Advancing a Preventive Rheumatology Agenda: Poster Session Abstracts

July 26, 2013
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Poster 1: Ideas from the 3rd International Conference on Cutaneous Lupus Erythematosus, Edinburgh, Scotland, 2013

Authors
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Abstract
Interested physicians and scientists from around the world came together for the third time in a meeting organized by the Rheumatologic Dermatologic Society, led by Dr. Victoria Werth. The first meeting of the ICCLE group was in Dusseldorf, Germany in 2004, and the second in Kyoto, Japan in 2008. This time at least twelve different countries and four continents were represented.

One aim of the meeting was to present and discuss updated information and ongoing research related to cutaneous lupus erythematosus (CLE) in order to maximize the exchange of ideas within a cooperative international group.

Skin involvement in individuals with lupus erythematosus is common and variable. The current classification system has been the basis for the understanding of skin lesions in lupus since the late 1970s. There is a need for more uniform definitions, enhanced diagnostic criteria and more specific classification of CLE and systemic lupus erythematosus associated skin lesions. This would help consistency in the field clinically and in studies.

Presentations were made and posters viewed. These covered such diverse aspects as the role of antimicrobial peptides in CLE, clinical subtypes of lupus seen in Asia, the epidemiology and prevalence of CLE, medications and cancer in Sweden, the current categorizations of CLE and lupus non-specific skin lesions, and the derivation and validation of Systemic Lupus International Collaborating Clinics (SLICC) classification criteria.

The second aim of the meeting was to review the history related to the current definitions, diagnosis and classification of CLE and lupus non-specific skin lesions. An approach to building consensus on these topics was discussed and the Delphi method was presented and initiated. This method has been used previously by the Outcome Measures in Rheumatology (OMERACT) rheumatoid flare group.
Attendees were divided into three working groups, each with a moderator and a recorder of minutes. The moderator’s job was to address specific concerns related to key questions about definitions and diagnosis on the first day and the classification of CLE on the second day, and to assure that every member of the group had a chance to verbalize his or her ideas, as well as to promote interactive discussion. After each session, collated minutes were presented by each moderator to all participants. Points of agreement and disagreement within and between groups were highlighted.

Conclusions
Presentations successfully promoted discussion and interchange of ideas, as well as the ambience for cooperation.

The initiation of the Delphi process for consensus building highlighted the need for a change in the categorization of skin related problems in lupus erythematosus. The definitions, diagnosis, and classification of CLE need updating and reorganizing to make them more functional for diagnosis and research data collection. The ideas collected are in the process of being organized and highlighted to begin a Delphi voting process and to build a consensus.
Poster 2: Fit & Strong! An evidence based community exercise program for older adults with osteoarthritis

Authors
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Abstract
Introduction
There are 26.9 million older adults with osteoarthritis. Older adults with lower extremity osteoarthritis (OA) are at risk for the development of disability. Increasing physical activity in this population is one strategy that may prevent the functional limitations typically seen in those with OA.

Goals
Fit & Strong! is a multi-component program of exercise and education, designed to increase aerobic fitness, muscle strength and self-efficacy for exercise and adherence. The program is low cost and easily replicated so it can be offered in the community.

Methods
Fit & Strong! is a 24 session program meeting for 90 minutes, 3x/wk, consisting of 1 hour of exercise and 30 min. of education and discussion. Exercises are designed to address aerobic fitness, strength, flexibility and balance. The education component covers exercise, OA, and strategies to promote lifelong adherence to physical activity and exercise. Outcomes include: timed sit to stand, 6 minute walk test, WOMAC, self-efficacy (SE) for arthritis self-management, exercise, and exercise adherence. Two randomized controlled trials provide evidence for the efficacy of Fit & Strong! A third trial evaluating dissemination of the program has also been completed. Support materials include: participant and instructor manuals as well as a website.

