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Abstract Number: 1

Pediatric Rheumatology Care and Outcomes Improvement Network Demonstrates Improvement on Quality Measures for Children with Juvenile Idiopathic Arthritis

C. April Bingham[1], Jesse Pratt[2], Cagri Yildirim-Toruner[3], Ronald Laxer[4], Beth Gottlieb[5], Jennifer Weiss[6], Tzielan Lee[7], Sheetal S. Vora[8], Jon Burnham[9], Julia Harris[10], Judyann C. Olson[11], Murray Passo[12], Michelle Batthish[13], Michael Shishov[14], Kerry Ferraro[15], Deborah M. Levy[16], Christine O'Brien[17], Kristi Whitney-Mahoney[17], Nancy Griffin[18], Anne Paul[19] and Esi Morgan[20], [1]Penn State Health Children's Hospital, Hershey, PA, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [3]Rheumatology, Nationwide Children's Hospital, Columbus, OH, [4]Div of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, [5]Pediatric Rheumatology, Cohen Children's Medical Center of New York, New Hyde Park, NY, [6]Hackensack University Medical Center, Hackensack, NJ, [7]Pediatric Rheumatology, Stanford University School of Medicine, Palo Alto, CA, [8]Pediatric Rheumatology, Levine Children's Hospital, Charlotte, NC, [9]Children's Hospital of Philadelphia, Philadelphia, PA, [10]Children's Mercy Kansas City, Kansas City, MO, [11]Ped/MACC Fund Research Ctr, Medical College of Wisconsin, Milwaukee, WI, [12]Division of Rheumatology PTD, Medical University of South Carolina, Charleston, SC, [13]Division of Pediatric Rheumatology, McMaster Children's Hospital, Hamilton, ON, Canada, [14]Pediatric Rheumatology, Phoenix Children's Hospital, Phoenix, AZ, [15]Pediatric Rheumatology Care and Outcomes Improvement Network, Cincinnati, OH, [16]Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, [17]The Hospital for Sick Children, Toronto, ON, Canada, [18]James M. Anderson Center for Health Systems Excellence, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [19]Anderson Center for Health Systems Excellence, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [20]Pediatric Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Plenary Abstract Session 1
Session Type: Abstract Submissions
Session Time: 2:00PM-3:00PM

Background/Purpose: Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN) is a growing multi-center network organized on a learning health system model designed to improve outcomes of care for children with juvenile idiopathic arthritis (JIA). Since 2011, data from JIA clinical encounters have been entered into a shared registry to track performance on process and outcome quality measures (QMs) to drive improved outcomes. Currently, 18 centers learn established quality improvement methodology to conduct quality improvement work and share best practices at biannual face-to-face learning sessions and monthly webinars.

Methods: Statistical process control methods are used to determine if there are changes in performance on the QMs. A centerline (the mean of the first 12 months of data) and control limits (±3 SD) are calculated, and control charts are monitored for special causes. Site specific and aggregate control charts are displayed monthly. If it is determined that a sustainable change has occurred, a new centerline and new control limits are calculated. Process QMs include measurement of: arthritis-related pain, physician global assessment of disease activity (PGA), joint counts, health related quality of life, physical function, medication counseling, as well as adherence to guidelines for uveitis screening, medication toxicity monitoring, and tuberculosis screening. Outcome QMs include: proportion of patients with clinical inactive disease (CID), mild to no pain, and optimal physical function; mean clinical Juvenile Arthritis Disease Activity Score 10 (cJADAS10); and percent of polyarthritis or oligoarthritis patients with inactive or low disease activity by cJADAS10.

Results: As of May 2016, 4722 JIA patients are enrolled, with over 28,000 visits recorded in the registry. Performance improvements have been achieved in process QMs, including percent of patients on Disease Modifying Anti Rheumatic

Drug (DMARD) who had appropriate toxicity lab monitoring (from 49 to 78%) and documented medication counseling with DMARD initiation (from 14 to 75%). In addition, PR-COIN sites reliably perform complete joint counts (99%), PGA (92%), measurement of arthritis-related pain (94%), and tuberculosis screening for patients newly prescribed biologic drugs (99%). Forty-six percent of all PR-COIN patients have CID, with marked center-to-center variability (range 26% to 58%) and statistical improvement in a subset of centers. Seventy-four percent of patients have mild to no pain, and 58% have optimal physical function. PR-COIN has shown improved outcomes in mean cJADAS10 scores (from 4.6 to 3.8) and percentage of patients with inactive or low disease activity by cJADAS10 (from 50 to 54%) from 2011 to present.

Conclusion: PR-COIN has demonstrated success in improving processes of care for management of JIA. There is, however, variability in performance across centers. The dichotomous outcome measure "clinical inactive disease" has been slow to show statistical improvement in aggregate. By adopting a continuous outcome measure, the cJADAS10, PR-COIN has been able to demonstrate incremental improvements in outcomes for patients with JIA.

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Abstract Number: 2

Murine Model of Arthritis Flare Identifies CD8+ Tissue Resident Memory T Cells in Recurrent Synovitis

Margaret H Chang[1], Anais Levescot[2], Allyn Morris[2], Nathan Nelson-Maney[3], Robert Fuhlbrigge[4] and Peter A. Nigrovic[2], [1]Immunology, Boston Children's Hospital, Boston, MA, [2]Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital, Boston, MA, [3]Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital, Boston, MA, [4]Children's Hospital Colorado, Aurora, CO

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Plenary Abstract Session 1

Session Type: Abstract Submissions

Session Time: 2:00PM-3:00PM

Background/Purpose: There are 75,000 children affected by JIA in the United States. Despite recent therapeutic advances, treatment often requires chronic therapy and is associated with considerable cost and morbidity, yet is still not curative as episodic flares are common. However, the pathophysiology of these flares is not well understood. There is a common observation that arthritis flares exhibit a strong tendency to recur in the same joints. This fixed pattern of joint involvement is highly individualized and persists for decades. To study this phenomenon, we established a murine model of recurrent, joint-specific inflammation.

Methods: Methylated bovine serum albumin (meBSA) or ovalbumin (OVA) is injected into the wrist, knee and ankle joints of B6 mice. The contralateral side was injected with vehicle as a negative control. For the OVA conditions, 5x10^6 CD3+ cells collected from peripheral lymph nodes of OT-I mice were transferred IV into the mice 1 day prior to intra-articular OVA injection. Interleukin-1 was concurrently injected into the footpad of the mice to stimulate the immune response. Arthritis flare was triggered by i.p. meBSA or OVA re-stimulation. At days 7 (acute inflammation), 28 (remission) and 31 (flare), the joints were analyzed for inflammation by measuring joint thickness, histological evaluation, and flow cytometry analysis of disaggregated synovium.

Results: 7 days after injection, there is measureable swelling and histological evidence of synovitis, specifically in the joints exposed to the antigen. In the synovium, there is a corresponding increase in CD4 and CD8 T cell populations. At 28 days after injection, inflammation subsides with normalization of both joint size and resolution of synovitis. During this post-inflammatory remission, we found a persistent population of antigen-specific cells with resident memory T cell (TRM) phenotype (CD45.2+CD3+CD8+CD44+CD62L-CD69+CD103+). These TRM cells are preferentially increased in the synovium of the joint exposed to antigen. Upon intraperitoneal challenge with antigen, there is a recurrent inflammation specifically in the joints previously exposed to antigen, and a corresponding expansion of antigen-specific CD8+ TRM cells in the synovium is also seen.

Conclusion: Here, we created an inducible model of recurrent, joint-specific inflammation. Our data suggests synovial resident memory T cells may represent the basis for joint-specific memory in inflammatory arthritis.

Disclosure: M. H. Chang, None; **A. Levescot**, None; **A. Morris**, None; **N. Nelson-Maney**, None; **R. Fuhlbrigge**, None; **P. A. Nigrovic**, None.

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Abstract Number: 3

Efficacy and Safety of Canakinumab in Patients With Systemic Juvenile Idiopathic Arthritis: Results From an Open-Label, Long-Term Follow-up Study

Hermine Brunner[1], Nicolino Ruperto[2], Pierre Quartier[3], Tamás Constantin[2], Ekaterina Alexeeva[2], Rayfel Schneider[4], Isabelle Koné-Paut[5], Kenneth N. Schikler[6], Katherine Marzan[4], Nico Wulffraat[2], Shai Padeh[7], Vyacheslav Chasnyk[7], Carine Wouters[7], Jasmin B. Kuemmerle-Deschner[7], Tilmann Kallinich[7], Bernard Lauwerys[8], Elie Haddad[4], Evgeny L Nasonov[7], Maria Trachana[7], Olga Vougiouka[7], Karolynn Leon[9], Antonio Speziale[10], Karine Lheritier[10], Eleni Vritzali[11], Alberto Martini[7] and Daniel Lovell[4], [1]Rheumatology, PRCSG, Cincinnati, OH, [2]PRINTO-Istituto Gaslini, Genoa, Italy, [3]Necker-Enfants Malades Hospital, Paris, France, [4]PRCSG, Cincinnati, OH, [5]Hôpital Kremlin Bicetre, University of Paris SUD, Paris, France, [6]PRCSG, Cincinatti, OH, [7]PRINTO-Istituto Gaslini, Genova, Italy, [8]Cliniques Universitaires Saint-Luc and Université Catholique de Louvain, Brussels, Belgium, [9]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [10]Novartis Pharma AG, Basel, Switzerland, [11]Immunology and Dermatology Franchise, Novartis Pharma AG, Basel, Switzerland

SESSION INFORMATION
Session Date: Thursday, May 18, 2017
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Session Time: 2:00PM-3:00PM

Background/Purpose: Canakinumab (CAN), a selective human anti-IL1 β monoclonal antibody, had demonstrated its efficacy and safety in patients (pts) with active systemic juvenile idiopathic arthritis (SJIA) in a comprehensive global clinical program consisting of one phase II and two phase III trials.[1,2] However, limited data was available on long-term efficacy and safety of CAN in SJIA. The study objective was to assess the long-term efficacy and safety of CAN treated SJIA pts over a 5-year (yr) follow-up observational period.

Methods: This was an open-label extension (OLE) study (NCT00891046) of SJIA pts participating in the global clinical trials of CAN.[3] Pts, 2 to <20 yrs of age at the time of enrollment in study, received subcutaneous CAN 4 mg/kg every 4 weeks. Baseline was defined as the starting point of the extension trial. Efficacy assessments were done every 3 months,

including adapted pediatric response criteria (aACR), clinical inactive disease, and clinical remission on medication (continuous 12 months of clinical inactive disease). Safety assessments included adverse events (AEs) and serious AEs (SAEs).

Results: Overall, 147 pts to the OLE study had a median treatment duration of 3.2 yrs; total treatment exposure was approximately 365 pt-yrs. Of 147 pts, 100 (68%) completed 96 weeks of treatment, whereas 47 (32%) pts discontinued the study. Another 25 pts (17%) discontinued the study after Week 96. Of the 107 pts with an aACR 30 at entry to the OLE study, 61.7%, 79.4%, and 86.0% have had aACR 100, 90, and 70 responses, respectively at last assessment. At baseline, 32.7% of patients were with inactive disease which increased up to 60%–70% between Week 36 and Week 168. Clinical remission on medication was achieved in 43% pts. In total, 137 (93.2%) pts reported at least 1 AE during the 3.2 yrs median exposure in the study corresponding to 2.009 AEs/100 pt-days (733.6 AEs/100 pt-yrs) with infections (202.7 per 100 pt-yrs) being the most common AE. Overall, 47 (32.0%) pts had at least 1 SAE corresponding to 0.089 SAE/100 pt-days (32.6 SAE/100 pt-yrs) with the most common being JIA (14 pts) denoting disease flares or worsening of SJIA. Ten patients (6.8%) with a total of 12 macrophage activation syndrome events were reported as SAE and 7 patients among them discontinued the study. No deaths were reported.

Conclusion: In patients previously treated with CAN in pivotal trials, response to treatment was sustained or improved during long-term treatment in the OLE study. Safety profile of CAN was consistent with safety findings from previous studies.

References:

1. Ruperto N, et al. *N Engl J Med*. 2012;367(25):2396-406.
2. Ringold S, et al. *Arthritis & Rheum*. 2013;65 (10):2499-512.
3. Ruperto N, et al. *Ann Rheum Dis*. 2015;74(2):608.

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Abstract Number: 4

Microbiota-Dependent Signals Regulate Inflammatory Myelopoiesis in a Murine Model of Macrophage Activation Syndrome

Lehn K. Weaver[1], Chhanda Biswas[1], Niansheng Chu[1] and Edward M. Behrens[2], [1]Pediatric Rheumatology, Children's Hospital of Philadelphia, Philadelphia, PA, [2]Rheumatology, Children's Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Plenary Abstract Session 1
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Background/Purpose: Targeting host-microbiota interactions to limit production of pathogenic myeloid cells that fuel chronic inflammatory responses is of therapeutic interest. Recent evidence suggests that this may be possible, as antibiotic-treated and germ-free mice have impaired myelopoiesis and have increased susceptibility to infection. To determine if microbiota-dependent processes regulate myelopoiesis during chronic inflammation, we tested whether broad-spectrum

antibiotics are protective in a murine model of macrophage activation syndrome (MAS). In this model, repeated TLR9 activation *in vivo* increases the production of TLR9 responsive monocytes through enhanced myelopoiesis, which is critical to sustain TLR9-induced immunopathology.

Methods: Broad-spectrum antibiotics were administered to C57BL/6 wild-type mice via their drinking water for 3 weeks prior to the induction of TLR9-mediated MAS. TLR9-mediated MAS was induced by intraperitoneal injection of CpG1826 into antibiotic-treated and control mice every other day for 5 doses. Systemic inflammation was determined 24 hours after the last dose of CpG by analysis of cytopenias, hypercytokinemia, hepatosplenomegaly, peripheral monocytosis, and inflammation-induced myelopoiesis. Initial TLR9 responses in antibiotic-treated and control mice were measured 24 hours after a single dose of CpG1826. Baseline numbers of TLR9 responsive monocytes and myeloid progenitors were enumerated in antibiotic-treated and control mice. The function of myeloid progenitors from antibiotic-treated and control mice were tested using *in vitro* myelopoiesis assays.

Results : Antibiotic-treated mice are completely protected from TLR9-induced MAS. Disease protection is not mediated by defective baseline TLR9 responses, as monocytes are present in antibiotic-treated mice and mount a normal inflammatory response to the initial TLR9 stimulus. Instead, disease protection correlates with failed induction of myelopoiesis and impaired peripheral monocyte accumulation. Baseline numbers and function of myeloid progenitors are reduced in antibiotic-treated mice, which correlates with reduced levels of serum myeloid-specific growth factors.

Conclusion : Our data suggest that microbiota-dependent signals sustain chronic TLR9-driven inflammation and immunopathology by promoting effective inflammatory myelopoiesis. These data implicate microbiota as a central pathogenic contributor to chronic inflammation, and provide rationale for future attempts to target microbiota-dependent regulation of inflammatory myelopoiesis for therapeutic benefit in TLR-driven chronic rheumatic diseases.

Disclosure: L. K. Weaver, None; **C. Biswas**, None; **N. Chu**, None; **E. M. Behrens**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/microbiota-dependent-signals-regulate-inflammatory-myelopoiesis-in-a-murine-model-of-macrophage-activation-syndrome

Abstract Number: 5

Effects of Puberty on Systemic Lupus Erythematosus: Results of a multi-center prospective longitudinal observational study in children entering puberty with SLE

Kathleen O'Neil[1], Hermine Brunner[2], Andrew Zeft[3], Anne Stevens[4], Suzanne Li[5], Tracey Wright[6], Emily von Scheven[7], B. Anne Eberhard[8], C. Egla Rabinovich[9] and Deborah M. Levy[10], [1]Pediatrics, Indiana University, Indianapolis, IN, [2]Rheumatology, PRCSG, Cincinnati, OH, [3]Pediatrics Rheumatology, Cleveland Clinic, Cleveland, OH, [4]University of Washington, Department of Pediatrics, Seattle, WA, [5]Pediatrics, Joseph M Sanzari Children's Hospital, Hackensack Meridian Health, Hackensack, NJ, [6]Pediatrics/Rheumatology, University of TX Southwestern, Dallas, TX, [7]Division of Rheumatology, Department of Pediatrics, University of California San Francisco, San Francisco, CA, [8]Cohen Children's Medical Center of New York, New Hyde Park, NY, [9]Pediatric Rheumatology, Duke University Medical Center, Durham, NC, [10]Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Friday, May 19, 2017
Session Title: Plenary Abstract Session 2
Session Type: Abstract Submissions
Session Time: 2:00PM-3:00PM

Background/Purpose: Lupus often presents during puberty, and when it affects pre-pubertal children, disease activity is

thought to increase at puberty. Sex hormones play some role in lupus expression, yet the picture is more complex then sex steroids alone, as shown by the SELENA trial. How lupus disease activity varies during the ~3 year process of puberty is surmised, but not documented by evidence.

Methods: Children fulfilling 4 or more ACR classification criteria for systemic lupus erythematosus who were between the ages of 8 and 12 years (girls) or 11 and 14 years (boys) whose pubertal development was Tanner 1 or early Tanner 2 were consented and enrolled in a prospective longitudinal observational study to assess what pubertal events and hormone changes affected lupus disease activity as measured by the SELENA SLEDAI. They were evaluated every 3 months until after the completion of puberty. Flares were defined as mild to moderate (MMF) if SLEDAI increased by 3 to 5 points, and severe (SvF) if 6 or more compared to the previous 3 monthly assessment. If SLEDAI decreased by at least 3 points, the visit was considered improved (IMP). Multivariate fitting after stepwise model slelection was used to correlate hormone changes with disease activity. Generalized equalizing equations were used to compare changes in disease activity over time and multiple regression analysis to compare factors potentially influencing disease activity. In some analyses, girls with pre-pubertal onset SLE (PreP) were compared to girls with post-pubertal (age 15 or more, PostP) SLE from two contemporaneously collected cohorts (HI Brunner).

Results: Of 55 girls with pre-pubertal onset lupus 100% had ds-DNA antibody vs 70% with SLE onset age >15 ($p=0.001$). PreP were twice as likely to have anemia (37 vs 18%, $p=0.01$) as PostP, and they had more nephritis at onset (60 vs 40%, $p<0.02$). Serum concentration of FSH, LH and estradiol did not correlate temporally with flare. In 270 visits from 65 pubertal children with SLE (55 F, 10 M), 48 had MMF (17.8%) and 19 had SvF (7.04%); 24.8% had any flare. In 63 visits (23.3%) SLEDAI decreased >3 points (IMP). 49% of visits had change in activity sufficient to consider alterring treatment. 16 entered puberty and 17 transitioned from Tanner 2-3. Flares were associated with Tanner stages 2 and 3 ($p=0.008$) vs Tanner 1. No severe flares happened in/after Tanner 4. Flares correlated with rapid falls in visfatin (OR 0.072, $p=0.002$), high adiponectin (OR 1.20, $p=0.0046$), and neither estradiol nor testosterone correlated with flare. IMP correlated with testosterone ($p=0.023$) and followed a drop in adiponectin (0.008) and rise in prolactin ($p=0.003$) and resistin ($p=0.026$).

Conclusion: Trasition from pre-puberty to early puberty is associated with flares in SLE, which falls after Tanner 4 is reached. Puberty is a tumultuous time for children with SLE with half the visits requiring medication adjustment because of flares and improvements. Adipokine changes in serum are temporally related to disease activity. Higher concentrations of testosterone appear to exert a calming effect on lupus disease activity.

Disclosure: K. O'Neil, None; **H. Brunner**, None; **A. Zeft**, 1,5; **A. Stevens**, 2,7; **S. Li**, None; **T. Wright**, None; **E. von Scheven**, None; **B. A. Eberhard**, None; **C. E. Rabinovich**, None; **D. M. Levy**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/effects-of-puberty-on-systemic-lupus-erythematosus-results-of-a-multi-center-prospective-longitudinal-observational-study-in-children-entering-puberty-with-sle

Abstract Number: 6

High Health Care Utilization Preceding Diagnosis of Systemic Lupus Erythematosus in Youth

Joyce Chang[1,2], David Mandell[3] and Andrea Knight[4,5,6], [1]Center for Clinical Epidemiology and Biostatistics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, [2]Children's Hospital of Philadelphia, Philadelphia, PA, [3]Psychiatry and Pediatrics, Center for Mental Health Policy and Services Research, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, [4]Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, [5]Center for Pediatric Clinical Effectiveness & PolicyLab, Philadelphia, PA, [6]Division of Pediatric Rheumatology, Children's Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION

Session Date: Friday, May 19, 2017

Session Title: Plenary Abstract Session 2
Session Type: Abstract Submissions
Session Time: 2:00PM-3:00PM

Background/Purpose: Childhood-onset SLE is associated with high risk for organ damage, which may be mitigated by early diagnosis and treatment. To identify points of health care interaction for potential intervention, we compared pre-diagnosis health care utilization patterns of youth with SLE to those of controls.

Methods: Using US administrative claims (OPTUM) from 2000 to 2013, we identified 682 youth ages 10-24 years with an incident diagnosis of SLE (≥3 International Classification of Diseases, Ninth Revision codes for SLE 710.0, each >30 days apart) and 1,364 controls, matched 2:1 by age and sex. We compared the incidence of ambulatory, emergency and inpatient visits one year before SLE diagnosis, and the frequency of primary diagnosis codes. We examined associations of SLE subject characteristics with pre-diagnosis utilization.

Results: Youth with SLE had significantly more visits in the year preceding diagnosis than controls across ambulatory (IRR 2.48, p<0.001), emergency (IRR 3.42, p<0.001) and inpatient settings (IRR 3.02, p<0.001) (Fig 1). The differences increased as diagnosis approached (Fig 2). Inpatient utilization was greater for SLE subjects with subsequent seizure/stroke and nephritis. Fever, venous thromboembolism, thrombocytopenia, chest pain and acute kidney failure were the most frequent diagnoses in acute care settings. The presence of a psychiatric diagnosis prior to SLE diagnosis was most strongly associated with increased utilization across all settings (Table).

Conclusion: Youth with SLE use significantly more health care in the year preceding diagnosis than peers without SLE, suggesting opportunities for earlier diagnosis, especially among those with neuropsychiatric or renal manifestations.

