%). Duration of the oldest injury/strain ranged from 1/0 to 58/70 years. Two-level models had a post-hoc power of 88% to detect an odds ratio (OR) of 3.0. Consistent with previous findings, specific injury had a significant effect on ROA progression (OR=3.26; 95% CI=1.29, 8.22). However, strain did not show an effect in the multivariable model (OR=1.09; 95% CI=0.52, 2.29). In 3-level models, the effects of specific knee injury were monotonic, and severe injury significant: moderate injury OR=1.32, 95% CI=0.32, 5.41; severe injury OR=5.80, 95% CI=1.83, 18.35. Knee strain showed no effect: moderate injury OR=1.23, 95% CI=0.52, 2.90; severe injury OR=0.66, 95% CI=0.19, 2.30.

Conclusion: We find no evidence that history of moderate or severe knee strain (including those severe enough to require a walking aid for at least 1 week) affects the progression of radiographic knee OA in a population with knee pain, after controlling for specific knee injury, age, sex, BMI and follow-up time between radiographs.