Results
Study 1 recruited 215 subjects, 115 were randomized to receive the program. Significant findings were seen at 2 months. These included exercise adherence (p=.000), SE for exercise (p=.001), WOMAC stiffness (p=.018) and 6MWD (p=.007). Results were maintained at 6 and 12 months, and additional improvements were seen for pain and SE for exercise adherence with maintenance of the improved 6MWD. Distance walked at baseline by the exercise group (mean) 350.6 m.; increased to 397.2 m. at 2 mos; and 396.9 m at 6 mos., which is a meaningful improvement.
Study 2, 443 participants received the program from certified exercise instructors randomized to different reinforcement strategies. The intervention again resulted in improvements in stiffness; 6MWD; and exercise adherence. Effects were also seen for timed stands test; self-efficacy for symptom management and managing exercise barriers.

Study 3, Fit & Strong! is offered in 7 states at 55 sites. There are 169 trained instructors. The total number of participants to date is 2,475. The program has been approved as an Evidence-Based Program by the Centers for Disease Control and Prevention; the Administration on Aging and the National Council on Aging.

Discussion
Osteoarthritis is one of the most prevalent diseases found in the older adult population. Community based strategies that have proven efficacy and effectiveness are one important avenue for maintenance of independent function in this population. Fit & Strong! has been found to be effective in reducing pain & stiffness, and improving physical function. Adoption of an active lifestyle has benefits to individuals as well as society.

Conclusion
Fit & Strong! is an effective community based option for older adults with OA to manage their disease and develop the skills needed to remain active. It is important to include lifestyle strategies in preventing OA disability.

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Poster 3: Seafood consumption and persistent organic pollutants as triggers of autoimmunity among Gullah African Americans

Presenting Author
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Abstract
Introduction / Background
Local seafood is a dietary staple among the African American Gullah population of South Carolina. High levels of persistent organic pollutants (POPs) have been found in local bottlenose dolphins, sentinel species for human health and consumers of many of the same fish as the Gullah. Links have been established between these bioaccumulating, ubiquitous compounds and deleterious health effects in humans. The objective was to determine whether levels of POPs, specifically perfluorinated compounds (PFCs), correlate with fish intake and markers of immune dysfunction in the Gullah, who have low non-African genetic admixture, environmental homogeneity, and a high prevalence of autoimmune diseases, particularly lupus.

Goals / Hypotheses
The overall hypothesis of the Persistent Organic Pollutants in Autoimmunity (POPAI) study is that POPs play a pathogenic role as environmental triggers of autoimmunity in genetically at-risk individuals.

Methods
At the onset of the Persistent Organic Pollutants in AutoImmunity (POPAI) study, one-on-one interviews were conducted with Gullah community members to validate a comprehensive environmental exposure questionnaire. The validated questionnaire, including a seafood intake survey, was then administered prospectively to patients with lupus, first-degree relatives of lupus patients, and unrelated nonlupus controls participating in the SLE in Gullah Health (SLEIGH) study. PFC levels (PFOS, PFOA and PFNA), antinuclear antibody titers and other autoantibodies were measured in the serum of participants drawn at the time of their study visit.

Results
Initial surveys returned by 103 of the SLE in Gullah Health participants confirmed that local seafood consumption is common, with 57% reporting they consumed locally caught seafood at least once a month, 25% catch fish from shores/piers/bridges, and 91% consumed species known or suspected to contain high levels of POPs in the Charleston Harbor area. Interviews with Gullah community members found that the majority who fish either do not understand or mistrust the posted Fish Advisories warning of potentially hazardous contamination. Preliminary results from 53 Gullah controls show that all have measurable serum levels of PFCs (specifically PFOS, PFOA and PFNA) from baseline and follow-up visits 7.3 ± 1.4
years apart. Annual servings of seafood directly correlated with baseline serum PFOS (p=0.02) and PFNA levels (p=0.03) and the strongest correlation was with reported intake of seafood known to have the highest concentrations of PFCs.