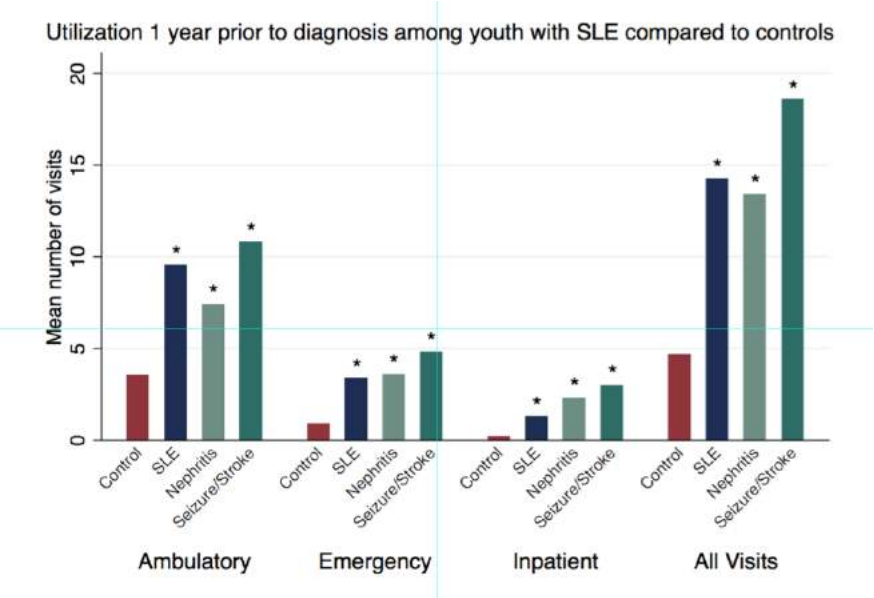

Figure 1. Mean health care visits one year prior to diagnosis in youth with SLE compared to controls. Mean visits for subgroups with nephritis and seizure/stroke at or after SLE diagnosis are also shown. * Indicates p-value < 0.001 in comparison to controls, calculated using negative binomial regression models adjusted for race and geographic region.

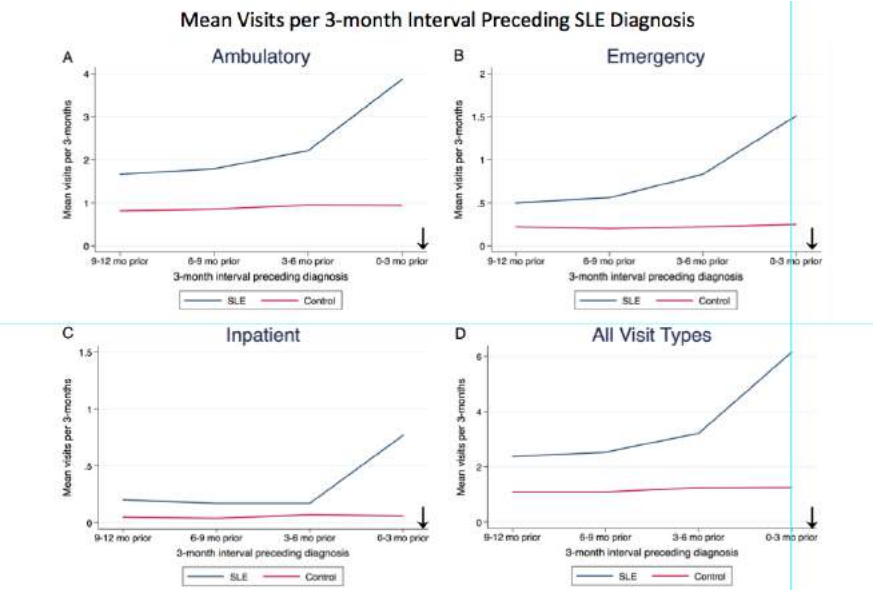

Figure 2. Mean visits at 3-month intervals leading up to the index date in youth with SLE compared to controls, stratified by a) ambulatory visits, b) emergency care visits, c) inpatient hospitalizations, and d) all visit types combined. Arrows indicate date of SLE diagnosis.

Table. Factors Associated with Pre-diagnosis Health Care Utilization in Youth with SLE

Factors	Ambulatory	Emergency	Inpatient
	Multivariate Incidence Rate Ratio (95% CI)		
Race/Ethnicity			
White	-	-	-
Black	0.8 (0.7-0.95)*	1.1 (0.8-1.5)	1.6 (0.7-3.5)
Hispanic	1.1 (0.9-1.3)	1.2 (0.9-1.6)	1.5 (0.6-3.6)
Asian	0.7 (0.5-0.95)*	0.5 (0.3-0.8)**	0.7 (0.2-2.4)
Age, years			
10-17	-	-	-
18-24	1.1 (1.0-1.3)	1.1 (0.9-1.3)	1.2 (0.7-2.2)
Female	1.4 (1.2-1.8)***	1.0 (0.8-1.4)	1.1 (0.4-2.7)
Region			
Midwest	-	-	-
Northeast	1.1 (0.9-1.4)	0.9 (0.6-1.3)	0.7 (0.2-2.0)
South	1.0 (0.9-1.2)	0.8 (0.6-1.0)	1.1 (0.5-2.2)
West	1.0 (0.8-1.2)	1.1 (0.8-1.5)	0.4 (0.2-1.2)
Highest household education			
High school or less	-	-	-
Beyond high school	1.2 (1.01-1.4)*	1.0 (0.8-1.2)	1.1 (0.5-2.2)
SLE nephritis§	0.8 (0.7-0.9)**	1.1 (0.8-1.4)	2.1 (1.02-4.3)*
Seizures or Stroke§	1.4 (1.1-1.7)**	1.4 (1.0-1.9)	2.6 (1.0-7.0)
Preceding psychiatric diagnosis	1.9 (1.6-2.2)***	2.1 (1.6-2.7)***	3.1 (1.4-7.1)**

Results from multivariable negative binomial regression models examining associations between demographic or disease factors and health care utilization. Separate models (n = 631) were used for ambulatory, emergency, and inpatient visits. * = p <0.05; ** = p < 0.01; *** = p < 0.001; § Indicates disease manifestation at or after SLE diagnosis

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Disclosure: J. Chang, None; **D. Mandell**, None; **A. Knight**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/high-health-care-utilization-preceding-diagnosis-of-systemic-lupus-erythematosus-in-youth

Abstract Number: 7

Activation of Immature, Transitional B cells by Integrated BCR, TLR and TACI signals promotes systemic autoimmunity in high BAFF settings

Holly Jacobs, Samuel Du, Tanvi Arkatkar and **Shaun Jackson**, Seattle Children's Research Institute, Seattle, WA

SESSION INFORMATION
Session Date: Friday, May 19, 2017
Session Title: Plenary Abstract Session 2
Session Type: Abstract Submissions
Session Time: 2:00PM-3:00PM

Background/Purpose:

B cell activating factor of the TNF family (BAFF, also known as BLyS) promotes B cell survival and activation by binding distinct B cell surface receptors, namely BAFF receptor (BAFF-R) and Transmembrane activator and CAML interactor (TACI). Although increased BAFF levels have been implicated in the pathogenesis of SLE, how excess BAFF promotes breaks in B cell tolerance is not completely understood. Since BAFF-R deletion results in loss of mature B cells, BAFF-R-dependent signals were presumed to explain BAFF-mediated autoimmunity. However, we made the surprising observation that B cell TACI signals are critical for BAFF-driven autoantibody production.

Methods:

To test the requirement for B cell receptor (BCR) and Toll-like receptor (TLR) signals in TACI-dependent autoantibody production, we crossed *Btk*$^{-/-}$, *Myd88*$^{-/-}$, *Tlr7*$^{-/-}$ and *Taci*$^{-/-}$strains with transgenic mice over-expressing BAFF (BAFF-Tg).

Results:

Despite prior studies suggesting that TACI signals negatively regulate B cell activation, we observed that TACI deletion results in a striking loss of class-switched autoantibodies and protection from immune-complex glomerulonephritis in BAFF-Tg mice. Importantly, lack of autoimmunity was not explained by alterations in peripheral B cell development, since both BAFF-Tg and *Taci*$^{-/-}$.BAFF-Tg mice exhibited similar B cell hyperplasia. Rather, whereas surface TACI expression is usually limited to mature B cells, we discovered that excess BAFF promotes increased TACI by an activated subset of developing transitional B cells. This novel TACI^{hi} transitional population exhibits an activated, cycling phenotype, is enriched for autoreactive BCR specificities and directly contributes to class-switched autoantibody formation in BAFF-Tg mice. To dissect the B cell-intrinsic signals required for transitional B cell TACI expression and autoantibody production, we crossed BAFF-Tg animals with mice deficient in the B cell signalling adaptor Bruton's tyrosine kinase (*Btk*). Notably, *Btk*$^{-/-}$.BAFF-Tg exhibited abrogated serum autoantibodies which correlated with loss of surface TACI on transitional B cells. In contrast, despite previous studies reporting a requirement for B cell-intrinsic TLR signals in BAFF-driven autoimmunity, deletion of either the TLR adaptor Myd88 or the endosomal RNA receptor TLR7 exerted no impact on transitional TACI expression. Rather, deletion B cell TLR signals exerted an isolated impact on transitional B cell class-switch recombination, without impacting BCR-dependent TACI upregulation; findings identifying distinct contributions of BCR and TLR signalling pathways to BAFF-driven autoantibody production.

Conclusion:

Our combined findings advance our understanding of how integrated B cell signals promote humoral autoimmunity, by highlighting a novel mechanism in which increased BAFF drives TACI-dependent activation of developing transitional B cells. In addition to informing the genesis of SLE, these findings are likely of particular relevance to the understanding of disease relapse after B cell-depletion with Rituximab; a state characterized by B cell reconstitution within a high BAFF environment.

Disclosure: H. Jacobs, None; **S. Du**, None; **T. Arkatkar**, None; **S. Jackson**, None.

Abstract Number: 8

Examination of Reported Risk Loci from Candidate Gene Studies of Systemic Juvenile Idiopathic Arthritis Identifies Link between IL1RN Variation and both Disease Susceptibility and Response to Interleukin-1 Directed Therapy

Victoria Arthur[1], Emily Shuldiner[1], Anne Hinks[2], The International Childhood Arthritis Genetics (INCHARGE) Consortium[3], Patricia Woo[4], Wendy Thomson[2], Elaine F. Remmers[5] and **Michael J. Ombrello**[1], [1]Translational Genetics and Genomics Unit, NIAMS, NIH, Bethesda, MD, [2]Arthritis Research UK Centre for Genetics and Genomics,The University of Manchester, Manchester, United Kingdom, [3]INCHARGE Consortium, Bethesda, MD, [4]Paediatric Rheumatology Unit, University College London, London, United Kingdom, [5]Inflammatory Disease Section, NHGRI, NIH, Bethesda, MD

SESSION INFORMATION
Session Date: Friday, May 19, 2017
Session Title: Plenary Abstract Session 2
Session Type: Abstract Submissions
Session Time: 2:00PM-3:00PM

Background/Purpose: Systemic JIA (sJIA) is a childhood inflammatory disease whose pathophysiology is poorly understood. sJIA is phenotypically heterogeneous with variable manifestations and responses to treatment. Until recently genetic investigations of sJIA have consisted of candidate gene studies in small patient collections. These studies found only modest associations, yet these associations are regularly included in discussions of sJIA pathophysiology. Therefore we examined the 11 sJIA candidate susceptibility loci in the INCHARGE Consortium collection, the largest sJIA study population assembled to date.

Methods: Single nucleotide polymorphism (SNP) genotypes within the *IL1A/B, GLI2, IL1RN/PSD4, IL1R2, IL10/20, IL6, MVK, CCR5, MIF, SLC26A2* and *TAPBP* loci were extracted from the INCHARGE dataset (701 sJIA, 6947 controls). Logistic regression was performed in 9 case-control strata and association results were meta-analyzed. SNPs were pruned for linkage disequilibrium (LD) to determine the number of independent SNPs and define the study's significance threshold. The effect of sJIA associated SNPs on gene expression was evaluated in paired whole genome (WGS) and RNA sequencing (RNAseq) data from lymphoblastoid cell lines (LCL) of 373 European 1000 Genomes Project subjects. The relative difference in gene expression between genotypes was evaluated with the Kruskal Wallis test. The relationship between sJIA-associated SNPs and response to interleukin-1 (IL-1) directed treatment was evaluated in 38 US patients for whom treatment response data were available.

Results: We examined the 26 SNPs with reported sJIA associations and did not find even nominal ($p<0.05$) association of any of these SNPs with sJIA. We expanded the analysis to determine whether the 11 loci containing the 26 SNPs harbored any sJIA risk SNPs. We examined 5479 SNPs from the 11 candidate regions, among which 500 SNPs were independent ($r^2<0.5$). This defined the study's significance threshold as $p<1E-4$. Association meta-analysis revealed only one significant association among the 11 candidate loci, the promoter region of *IL1RN*, where 3 SNPs showed significant association. The top 7 SNPs were in strong LD and resided on a common haplotype. Analysis of LCL data showed that the associated SNPs correlate with *IL1RN* expression, with an inverse correlation between sJIA risk and *IL1RN* expression. Importantly, the presence of homozygous *IL1RN* high expression alleles correlated strongly with non-response to IL-1 directed therapy (p=9.8E-4, OR 17.3 [2.8, 108.1]).

Conclusion: *IL1RN* was the only candidate locus associated with sJIA in our study. The implicated SNPs are among the strongest known determinants of *IL1RN* and IL1RA levels, linking low expression with increased sJIA risk. Although high expression alleles were protective against sJIA, patients with 2 high expression alleles were significantly less likely to respond to IL-1 directed therapy than those with 1 or 2 low expression alleles. Despite the fact that exogenously administered IL1RA (anakinra) ameliorates or reduces inflammation in some sJIA patients, this is the first report to link sJIA risk and response to IL-1 directed therapy with genetically determined capacity to produce *IL1RN* or IL1RA.

Disclosure: V. Arthur, None; **E. Shuldiner**, None; **A. Hinks**, None; **T. International Childhood Arthritis Genetics (INCHARGE) Consortium**, None; **P. Woo**, None; **W. Thomson**, None; **E. F. Remmers**, None; **M. J. Ombrello**, None.

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Abstract Number: 9

Biologically-Based Approach for Classifying Chronic Childhood Arthritis

Elham Rezaei[1], Daniel Hogan[2], Brett Trost[2], Anthony Kusalik[2], Susanne Benseler[3], Gilles Boire[4], David A. Cabral[5], Bonnie Cameron[6], Sarah Campillo[7], Gaëlle Chédeville[8], Paul Dancey[9], Ciarán M. Duffy[10], Karen N Watanabe Duffy[11], Janet Ellsworth[12], Simon Eng[13], Brian M. Feldman[14], John Gordon[2], Jaime Guzman[15], Kristin Houghton[16], Adam Huber[17], Quaid Morris[13], Bianca Lang[18], Deborah M. Levy[19], Loren Matheson[20], Kiem Oen[21], Ross Petty[22], Suzanne Ramsey[23], Johannes Roth[24], Dax Rumsey[25], Claire Saint-Cyr[26], Rayfel Schneider[27], Rosie Scuccimarri[28], Earl Silverman[19], Lynn R. Spiegel[29], Elizabeth Stringer[18], Shirley M.L. Tse[30], Lori Tucker[31], Rae S.M. Yeung[32] and Alan Rosenberg[1], [1]Pediatrics, University of Saskatchewan, Saskatoon, SK, Canada, [2]University of Saskatchewan, Saskatoon, SK, Canada, [3]Pediatric Rheumatology, University of Calgary, Alberta Children's Hospital, Calgary, AB, Canada, [4]Rheumatology Division, CHUS - Sherbrooke University, Sherbrooke, QC, Canada, [5]Pediatrics/Rm K4-121, BC Children's Hospital, Vancouver, BC, Canada, [6]The Hospital for Sick Children, Toronto, ON, Canada, [7]Montreal Children's Hospital, Montreal, QC, Canada, [8]Rheumatology, McGill University, Montreal, QC, Canada, [9]Pediatrics, Janeway Children's Hospital, St. John's, NL, Canada, [10]Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, ON, Canada, [11]Rheumatology, Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, ON, Canada, [12]University of Alberta, Edmonton, AB, Canada, [13]University of Toronto, Toronto, ON, Canada, [14]Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, [15]Rheumatology, BC Children's Hospital, Vancouver, BC, Canada, [16]Rheumatology/Pediatrics, British Columbia Childrens Hos, Vancouver, BC, Canada, [17]IWK Health Centre, Halifax, NS, Canada, [18]Dalhousie University, Halifax, NS, Canada, [19]Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, [20]University of Saskatchewan, Ottawa, ON, Canada, [21]University of Manitoba, Winnipeg, MB, Canada, [22]Pediatric Rheumatology, Division of Rheumatology, BC Children's Hospital, Vancouver, BC, Canada, [23]Pediatric Rheumatology, IWK Health Centre, Halifax, NS, Canada, [24]Pediatric Rheumatology, Children's Hospital Eastern On, Ottawa, ON, Canada, [25]Stollery Children's Hospital, Edmonton, AB, Canada, [26]Pediatrics, CHU Sainte-Justine, Montreal, QC, Canada, [27]Division of Rheumatology, Hospital for Sick Children, Toronto, ON, Canada, [28]Division of Pediatric Rheumatology, Montreal Children's Hospital/McGill University Health Centre, Montreal, QC, Canada, [29]Rheumatology/Pediatrics, The Hospital for Sick Children, Toronto, ON, Canada, [30]Rheumatology, The Hospital for Sick Children and University of Toronto, Toronto, ON, Canada, [31]Pediatric Rheum/Rm K4-120, BC Childrens Hospital, Vancouver, BC, Canada, [32]Paediatrics, Immunology and Medical Science, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Saturday, May 20, 2017

Session Title: Plenary Abstract Session 3

Session Type: Abstract Submissions

Session Time: 2:30PM-3:00PM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) comprises a heterogeneous group of conditions that share chronic arthritis as a common characteristic. International uniformity in classifying JIA, based predominantly on clinical

characteristics at onset, has helped propel

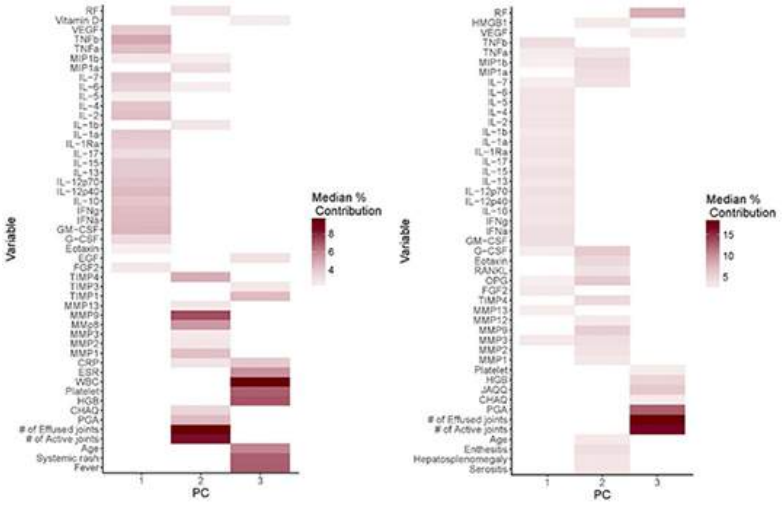

Figure. Principal component contributions of variables at Visit 1 (A) and Visit 2 (B)

collaborative efforts to improve understanding of subset-specific pathophysiology, treatment responses, and outcomes. The purpose of this study was to consider the added value of combining biomarker-based attributes with clinical characteristics to classify chronic childhood arthritis in a biologically-based context.

Methods: Data were derived from a prospective, nation-wide, longitudinal cohort study titled Biologically-Based Outcome Predictors in JIA (The BBOP Study). Newly diagnosed, treatment naïve children with JIA were evaluated at baseline and after six months. Data included clinical manifestations and plasma inflammation-related biomarkers. Categorical (nonlinear) principal component analysis (CAT-PCA), factor analysis of mixed data (FAMD), and probabilistic principal component analysis (PPCA) were used for dimensionality reduction purposes. To identify groups in the data, K-medoids clustering and Gaussian mixture modeling (GMM) were applied. Four common metrics were used to validate the clustering configurations: Davies–Bouldin, Dunn2, average silhouette width, and Calinski and Harabasz indices. The results were compared with the JIA subgroups defined by International League of Associations for Rheumatology criteria.

Results: A total of 150 JIA patients were enrolled. Data consisted of 191 variables. PCA reduced variables into 3 clinically relevant principal components (PCs) (Figure). Using PCs, three clusters were identified at baseline by both methods. At six months, three clusters were identified by K-medoids, and GMM recognized five clusters; new clusters were also revealed at six months (Figure). PCs recovered 33% and 47% of variance in the patient profiles in visit 1 and 2, respectively. Clustering validation indices showed that PPCA-GMM is the most reliable clustering method. At first presentation, clusters revealed in this analysis exposed different and more homogenous subgroups compared to the seven JIA ILAR subgroups. A large subset of patients with oligoarthritis and rheumatoid factor negative polyarthritis grouped into one cluster.

Conclusion: Using data-driven, unsupervised machine learning algorithms these analyses recognized distinctive patterns that provide insight into the underlying biology of chronic childhood arthritis and enable categorization of disease based on a combination of clinical and biomarker profiling.

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Abstract Number: 10

Severe Juvenile Arthritis Associated with a De Novo Gain-of-Function Germline Mutation in MYD88

Keith A. Sikora[1], Joshua R. Bennett[1], Zuoming Deng[2], Wanxia Li Tsai[3], April D. Brundidge[3], Fatemeh Navid[3], Gerlinde Layh-Schmitt[3], Eric Hanson[4], Massimo G. Gadina[5], Louis M. Staudt[6], Thomas A. Griffin[7] and Robert Colbert[3], [1]Pediatric Translational Research Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [2]Biodata Mining & Discovery, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [4]Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [5]Translational Immunology, Office of Science and Technology, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [6]National Cancer Institute, National Institutes of Health, Bethesda, MD, [7]Levine Children's Hospital at Carolinas Medical Center, Charlotte, NC

SESSION INFORMATION

Session Date: Saturday, May 20, 2017

Session Title: Plenary Abstract Session 3

Session Type: Abstract Submissions

Session Time: 2:30PM-3:00PM

Background/Purpose: Myeloid differentiation primary response 88 (MyD88) is a critical adaptor protein that connects Toll-like and IL-1 receptor signaling to activation of NF-κB. Germline loss-of-function mutations in MyD88 cause immunodeficiency, while somatic gain-of-function mutations have been linked to lymphoma. We investigated a child with a progressively destructive small-to-medium joint polyarticular JIA since the age of 2 with persistent neutrophil predominant synovial infiltrates.