Local serum levels of PFCs among the Gullah at baseline (2003-2004) are significantly higher compared to NHANES non-Hispanic black serum levels from 2003-2004 (p<0.01 for PFOS, PFOA and p=0.01 for PFNA). ANA positive controls (48% of controls at baseline) had higher median levels compared to ANA negative controls for PFOS (62.3 vs 46.4 ng/ml, p=0.05), PFOA (6.1 vs 5.4, p=NS) and PFNA (2.8 vs 1.6, p=0.03).

Conclusions
Genetically at-risk, autoantibody-positive but clinically asymptomatic populations can give us valuable insights into environmental triggers of progression to autoimmune disease. These ongoing studies address concerns of the Sea Island Gullah community regarding the potential immune health effects of the bioaccumulating pollutants found in local dietary staples such as fish.
Poster 4: Serum Urate Association with Hypertension in Young Adults: Analysis from the Coronary Artery Risk Development in Young Adults Cohort

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Abstract
Objective
To determine if serum urate concentration is associated with development of hypertension in young adults.

Methods
Retrospective cohort analysis from 4752 participants with available serum urate and without hypertension at baseline from the Coronary Artery Risk Development in Young Adults (CARDIA) study; a mixed race (African-American and White) cohort established in 1985 with 20 years of follow-up data for this analysis. Associations between baseline serum urate concentration and incident hypertension (defined as a blood pressure greater or equal to 140/90 or being on antihypertensive drugs) were investigated in sex-stratified bivariate and multivariable Cox-proportional analyses.

Results
Mean age (SD) at baseline was 24.8 (3.6) years for men and 24.9 (3.7) years for women. Compared with the referent category, we found a greater hazard of developing hypertension starting at 345 mmol/l (5.8 mg/dl) of serum urate for men and 214 mmol/l (3.6 mg/dl) for women. There was a 25% increase in the hazard of developing hypertension in men (HR 1.25 (95% CI 1.15 to 1.36)) per each mg/dl increase in serum urate but no significant increase in women (HR 1.06 (95%CI 0.97 to 1.16)).

Conclusions
We found a significant independent association between higher serum urate concentrations and the subsequent hazard of incident hypertension, even at concentrations below the conventional hyperuricaemia threshold of 404 mmol/l (6.8 mg/dl).
**Poster 5: Manual therapy, exercise therapy, or both for osteoarthritis of the hip or knee. Economic evaluation alongside a randomized controlled trial**

**Presenting Author**  
Daniel Pinto  
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**Abstract**

**Introduction**  
Multiple interventions exist for managing hip and knee OA with conservative treatments, primarily exercise therapy, recommended as first line treatments. Additionally, guidelines suggest referral to a physiotherapist for instruction in exercise may be beneficial. Preliminary evidence suggests manual mobilizations of the joints and surrounding soft tissue (manual physical therapy) may also reduce pain and improve function in patients with hip and knee OA.

**Objective**  
To evaluate the cost effectiveness of manual physiotherapy, exercise physiotherapy, and a combination of these therapies for patients with osteoarthritis of the hip or knee.

**Methods**  
206 adults who met the American College of Rheumatology criteria for hip or knee osteoarthritis were included in an economic evaluation from the perspectives of the New Zealand health system and society alongside a randomized controlled trial. Resource use was collected using the Osteoarthritis Costs and Consequences Questionnaire. Quality-adjusted life years (QALYs) were calculated using the Short Form 6D. Willingness-to-pay threshold values were based on one to three times New Zealand’s gross domestic product (GDP) per capita of NZ$29,149 (in 2009).

**Results**  
All three treatment programmes resulted in incremental QALY gains relative to usual care. From the perspective of the New Zealand health system, exercise therapy was the only treatment to result in an incremental cost utility ratio under one time GDP per capita at NZ$26,400 (~$34,081 to $103,899). From the societal perspective manual therapy was cost saving relative to usual care for most scenarios studied. Exercise therapy resulted in incremental cost utility ratios regarded as cost effective but was not cost saving. For most scenarios combined therapy was not as cost effective as the two therapies alone.

**Conclusions**  
In this study, exercise therapy and manual therapy were more cost effective than usual care at policy relevant values of willingness-to-pay from both the perspective of the health system and society.
Poster 6: Lower Serum Dehydroepiandosterone and Androstenedione Levels in Pre-Rheumatoid Arthritis versus Normal Control Women: Correlations with Lower Serum Cortisol Levels

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Abstract

Background
Rheumatoid arthritis (RA) is a leading cause of disability, occurring three times more frequently in women, and increasing in incidence during adult aging. Low serum adrenal androgens, including androstenedione (Δ4A), dehydroepiandosterone (DHEA), and its sulfate (DHEAS), have previously been reported in female RA patients. As yet, no study has been performed of adrenal androgen levels before onset of RA.

Objective
This study investigates a broad panel of adrenal steroids, including glucocorticoids and androgens, and their enzymatic pathways, to determine if differences occur between women who later develop RA versus matched controls.

Study Method
“Operation CLUE” is a nested case-control cohort study which enrolled 21,061 adult residents of Washington Co., Maryland, in 1974. After baseline entry, pre-RA cases had onset of American College of Rheumatology (ACR) criteria-positive RA (1977–1992), and were patients of the sole community rheumatologist. Four controls (CN) were matched to each pre-RA case on gender, race, and cohort entry age. The baseline 1974 stored sera were available on most subjects for assays of a comprehensive panel of steroid hormones. Hormonal levels were standardized by menopausal status and compared in 36 female pre-RA vs 144 CN, by t-tests and age-adjusted partial correlations.

Results
Mean Δ4A levels were lower in total pre-RA vs CN subjects (p=0.015). When analyses were restricted to women with cortisol levels less than the population mean, the preceding Δ4A difference was magnified in these subjects (p=0.005), and explained the total difference. In subjects having lower cortisol, the mean DHEA level was also lower in pre-RA vs CN women (p=0.012). The enzyme leading to Δ4A production, 17,20 lyase,
was evaluated by the ratio of its product ($\Delta 4A$) to its precursor (17-hydroxyprogesterone). This ratio also tended ($p=0.053$) to be lower in pre-RA than CN, among subjects having lower mean cortisol values. The pre-RA women who had lower $\Delta 4A$ levels tended ($p=0.097$) to develop clinical RA sooner after entry than their cohorts.

Conclusions
Study data indicate that women who later developed clinical RA had combined lower baseline cortisol and adrenal androgens (AAs), DHEA and $\Delta 4A$, than matched cohort women. Physiologically, cortisol levels remain constant during aging, but AAs progressively diminish. Adrenal function may also decline more rapidly with aging in a subset of pre-RA women having combined lower cortisol and AA levels, than occurs in a control population. Women with relative adrenal insufficiency may have lesser control of inflammatory pathways involved in the multifactorial development of RA.
**Poster 7: Targeting rheumatoid arthritis prevention strategies to high-risk populations based on family history, genetic and environmental factors**

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**Abstract**

**Background**
The identification of high-risk groups is crucial for RA prevention strategies. Family history (FH) of autoimmunity, genetics, and environmental factors has been associated with RA. The area under the receiver operating characteristic curve (AUC) can measure the ability of prediction models to discriminate between cases and controls.

**Goal**
We aimed to evaluate the performance of prediction models for RA stratified by serologic phenotypes based on family history, environment, and genetics.

**Methods**
We developed RA prediction models in a nested case-control study within the Nurses’ Health Study (NHS) and replicated in women in the Swedish Epidemiological Investigation in RA (EIRA) study. NHS cases were validated by chart review and matched to controls by age, menopausal status and post-menopausal hormone use. EIRA new-onset RA cases were matched to controls by age and region. All cases were Caucasian and satisfied the 1987 ACR criteria for RA classification. FH data were obtained from questionnaires (NHS) and registries (EIRA). Serologic status was defined as seropositive (+RF/ACPA) for NHS and as ACPA+ or ACPA- for EIRA. Weighted genetic risk scores were calculated for cases and controls based on 39 genetic markers associated with RA in prior genome-wide association studies. Logistic regression models were used to calculate the AUC and 95% confidence intervals (CI) for seropositive/ACPA+ RA and seronegative/ACPA- RA. Model components were based on family history (FH, any first-degree relative with RA or lupus in NHS and any first-degree relative with RA in EIRA), environment (E: matching factors, smoking pack-years, body mass index, alcohol intake, education, and parity), genetics (G), and shared
epitope-cigarette smoking interaction (GEI). Analyses stratified by FH were performed using E, G, and GEI model components.