Methods: We evaluated the patient and family members by whole exome sequencing (WES), peripheral blood immunophenotyping, and phosphorylated-STAT3 (p-STAT3) quantitation. Functional studies in monocytes and dermal fibroblasts included gene/protein expression, quantitation of neutrophil chemotaxis, and siRNA-mediated knockdown of MyD88 and NF-κB subunit p65 (p65). Wild type (WT) or S222R MyD88-AU1 fusion proteins were re-expressed in MyD88-deficient THP-1 cells. NF-κB activity in THP-1 cells was measured via p65 phosphorylation. Molecular mechanistic studies assessing capacity of S222R MyD88 to aggregate, which is necessary for pathway signaling, were performed via centrifugal sedimentation and immunofluorescence imaging.

Results: WES revealed a *de novo* heterozygous missense mutation in *MYD88* (c.666T>G, p.Ser222Arg), which was confirmed by Sanger sequencing in both peripheral leukocytes and dermal fibroblasts. Immunophenotyping showed a persistent absence of CD16+ monocytes, an expansion of CD4+ Th17 T cells, and the presence of a previously uncharacterized CD123+CD11c+ dendritic cell population, as well as markedly increased basal and stimulated p-STAT3 in monocytes and T and B lymphocytes in the patient. Peripheral monocytes exhibited a baseline interferon gene expression signature and increased expression of neutrophil and monocyte chemokines. Fibroblasts exhibited significantly greater baseline expression of CXCL chemokines compared to controls, which abated upon MyD88 or p65 knockdown. Re-expression of WT or S222R MyD88-AU1 fusion protein in MyD88-knockout THP-1 cells demonstrated increased p65 phosphorylation in S222R-MyD88-expressing cells compared to WT. Similar to L265P, the most common lymphoma-associated MyD88 gain-of-function somatic mutation, S222R-MyD88 aggregated in THP-1 cells to a greater extent than WT MyD88 protein, which was visualized by immunoblotting of re-solubilized aggregates as well as immunofluorescence microscopy.

Conclusion: This is the first description of a *de novo* germline MyD88 mutation associated with severe polyarticular JIA. Gain-of-function effects demonstrated in the patient's hematopoietic and non-hematopoietic cells, occurring through increased MyD88-S222R aggregation, offer a plausible mechanism for arthritis and support a role for single gene defects contributing to extreme JIA phenotypes.

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Abstract Number: 11

Safety of Adalimumab ± Methotrexate for the Treatment of Polyarticular Juvenile Idiopathic Arthritis (pJIA): STRIVE Registry

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SESSION INFORMATION

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Session Title: Clinical and Therapeutic Poster Breakout I

Session Type: Abstract Submissions

Session Time: 4:45PM-5:15PM

Background/Purpose:

JIA is the most common chronic inflammatory rheumatic disease of childhood. Due to their known safety and efficacy, TNF inhibitors are used for long-term control of pJIA disease. The purpose of this analysis was to evaluate the 7 year (y) safety of Adalimumab treatment with or without methotrexate (ADA±MTX) when used in current clinical practice for treatment of patients (pts) with active pJIA.

Methods:

This is a 7 y interim analysis of an ongoing, multicenter, non-interventional, observational registry of pts with pJIA with up to10 y safety follow-up. Included pts were treated with either ADA±MTX or MTX alone as comparison arm according to routine clinical care in US, EU, and Australia. MedDRA observational adverse events (AEs) were recorded from 1st day in the registry through last contact, irrespective of the duration of registry treatment.

Results:

In January 2014, enrollment was complete. As of June 1, 2016 cut-off date, 838 pts (301- MTX arm and 537 - ADA±MTX arm) were treated in the registry. There were 39 pts who rolled over from MTX to the ADA±MTX arm. At registry entry mean pJIA disease duration was 1.3 y and 3.7 y and mean AJC71 was 5.8 and 5.2 for MTX and ADA±MTX arms, respectively. CHAQ disability index was 0.6 for both arms. The mean duration of study drug exposure in registry was 2.0 y (range: 0.0 – 7.1) and 2.5 y (range: 0.0 – 7.9) for MTX and ADA±MTX arms, respectively. The mean duration of observation in registry was 3.9 y (range: 0.0 – 7.2) and 3.5 y (range: 0.0 – 7.9) for MTX and ADA±MTX arms, respectively. Overall, 213 pts (70.8%) in MTX and 225 pts (41.9%) in ADA±MTX arms discontinued registry drug through 7 y. The main reasons for registry drug discontinuation for MTX arm: pts required additional therapy (32.6%), other (13.3%), lack of efficacy (11.6%), AEs (9.3%), or pts achieved JIA remission (8.6%), and for ADA±MTX arm: lack of efficacy (17.9%), other (7.3%), lost to follow-up (5.6%), AEs (5.4%), or pts achieved JIA remission (5.0%).

Frequencies and rates of treatment-emergent AEs (from 1st dose date of registry drug in registry up to last dose + 70 days in registry, excluding AEs occurring during treatment interruption) were similar to those reported for observational AEs (from 1st day in registry up to last contact irrespective of drug treatment duration) **(Table)**. The rate of serious infections was similar between MTX and ADA±MTX arms. One pt (0.2%) reported an event of opportunistic infection (fungal oesophagitis) in ADA±MTX arm. No reports of deaths, malignancies, active tuberculosis, oral candidiasis, demyelination, or congestive heart failure. Data on safety and effectiveness of ADA±MTX background therapy compared to MTX alone will be presented, that adjusts for differences in treatment durations.

Conclusion:

Overall, ADA±MTX was well-tolerated in these pts with pJIA with no new safety signals. The retention rate for registry drug was higher in ADA±MTX arm compared to MTX arm.

Table. Overview of the Observational Adverse events

	MTX		ADA±MTX			
			ADA only		ADA + MTX[a]	
	N=301 n (%)	PYs=1170.3 E (E/100 PYs)	N=160 n (%)	PYs=517.0 E (E/100 PYs)	N=377 n (%)	PYs=1338.5 E (E/100 PYs)
Any AE	157 (52.2)	505 (43.2)	66 (41.3)	216 (41.8)	178 (47.2)	553 (41.3)
AE at least "possibly drug related" per the investigator	87 (28.9)	197 (16.8)	30 (18.8)	66 (12.8)	88 (23.3)	177 (13.2)
Severe AE	17 (5.6)	23 (2.0)	14 (8.8)	22 (4.3)	25 (6.6)	41 (3.1)
Serious AE	32 (10.6)	52 (4.4)	21 (13.1)	39 (7.5)	56 (14.9)	95 (7.1)
AE leading to discontinuation of study drug or study	28 (9.3)	36 (3.1)	13 (8.1)	19 (3.7)	25 (6.6)	40 (3.0)
Infectious AE	87 (28.9)	179 (15.3)	38 (23.8)	75 (14.5)	105 (27.9)	187 (14.0)
Serious infectious AE	14 (4.7)	17 (1.5)	6 (3.8)	8 (1.5)	22 (5.8)	30 (2.2)
Injection site-related AE	6 (2.0)*	8 (0.7)	5 (3.1)	6 (1.2)	24 (6.4)	32 (2.4)

E, events; PYs, patient years (Observation time irrespectively of study drug treatment duration). *3 patients experienced injection site -related AEs with etanercept injections. During the registry, 52 (17.3%) pts in MTX arm and 45 (8.4%) pts in ADA arm started with a biologic DMARD.
[a]MTX was used at any point of time during the course of the registry.

Disclosure: H. Brunner, 5,8; **N. Ruperto**, 2,8; **K. Nanda**, 5; **M. Toth**, None; **I. Foeldvari**, 9; **J. F. Bohnsack**, 5; **D. Milojevic**, 5; **C. E. Rabinovich**, 2; **D. Kingsbury**, 2; **K. Marzan**, 2; **P. Quartier**, 5,2,9; **K. Minden**, 2,5; **E. Chalom**, 8; **G. Horneff**, 2,8; **R. M. Kuester**, 2; **J. A. Dare**, 2; **M. Bereswill**, 1; **J. Kalabic**, 1; **H. Kupper**, 1; **D. J. Lovell**, 5,8,9; **A. Martini**, 2,8.

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Abstract Number: 12

Use of Ultrasound to Determine Remission Status in Children with Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Breakout I

Session Type: Abstract Submissions

Session Time: 4:45PM-5:15PM

Background/Purpose: The ultimate goal for clinicians caring for children with Juvenile idiopathic arthritis (JIA) is to attain disease remission off medications. Correct identification of remission is crucial in the decision to withdraw medications. Ultrasound (US) is a non-invasive and sensitive technique used to detect the presence of active synovitis. Between 30-40% of JIA patients in physician diagnosed clinical remission demonstrated persistent active synovitis with ultrasound in published experiences, and withdrawal of medications in these patients may precipitate a disease relapse. The purpose of this study is to assess whether or not the use of ultrasound can better enable pediatric rheumatologists to determine clinical remission in children with JIA.

Methods: We recruited 41children with either oligoarticular or polyarticular JIA, 17 with clinically active disease and 24 in clinical remission. Three to 6 joints were scanned using US in each child, including the currently or previously most active joints. Joint effusion, synovial thickening, erosions and synovial hyperemia by Power Doppler signal were recorded within each joint. These four variables were scored on a scale from 0-3 and a score of 2 or 3 was considered to represent significant clinical change. Univariate and multivariate logistic regression analyses were performed, to best distinguish the two groups. Inter-reader reliability was calculated using Cohen's kappa statistics between two independent ultrasonographers.

Results: Of the 41 subjects, 73.2% were female, 90.3% were Caucasian and 48.8% were polyarticular. 156 joints were scanned; 63 in the active group and 93 in the remission group. The most commonly scanned joints were MCP's (50), PIP's (50) and knees (29). Overall 57.7% of joints had significant US abnormalities: 74.6% in the active group, and 46.2% in the remission group (p=0.003). 64% of MCP joints had abnormal findings on US: 84.2% in the active group, and 51.6% in the remission group (p=0.053). 33.3% of ankle joints had abnormal findings: 62.5% in active group, and 0.0% in remission group (p=0.03). The calculated kappa coefficient of 0.68 indicates a high degree of inter-reader agreement. The most common abnormal finding was Power Doppler signal 47.4%. PIPs were the joints most commonly abnormal in the remission group. None of the patients in clinical remission who had normal ultrasound findings had elevated ESRs, but 42.1% of the patients with abnormal ultrasound findings had elevated ESRs (P = 0.5).

Table 1: Frequency of ultrasound abnormalities by group					
	All patients (N=41)	Active (N=17)	Remission (N=24)	p-value	Odds Ratio
All joints	90/156 (57.7%)	47/63 (74.6%)	43/93 (46.2%)	0.003	3.51 (1.53, 8.04)
Elbow	3/4 (75.0%)	2/2 (100.0%)	1/2 (50.0%)	0.25	
Wrist	4/6 (66.7%)	2/2 (100.0%)	2/4 (50.0%)	0.47	
MCPs	32/50 (64.0%)	16/19 (84.2%)	16/31 (51.6%)	0.053	5.07 (0.98, 26.3)
PIPs	35/50 (70.0%)	16/19 (84.2%)	19/31 (61.3%)	0.12	3.66 (0.67, 19.9)
DIPs	1/2 (50.0%)	1/1 (100.0%)	0/1 (0.0%)	0.16	
Knee	10/29 (34.5%)	5/12 (41.7%)	5/17 (29.4%)	0.53	1.81 (0.20, 16.3)
Ankle	5/15 (33.3%)	5/8 (62.5%)	0/7 (0.0%)	0.03	

Conclusion: There were higher than expected findings of active synovitis (46%) in children believed to have been in clinical remission, with the most common active joints being the PIP, MCP, and ankle joints. Use of US with Power Doppler of these specific joints may prove to be helpful in assisting clinicians to more accurately define remission in children with JIA.

Disclosure: O. Kristinsson, None; **L. Scalzi**, None; **M. Bruno**, None; **C. French**, None; **V. Chinchilli**, None; **B. Groh**, None.

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Abstract Number: 13

Prevalence of Celiac Antibodies and IgA deficiency in Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Clinical and Therapeutic Poster Breakout I
Session Type: Abstract Submissions

Session Time: 4:45PM-5:15PM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) is the most common chronic arthritis of childhood. The prevalence of autoimmunity is higher in JIA cases and relatives. The prevalence of celiac disease (CD) in JIA has been reported to be 0.1% to 7% in small studies. CD is 3 to 10-fold higher in asymptomatic individuals with other autoimmune diseases or chromosomal abnormalities for which screening is recommended. Tissue transglutaminase (tTG) IgA has high specificity for CD in individuals with normal IgA levels. The prevalence of IgA deficiency ranges between 1 in 330 to 2200 persons, and has been reported to be higher in JIA. Our aims were to estimate the prevalence of IgA deficiency and tTG IgA in a cohort of JIA followed in two large academic medical centers.

Methods: Subjects were 830 cases with JIA per the ILAR criteria (ages 3 to 21 at the time of collection) and 205 healthy controls (ages 3 to 69). Serum was collected and stored from all subjects and analyzed in a reference laboratory for total IgA (Quantitative Nephelometry) and tTG IgA antibody levels (Semi-Quantitative Enzyme-Linked Immunosorbent Assay). Standard reference levels of tTG IgA 0-3 U/mL as negative, 4-10 U/mL as weak positive and >10 U/mL as positive; and IgA <7 mg/dl for IgA deficiency were applied. Those with IgA deficiency were excluded from the tTG IgA analysis. Fisher's exact tests were performed for statistical significance.

Results: Ten JIA cases (1.2%) and none of the controls had IgA deficiency (p = ns). Cases with IgA deficiency were mostly female (70%), and had the following JIA subtypes: oligoarticular = 5, polyarticular Rheumatoid Factor (RF)-negative = 2, polyarticular RF-positive = 2, and enthesitis-related = 1. In all 16 cases (2%), and 8 controls (3.9%) had an abnormal tTG (p =ns). After excluding the weak positives, we observed 7 cases (0.8%) and 3 controls (1.5%) with tTG IgA >10u/mL (p=ns). Cases with tTG IgA >10 u/mL were mostly female (71%), and were oligoarticular =3, polyarticular RF-negative =1, polyarticular RF-positive = 2 and enthesitis-related =1. From the healthy group with tTG IgA >10 u/mL the majority were female (67%).

Conclusion: Using the largest JIA cohort to date to investigate prevalence of celiac antibodies, we show that the prevalence of positive tTG IgA was 0.8% and the prevalence of IgA deficiency was 1.2%. Our results did not demonstrate a higher prevalence of abnormal tTG IgA in JIA. We do not recommend routine screening of asymptomatic JIA patients for CD.

Disclosure: A. Taneja, None; **S. Prahalad**, None; **A. O. Hersh**, None; **L. Ponder**, None; **L. H. K. Chan**, None; **K. A. Rouster-Stevens**, None; **A. E. Tebo**, None; **S. Kugathasan**, None; **J. F. Bohnsack**, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/prevalence-of-celiac-antibodies-and-iga-deficiency-in-juvenile-idiopathic-arthritis

Abstract Number: 14

Efficacy and Safety of Canakinumab in Patients with Periodic Fever Syndromes (Colchicine-Resistant FMF, HIDS/MKD and TRAPS): Results from a Phase 3, Pivotal, Umbrella Trial

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SESSION INFORMATION

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Session Type: Abstract Submissions
Session Time: 4:45PM-5:15PM

Background/Purpose: Open-label studies have suggested the efficacy of canakinumab (CAN), a fully human, highly specific anti-IL-1β neutralizing monoclonal antibody, in colchicine-resistant-FMF (crFMF), hyper-immunoglobulin (Ig) D syndrome/mevalonate kinase deficiency (HIDS/MKD), and tumour necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS).[1-3] We report the efficacy and safety of CAN from the randomized treatment epoch of the Phase 3 pivotal study in patients (pts) with crFMF, HIDS/MKD or TRAPS.

Methods: The study (NCT02059291) consists of 3 disease cohorts (crFMF, HIDS /MKD and TRAPS) and 4 study epochs: a screening epoch (E1) of up to 12 wks, a randomized treatment epoch (E2) of 16 wks, a randomized withdrawal epoch (E3) of 24 wks and an open-label treatment epoch (E4) of 72 wks. Pts (aged ≥2 years) with a flare during E1were randomized (1:1) in E2 to receive CAN or placebo (PBO). Primary objective was to demonstrate that CAN 150 mg (or 2 mg/kg for pts ≤40 kg) sc q4w is superior to PBO. Safety assessments included adverse events (AEs) and serious AEs(SAEs).

Results: Of 181 pts (crFMF, n=63; HIDS/MKD, n=72; TRAPS, n=46) randomized in E2, 6 discontinued the study (5 PBO; 1 CAN). In all 3 disease cohorts, the proportion of responders for the primary outcome at Wk 16 was significantly higher with CAN vs PBO. At Wk 16, a significantly higher proportion of pts achieved a physician's global assessment (PGA) score <2, C-reactive protein (CRP) ≤10 mg/L and serum amyloid A (SAA) ≤10 mg/L in the CAN group vs PBO in all 3 cohorts. The most frequently affected system organ class across 3 cohorts was infections and infestations typically involving the upper respiratory tract. The incidence of SAEs was 8.6%, 4.7% and 11.8% in crFMF, TRAPS and HIDS/MKD cohorts, respectively.

Conclusion: These results demonstrated superior efficacy of canakinumab after a 16-week treatment period compared with placebo. The overall safety profile was not distinct from those reported in previous controlled studies.

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Abstract Number: 15

An Internet-based Self-management Program for Adolescents with Juvenile Idiopathic Arthritis – A Randomized Controlled Trial

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SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Clinical and Therapeutic Poster Breakout I
Session Type: Abstract Submissions
Session Time: 4:45PM-5:15PM

Background/Purpose:

Juvenile Idiopathic Arthritis (JIA) is a common chronic childhood illness associated with physical and emotional symptoms that can negatively impact health-related quality of life (HRQL). Adolescents are expected to assume greater responsibility in disease management as they mature. This can prevent worsening of the disease and symptoms, and facilitate the transition to adult health care. However, the vast majority of adolescents with JIA do not receive comprehensive self-management education. Internet-based interventions provide an innovative approach to improve the *accessibility* and *acceptability* of self-management programs for adolescents with chronic illnesses. A randomized control trial was conducted to determine the effectiveness of an Internet intervention, which consisted of education about JIA, self-management strategies, and social support.

Methods:

Participants were between 12-18 years old with JIA across 11 pediatric centers in Canada. Most teens participated with a parent/caregiver. Teens in the intervention reviewed 12 modules focused on disease education and self-management strategies. Teens in the control condition reviewed standard disease education modules without self-management material. As part of the 3-month program, teens had monthly telephone check-ins with health coaches, but only intervention participants reviewed modules with their coach. Parents in both groups reviewed modules focused on promoting independence and disease self-management in their teen. Teens and parents completed outcome measures at 4 time points: baseline, at program completion, 3-months, and 6-months after the program. The primary outcomes measured were: pain and HRQL. The secondary outcomes were: emotional symptoms, adherence, coping, knowledge, and self-efficacy.

Results:

In total, 333 teens (n = 109 male, n = 224 female; mean age = 14.5, SD = 1.7) and 306 parents (n = 52 male, n = 254 female; 81.1% biological mothers) were enrolled. Of the 164 participants in the intervention group, 62.8% (n = 103) completed the study and 50.1% (n = 87) completed all modules and coach calls. Of the 169 control participants, 87.0% (n = 147) completed the study and 85.8% (n = 145) completed all modules and coach calls. On average, participants took 189.8 days (SD = 113.5) to complete the intervention and 123.6 days (SD = 70.6) days to complete the control program.

Pauses in the program were allowed for exams, illness, and vacations. Preliminary analyses indicate a trend for increased self-efficacy ($p = 0.026$) for intervention teen participants and decreased (1) pain ($p = 0.072$), (2) pain interference with sleep ($p = 0.064$) and enjoying daily life ($p = 0.004$), and (3) daily interference in quality of life ($p = 0.027$), compared to the control. Parent quantitative analyses are ongoing. The majority of teens in the intervention found the coach calls helpful and were satisfied with the frequency of the calls. Most also found the website text content, the online videos, graphics/animations, and relaxation exercises helpful.

Conclusion:

Teens and parents enjoyed being part of the study and trends for some benefits in outcome measures were noted. The intervention website will be launched for public release in the coming months.

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View Abstract and Citation Information Online - http://acrabstracts.org/abstract/an-internet-based-self-management-program-for-adolescents-with-juvenile-idiopathic-arthritis-a-randomized-controlled-trial

Abstract Number: 16

Novel Serum Broad-Based Proteomic Discovery Analysis Identifies Proteins and Pathways Dysregulated in Juvenile Dermatomyositis (JDM) Myositis Autoantibody Groups

Hanna Kim[1], Angélique Biancotto[2], Foo Cheung[3], Terrance P. O'Hanlon[4], Ira N. Targoff[5], Yan Huang[6], Frederick Miller[4], Raphaela Goldbach-Mansky[6] and Lisa G. Rider[4], [1]Pediatric Translational Research Branch, NIAMS/NIH, Bethesda, MD, [2]Center for Human Immunology, Autoimmunity and Inflammation (CHI), NHLBI, NIH, Bethesda, MD, [3]Center for Human Immunology Autoimmunity and Inflammation (CHI), NHLBI, NIH, Bethesda, MD, [4]Environmental Autoimmunity Group, NIEHS, NIH, Bethesda, MD, [5]VA Medical Center, University of Oklahoma Health Sciences Center, Oklahoma Medical Research Foundation, Oklahoma City, OK, [6]Translational Autoinflammatory Disease Studies (TADS), NIAID, NIH, Bethesda, MD

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Genetics and Pathogenesis Poster Breakout I

Session Type: Abstract Submissions

Session Time: 4:45PM-5:15PM

Background/Purpose: Juvenile dermatomyositis (JDM) is a complex heterogeneous autoimmune disease. Myositis-specific autoantibodies (MSAs), present in up to 80% of JDM patients, help define distinct phenotypes within JDM and may indicate distinct pathogeneses. To define biomarkers and better understand JDM pathogenesis, aptamer-based proteomic technology was used to mine the serum proteome in a well-characterized JDM cohort.

Methods: Sera from 41 JDM patients (prevalent cases on variable treatment) selected for higher disease activity (physician global activity or PGA median 4.0 (IQR 3.0-5.0)) with anti-p155/140 or TIF1 (n=21), NXP2 (n=10), and MDA5 (n=10) MSAs, were compared with 28 age- and gender-matched healthy controls (HC). Broad proteomic analysis of 1306 targets using SOMAscan assay of slow off-rate modified aptamers (SomaLogic, CO) generated simultaneous quantitative serum levels. Individual MSA group vs. HC proteins with Mann-Whitney FDR-corrected p values of <0.05 with expression ratio of >1.3 were analyzed using Ingenuity Pathway Analysis or IPA (Qiagen, CA).

Results: 62, 41, and 67 proteins, met above criteria with overexpression (>1.3 ratio versus HC) with 13, 4, and 13

proteins specific to TIF1, NXP2, and MDA5 MSA groups respectively and 26 shared in all 3 groups and 31 shared in 2 groups (Figure 1). Top 10 proteins by MSA group are listed in Table 1. Within the top 20 dysregulated pathways by MSA group by IPA, Th1 and Th2 activation, acute phase response, IFN, and glucocorticoid receptor signaling were shared to all 3 MSA groups. Further analysis by MSA group is ongoing.

Conclusion: Preliminary broad quantitative proteomic analysis by MSA group compared to HC identified Th1/ Th2, acute phase response, IFN, and glucocorticosteroid receptor signaling shared in all MSA groups. Unique protiens were identified by MSA group, but further analysis by MSA group is pending. While in need of confirmation in other cohorts, these proteins identified through a high-throughput screen bring to light new pathways that may be important in JDM and potential MSA-group specific pathogenesis.

This research was supported by the Cure JM Foundation and the Intramural Research Program of the NIH, NIAMS, NIEHS, NHLBI, NIAID, and the CC.

Figure 1. Somamers (Proteins) By MSA group

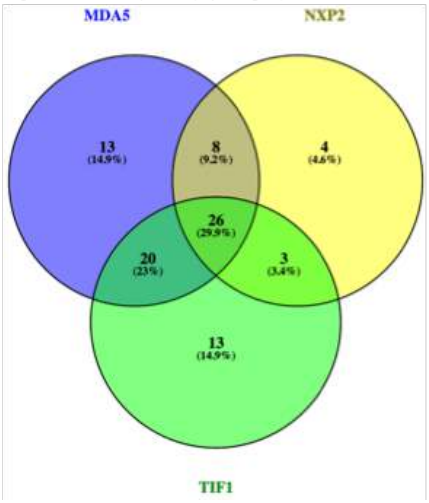

Table 1: Top Upregulated Proteins by MSA group versus HC

MSA Group	Target	Protein Target Full Name	JDM/ HC Expression Ratio
TIF1 (N=21)	MMP3	Stromelysin-1	6.609
	LTA4H	Leukotriene A-4 hydrolase	6.295
	APOB	Apolipoprotein B	5.921
	CXCL10	C-X-C motif chemokine 10	5.707
	HIST1H2A	Histone H2.1	5.384
	ISG15	Ubiquitin-like protein ISG15	4.952
	C3	Complement C3b	4.842
	CXCL11	C-X-C motif chemokine 11	4.168
	CCL7	C-C motif chemokine 7	4.149
	GPD1	Glycerol-3-phosphate dehydrogenase [NAD(+)], cytoplasmic	3.184
NXP2 (N=10)	MMP3	Stromelysin-1	6.060
	ISG15	Ubiquitin-like protein ISG15	4.693
	CXCL10	C-X-C motif chemokine 10	3.851
	C3	Complement C3b	2.806
	LTA4H	Leukotriene A-4 hydrolase	2.585
	OAS1	2'-5'-oligoadenylate synthase 1	2.209
	IL1RL1	Interleukin-1 receptor-like 1	2.109
	GDF15	Growth/differentiation factor 15	2.081
	FGF2	Fibroblast growth factor 2	2.071
	STAT1	Signal transducer and activator of transcription 1-alpha/beta	2.011
MDA5 (N=10)	LTA4H	Leukotriene A-4 hydrolase	8.750
	ISG15	Ubiquitin-like protein ISG15	7.017
	IL1RL1	Interleukin-1 receptor-like 1	6.605
	CXCL10	C-X-C motif chemokine 10	5.139
	FTH1 FTL	Ferritin	4.619
	IFNL1	Interferon lambda-1	4.423
	PIGR	Polymeric immunoglobulin receptor	4.309
	C3; 3	Complement C3b	4.282
	MMP3	Stromelysin-1	3.707
	GPD1	Glycerol-3-phosphate dehydrogenase [NAD(+)], cytoplasmic	3.702

Disclosure: H. Kim, 2; **A. Biancotto**, None; **F. Cheung**, None; **T. P. O'Hanlon**, None; **I. N. Targoff**, 6; **Y. Huang**, None; **F. Miller**, None; **R. Goldbach-Mansky**, None; **L. G. Rider**, 2.

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Abstract Number: 17

Anti-endothelial cell antibodies in juvenile dermatomyositis

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SESSION INFORMATION
Session Date: Thursday, May 18, 2017
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Background/Purpose: Juvenile dermatomyositis (JDM) is the most common form of inflammatory myopathy in children. Although classified as a myopathy, involved tissues in JDM are characterized by prominent vascular and perivascular inflammation that are believed to be directly involved in the clinical features of the disease. Thus, JDM also can be characterized as a form of vasculitis. Anti-endothelial cell antibodies (AECA) are detected in multiple autoimmune, infectious, and inflammatory diseases, including vasculitis. We aimed to determine whether such antibodies are present in JDM and, if so, to comprehensively detect their target antigens using a proteomics approach. **Methods:** To detect antibodies in sera from patients with JDM, proteins extracted from human aortic endothelial cells (HAEC) were used as antigen sources by SDS-PAGE and immunoblotting. To comprehensively detect target antigens for AECA, we separated proteins extracted from HAEC by two-dimensional electrophoresis (2DE) and then transferred them onto membranes. Autoantigens that were positive only in sera from children with JDM but not in sera from healthy children were detected by western blotting (WB). The detected proteins were then identified by mass spectrometry (MS). Bound IgG antibodies to antigens were detected using standard methods. **Results:** Five candidate protein spots as JDM-specific proteins were detected in 2DE-WB. From these spots, we successfully identified 34 proteins which we characterized broadly according to their functions: (1) 62% were ATP-related proteins such as proteins of the tricarboxylic acid (TCA) cycle (e.g., pyruvate kinase PKM and 78kDa glucose-regulated protein; (2) 21% were muscle-related proteins, including myosin-9 and Cdc42-interacting protein 4; (3) 18% were calcium regulated proteins and/or calcium binding proteins (e.g., annexin A6 and N-acetylglucosamine-6-sulfatase). We also identified eight proteins that act as chaperones or co-chaperones in intracellular protein trafficking. Furthermore 22 of the 34 identified antigens represented membrane proteins. Using Ingenuity Pathway Analysis (IPA), 27 of the 34 candidate target antigens for AECA in JDM were predicted to interact with chaperone proteins, which regulate the correct folding, stabilization, and translocation of proteins. **Conclusion:** IgG antibodies to proteins in the proteome of HAEC are present in the sera of JDM. The presence of AECA in JDM could implicate these antibodies in the pathobiology of the vascular/perivascular inflammation that is a proment feature of JDM.

Disclosure: R. Karasawa, None; **M. Tamaki**, None; **T. Sato**, None; **M. Tanaka**, None; **K. Yudoh**, None; **J. Jarvis**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/anti-endothelial-cell-antibodies-in-juvenile-dermatomyositis

Abstract Number: 18

Bridging the gap between GWAS and mechanism in juvenile idiopathic arthritis using a novel high-throughput experimental screen

Gang Li[1], Marta Martinez-Bonet[1], Di Wu[2], Jing Cui[3] and **Peter A. Nigrovic**[1,4], [1]Brigham and Women's Hospital, Boston, MA, [2]University of North Carolina, Chapel Hill, Chapel Hill, NC, [3]Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [4]Division of Immunology, Boston Children's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Genetics and Pathogenesis Poster Breakout I

Session Type: Abstract Submissions
Session Time: 4:45PM-5:15PM

Background/Purpose: Genome wide association studies (GWAS) have identified 27 non-HLA loci that convey risk for oligoarticular and seronegative polyarticular JIA. Most associated haplotypes bear no coding polymorphisms, implicating regulatory variants as a major driver of genetic predisposition. Unfortunately, predicting regulatory variants has proven extremely difficult, leaving obscure the mechanisms by which genes drive JIA risk.

Methods: We devised an unbiased high-throughput screen that employs enzymatic restriction to identify genetic variants that allelically modulate the binding of regulatory proteins to DNA. In this method, termed Single Nucleotide Polymorphism-next generation sequencing (**SNP-seq**), each potentially regulatory variant is engineered into an individual DNA construct. A pool of constructs is then incubated with nuclear extract containing regulatory proteins such as transcription factors. PCR and next generation sequencing are then employed to amplify and quantitate sequences that bind nuclear proteins and are therefore spared from enzymatic degradation. To identify these bound proteins, we applied Flanking Restriction Enhanced Pulldown (**FREP**, Li...Nigrovic *PLOS Genetics* 2016;e1006292), an efficient method to employ SNP-containing sequences as bait constructs for protein identification by mass spectrometry.

Results: We piloted SNP-seq + FREP on the *CD40* locus, associated with rheumatoid arthritis, identifying three SNPs that determined expression of this co-stimulator via a previously unrecognized protein complex. We then performed a high-throughput screen across 1223 alleles of 608 SNPs in LD R^2>0.8 with 27 JIA loci, using peripheral blood mononuclear cells as protein source, resulting in identification of 148 candidate regulatory variants. Confirmatory testing at the *STAT4* locus established two novel regulatory DNA-protein interactions that regulate this T cell-associated gene in a manner implicated in JIA risk.

Conclusion: We have developed a novel experimental strategy to identify genetic variants that modulate disease risk by altering the binding of transcription factors and other regulatory proteins. Application of this strategy to JIA has allowed us to begin to bridge the gap between GWAS and mechanism in this important but poorly-understood disease.

Disclosure: G. Li, None; **M. Martinez-Bonet**, None; **D. Wu**, None; **J. Cui**, None; **P. A. Nigrovic**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/bridging-the-gap-between-gwas-and-mechanism-in-juvenile-idiopathic-arthritis-using-a-novel-high-throughput-experimental-screen

Abstract Number: 19

The Lymphocyte Repertoire in Juvenile Dermatomyositis

Kacie Hoyt[1], Edwin Anderson[1,2], Megan L. Curran[3], Robert Fuhlbrigge[4], Luigi Notarangelo[5], Lauren M. Pachman[6], Susan Kim[7] and **Lauren Henderson**[8], [1]Division of Immunology, Boston Children's Hospital, Boston, MA, [2]Clinical Research Center/Rheumatology, Boston Children's Hospital, Medford, MA, [3]Pediatric Rheumatology, Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, [4]Children's Hospital Colorado, Aurora, CO, [5]National Institute of Allergy and Infectious Diseases, Bethesda, MD, [6]Cure JM Program of Excellence in Juvenile Myositis Research, Stanley Manne Children's Research Institute, affiliated with Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, [7]Pediatric Rheumatology, University of California, San francisco School of Medicine, San Francisco, CA, [8]Division of Immunology, Boston Children's Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION
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Session Type: Abstract Submissions
Session Time: 4:45PM-5:15PM

Background/Purpose: In adult dermatomyositis (DM), clonal populations of T and B cells with shared variable (V) gene usage have been identified in affected muscle, suggesting aberrant lymphocyte responses to a common antigen. Using next generation sequencing (NGS), we aimed to determine if these previously identified repertoire abnormalities in the muscle of adult DM patients could be detected in the peripheral blood (PB) of children with juvenile DM (JDM).

Methods: PB was obtained from JDM patients with skin and muscle disease (classic JDM) at diagnosis, during active disease, and at remission when patients were off medication. Amyopathic patients and healthy controls were also studied. $CD8^+$ T and $CD19^+$ B cells were isolated from PB mononuclear cells (PBMC) by magnetic beads. The remaining lymphocyte populations were isolated by fluorescence activated cell sorting: CD4/CD8 naïve (N) T cells ($C3^+CD4^+/CD8^+CD45RA^+CCR7^+$), CD4/ CD8 memory (M) T cells ($CD3^+CD4^+/CD8^+CD45RA^-$), Treg cells ($CD3^+CD4^+CD25^+CD127^{lo}$), Teff cells ($CD3^+CD4^+CD25^-$), Naïve B cells ($CD19^+IgD^+CD27^-$), and $CD21^{lo}$ B cells ($CD19^+CD21^{lo}CD38^{lo}$). The TCR β (*TRB*) and BCR heavy (*IgH*) chains were amplified by multiplex PCR with a standard quantity of genomic DNA serving as the template (ImmunoSEQ™). Illumina HiSeq platform was used for sequencing. Productive sequences were analyzed using the ImmunoSEQ set of online tools. Mann Whitney and 1-way ANOVA tests were used to compare the clonality index, Shannon entropy, and clone sharing in study groups. 2-way ANOVA with Bonferroni correction was used to compare TCRVβ family usage.

Results: Clinical characteristics of the patients are in Table 1. $CD21^{lo}$ B cells, a population of B cells associated with autoimmunity, were more clonal in classic JDM patients with active disease compared to those in remission ($p=0.03$). Similarly, the Treg repertoire was significantly more clonal in classic JDM patients with active disease than JDM patients in remission ($p<0.0001$) and amyopathic patients ($p=0.002$). CD19, CD19N, CD8, CD4/8 N/M, and Teff cells were polyclonal and diverse in all JDM patient groups. In Treg and Teff subsets, TCRVβ families 7, 10, and 28 were used more and Vβ families 3, 5, and 19 were used less in classic JDM patients with active disease compared to controls ($p<0.0001$for Treg and Teffs). Inter-individual sharing of Teff clonotypes was observed in JDM patients with active disease compared to controls ($p<0.001$).

Conclusion: Clonal expansions in $CD21^{lo}$ B and Treg cells noted in JDM patients with active disease resolved upon remission. Skewed TCRVβ family usage was observed in active JDM patients with increased usage of Vβ7, a Vβ family that has been linked with other autoimmune conditions. Inter-individual sharing of Teff clonotypes was also observed. Our pilot results suggest that lymphocyte repertoire abnormalities may contribute to disease pathogenesis in JDM and can be detected in PB by NGS.

Table 1. Characteristics of Study Subjects

Sample Name	Clinical Status	Age (years)	Sex	Auto-antibodies	Disease Duration (mo)	MMT8 Score	DAS (total/muscle/skin)	Medications
Classic JDM1	Diagnosis	4.7	M	MJ	6.0	N/A	N/A	None
Classic JDM2	Diagnosis	9.2	F	p155/140	7.0	76	N/A	None
Classic JDM3	Diagnosis	9.4	M	Neg	2.0	58	N/A	Pred, MTX
Classic JDM4	Diagnosis	2.1	F	N/A	5.0	N/A	N/A	None
Classic JDM5	Diagnosis	3.3	M	N/A	2.0	58	N/A	None
Classic JDM6	Diagnosis	7.4	M	N/A	0.8	60	N/A	None
Classic JDM7	Diagnosis	7.9	F	Anti-Jo	24.0	78	N/A	None
Classic JDM8	Active	6.6	M	MJ	7.5	N/A	4/3/1	MTX
Classic JDM9	Active	5.9	M	Neg	38.4	N/A	7.5/5.0/2.5	MTX, HCQ
Classic JDM10	Active	6.2	F	p155/140	4.0	N/A	12/14/8	MTX
Amyo JDM1	Amyopathic	11.9	F	Neg	108.0	N/A	4	HCQ
Amyo JDM2	Amyopathic	4.5	F	MDA	23.0	N/A	6	IVIG, CellCept
Amyo JDM3	Amyopathic	9	F	MDA	5.0	N/A	6	MTX Cellcept
Amyo JDM4	Amyopathic	10.4	M	MDA	57.0	N/A	7	CellCept
Classic JDM 11	Remission	11.2	F	p155/140	72.4	N/A	0/0/0	None
Classic JDM12	Remission	11.8	F	p155/140	75.8	N/A	0/0/0	None
Classic JDM13	Remission	11.2	M	MJ	63.6	N/A	0/0/0	None
Classic JDM14	Remission	13.1	F	p155/140	86.9	N/A	0/0/0	None
Classic JDM15	Remission	5.9	M	Neg	47.0	80	0/0/0	None
Adult HC1	Control	35	M					
Adult HC2	Control	32	M					
Adult HC3	Control	35	F					
Adult HC4	Control	32	F					
Pedi HC1	Control	13.1	F					
Pedi HC2	Control	16.1	M					
Ped HC3	Control	9.2	M					

MMT8, manual muscle testing 8; DAS, disease activity score; pred, prednisone; MTX, methotrexate; HCQ, hydroxychloroquine; IVIG, intravenous immunoglobulin

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Disclosure: K. Hoyt, None; **E. Anderson**, None; **M. L. Curran**, None; **R. Fuhlbrigge**, None; **L. Notarangelo**, None; **L. M.**

Pachman, None; **S. Kim**, None; **L. Henderson**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-lymphocyte-repertoire-in-juvenile-dermatomyositis-2

Abstract Number: 20

Enthesitis-Related Arthritis: Non-Peripheral Pattern is Associated with an Expansion of Peripheral Th17 Populations

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SESSION INFORMATION
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Session Type: Abstract Submissions
Session Time: 4:45PM-5:15PM

Background/Purpose:

Enthesitis-related arthritis (ERA) is a category of juvenile idiopathic arthritis. Different proinflammatory cytokines linked to the Th1 and Th17 T- cell subsets have been implicated in its pathogenesis. Limited data are currently available about the relationship between disease activity and the clinical pattern and the percentage of Th1/ Th17 T- cell subsets. Our objectives were to analyze Th1 and Th17 cell subsets in patients with ERA and to compare with age-matched healthy controls. To assess the association between disease activity and disease clinical pattern with Th1and Th17 cells subsets

Methods: Patients with ERA (according to ILAR criteria) were included in a cross sectional study. Disease activity measures were collected in random visits: active joint count (AJ), pain score (0-10), active enthesitis (AE), sacroiliac pain (SIP) , lumbar pain (LP),lumbar limitation (LL) by Schöber´s test, wellbeing according to the patient using a visual analogue scale (VASp, 0-10), disease activity according to the physician (VASphy), JADAS-10, JSpADA, and ESR were evaluated. Patients were classified based on the articular pattern (peripheral and non-peripheral) depending on the presence or absence of AJ and/or AE. Functional capacity by CHAQ. Presence of radiologic sacroiliitis (MRI/X-rays) and treatment were recorded. Th-17 and Th-1 cells were quantified by flow cytometry in PBMCs stimulated with PMA/IO. Age-matched healthy children without disease or medication were recruited as normal control. Statical analysis:Mann-Whitney U test and correlation tests.

Results: 29 patients (90 % M) fulfilled inclusion criteria. HLA-B27 was positive in 13 (45%). Median age was 12 years and disease duration was 2.1 years at observation. Activity and functional measures were (medians): AJ 1, pain 0.25, VASp 0.5, VASphy 1, JADAS-10 7, JSpADA 1.75, ESR 15 mm/h; CHAQ ≥ 0.5 occurred in 8 patients (27%). AE was present in 1 (3%), SIP in 7 (24 %), LP in 6 (21%), and LL in 12 (41%) children. Nineteen (65%) patients showed JADAS >1 and 21 (76%) JSpADA>0. Radiologic sacroilitis was recorded in 21(72%) children. Fourteen (48%) patients were treated with TNFi. Th1cell percentage in ERA was 8.5±3.4% (range, 4-17.4) while healthy controls was 5.8±3.8% (range, 1.2-14.2), p=0.023. Th17cell% in ERA was 0.90±0.44(range, 0.39-2.34%) while controls was 0,55±0.38 (range, 0,17-1,61%); p=0.004. There was no difference between T-cells and active/inactive disease according scores. Eighteen (62%) children showed peripheral pattern, while 11(38%) exhibited non-peripheral. Peripheral and non-peripheral groups showed Th17% cells 0.90(0.39-1.74) vs 1.14(0.64-2.44) respectively(p=0.018).Significant correlations with Th1: AJ (r=0.45 p=0.004) and with Th17: LP (r=0.83 p=0,0001), LL (r=0.47 p=0.03).

Conclusion:

Th1 and Th17 cells subsets were significantly higher in ERA compared with healthy controls. However, T-cells showed no significant difference between patients with active versus inactive disease.Interestingly, non-peripheral pattern showed higher Th17% cells with respect to patients with peripheral disease pattern. ERA with axial arthritis may benefit most from Th-17 blocking strategies.

Disclosure: M. M. Katsicas, None; **C. Carrara**, None; **A. Bernasconi**, None; **J. Rossi**, None; **R. Russo**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/enthesitis-related-arthritis-non-peripheral-pattern-is-associated-with-an-expansion-of-peripheral-th17-populations

Abstract Number: 21

Enhancing Quality of Care in Childhood-Onset Systemic Lupus Erythematosus by Improving Performance on Quality Indicator Measures in Cardiovascular and Bone Health

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SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Quality, Health Services and Education Research Poster Breakout I
Session Type: Abstract Submissions
Session Time: 4:45PM-5:15PM

Background/Purpose: Childhood-onset SLE (cSLE) leads to poor health outcomes, including cardiovascular and bone health, due to high rates of potentially devastating disease complications and medication toxicities. Initial benchmarking of cSLE quality indicator measures revealed suboptimal performance and significant variation in cardiovascular and bone health processes of care. The aim of this study was to develop a reliable process to improve performance and decrease variability from baseline on bone mineral density testing via dual x-ray absorptiometry (DXA), serum lipid profiles, and serum vitamin D screenings.