Results
We analyzed 492 cases and 501 controls in NHS women and 1,244 cases and 971 controls in EIRA women with FH data. The complete model (FH+E+G+GEI) for seropositive/ACPA+ RA had an AUC of 0.71 (95% CI 0.67-0.75) in NHS and 0.78 (95% CI 0.76-0.80) in EIRA. After stratification for FH, women with +FH had an AUC of 0.85 (95% CI 0.77-0.92) in the complete model (E+G+GEI) for seropositive RA in NHS and an AUC of 0.85 (95% CI 0.78-0.92) for ACPA+ RA in EIRA. For seronegative/ACPA- RA with +FH, complete models had an AUC of 0.85 (95% CI 0.63-0.72) in NHS and an AUC of 0.80 (95% CI 0.69-0.91) in EIRA. For seropositive/ACPA+ RA with +FH, models using only the E component (AUC 0.82 in NHS and 0.77 in EIRA) performed better than models using only the G component (AUC 0.63 in NHS and 0.74 in EIRA).

Conclusions/Implications
We have developed and replicated prediction models for RA in women using family history, environment, and genetics. These models had highest discrimination for seropositive/ACPA+ RA and performed best in stratified analyses for those with family history. This study suggests that RA prevention strategies should be targeted to those with family history of autoimmunity. Amongst those with family history, environmental and genetic data may further identify those at high risk for developing RA and suitable for prevention strategies.
Poster 8: Impact of Rheumatoid Arthritis on Recognition of Hypertension in a US Medically Homed Population

Presenting Author
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Abstract
Objective
Despite numerous studies reporting increased cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA), the impact of RA on management of modifiable risk remains understudied.

Hypothesis
We tested the hypothesis that RA is a risk factor for missed hypertension diagnosis.

Methods
Using a cohort design we studied all medically homed adult patients from a large multispecialty practice who met Joint National Committee-7 (JNC-7) hypertension criteria but lacked baseline diagnosis or treatment to compare new diagnosis of hypertension in patients with and without RA. “Medically homed” required ≥2 primary care visits over>24 months including at least one visit in the most recent 24 months (2009-11). RA/inflammatory polyarthritis arthritis required two ICD-9 claims of 714 in 24 months. The outcome of new hypertension diagnosis included: (a) an ICD-9 hypertension diagnosis (Tu 2007), (b) a code for elevated blood pressure without hypertension (796.2), or a new antihypertensive prescription. Kaplan Meier Survival and Cox proportional hazard modeling were used to examine the impact of RA on hypertension diagnosis.

Results
Among 14,974 patients with undiagnosed hypertension, 201 patients had RA codes. After up to 4 years, the likelihood of hypertension diagnosis was 36% in RA patients compared to 51% without RA. RA patients had equal primary care visits (mean 2.5 v. 2.6), and more total visits (7.9 v. 4.9). In multivariate modeling controlling for sociodemographics, comorbidity, and utilization, RA decreased hypertension diagnosis by 29% [Hazard Ratio 0.71, 0.55-0.93]. RA showed larger gaps than all other tested comorbidities. Declines in RA stood in contrast to increased hypertension recognition with diabetes [HR 1.27, 1.14-1.63].

Conclusions
Among medically homed patients meeting JNC-7 hypertension criteria, RA patients were 29% less likely to be diagnosed despite more visits than those without RA. Given that hypertension and RA both increase CVD, rheumatologists and primary care may need to actively collaborate to improve hypertension diagnosis to modify CVD risk in RA patients.