Methods: The intervention took place from September 2016 to January 2017 at a tertiary care pediatric rheumatology clinic. Eligible patients with SLE diagnosis code were identified using disease registry functionality within the electronic health record. Rigorous implementation science methodology was applied including process maps, failure modes effect analysis (FMEA), and key driver diagrams. Performance at baseline was benchmarked, and failures were identified through Pareto analysis. Through multiple Plan-Do-Study-Act (PDSA) cycles, we adopted the primary intervention to standardize pre-visit planning and pend orders. Primary outcome measures included percentage of patients with results for a baseline DXA, lipid profile in the past year, and vitamin D in the past year. Performance on these measures was tracked over time using run charts and control charts.

Results: Our baseline performance was DXA in 54%, lipid profile in 54%, and vitamin D screening in 60% of patients. During the intervention period, a total of 77 patients (14% male, mean age 18.4 years) were evaluated. We improved our performance in the intervention group to DXA in 73%, lipid profile in 73%, and vitamin D screening in 79% of patients (Figure 1). The majority of failures were due to add-on clinic visits and patient factors (Figure 2).

Conclusion: We were able to achieve improvement in performance on process measures for cardiovascular and bone

health through standardization of pre-visit planning. We are currently pursuing additional interventions to target patient engagement, education, and self-management support. We are considering further modification of pre-visit planning to better address add-on visits to reach our improvement goal of > 80% reliability. Future plans include adapting this change package to include additional process measures in cSLE, and ultimately measure the impact on health outcomes.

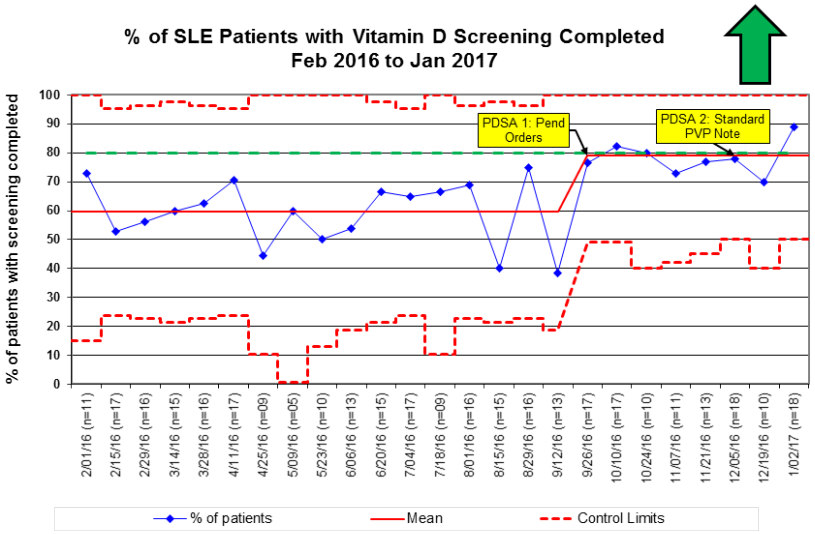

Figure 1. Example control chart for vitamin D screenings.

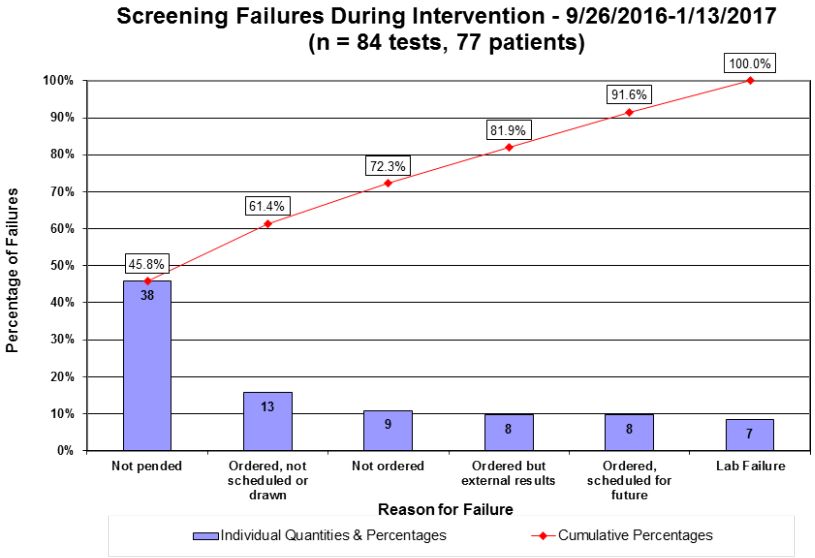

Figure 2. Pareto analysis of reasons for failures for DXA, lipid, and vitamin D screenings.

Disclosure: E. A. Smitherman, None; **A. Furnier**, None; **J. Taylor**, None; **M. B. Burns**, None; **H. Brunner**, None; **E. Morgan**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/enhancing-quality-of-care-in-childhood-onset-systemic-lupus-erythematosus-by-improving-performance-on-quality-indicator-measures-in-cardiovascular-and-bone-health

Abstract Number: 22

Patient perception of barriers to taking medication in Juvenile Idiopathic Arthritis

Gabriela Guefen[1], Kirsten Jenkins[2], Lori Ponder[2], Kelly A. Rouster-Stevens[2,3], Patricia Vega-Fernandez[2,3], Elaine S

Ramsay[2,3], Sheila Angeles-Han[2,3] and Sampath Prahalad[2,3,4], [1]College of Arts and Sciences, Emory University, Atlanta, GA, [2]Children's Healthcare of Atlanta, Atlanta, GA, [3]Pediatrics, Emory University School of Medicine, Atlanta, GA, [4]Human Genetics, Emory University School of Medicine, Atlanta, GA

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Quality, Health Services and Education Research Poster Breakout I

Session Type: Abstract Submissions

Session Time: 4:45PM-5:15PM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) is the most common rheumatic disease of childhood. Treatments include disease modifying anti-rheumatic drugs, commonly methotrexate (MTX), biologics including Etanercept (ETN) and Adalimumab (ADA). However, medication adherence may be impaired by fear of starting medication, access to these medications, or their side effects (barriers). Common side effects of MTX are nausea, abdominal pain, transaminitis, oral ulcers, and leukopenia. Side effects of biologics are infections, possible malignancy, and injection site reactions (ISRs). We describe patient perceptions of potential barriers to medication adherence in JIA.

Methods: We enrolled 101 children diagnosed with JIA and treated with MTX, ETN and/or ADA for at least 3 months or greater than 24 months. Subjects and their parents completed self-administered questionnaires about perceived barriers to medication adherence compliance.

Results: Of all subjects, 96 used MTX alone or with ETN/ADA. One or more barriers to MTX use was reported by 58% of subjects (Table 1) whereas 42% of subjects reported no barriers. While taking MTX, 52% reported nausea/vomiting (Table 2). In all 14% of patients discontinued MTX due to side effects.

ETN was used by 21 patients. One or more barriers to ETN use was reported by 57% of subjects including difficulty with access (19%) whereas 43% of subjects reported no barriers. While taking ETN, 43% reported ISRs as a side effect. In all, 15% discontinued ETN due to side effects.

ADA was used by 35 patients. One or more barriers to ADA use was reported by 71% of subjects, including difficulty with access (31%), whereas no barriers were experienced by 29% of patients. While taking ADA, 63% reported ISRs. In all, 20% of patients discontinued ADA due to side effects.

For all three drugs, patients reported a decrease in their fear after they used them for at least 3 months (Table 1 pre and post). In fact, 65% stated that they wished they had begun a biologic medication sooner.

Conclusion: While a majority of subjects expressed concerns prior to starting medications, these lessened after taking them. A substantial proportion of respondents indicated they would have started a biologic sooner. Providing this information to patients prior to starting biologics may help alleviate their concerns and improve medication adherence.

Table 1. Patient perceived barriers before starting medication (pre) and after being on medication for at least 3 months (post)

Patient Barriers						
Patient Barriers (%)	MTX (n=96)		ETN (n=21)		ADA (n=35)	
	Pre	Post	Pre	Post	Pre	Post
Fear of needles	35	26	29	19	40	34
Fear of side effects	29	31	38	14	34	29
Fear of long term effects	28	19	38	24	31	23
No Barriers	42	43	43	57	29	43

Table 2. Common side effects of methotrexate, etanercept and adalimumab

Patient Side Effects (%)			
	MTX (n=96)	ETN (n=21)	ADA (n=36)
Nausea/Vomiting	52	10	20
Abdominal Pain	31	10	6
Headache	19	14	11
Infections	22	24	9
Injection Site Reaction	26	43	63
Stopped Medication Due to Side Effects	14	15	20

Disclosure: G. Guefen, None; **K. Jenkins**, None; **L. Ponder**, None; **K. A. Rouster-Stevens**, None; **P. Vega-Fernandez**, None; **E. S. Ramsay**, None; **S. Angeles-Han**, None; **S. Prahalad**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/patient-perception-of-barriers-to-taking-medication-in-juvenile-idiopathic-arthritis

Abstract Number: 23

Impact of an Institutional Specialty Pharmacy on Adherence to Biologic Therapies

Kelly Wise[1], Dustin Lewis[2], Bethanne Thomas[2], Karla Jones[3], Stephanie Lemle[2], Darby MacDonald[2], Fatima Barbar-Smiley[2], Vidya Sivaraman[2] and Cagri Yildirim-Toruner[3], [1]Pharmacy/Rheumatology, Nationwide Children's Hospital, Columbus, OH, [2]Nationwide Children's Hospital, Columbus, OH, [3]Rheumatology, Nationwide Children's Hospital, Columbus, OH

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Quality, Health Services and Education Research Poster Breakout I

Session Type: Abstract Submissions

Session Time: 4:45PM-5:15PM

Background/Purpose: Biologic therapies have become a standard of care for many pediatric rheumatic diseases such as juvenile idiopathic arthritis (JIA) and periodic fever syndromes. Biologics, including adalimumab, etanercept, canakinumab, and tocilizumab, are categorized as specialty medications. Specialty medications are generally defined by the following: use in the treatment of complex chronic conditions, high cost (typically >$600 per month), usually requiring special storage, handling, and site-of-care administration, and involving a significant degree of patient education, monitoring, and management. Barriers that can prevent patients from obtaining specialty medications include need for prior authorizations, high copayments, directing prescriptions to the preferred specialty pharmacies, and coordinating delivery of medications from the specialty pharmacy. Pharmacists can be used in the ambulatory setting to aid in procurement and management of specialty medications. Nationwide Children's Hospital (NCH) has instituted a specialty pharmacy for the division of rheumatology to aid in prior authorization, injection teaching, and medication management of select biologic therapies. This is expected to result in increased adherence to treatment and achievement of inactive disease. The primary aim of this pilot study is to assess the medication possession ratio (MPR) for individuals on adalimumab, etanercept, canakinumab, and tocilizumab that were enrolled in NCH Specialty Pharmacy for an index period of October 2016 to January 2017.

Methods: A retrospective review of prescriptions filled at NCH Specialty Pharmacy over a 4 month period assessed overall number of prescriptions, number of specialty prescriptions, patients enrolled, and MPR for adalimumab, etanercept, canakinumab, and tocilizumab. MPR was calculated for patients with >1 fills at NCH Specialty Pharmacy. An MPR of 1 reflects 100% adherence.

Results: In the first four months, NCH Specialty Pharmacy filled a total of 446 prescriptions and 132 specialty medications (adalimumab n=55; etanercept n=37; canakinumab n=19; tocilizumab n=11; other n=10) for 46 rheumatology patients. Average and median MPRs were assessed for adalimumab (0.95, 1) etanercept (0.95, 1), canakinumab (0.99, 1), and tocilizumab (1, 1), respectively. Overall, the average MPR was 0.96 and median MPR was 1.

Conclusion: The implementation of an institutional specialty pharmacy has added services to improve outcomes for children with rheumatic diseases. NCH was able to ensure a median MPR of 1 for all biologics filled at NCH Specialty Pharmacy during the pilot phase. It is expected that improvement in medication adherence will result in achievement of inactive disease. Strategies used by NCH Specialty Pharmacy to maintain an MPR of 1 include coordination of prior authorization, injection teaching by a pharmacist, and medication management consisting of monthly follow up with the patient or caregiver to schedule medication delivery. Rheumatologists at NCH will continue to enroll patients with JIA and other autoinflammatory diseases in NCH Specialty Pharmacy to ensure streamlined care and improved patient outcomes.

Disclosure: K. Wise, None; **D. Lewis**, None; **B. Thomas**, None; **K. Jones**, None; **S. Lemle**, None; **D. MacDonald**, None; **F. Barbar-Smiley**, None; **V. Sivaraman**, None; **C. Yildirim-Toruner**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/impact-of-an-institutional-specialty-pharmacy-on-adherence-to-biologic-therapies

Abstract Number: 24

Development and Implementation of a "Data-In-Once" Model for a Pediatric Rheumatology Learning Health System

Tzielan Lee[1], Sharon Bout-Tabaku[2], Joshua Conkle[3] and Esi Morgan-Dewitt[3], [1]Pediatric Rheumatology, Stanford University School of Medicine, Palo Alto, CA, [2]Nationwide Children's Hospital, Columbus, OH, [3]Cincinnati Children's Hospital, Cincinnati, OH

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Quality, Health Services and Education Research Poster Breakout I

Session Type: Abstract Submissions

Session Time: 4:45PM-5:15PM

Background/Purpose:

Medical institutions are adopting electronic health records (EHR) in accordance with Meaningful Use. This affords the opportunity for standardizing and capturing patient data to build the backbone for registry information serving Learning Health Systems (LHS). LHS leverage clinical data to generate new evidence and knowledge improving clinical practice; ensuring quality, safety, and value; and driving innovation in health care.

The Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN) is a 17 center learning network designed to improve the outcomes of rheumatic disease care. Teams collect and analyze point of care data on process and outcomes that guide improvement activities. Data collection at most centers currently involves manual data entry that is duplicative: (1) patients and providers fill out paper forms; (2) providers document clinical visits in the EHR; (3) staff complete paper case report forms (CRF); and (4) staff enter data from CRFs into the registry database. This time consuming process increases the risk for data entry errors. In addition, patient level EHR data can appear in different areas interfering

with timely viewing, evaluating, and responding.

We describe a PR-COIN and EHR vendor (Epic Systems Corporation) collaboration to design, build, and implement a technical architecture to make clinical documentation more efficient, standardize data collection, improve data display methods, and enable easy access to more informed clinical visits.

Methods:

Development entailed direct interaction of the EHR vendor with three institutions' information systems departments. Twice a month meetings occurred to discuss collection form and note template builds, data element standardization, and process workflows. Our goals were: (1) to support a "data-in-once" strategy for registry data collection minimizing re-work and integrating data capture into routine patient clinical visit documentation; (2) to develop automated pre-visit planning reports embedded in the EHR supporting QI measure compliance and evidence based chronic care patient management.

Results:

Components of the "data-in-once" build developed include: (1) point of care seamless discrete standardized data exchange between the clinical documentation and PR-COIN registry data collection elements within the EHR; (2) capability for ongoing electronic transfer of the EHR PR-COIN registry data to the external PR-COIN registry. Automated pre-visit planning reports are strategically localized in various areas of the EHR for ease of access and use. Four institutions are piloting system implementation with subsequent roll-out planned to other Epic users in the learning network.

Conclusion:

Learning health systems can be the foundation for improved quality of clinical care and patient outcomes. Using the EHR platform to obtain registry data directly from the patient care process, we developed a method to efficiently and unobtrusively collect patient data accelerating the rate of useful data accumulated for analysis with enhanced presentation of clinically meaningful data to users.

Disclosure: T. Lee, None; **S. Bout-Tabaku**, None; **J. Conkle**, None; **E. Morgan-Dewitt**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/development-and-implementation-of-a-data-in-once-model-for-a-pediatric-rheumatology-learning-health-system

Abstract Number: 25

Reliability of the Physician Global Assessment Scores for Determination of Disease Activity Status within the Pediatric Rheumatology Care and Outcomes Improvement Network

Brandt Groh[1], Ottar Kristinsson[2], Lisabeth V. Scalzi[3], C. April Bingham[4], Ronald Laxer[5], Cagri Yildirim-Toruner[6], Esi Morgan[7], Michelle Batthish[8], Beth Gottlieb[9], Julia G. Harris[10], Murray Passo[11], Michael Shishov[12] and Sheetal S. Vora[13], [1]Pediatrics, Penn State Milton S. Hershey Medical Center, Hershey, PA, [2]Pediatrics, Penn State Children's Hospital, Hershey, PA, [3]Department of Rheumatology, Penn State Hershey Children's Hospital, Hershey, PA, [4]Penn State Health Children's Hospital, Hershey, PA, [5]Div of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, [6]Rheumatology, Nationwide Children's Hospital, Columbus, OH, [7]Pediatric rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [8]Division of Pediatric Rheumatology, McMaster Children's Hospital, Hamilton, ON, Canada, [9]Pediatric Rheumatology, Cohen Children's Medical Center of New York, New Hyde Park, NY, [10]Children's Mercy - Kansas City, Kansas City, MO, [11]Division of Rheumatology PTD, Medical University of South Carolina, Charleston, SC, [12]Pediatric Rheumatology, Phoenix Children's Hospital, Phoenix, AZ, [13]Pediatric Rheumatology, Levine Children's Hospital, Charlotte, NC

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Quality, Health Services and Education Research Poster Breakout I

Session Type: Abstract Submissions

Session Time: 4:45PM-5:15PM

Background/Purpose: Within the Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN), the Physician Global Assessment (PhGA) metric is a key determinant of Òclinically inactiveÓ juvenile idiopathic arthritis (JIA)—the target to which all participating centers are encouraged to treat. While reliability has been documented within a single center, it has not been investigated whether or not there may be significant variation in how PhGA is assigned among centers across this network.

This study aims to determine if there is significant PhGA variability among centers across the PR-COIN network.

Methods: 15 PR-COIN centers were included with a total sample size of 5,888 patient entered in the database as of May 1, 2016. Utilizing the most recent PhGA score entered for each patient, we calculated the mean PhGA scores for the following JIA subsets: RF negative poly JIA; RF positive poly JIA; persistent oligo JIA; extended oligo JIA; psoriatic arthritis; enthesitis-related arthritis; and undifferentiated arthritis. To compare PhGA scores among centers, we used either center-specific mean data combining scores for all subtypes or center-specific mean data for a single subtype of interest. One-way ANOVA statistics were calculated to compare means among centers.

Results: Among participating centers, the mean PhGA values for all included ILAR JIA subtypes as a composite were significantly different ($p = 0.04$). PhGA remained significantly different with a restriction of the analysis to the five centers with total enrollments over 500 patients ($n = 3,644$) ($p < 0.0001$) and also with the restriction to a relatively homogeneous subtype, RF negative poly JIA ($n = 1,903$) ($p < 0.0001$). Limiting the analysis both to the larger centers and to the RF negative poly JIA subtype ($n = 1,086$; Table 1) again resulted in a significant difference between PhGA means ($p < 0.0001$). This analysis indicates significant variability of mean PhGA scores among centers. While it remains possible that mean PhGA differences among centers reflect true differences in patient outcomes, it is also possible that the subjective nature of this metric accounts for this variability.

Conclusion: To continue use of PhGA scores in the determination of disease activity in JIA, efforts should be made to better standardize this metric both within and among participating PR-COIN centers. Alternatively, a better defined composite metric could be substituted for the PhGA, or the determination of disease activity could be limited to joint counts. Further study is needed to determine if mean joint count scores correlate well with mean PhGA scores.

Table 1: Physician Global Assessment scores for RF-negative poly JIA patients at PR-COIN centers with total enrollments > 500 patients

Centers	1	2	3	4	5
N	294	182	154	199	257
Mean	4.95	3.71	3.12	3.58	2.65
SD	3.80	3.13	3.41	3.58	3.31
Range	0 – 10	0 – 7	0 – 8	0 – 10	0 - 10

Disclosure: B. Groh, None; **O. Kristinsson**, None; **L. V. Scalzi**, None; **C. A. Bingham**, None; **R. Laxer**, 5; **C. Yildirim-Toruner**, None; **E. Morgan**, None; **M. Batthish**, None; **B. Gottlieb**, 5; **J. G. Harris**, None; **M. Passo**, 5; **M. Shishov**, 5; **S. S. Vora**, None.

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Abstract Number: 26

Gray Matter Volume Loss in Youth with SLE

Andrea Knight[1], Michelle Vickery[2], Arastoo Vossough[3], Guray Erus[4], Jimit Doshi[5] and Susan Furth[6], [1]Center for Pediatric Clinical Effectiveness & PolicyLab, Philadelphia, PA, [2]PolicyLab, Children's Hospital of Philadelphia, Philadelphia, PA, [3]Radiology, Children's Hospital of Philadelphia, Philadelphia, PA, [4]Section on Biomedical Image Analysis, University of Pennsylvania, Philadelphia, PA, [5]Section of Biomedical Image Analysis, University of Pennsylvania, Philadelphia, PA, [6]Division of Nephrology, Children's Hospital of Philadelphia, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Saturday, May 20, 2017
Session Title: Clinical and Therapeutic Poster Breakout II
Session Type: Abstract Submissions
Session Time: 5:15PM-5:45PM

Background/Purpose: Neuropsychiatric SLE in children and adolescents presents diagnostic challenge due to limitations of conventional magnetic resonance imaging (MRI) to detect clinically relevant brain changes. We examined structural brain abnormalities in pediatric-onset SLE (pSLE) utilizing advanced MRI techniques.

Methods: We conducted a cross-sectional analysis of clinically-obtained brain MRI images from subjects with pSLE, and compared them to existing brain MRI images from age and sex-matched controls from another study. All images were obtained between 2007 and 2015 on the same scanner at 3T using a T1-weighted MPRAGE (magnetization-prepared rapid, acquisition gradient echo) protocol. We used an advanced multi-atlas segmentation algorithm to divide the brain into 154 anatomical regions of interest (ROIs), organized hierarchically within larger brain structures. We calculated volumes of individual ROIs and larger brain structures, and compared volumetric measurements from pSLE and control subjects using univariate paired t-tests. ROIs with significant group differences after Bonferroni correction for multiple comparisons ($q<0.01$, where $q=p/\#ROIs$ tested) were reported. A neuroradiologist, blinded to the volumetric results, performed conventional re-reads of MRIs for pSLE subjects.

Results: We matched 28 SLE adolescents to 28 controls, comprised of 89% females with a mean age of 15.9 (SD=3.6). Median disease duration for SLE subjects was 1.1 years (interquartile range, IQR 0.3, 2.9), and median SLEDAI score was 5 (IQR 1, 11). There was a history of nephritis in 12 (43%), seizures and/or stroke in 5 (18%), anti-phospholipid syndrome in 3 (11%), depression and/or anxiety in 18 (64%). Glucocorticoids were used by 89% of pSLE subjects at the time of MRI (median prednisone dose=5 mg, IQR=10,25). Conventional pSLE MRI reads indicated T2 hyperintensities in 48% and mild diffuse volume loss in 28%. Using advanced segmentation, total brain volume did not differ between groups, but volumes in specific gray matter ROIs were significantly decreased in pSLE subjects compared to controls ($q<0.01$). These ROIs are involved in: decision-making, memory, and social cognition (right medial frontal cortex); empathy, emotional memory and processing (right temporal pole, left anterior cingulate gyrus); topographical and facial recognition (right lingual gyrus); language processing (left parietal lateral cortex, bilateral planum polare, frontal operculum); visual and spatial attention (bilateral cuneus).

Conclusion: Compared to healthy peers, children and adolescents with SLE have decreased gray matter volumes in regions involved in executive function, social cognition, language and emotional processing. Future study should examine the functional correlates of these structural brain abnormalities.

Disclosure: A. Knight, None; **M. Vickery**, None; **A. Vossough**, None; **G. Erus**, None; **J. Doshi**, None; **S. Furth**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/gray-matter-volume-loss-in-youth-with-sle

Abstract Number: 27

Assessing the Safety of Kidney Biopsies Performed on Childhood-onset Systemic Lupus Erythmatosus Patients

Shreya Goyal[1], Daniel Ashton[2,3], Kamlesh Kukreja[3,4], Michael C. Braun[5,6] and Scott E. Wenderfer[5,7], [1]Pediatrics, Baylor College of Medicine, Houston, TX, [2]Interventional Radiology, Texas Children's Hospital, Houston, TX, [3]Radiology, Baylor College of Medicine, Houston, TX, [4]Interventional RAdiology, Texas Children's Hospital, Houston, TX, [5]Texas Children's Hospital, Houston, TX, [6]Pediatrics-Renal, Baylor College of Medicine, Houston, TX, [7]Pediatrics-Renal, Baylor College of Medicine, Texas Children's Hospital, Houston, TX

SESSION INFORMATION

Session Date: Saturday, May 20, 2017

Session Title: Clinical and Therapeutic Poster Breakout II

Session Type: Abstract Submissions

Session Time: 5:15PM-5:45PM

Title: Assessing the Safety of Kidney Biopsies Performed on Childhood-onset Systemic Lupus Erythematosus Patients

Background/Purpose:

There is very little data in the literature on the rates of adverse events after percutaneous kidney biopsy specifically in childhood-onset lupus (cSLE) patients. In children with and without SLE, studies show that post-biopsy complication rates range from 5 to 23%. Children with SLE often develop anemia, thrombocytopenia, and/or prothrombotic autoantibodies, which may predispose them to biopsy-related complications. Clinicians would benefit tremendously from scientific evidence specifically addressing whether rates of pain or bleeding differ after kidney biopsy in children with SLE.

Methods:

Inclusion criteria: 1) diagnosis of cSLE according to American College of Rheumatology classification criteria, 2) kidney biopsy between January 1, 2011 and December 31, 2015 at Texas Children's Hospital, and 3) age < 18 years at the time of biopsy. Our cohort included 107 lupus biopsies (77% female, 50% Hispanic, 26% African American, 16% Caucasian, 5% Asian, 2% mixed, 1% Vietnamese). Routine post-biopsy care of cSLE patients includes overnight observation in the hospital. Charts were reviewed for biopsy-related complications both during and after procedures performed by either nephrologists or radiologists. Nephrologists performed 87% and radiologists 13% were performed by radiologists. Procedural complications were classified using the Society of Interventional Radiology (SIR) scale (class A and B minor complications, classes C, D, E, and F major complications). Anesthesia complications were classified using the Surgical Apgar Score (SAS).

Results:

The rate of major complications was 12%. *Table 1* below shows the most common kidney biopsy-related events. No anesthesia complications were observed. There were no deaths, nephrectomies, or permanent disabilities, and >50% of major complications were class C. The most frequent complications were pain (71%) and gross hematuria (12%). One patient required angiography to correct the bleeding and 5 patients had prolonged hospitalization due to biopsy-related complication.

Conclusion:

Percutaneous kidney biopsies are a relatively safe procedure to perform in cSLE patients. Although small perinephric hematomas are common, most are asymptomatic or resolve with acetaminophen alone. The need for IV narcotics to treat pain in a significant portion of our patients justifies the practice of overnight observation following kidney biopsy for this indication. As in biopsies performed for non-SLE indications, the rate of major complications is low.

Table 1: Event Rates following Percutaneous Kidney Biopsy in Children with Systemic Lupus Erythematosus (n=107)

Event	SIRS Classification	N	Percent
Bleeding:			
Perinephric hematoma	A	52	56.5%
Gross hematuria w/ no admission *	A	6	5.%
Gross hematuria w/ <24hr prolonged hospitalization *	C	1	0.9%
Gross hematuria w/ >24hr prolonged hospitalization *	D	3	2.8%
Intervention for Bleeding:			
DDAVP	B	3	2.8%
IR Embolization	C	1	0.9%
Transfusion	C	3	2.8%
Surgery	D	0	0%
Urologic Intervention	D	0	0%
Nephrectomy	E	0	0%
Pain:			
Need for acetaminophen	B	35	32.7%
Need for oral narcotics	B	1	0.9%
IV Narcotics w/ no admission *	B	27	25.2%
IV Narcotics w/ <24hr prolonged hospitalization *	C	1	0.9%
IV Narcotics w/ >24hr prolonged hospitalization *	D	1	0.9%
Prolonged Length of Stay:			
Outpatients, admitted <24hr	C	1	1.8%
Inpatients, prolonged 24-48hr	C	2	3.9%
Outpatients, admitted >24hr	D	2	3.6%
Other Complications:			
AV fistula requiring intervention	E	0	0%
Infection	C	1	0.9%

*an additional hospitalization beyond 23-hour observation

Disclosure: S. Goyal, None; **D. Ashton**, None; **K. Kukreja**, None; **M. C. Braun**, None; **S. E. Wenderfer**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/assessing-the-safety-of-kidney-biopsies-performed-on-childhood-onset-systemic-lupus-erythmatosus-patients

Abstract Number: 28

Dyslipidemia in Juvenile Dermatomyositis

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Northwestern University Feinberg School of Medicine, Department of Pediatrics, Chicago, IL, [7]Program of Excellence in Cure-Juvenile Myositis (JM) Research, Stanley Manne Children's Research Institute, affiliated with Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, [8]Cure JM Program of Excellence in Juvenile Myositis Research, Stanley Manne Children's Research Institute, affiliated with Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, [9]Rheumatology/Immunology, Ann & Robert H. Lurie Children's Hosptial of Chicago, Chicago, IL

SESSION INFORMATION

Session Date: Saturday, May 20, 2017

Session Title: Clinical and Therapeutic Poster Breakout II

Session Type: Abstract Submissions

Session Time: 5:15PM-5:45PM

Background/Purpose: Juvenile Dermatomyositis (JDM) is a multisystem pediatric autoimmune disease characterized by chronic inflammation of muscle and skin. Premature atherosclerosis is an important cause of mortality in adults with rheumatic diseases, which is attributed to chronic inflammation, hypertension and dyslipidemia (low HDL and elevated triglyceride). Older patients who had JDM in childhood have higher risk of atherosclerosis evident by increased intima media thicknes and cardiovascular damage. There are limited data on the prevalence of dyslipidemia in children with JDM.

Methods: This was a retrospective study conducted at The CureJM Center, Ann & Robert H. Lurie Children's Hospital. We included all JDM patients (n= 210, 73% female) who had either a random (n= 65) or fasting lipid profile (n= 145) and a disease activity score close to the time of sampling. Based on the 2011 AAP guidelines for cardiovascular health, the lipid profile data was divided into three groups: acceptable, borderline and abnormal. One way ANOVA was conducted to compare the means of these three groups using SPSS. IRB approval was obtained (IRB# 2012-14858).

Results: 210 JDM patients (145 with fasting lipid profile) were included in this study. 32% of the patients had elevated fasting triglyceride (TG) level. One third of the subjects had low HDL (Table 1). Elevated fasting TG is associated with higher Skin, Muscle and Total Disease Activity Score (DAS) (Table 2). Surprisingly, there was no significant correlation between abnormal fasting TG level and lipodystrophy, which can be explained by the high prevalence of abnormal TG, not only in lipodystrophy patients, but also in the other groups, who were each taking a range of immunosuppressive medications.

Conclusion: We found that many JDM patients have elevated fasting TG (32%) and/or low HDL (30%), which is similar to the reported dyslipidemia in other rheumatic diseases. Of note, dyslipidemia in this study was associated with an increased Total Disease Activity Score, raising the possibility that chronic inflammation may contribute to the generation of dyslipidemia in JDM. On the other hand, this association could be due to immunosuppressive medications such as corticosteroids. We suggest annual monitoring of lipid profile in JDM patients with early institution of dietary intervention and exercise, for this high prevalence of dyslipidemia is associated with an increased risk of cardiovascular disease in adults with JDM in childhood.

Table 1: Prevalence of Dyslipidemia in JDM Patients

	Triglyceride		LDL		HDL		Total Cholesterol	
	Fasting	Random	Fasting	Random	Fasting	Random	Fasting	Random
Acceptable	76 (53%)	24 (38%)	111 (84%)	30 (71%)	79 (57%)	35 (76%)	107 (74%)	38 (58%)
Borderline	22 (15%)	10 (16%)	15 (11%)	7 (17%)	18 (13%)	1 (2%)	29 (20%)	16 (25%)
Abnormal	46 (32%)	29 (46%)	6 (5%)	5 (12%)	42 (30%)	10 (22%)	9 (6%)	11 (17%)

Table 2: Association of Fasting Triglyceride Level and Disease Activity Score

Fasting TG	Age (years)	Disease duration (months)	Skin DAS	Muscle DAS	Total DAS	BMI percentile
Acceptable	14.2 ± 4.9 ***	88 ± 54	2 ± 2.6*	1.5 ± 2.3 **	3.5 ± 4.2 **	61.1 ± 31
Borderline	10.4 ± 4.1 ***	63 ± 46	2 ± 2.1*	1.9 ± 2.6 **	3.9 ± 4.2 **	75.3 ± 33
Abnormal	9.1 ± 4.2 ***	70 ± 196	3.4 ± 3.1*	2.9 ± 3.2 **	6.3 ± 5.7 **	67 ± 31.

* P value <0.05 ** P value <0.01 *** P value <0.001

Disclosure: A. Kadakia, None; **A. Khojah**, None; **G. A. Morgan**, None; **M. L. Curran**, None; **I. Benuck**, None; **C. C. Huang**, None; **D. Xu**, None; **L. M. Pachman**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/dyslipidemia-in-juvenile-dermatomyositis

Abstract Number: 29

Spinal Cord Inflammation in Children with Small Vessel Primary CNS Vasculitis

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SESSION INFORMATION

Session Date: Saturday, May 20, 2017

Session Title: Clinical and Therapeutic Poster Breakout II

Session Type: Abstract Submissions

Session Time: 5:15PM-5:45PM

Background/Purpose: Small vessel childhood primary angiitis of CNS (SVcPACNS) is an increasingly recognized inflammatory brain disease requiring rapid targeted investigation and initiation of tailored therapies to prevent brain damage. Spinal cord involvement has never been systematically investigated. Objective: To determine the presenting clinical and laboratory features, neuroimaging, treatment and outcome of children with spinal cord involvement in SVcPACNS.

Methods: A single center cohort study of children with small vessel primary CNS vasculitis diagnosed between 2002 and 2016 was conducted. Children were included, if they were 1) age ≤18years, 2) met Calabrese criteria and 3) had evidence of spinal cord inflammation. Data were captured in the BrainWorks database. Outcome: Neurological function at 12 months was determined using the Pediatric Stroke Outcome Measure; secondary outcomes included the estimated disease activity and damage.

Results: A total of 158 children were diagnosed with primary CNS vasculitis; 52 (33%) were found to have SVcPACNS, of whom 20 had spinal cord imaging for clinical concerns. These were 13 girls and 7 boys; median age was 10.1 years (range 5.4-17.7). The median time from onset of symptoms to diagnosis was 57 days (range 10-1041). A total of 11 (55%) had evidence of spinal inflammatory lesions on MRI. Their clinical features at diagnosis included hemiparesis (13), visual impairment (10), optic neuritis (4) and status epilepticus (4). At diagnosis, 8/9 tested (89%) had abnormal serum inflammatory markers (ESR 6/9, CRP 3/9) or vWF antigen (3/7, 42%). Raised CSF cell count was seen in 7/9 (78%). Imaging: 21 lesions were detected; the spinal lesion load was 1.9 per patient. Distribution: Nine lesions were located in

the cervical, 10 in the thoracic and 2 in the lumbar spine. 17 lesions (81%) were long segments (> 3 vertebrae). Gadolinium enhancement was seen in 7/9 (78%), cord swelling in 3/11 (27%). All children were treated with the BrainWorks SVcPACNS protocol. Outcome: A total of eight patients (73%) had a no functional neurological deficit at 12 months. The median disease activity was 3/10 (range 0.5-8) and estimated disease damage 1/10 (range 0.1-3) at 12 months.

Conclusion: One in five children with brain biopsy confirmed primary CNS vasculitis had symptomatic spinal cord inflammation. The differential diagnosis of myelitis should include SVcPACNS. Rapid diagnosis and targeted therapy may improve the outcome.

Disclosure: A. Dropol, None; **N. Dhillon**, None; **M. Twilt**, None; **F. Nishat**, None; **S. Sheikh**, None; **H. Branson**, None; **S. Benseler**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/spinal-cord-inflammation-in-children-with-small-vessel-primary-cns-vasculitis

Abstract Number: 30

Cross-sectional Analysis of Depression and Medication Non-Adherence in Childhood-onset Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Saturday, May 20, 2017

Session Title: Clinical and Therapeutic Poster Breakout II

Session Type: Abstract Submissions

Session Time: 5:15PM-5:45PM

Background/Purpose: The objectives of this study were to estimate prevalence of depression and medication non-adherence, describe demographic and disease characteristics associated with depression and medication non-adherence, and evaluate the association between depression and medication non-adherence among patients with childhood-onset systemic lupus erythematosus (cSLE).

Methods: Participants (n = 51) completed validated screening tools to identify depression and medication non-adherence, Patient Health Questionnaire-9 (PHQ-9) and Medication Adherence Self-report Inventory (MASRI), respectively. Eligibility criteria included a diagnosis of cSLE confirmed using the American College and Rheumatology or Systemic Lupus International Collaborating Clinics classification criteria, presence of prescribed medication for management of SLE for at least 1 month, and ability to complete the consent form and study questionnaires in English. Demographic and disease characteristics for each enrolled participant were obtained via chart abstraction and compared between groups of depression and medication non-adherence. A multivariable linear regression model adjusting for propensity scores was conducted to evaluate the association between depression and medication non-adherence.

Results: The prevalence of a positive depression screen was 58.8% and four patients reported suicidal ideation (13.7%). The prevalence of self-reported medication non-adherence was 19.7%. There were no statistically significant differences for measured demographic and disease characteristics between patients with a positive vs. negative depression screen. Patients reporting medication non-adherence were more likely to have longer disease duration (2.6 vs. 4.8 years, $p = 0.035$). As the severity of depression symptoms increased, the degree of medication non-adherence also increased ($\beta = -1.89$; $p = 0.011$).

Conclusion: The prevalence of depression and medication non-adherence is high in cSLE, and these two factors are

directly related. Prospective, multi-center studies are needed to better characterize the relationship between depression and medication non-adherence to inform development of interventions that address these factors and improve outcomes in cSLE.

Table 1: Demographics and Disease Characteristics by Depression Screen

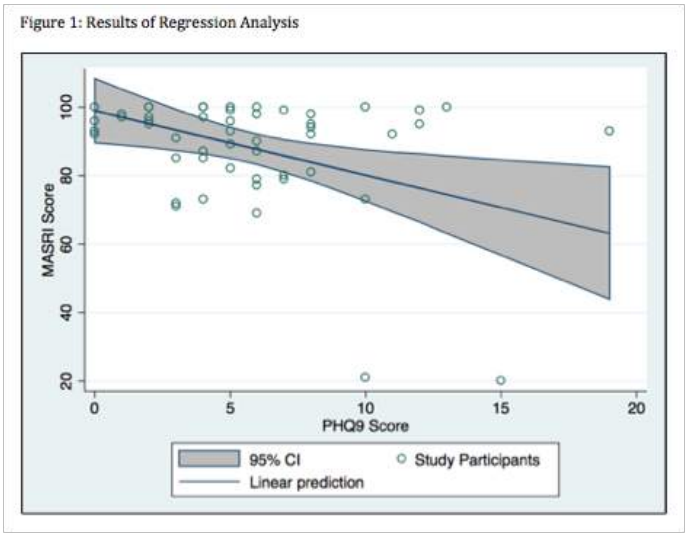
	PHQ-9 score < 5 N = 21	PHQ-9 score ≥ 5 N = 30	p-value
Age (years)	16.3 ± 3.0	16.0 ± 3.6	0.721
Sex			
Male	3 (14.3)	1 (3.3)	0.293
Female	18 (85.7)	29 (96.7)	
Race/Ethnicity			
Caucasian	8 (38.1)	7 (23.3)	
Black	8 (38.1)	19 (63.3)	0.098
Hispanic	3 (14.3)	0 (0)	
Asian	2 (9.52)	3 (10.0)	
Other	0 (0)	1 (3.3)	
Insurance			
Commercial	8 (38.1)	13 (43.3)	0.639
Medicaid	12 (57.1)	17 (56.7)	
Tricare	1 (14.8)	0 (0)	
Age at diagnosis (years)	13.6 ± 2.5)	12.8 ± 3.3	0.602
Disease duration (years)	2.8 ± 2.6	3.2 ± 3.2	0.841
SLEDAI score	4.7 ± 4.0	5.4 ± 5.6	0.953
No. of medications	6.0 ± 2.4	7.3 ± 2.9	0.153
Oral Steroids			
No	5 (23.8)	2 (6.7)	0.109
Yes	16 (76.2)	28 (93.3)	
Prednisone dose (mg/kg/day)	0.12 ± 0.09	0.14 ± 0.12	0.471
Presence of lupus nephritis	6 (28.6)	14 (46.7)	0.193
Receives mental health services	4 (19.0)	12 (40.0)	0.112

Values are presented as mean ± standard deviation (SD) or N (%). An asterisk (*) indicates statistical significance ($p \leq 0.05$).

Table 2: Demographics and Disease Characteristics by Medication Adherence

	MASRI score ≥ 80 N = 41	MASRI score < 80 N = 10	p-value
Age (years)	16.3 ± 4.3	16.1 ± 3.1	0.591
Sex			
Male	4 (9.8)	0 (0)	0.573
Female	37 (90.2)	10 (100)	
Race/Ethnicity			
Caucasian	11 (26.8)	4 (40.0)	
Black	21 (51.2)	6 (60.0)	0.788
Hispanic	3 (7.3)	0 (0)	
Asian	5 (12.2)	0 (0)	
Other	1 (2.4)	0 (0)	
Insurance			
Commercial	17 (41.5)	4 (40.0)	1.00
Medicaid	23 (56.1)	6 (60.0)	
Tricare	1 (2.4)	0 (0)	
Age at diagnosis (years)	13.4 ± 2.9	11.7 ± 3.2	0.096
Disease duration (years)	2.6 ± 2.7	4.8 ± 3.2	0.035*
SLEDAI score	5.5 ± 5.3	3.4 ± 3.1	0.359
No. of medications	6.5 ± 2.8	7.8 ± 3.0	0.144
Oral Steroids			
No	4 (12.2)	2 (20.0)	0.612
Yes	36 (87.8)	8 (80.0)	
Prednisone dose (mg/kg/day)	0.14 ± 0.11	0.08 ± 0.06	0.162
Presence of lupus nephritis	15 (36.6)	5 (50.0)	0.486
Receives mental health services	10 (24.4)	6 (60.0)	0.054

Values are presented as mean ± standard deviation (SD) or N (%). An asterisk (*) indicates statistical significance ($p \leq 0.05$).



Disclosure: A. M. Davis, None; **T. B. Graham**, None; **Y. Zhu**, None; **M. L. McPheeters**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/cross-sectional-analysis-of-depression-and-medication-non-adherence-in-childhood-onset-systemic-lupus-erythematosus

Abstract Number: 31

Predicting therapy response to IL-1 blockade in systemic JIA: a biomarker search

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SESSION INFORMATION
Session Date: Saturday, May 20, 2017
Session Title: Genetics and Pathogenesis Poster Breakout II
Session Type: Abstract Submissions
Session Time: 5:15PM-5:45PM

Background/Purpose: Systemic onset juvenile idiopathic arthritis (sJIA) is an autoinflammatory disease, characterized by fever, rash and arthritis. The IL-1 and IL-6 pathway are crucial in sJIA, exemplified by excellent responses to IL-1 and IL-6 blocking therapy. However, so far it has not been feasible to base treatment choice on individual inflammatory characteristics of patients. Moreover, we cannot predict which patients can safely stop therapy in inactive disease. Here, we aim to identify biomarkers that predict which sJIA patients will respond to IL-1 blockade and which patients will sustain clinical remission when IL-1 blockade is stopped in clinically inactive disease.

Methods:

All patients were treated with recombinant human IL-1 receptor antagonist (rhIL1RA) as first-line therapy. If the response

to rhIL1RA was insufficient, either low dose corticosteroids were added or the patients were switched to other biologicals. If patients acheived clinically inactive disease at time point 3 months after start of rhIL1RA, we attempt to taper and stop rhIL1RA. Biomarker discovery was performed in the serum of patients at onset (before start of rhIL1RA) and at time point 3 months in patients with clinically inactive disease on rhIL1RA, using cytokine analysis (Luminex multiplex assay), determination of S100A12 and Mrp8/14 (ELISA) and miRNAs (qPCR). We used Mann-Whitney U tests, with false discovery rate (FDR) correction by Benjamini-Hochberg methodology.

Results: In total, serum of 19 patients at disease onset and 20 patients at inactive disease was available. Fifty-five proteins and 10 miRNAs were significantly different between patients at onset and at inactive disease after FDR-correction. Proteins included known biomarkers as S100A12, Mrp8/14, IL-6 and IL-18, but also novel markers including metalloproteinases and angiogenesis-related proteins.

Within the onset patients, thirteen patients had a complete response with rhIL1RA monotherapy (CR), while five patients needed additional therapy/switch of therapy (NR) because of persistent fever (n=2), arthritis (n=2) or both fever and arthritis (n=1). One patient had a partial response on rhIL1RA monotherapy. On univariate (uncorrected) testing, 3 proteins and 35 miRNAs were significantly different between CR and NR. After FDR-correction none remained significant.

In the stop-prediction part of this study, ten patients flared during tapering or stopping therapy, while nine patients remained in remission. The PCA of the Luminex data showed that patients that will flare cluster separately from patients that will maintain clinical remission. On univariate analysis, 16 proteins and 2 miRNAs were significantly different, however none were significant after FDR correction.

Conclusion: This study aimed to identify novel biomarkers for the prediction of treatment response to rhIL1RA in new-onset sJIA patients. Although in our small cohort no markers tested significantly after FDR correction, our results provide potentially interesting novel biomarkers that need further modelling and validation.We recently started a prospective study optimising our stop-strategy of rhIL1RA, providing the opportunity to validate the predictive value of suggested biomarkers.

Disclosure: N. M. ter Haar, None; **R. C. Scholman**, None; **W. de Jager**, None; **N. Ryter**, 3; **A. de Ganck**, 3; **D. Foell**, 2; **S. de Roock**, None; **B. Vastert**, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/predicting-therapy-response-to-il-1-blockade-in-systemic-jia-a-biomarker-search

Abstract Number: 32

High Mobility Group Box 1 Protein in Children with Kawasaki Disease and Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION
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Session Type: Abstract Submissions
Session Time: 5:15PM-5:45PM

Background/Purpose: High Mobility Group Box 1 Protein (HMGB1) is a nuclear protein that stabilizes DNA and modulates gene expression. In sepsis and in certain other systemic inflammatory conditions HMGB1 is released

extracellularly to mediate an array of cell signaling pathways that promote downstream release of pro-inflammatory cytokines. Elevated blood levels of HMGB1 are found in association with sepsis and a variety of conditions characterized by systemic inflammation. The purpose of this study was to determine if HMGB1 levels could serve as a discriminating biomarker in early Kawasaki Disease (KD) compared to new onset systemic juvenile idiopathic arthritis (sJIA).

Methods: Children (age ≤ 16 years) with KD and, for comparison, those with sepsis (systemic inflammatory response syndrome or bacteremia) and other non-infectious/non-inflammatory conditions were prospectively enrolled at the time of hospital admission. Prospectively collected data from new onset, treatment naive sJIA participants were derived from the BBOP Study (Biologically-based Outcome Predictors in JIA; www.bbop.ca). Blood was collected in P100 vacutainers (BD) and plasma stored at -80^{0}C until assayed. HMGB1 was measured in duplicate (1:100 dilution) by enzyme immunoassay (Biomatrix). Inter-group differences were compared by independent samples t tests and correlations by Pearson correlation coefficients.

Table: HMGB1 Levels in Study Groups

Diagnosis	N (%)	Mean HMGB1 (±SD) pg/ml
KD	14 (20)	1026±306
Systemic JIA	23 (33)	425±478
Sepsis	26 (37)	829±728
Other	7 (10)	519±502

Results: The study population comprised 70 participants (Table). HMGB1 levels were significantly higher in KD compared to sJIA (t= 4.19; p<.001; CI= 310-892) and to patients with other conditions (t=2.89; p=.009; CI=140-875) but were not different from HMGB1 levels in sepsis (t=.82; p=0.42; CI=-246-582). Participants with sJIA had significantly lower levels of HMGB1 compared to those with sepsis (t=2.42; p=.019; CI=73-792) and did not differ from those with other conditions. HMGB1 levels were significantly higher in younger children (r=.26); children 3 years of age or younger had higher HMGB1 levels than those older than age 3 (p=.028; CI=34-600). There was no correlation between HMGB1 levels and c-reactive protein in any of the groups. No sex differences in HMGB1levels were observed.

Conclusion: Results of this study show that HMGB1 levels are significantly higher in children with KD than in sJIA and comparable to levels seen in children with sepsis. HMGB1 levels in sJIA are not different than in children with other non-infectious/non-inflammatory conditions. Further prospective studies in larger cohorts are required to determine if HMGB1 could serve as a biomarker to predict disease course and outcomes in KD and as an early biomarker useful for distinguishing KD from sJIA. Results suggest that HMGB1 has a role in mediating KD pathogenesis and that HMGB1, as a pro-inflammatory mediator, might be a potential target for biologically-based therapy in acute KD.

Disclosure: H. Y. Ng, None; **S. Slomp**, None; **T. Wilson-Gerwing**, None; **J. Dietz**, None; **A. Lodhi**, None; **T. Holt**, None; **A. Rosenberg**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/high-mobility-group-box-1-protein-in-children-with-kawasaki-disease-and-systemic-juvenile-idiopathic-arthritis

Abstract Number: 33

An extracellular ionic milieu renders human granulocytic S100A12 into a pro-inflammatory TLR4-binding alarmin

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SESSION INFORMATION

Session Date: Saturday, May 20, 2017

Session Title: Genetics and Pathogenesis Poster Breakout II

Session Type: Abstract Submissions

Session Time: 5:15PM-5:45PM

Background/Purpose: Granulocytic S100A12 is a member of the calgranulin-subgroup within the S100 family of calcium-binding proteins. Similar to other S100 proteins S100A12 can bind divalent metal ions, preferentially Ca^{2+} and $Zn^{2+}$and subsequently arrange into different homo-multimeric complexes. Although S100A12 is highly overexpressed in auto-inflammatory diseases such as systemic juvenile idiopathic arthritis (sJIA) or familial mediterenean fever (FMF) the protein's intracellular function is poorly defined. Yet, it is well accepted that once released from granulocytes S100A12 can operate as damage associated molecular pattern (DAMP) molecule or 'alarmin'. In this function S100A12 was originally reported as ligand of the receptor for advanced glycation endproducts (RAGE), while we recently described human monocytes to respond to S100A12 stimulation in an exclusively toll like receptor 4 (TLR4)-dependent manner.

Methods: Oligomers of recombinant as well as native S100A12 were isolated from serum samples and freshly isolated human granulocytes after cross-linking. Eluted S100A12 oligomers from patients' serum were further applied to size exclusion chromatography. TLR4/MD2-binding assay and surface plasmon resonance assays were performed to investigate ligand-receptor interactions. Monocytic cells lines and primary human monocytes were used for stimulation experiments using defined S100A12 complexes.

Results: Here we demonstrate that binding and signaling of S100A12 through TLR4 is dependent on the protein's arrangement into a hexameric quarternary structure. Hexameric S100A12 triggers pro-inflammatory cytokine production by human monocytes and TLR4-expressing cell lines, which is sensitive to TLR4 and CD14 but not MD2 blockade. Importantly, the arrangement of S100A12 into its hexameric structure appears to depend on extracellular Ca^{2+} and Zn^{2+}ion strengths. While S100A12-hexamers are not detectable inside human granulocytes, these protein complexes can be found in and isolated from human serum specimens, particularly sera obtained from patients with auto-inflammatory disease.

Conclusion: Our data demonstrate that extracellular ion levels can serve as a molecular switch rendering a protein with non-inflammatory cell-intrinsic function into a pro-inflammatory DAMP. Hexameric S100A12 complexes are responsible for the pro-inflammatory functions of the protein. A detection system specifically quantifying its hexameric forms in human serum will improve the performance of S100A12 biomarker assays. Specific blockade of hexameric S100A12 may provide a novel therapeutic target.

Disclosures: The authors declare no conflict of interest. The described findings and principles are part of an international patent application (WO2016/178154A1).

Disclosure: C. Kessel, None; **S. Fuehner**, None; **B. Zimmermann**, None; **D. Holzinger**, None; **H. Wittkowski**, None; **C. Hinze**, None; **D. Foell**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/an-extracellular-ionic-milieu-renders-human-granulocytic-s100a12-into-a-pro-inflammatory-tlr4-binding-alarmin

Abstract Number: 34

The SLCO1B1 *14 Allele is Associated with Poor Response to Subcutaneous Methotrexate in Patients with Juvenile Idiopathic Arthritis

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SESSION INFORMATION

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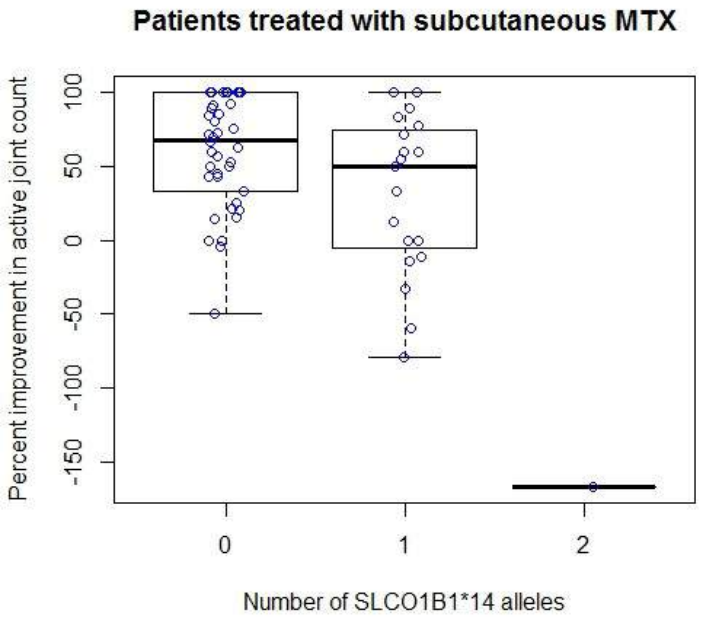
Session Time: 5:15PM-5:45PM

Background/Purpose: Variants in the *SLCO1B1* gene, encoding a hepatic methotrexate (MTX) transporter, affect clearance of high-dose MTX in leukemia patients. We aimed to assess the influence of this gene on the response to MTX in juvenile idiopathic arthritis (JIA) patients.

Methods: 314 JIA patients treated with methotrexate monotherapy enrolled in the local clinic over more than 30 years or in multi-center gene expression studies comprised the initial cohort. Active joint counts at baseline and follow up (visit closest to six months of treatment) were available for all patients and used to evaluate response. Patients were excluded if they had less than two active joints (n=3) at the baseline visit, had Down Syndrome (n=3), if their subtype was ERA (n=3) or systemic (n=8). Data on the route of administration of MTX was available on 174 patients. Genotyping of 3 SNPs in *SLCO1B1* (rs4149056, rs2306283 and rs11045819) was performed successfully on 286 patients with TaqMan probes or available from genome-wide arrays. A patient's *SLCO1B1* diplotype was determined by these three SNPs that make up the *1a, *1b, *4, *5, *14 and *15 alleles. Percent change in active joint count at follow-up was used as the dependent variable in a linear regression.

Results: In a univariate analysis, the *SLCO1B1* *14 allele was associated with less response to MTX (p=0.048). In univariate analyses for other variables, the route of administration of MTX and sex were marginally associated with response (better response with subcutaneous MTX and in females, p=0.07 for each). Variables tested but not associated with response to MTX were: number of active joints at baseline, MTX dose at baseline, follow-up time, age, race, and JIA subtype. In a multivariate model including sex (p=0.04), route (p=0.06) and number of *14 alleles (p=0.09), 4% of the variability in response was explained. Among the 286 patients included in the study, there were 62 patients treated with subcutaneous MTX. The *14 allele explains 18.7% of the variability in response (p=0.00026) in the patients where MTX was administered subcutaneously (Figure) but is not associated with response in the 112 patients treated with oral MTX.

Conclusion: The *SLCO1B1**14 allele may be associated with poor response to subcutaneous MTX for JIA patients. This allele has been associated with fast clearance and low exposure after high dose MTX in leukemia patients. Thus, the *SLCO1B1* *14 allele may be informative for precision dosing of MTX in JIA patients. Patients carrying this allele may require a higher dose than non-carriers to achieve a similar response to subcutaneous MTX.



Lovell, 5,2; **S. D. Thompson**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-slco1b1-14-allele-is-associated-with-poor-response-to-subcutaneous-methotrexate-in-patients-with-juvenile-idiopathic-arthritis

Abstract Number: 35

Kv1.3 Expression on Urinary Leukocytes in Lupus Nephritis: Potential for Targeted Immunotherapy

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SESSION INFORMATION
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Session Title: Genetics and Pathogenesis Poster Breakout II
Session Type: Abstract Submissions
Session Time: 5:15PM-5:45PM

Background/Purpose: Lymphocyte activation depends upon a calcium signaling cascade that is regulated by voltage-gated potassium channels. Effector memory T cells (T_{EM}), which are implicated in the immunopathogenesis of a panel of autoimmune diseases, dramatically upregulate the potassium channel Kv1.3, and become dependent on it for cytokine expression and proliferation. Dalazatide is a potent peptide inhibitor of the Kv1.3 channel that has shown potential efficacy in a Phase 1b plaque psoriasis trial. That inflammatory cytokine producing T_{EM} cells have been implicated in in the pathogenesis of lupus nephritis suggests that targeting Kv1.3 may be a successful strategy in lupus nephritis as well.

Methods: Urinary cells were isolated from patients with systemic lupus erythematosus (SLE). Immunofluorescence was performed to quantify and characterize cells expressing Kv1.3. Peripheral blood T lymphocyte subsets were assayed *ex vivo* for Kv1.3 expression by flow cytometry. The effect of dalazatide on phorbol myristate acetate (PMA)/ionomycin-induced inflammatory cytokine expression by T_{EM}cells was evaluated by intracellular cytokine staining.

Results: In the urine, cells expressing Kv1.3 were found in every subject studied. Kv1.3 expression was detected on CD3+ lymphocytes in 13 of 13 samples studied (mean of 52%,range 10-100%). In 4 of 6 samples, Kv1.3 was detected on CD20+ B lymphocytes (mean 35%, range 0-100%), and CD14+ monocytes/macrophages (mean 50%, range 0-100%).

In the blood, Kv1.3 expression by $CD8^+$ T_{EM} cells was significantly higher in patients with active lupus nephritis when compared to patients with inactive SLE or healthy controls. Dalazatide inhibited IFN-g, IL-17 and TNF-a production by both $CD4^+$ and $CD8^+$ T_{EM} cells from SLE patients in a dose-dependent manner. Higher levels of dalazatide-mediated inhibition were observed in IFN-g and TNF-a-expressing $CD4^+$ T_{EM}cells from patients with active SLE when compared to samples from SLE patients with inactive disease.

Conclusion: Kv1.3 is detectable on urinary B lymphocytes, T lymphocytes, and macrophage, implying that inflammatory cells in the kidney may be targeted by this channel. Peripheral blood cell expression and functional data suggest that SLE T cells are more susceptible to inhibition by dalazatide than healthy T cells.

Disclosure: A. Stevens, 2,7; **A. Hinkle**, None; **M. Yuasa**, None; **D. Peckham**, 3; **C. Olsen**, 3; **C. Philips**, 3; **S. P. Iadonato**, 3; **P. Probst**, 3.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/kv1-3-expression-on-urinary-

leukocytes-in-lupus-nephritis-potential-for-targeted-immunotherapy

Abstract Number: 36

The Association of Obesity with Pediatric Psoriatic Arthritis

Cynthia Manos[1], Rui Xiao[2], Timothy G. Brandon[1], Alexis Ogdie-Beatty[3] and Pamela Weiss[4], [1]Rheumatology, Children's Hospital of Philadelphia, Philadelphia, PA, [2]Department of Biostatistics and Epidemiology, University of Pennsylvania, Philadelphia, PA, [3]Rheumatology, Hospital of the University of Pennsylvania, Philadelphia, PA, [4]Division of Rheumatology, Center for Pediatric Clincial Effectiveness, Children's Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION

Session Date: Saturday, May 20, 2017

Session Title: Quality, Health Services and Education Research Poster Breakout II

Session Type: Abstract Submissions

Session Time: 5:15PM-5:45PM

Background/Purpose: Obesity is associated with a significantly increased risk of inflammatory arthritis in adult patients with psoriasis. Obese adults with psoriatic arthritis (PsA) also have more difficult to treat arthritis, however weight loss may improve their response to treatment. It is not yet known if obesity plays a role in the development of arthritis in children with psoriasis. We evaluated the association of obesity with pediatric psoriasis and PsA.

Methods: We conducted a retrospective cohort study of children with psoriasis and PsA enrolled in The Health Improvement Network (THIN) database between 1994 and 2015. All psoriasis, PsA, and arthritis, cases in the cohort had ≥ 1 READ code for psoriasis, psoriasis and arthritis, or arthritis, respectively. Controls were matched on age, sex, and practice at a 5:1 ratio. Age- and sex-specific z-scores for BMI (zBMI) were calculated. Differences in demographic and clinical characteristics, including overall prevalence of obesity, were assessed using the t-test, test for the equality of proportions, and Wilcoxon rank sum test. Cox proportional hazard regression was performed to assess risk of developing arthritis in children with psoriasis who were overweight or obese compared to normal or underweight, adjusting for age and sex.

Results: There were 234 children with PsA, 6036 with other types of arthritis, 13162 with psoriasis, and 63262 controls. Median age at PsA diagnosis was 11.3 (IQR 7.8-14.0) years and psoriasis diagnosis was 10.1 (IQR 6.9-13.1) years. Amongst those children who had both psoriasis and arthritis, approximately 2/3 developed psoriasis first. Figure 1 shows the probability of remaining arthritis-free in psoriasis patients. Overall, the risk of arthritis was low among psoriasis patients with a cumulative probability of approximately 2.6% during the follow-up period. Approximately half of the children with psoriasis who went on to develop arthritis did so within 5.5 years of the diagnosis of psoriasis. As shown in Table 1, patients with psoriasis had a significantly higher zBMI compared to healthy controls (p <0.001). Arthritis patients had a significantly lower zBMI than controls (p 0.03). Although the difference did not reach statistical significance, PsA patients also had a smaller zBMI than controls. There was no significant association between zBMI at time of psoriasis diagnosis and risk of later developing arthritis (HR 0.87, p 0.10).

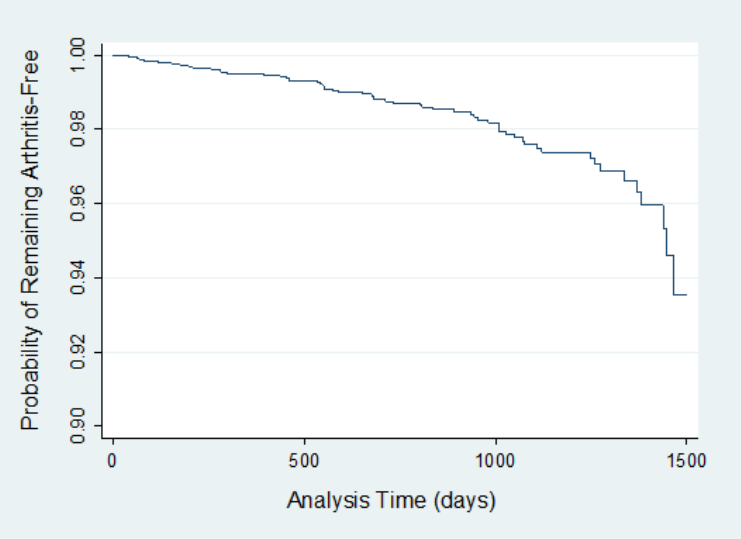
Conclusion: In contrast to adult data, obesity was not associated with development of psoriatic arthritis in children. Moreover, children with arthritis, including PsA, were leaner than the control population.

Table 1: Comparison of Mean zBMI in Psoriasis, Arthritis, and Healthy Controls

	PsA (n=135)	Arthritis (n=2,722)	Psoriasis (n=5,878)	Controls (n=27,389)	PsA vs. psoriasis p-value	Psoriasis vs. controls p-value	Arthritis vs. controls p-value	PsA vs. controls p-value
zBMI, mean (SD)	0.40 (1.34)	0.43 (1.40)	0.59 (1.38)	49. (1.49)	0.10	<0.001	0.03	0.44

Legend. zBMI (BMI z-score) was calculated from the recorded weight and height, taking into account patient sex and age.

Figure 1: Time from Psoriasis to Arthritis



Legend. Time from development to arthritis among all children with psoriasis.

Time	Beg. Total	Fail	Survivor Function	Std. Error	[95% Conf.	Int.]
500	11869	22	0.9983	0.0004	0.9974	0.9989
1000	10546	22	0.9963	0.0006	0.9950	0.9973
1500	9302	18	0.9945	0.0007	0.9930	0.9957
2000	8130	26	0.9916	0.0009	0.9896	0.9932

Disclosure: C. Manos, None; **R. Xiao**, None; **T. G. Brandon**, None; **A. Ogdie-Beatty**, None; **P. Weiss**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-association-of-obesity-with-pediatric-psoriatic-arthritis

Abstract Number: 37

Increased Involvement of Teenagers with Juvenile Idiopathic Arthritis in Treatment Decisions Using Medication Choice Cards: Preliminary Report from a Case-Control Study

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SESSION INFORMATION

Session Date: Saturday, May 20, 2017

Session Title: Quality, Health Services and Education Research Poster Breakout II

Session Type: Abstract Submissions

Session Time: 5:15PM-5:45PM

Background/Purpose:

Shared Decision Making (SDM) is an interactive process whereby the clinician-patient-parent triad arrives at a treatment decision after reviewing treatment goals, best available medical evidence and patient and parent preferences. SDM tools have been shown to improve patients' risk perception and knowledge of treatment in both adult and pediatric settings. However, the role of these decision aides in childhood rheumatologic diseases has not been well established. Our objective was to investigate the impact of 'JIA Medication Choice Cards,' an SDM tool developed by Pediatric Rheumatology Care and Outcome Improvement Network (PR-COIN) on parent and patient involvement in treatment decisions in adolescents with JIA.

Methods:

Patients diagnosed with JIA (using International League of Associations for Rheumatology criteria) between the ages 12 and 17 were enrolled if they required change or addition of disease modifying drugs. Medication Choice Cards were used to facilitate decision making and discussion in the case group. The cards were not used in the control group. Anonymous survey responses from all patient-parent dyads were used to measure and analyze the following:

1. CollaboRATE (a fast and frugal patient and parent-reported measure of shared decision making, scored 0-9 on a Likert scale):

- Q1: Effort made to help parent/patient understand health issues.
- Q2: Effort made to listen to patient and parent primary health concerns.
- Q3 Effort made to include the primary health concerns in choosing next treatment step.

1. Parental SURE questions (a four item, binary screening measure of decisional conflict)
2. Patients' actual decision roles (Likert scale)
3. Patients' preferred decision role (Likert scale)

Statistical analysis included mean + standard deviation (SD). Fisher's Exact Test and t-test were used to compare results between case and control groups. Statistical significance was defined as $p<0.05$

Results:

Patient-parent encounter-based dyads were divided in the cases (Medication Choice Cards were used, n=30) and controls (No Medication Choice Cards used, n=16).

Table 1: Patient-perceived decision roles in case and control groups

Patients' Perception of Decision Role(s)	Controls	Cases	Total
Decision by parents and the physician	3 (18.7%)	1 (3.3%)	4
Final decision by parents after consideration of patient opinion	10 (62.5%)	4 (13.3%)	14
Shared decision between patient and parent	3 (18.7%)	16 (53.3%)	19
Final decision by patient after consideration of parent opinion	0 (0%)	7 (23.3%)	7
Final decision by patient	0 (0%)	2 (6.6%)	2

p=0.0003

Use of medication choice cards was associated with significantly higher number of patients reporting actual SDM compared to the control group with no medication choice cards. Overall, the patients in the case group demonstrated significantly greater autonomy in making treatment decisions (Table-1)

Patient and parent CollaboRATE measures (Q1-Q3) and parental decisional conflict (SURE measures) were not significantly different between case and control groups.

Conclusion:

Ours is the first study to show that use of Medication Choice Cards significantly enhanced shared decision making in treatment of adolescents with JIA, through increased patient engagement. Parent satisfaction and decisional conflict remained unchanged regardless of use of Choice Cards.

Disclosure: S. Ganguli, None; **S. Hoffmann**, None; **M. Akerman**, None; **H. Walters**, None; **B. Gottlieb**, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/increased-involvement-of-teenagers-with-juvenile-idiopathic-arthritis-in-treatment-decisions-using-medication-choice-cards-preliminary-report-from-a-case-control-study

Abstract Number: 38

Knowledge Translation in Juvenile Idiopathic Arthritis Research in Canada: A Focus on Pediatric Rheumatologists and Allied Health Professionals

Benjamin Rose-Davis[1], Janet Curran[2], Tania Cellucci[3], Ciarán M. Duffy[4], Lori Tucker[5,6], Michelle Batthish[7], Adam Huber[8], Bianca Lang[9,10], Deborah M. Levy[11], Dax Rumsey[12], Karen N Watanabe Duffy[13] and Elizabeth Stringer[14], [1]Division of Pediatric Rheumatology, IWK Health Centre, Halifax, NS, Canada, [2]Department of Pediatrics, IWK Health Centre, Halifax, NS, Canada, [3]Pediatrics/Rheumatology, McMaster Children's Hospital, Hamilton, ON, Canada, [4]Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, ON, Canada, [5]Rheumatology, BC Childrens Hospital, Vancouver, BC, Canada, [6]Pediatric Rheum/Rm K4-120, BC Childrens Hospital, Vancouver, BC, Canada, [7]Division of Pediatric Rheumatology, McMaster Children's Hospital, Hamilton, ON, Canada, [8]IWK Health Centre, Halifax, NS, Canada, [9]Pediatrics, IWK Health Centre, Halifax, NS, Canada, [10]Rheumatology, IWK Health Centre, Halifax, NS, Canada, [11]Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, [12]Stollery Children's Hospital, Edmonton, AB, Canada, [13]Rheumatology, Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa, ON, Canada, [14]Department of Rheumatology, IWK Health Centre, Halifax, NS, Canada

SESSION INFORMATION
Session Date: Saturday, May 20, 2017
Session Title: Quality, Health Services and Education Research Poster Breakout II
Session Type: Abstract Submissions
Session Time: 5:15PM-5:45PM

Background/Purpose: Knowledge Translation (KT) is an iterative process that includes synthesis, dissemination, and application of knowledge to improve health. The aim of this study is to identify the barriers and facilitators identified by Pediatric Rheumatologists (PRs) and Allied Health Professionals (AHPs) to incorporating research findings from Canadian JIA research in clinical care.

Methods: Canadian PRs and AHPs who care for children with JIA were invited to participate via an email survey. Purposeful sampling was used to choose subjects from across the country, including small and large centres. Telephone interviews, which focused on the use of information obtained from the ReACCh-Out Study (Research in Arthritis in Canadian Children emphasizing Outcomes) by PRs/AHPs in clinical care, were conducted using a standardized interview guide. The ReACCh-Out inception cohort characterizes outcomes for over 1000 Canadian children with JIA. Transcripts were coded (BRD, ES) in NVivo 11 using the validated Theoretical Domains Framework (TDF). The 14 domains of the TDF provide a framework for qualitative data analysis informing interventions aimed at behavior change, improving knowledge uptake and patient counselling.

Results: 8 PRs and 10 AHPs (4 PTs, 3 RNs, 3 OTs) representing 11 centres were interviewed. All PRs had knowledge of the ReACCh-Out study. 3/10 AHPs were not aware of the study, 4/10 had heard of it, and 3/10 had a more in-depth knowledge. The PRs and AHPs feel it is their role to share the most up-to-date information with families. It is important to them for a variety of reasons, including the potential to improve shared decision-making and self-management, and decrease anxiety for families. Domains of the TDF and specific beliefs deemed to be important barriers and facilitators are found in Tables 1 and 2.

Table 1: Barriers and Facilitators PRs (n=8)

Domains likely to be barriers for PRs	**Specific Beliefs (frequency) and sample quote**
Memory, Attention, Decision Process	**It is difficult to recall the results of the research** (7/8) "*the manuscript itself is very information heavy…I think that reading it is all fine and well but to keep the number at hand is hard"*
Environment, Context, Resources	**Receptiveness, emotional state, and literacy of the patient can be barriers** (7/8) *"they are not in the right frame of mind to have that kind of discussion. They are too upset, or overwhelmed…"* **There is a lack of time to search/read the literature** (6/8) **and in the clinic** (6/8) *"Taking the time to synthesize the data and then to be able to create the necessary dialogue with families. I think that is probably more of the barrier for me."* "*I would say that how much time I have with the patients in the clinic. How, you know, busy the rest of my day is outside of clinic might affect the amount of quality time I can spend on this interaction."* **There is a lack of non-verbal means to provide research information** (7/8) *"like sometimes I guess if the information is very technical it is a bit hard to put into layman's terms, so maybe some aid, like visual aids to help with that."*
Domains likely to be facilitators for PRs	
Memory, Attention, Decision Process	**Triggers for sharing information (diagnosis, flares, medication changes)** (8/8) *"…that happens in three different situations. One is when I am making a new diagnosis of a patient and trying to tell the families what is going to happen. Second is when I'm prescribing treatments for patients with arthritis or other conditions and trying to describe the possible things that are going to happen. Third is when families ask me about what the future holds and why we make certain decisions…"*
Behavioral Regulation	**A tool or trigger to facilitate knowledge translation** (4/8) *"… it would be very helpful to me to have like some kind knowledge translation tool to be able to practice it better I think."*

Table 2: Barriers and Facilitators AHPs (n=10)

Domains likely to be barriers for AHPs	**Specific Beliefs (frequency) and sample quote**
Memory, Attention, Decision Process	**It is difficult to recall the results of the research** (8/10) *"right off the top of my head I might not remember all the specifics of the research"*
Environment, Context, Resources	**There is a lack of time to search/read the literature** (9/10) **and in the clinic** (6/10) *"we don't always have time to go and look for the most current information"* **Perceived patient ability and readiness causes clinician to hold back info** (5/10) *"for some too much information is overwhelming"*
Knowledge	**Unaware of recent research** (7/10) *"in the last while I have not been up on the research"* **Relying on anecdotal evidence** (5/10) *"It's more my clinical knowledge...and what's been reported by other patients"*
Professional Role and Identity	**Perceive it is not their primary role to communicate this information** (7/10) *"I think like actually discussing those outcomes…would be more the owned by the rheumatologist"*
Domains likely to be facilitators for AHPs	
Social Influences	**Learning about using research from peers** (9/10) *"just having rheumatologist around to talk about the research they're involved in can help to kind of spur that on"*
Memory, Attention, Decision Process	**Triggers for sharing information (diagnosis, flares, medication changes)** (5/10) *"any sort of changing in clinical status…a change in therapy, then for sure that's probably the most common time that I would be accessing research"*
Behavioral Regulation	**A tool or trigger to facilitate knowledge translation** (6/10) *"one thing that we've often wished to have is more, sort of, updates that…would support the clinician"*

Conclusion: PRs and AHPs find it challenging to recall specific study results, stay abreast of current research and distill it down for patients. Lack of time is a factor in the clinic, as well as the perception that families are not ready or able to understand information presented to them at certain times. Availability of KT tools are likely to be important, both as resources and regulators of behavior, particularly at specific time points in care (e.g. diagnosis, discussions around medication changes). Future work will be aimed at addressing barriers and leveraging facilitators in the design of KT interventions in the clinical setting.

Disclosure: B. Rose-Davis, None; **J. Curran**, None; **T. Cellucci**, None; **C. M. Duffy**, None; **L. Tucker**, None; **M. Batthish**, None; **A. Huber**, None; **B. Lang**, None; **D. M. Levy**, None; **D. Rumsey**, None; **K. N. Watanabe Duffy**, None; **E. Stringer**, None.

Abstract Number: 39

Rheumapalooza: A rheumatology curriculum in evolution

Kristen Hayward[1] and Helen M. Emery[2], [1]Pediatric Rheumatology, University of Washington & Seattle Children's Hospital, Seattle, WA, [2]rheumatology, Seattle Childrens Hospital, Seattle, WA

SESSION INFORMATION
Session Date: Saturday, May 20, 2017
Session Title: Quality, Health Services and Education Research Poster Breakout II
Session Type: Abstract Submissions
Session Time: 5:15PM-5:45PM

Background/Purpose: Rheumapalooza was implemented in 2008 as an elective course with support from an ACR/REF Clinical Scholar Educator Award.[1] The course was incorporated into the required UW Medical School 2nd year curriculum in 2010 and expanded to 3 half days. In 2015 and 2016 a flipped classroom instructional model was incorporated. The UW implemented an entirely new 18 month preclinical curriculum for entering first year students in 2015 presenting new educational challenges. We describe lessons learned from ongoing curriculum revision with emphasis on increasing learner engagement.

Methods: The course was designed for 3 consecutive half-day sessions. Day 1 was structured as a series of foundational lectures;[1] Day 2 was initially delivered in large-group lecture format and was revised to place more emphasis on basic rheumatologic disorders and opportunities for active learning. Students are given required reading and 4 case studies (RA, Gout, JIA and SLE) to prepare prior to class. Faculty facilitate student discussion of cases in a small-group format. On day 3, students rotate through 14 stations, including adult and pediatric rheumatology patients, demonstrations of physical therapy, pathology specimens and imaging modalities. In the new curriculum course content is dispersed throughout several different blocks and there are decreased hours for in-class instruction. The other new challenges is that course presentation must be equivalent at 6 regional teaching sites. These constraints have lead to development of detailed faculty guides and incorporation of a webinar format. The patient panel experience will become an elective option in Seattle until alternate regional solutions are developed.

Multiple choice exams assess mastery of course material. Students complete course evaluations including numerical and qualitative responses for overall rating, achievement of learning objectives, ratings of specific lectures and days.

Results: The patient panel has received consistently high student ratings (Figure 1). Feedback on lectures indicated students felt overloaded and requested more opportunities for cementing knowledge. Modification of the 2nd day to a small-group flipped classroom model was associated with improvement in student's rating of active learning opportunities and overall satisfaction (Figure 1). However, students indicated concern about less coverage of rare disorders and inconsistencies between small group instructors.

Conclusion: Integration of a case-based flipped classroom model into the Rheumapalooza curriculum was associated with improved student satisfaction, however, the breadth of information covered decreased. These findings have important ramifications for future medical school curricula given increasing emphasis on active learning delivery models and shorter duration of pre-clinical teaching hours. Future work will focus on partnership with clinical year course directors to ensure adequate coverage of essential concepts across the entire curriculum while meeting the challenge of uniform content presentation over a five state area.

Reference:

1. Emery, Helen, Gardner, Gregory. [abstract]. Arthritis Rheum 2010;62 Suppl 10 :1433 DOI: 10.1002/art.29199.

Disclosure: K. Hayward, None; **H. M. Emery**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/rheumapalooza-a-rheumatology-curriculum-in-evolution

Abstract Number: 40

Perspectives of young people with Juvenile Idiopathic Arthritis, their caregivers, and health care providers on transition to adult care: Informing development of a transition toolkit

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SESSION INFORMATION
Session Date: Saturday, May 20, 2017
Session Title: Quality, Health Services and Education Research Poster Breakout II
Session Type: Abstract Submissions
Session Time: 5:15PM-5:45PM

Background/Purpose:

A seamless transition from pediatric to adult care is critical to ensure optimal health outcomes in adolescents and young adults with Juvenile Idiopathic Arthritis (JIA); however, there are obstacles at the patient, caregiver, health care provider (HCP), and health care system level. A "transition tool-kit" has the potential to overcome some of the existing barriers by providing a standardized approach to the transition process. A needs assessment was conducted to determine the most important factors and tools that users would value as part of a transition tool-kit.

Methods:

In total, 8 semi-structured focus groups (approximately 5-7 subjects in each) and 22 individual interviews were conducted for all user types (adolescents, young adults, caregivers, and pediatric and adult multidisciplinary HCPs), at three rheumatology centers in Canada. Data collection at a fourth study site is ongoing (4 focus groups scheduled). Participants were asked about preparations, concerns and wishes regarding the transition process, and how these issues could be addressed using a transition tool-kit. Qualitative data were analyzed using simple descriptive content analysis. Demographic and disease-related (if applicable) data were collected and analyzed using descriptive statistics.

Results:

To date, 20 adolescents (60% female; mean age = 15.9±1.3), 5 young adults (60% female; mean age = 19.8± 0.8), 19 caregivers (89.5% female; mean age = 44.7± 6.7), 20 pediatric HCP (90% female; mean number of years practicing = 14.3±7.6), and 8 adult HCP (87.5% female; mean number of years practicing = 12.0±13.8) have participated in the study. Main themes from the qualitative analysis were: (1) transition process: most participants felt that patients were not

properly prepared and expressed concerns about the transition, with a small number of adolescent participants expressing no concerns; (2) treatment decision making: most participants agreed that patients should be the ultimate decision makers following discussion with their caregivers and HCPs but that they need access to accurate and comprehensive information resources before making a decision; patients mostly receive or seek disease-related information from HCPs, their caregivers, and the Internet; (3) transition tools: most participants thought that the tool-kit would streamline the transition process and provided thoughts and suggestions for potential components of the tool-kit, such as a calendar feature to remind patients of appointments and to take medication, and an online self-guided JIA resource website. Most participants thought that the tool-kit would be best suited as a website or mobile application (rather than as a paper-based tool).

Conclusion:

Generally, participants responded positively to the idea of a transition tool-kit and indicated that they would use it. They identified key features of this tool, including a calendar reminder system and a JIA resource website. The results from the current study will inform the development of a standardized transition tool-kit for patients with JIA.

Disclosure: N. Luca, None; **E. Rozenblyum**, None; **A. Elliott**, None; **L. R. Spiegel**, None; **N. Johnson**, None; **S. Ahola Kohut**, None; **Y. Brandelli**, None; **C. Johns**, None; **S. Luca**, None; **D. P. Mosher**, None; **G. Soon**, None; **K. Toupin-April**, None; **G. Uifalusi**, None; **J. N. Stinson**, None.

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Abstract Number: 41

Identification of Optimal Subcutaneous Doses of Tocilizumab in Children With Polyarticular-Course Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Clinical and Therapeutic Poster Session
Session Type: Abstract Submissions
Session Time: 5:30PM-7:00PM

Background/Purpose: The efficacy and safety of intravenous (IV) tocilizumab (TCZ), an interleukin-6 receptor-alpha inhibitor, have been demonstrated in patients (pts) with polyarticular-course juvenile idiopathic arthritis (pcJIA) (Brunner HI et al. *Ann Rheum Dis*. 2014;74:1110-7). This study investigated appropriate dosing regimens of subcutaneous (SC) TCZ in pts with pcJIA.

Methods: We enrolled pts aged 1-17 years with pcJIA and previous inadequate response/intolerance to methotrexate who were TCZ naive or were receiving TCZ IV with adequate disease control. TCZ SC was administered open label according to a body weight (BW)–based dosing regimen designed following PK simulations of the approved IV dosing in pcJIA and SC dosing in adult rheumatoid arthritis: pcJIA pts weighing <30 kg received TCZ 162 mg every 3 weeks (Q3W) and pcJIA pts weighing ≥30 kg received TCZ 162 mg Q2W for 52 weeks. Model-computed pharmacokinetic (PK) and pharmacodynamic (PD) parameters and safety and efficacy (exploratory) were assessed.

Results: Fifty-two pts were enrolled; 27 <30 kg BW received TCZ 162 mg SC Q3W and 25 ≥30 kg BW received TCZ 162 mg SC Q2W. Overall, 69% of pts were female. Median baseline age was 6.0 years for the <30 kg BW group and 15.0 years for the ≥30 kg BW group; 85% and 56%, respectively, were TCZ naive. Because no notable differences in steady state PK occurred between naive vs non-naive pts, pooled data are presented. Median C_{min} was similar between BW groups and higher than previously established with TCZ IV (TCZ IV median C_{min}: 3.2 µg/mL for TCZ 10 mg/kg <30 kg BW and 7.3 µg/mL for TCZ 8 mg/kg ≥30 kg BW), ensuring adequate exposure from SC doses. Median C_{max} from SC dosing was lower than from IV dosing in both BW groups (TCZ IV median C_{max}: 191 µg/mL for TCZ 10 mg/kg <30 kg BW and 201 µg/mL for TCZ 8 mg/kg ≥30 kg BW). C_{max} and $AUC_{12weeks}$ were higher with TCZ SC in the <30 kg BW group than the ≥30 kg BW. Changes in PD parameters for TCZ-naive pts were consistent with those previously observed for TCZ IV and suggest improvement of inflammation. JADAS-71 generally improved in both BW groups (Table), with trends consistent with those observed for TCZ IV. Infections were the most frequent adverse event (AE), reported in 20 pts in the <30 kg BW group and 16 pts in the ≥30 kg BW group (Table). Injection site reactions were more common in the ≥30 kg BW group (Table). The most common symptoms were erythema, swelling, hematoma, pain, and pruritus. No serious hypersensitivity, AE leading to withdrawal, opportunistic infection, serious hepatic AE, or death occurred. There were 2 serious AEs (croup and varicella) in 1 pt in the <30 kg group and 2 serious AEs (anorexia and arthralgia) in 2 pts in the ≥30 kg group; the overall rate was 7.9/100 pt-years, consistent with that for TCZ IV.

Conclusion: The BW-based TCZ SC dosing regimens for pcJIA provided adequate exposure to support efficacy comparable to that of TCZ IV, with an acceptable benefit-risk profile.

Table. Results

	TCZ 162 mg SC Q3W BW <30 kg (n = 27)	**TCZ 162 mg SC Q2W BW ≥30 kg (n = 25)**
Model-computed steady state PK parameters, median [range]		
C_{min}, µg/mL	13.4 [0.2, 52.3]	12.7 [0.2, 23.8]
C_{max}, µg/mL	62.4 [39.4, 121.1]	29.7 [7.6, 50.3]
$AUC_{12weeks}$, µg/mL×day	2998 [1465, 7708]	1933 [324, 3098]
Change from baseline to week 52[a] in observed levels of PD markers, median [range]; TCZ-naive pts		
IL-6, pg/mL	27.3 [3.5, 173.9], n = 11	12.2 [–6.2, 30.9], n = 9
sIL-6R, ng/mL	612.1 [399.4, 808.4], n = 14	429.3 [245.5, 585.6], n = 11
CRP, mg/L	–1.3 [–17.0, 0.5], n = 21	–0.8 [–22.9, 0.0], n = 12
ESR, mm/h	–11.0 [–40.0, 0.0], n = 21	–6.0 [–35.0, 0.0], n = 12
Efficacy at week 52[a], TCZ-naive pts		
Change from baseline in JADAS-71	–16.8 [–40.3, –4.4], n = 21	–12.9 [–48.1, –2.3], n = 12
Safety over 52 weeks; all pts		
Infection AEs, n (%)	20 (74)	16 (64)
SAEs, n (%)	1 (4)	2 (8)
ISR, n (%)	4 (15)	11 (44)

[a]Week 51 for Q3W group. AE, adverse event; AUC, area under the concentration curve; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; ISR, injection site reaction; JADAS-71, Juvenile Arthritis Disease Activity Score-71; pts, patients; SAE, serious adverse event; sIL-6R, soluble IL-6 receptor.

Disclosure: H. Brunner, None; **N. Ruperto**, 5,8; **A. Martini**, 5,8; **A. Ramanan**, 8; **R. Cuttica**, 5,8; **J. E. Weiss**, None; **M. Henrickson**, None; **H. Schmeling**, 2; **J. Anton**, 2; **K. Minden**, 2,8; **J. Hsu**, 3; **K. Bharucha**, 3; **S. Wimalasundera**, 3; **A. K. Kadva**, 3; **R. Upmanyu**, 3; **N. L. Mallalieu**, 1,3; **D. Lovell**, 5,2; **F. De Benedetti**, 2.

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Abstract Number: 42

Evaluation of a Dosing Regimen for Tocilizumab in Patients Younger Than Two Years of Age With Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Thursday, May 18, 2017
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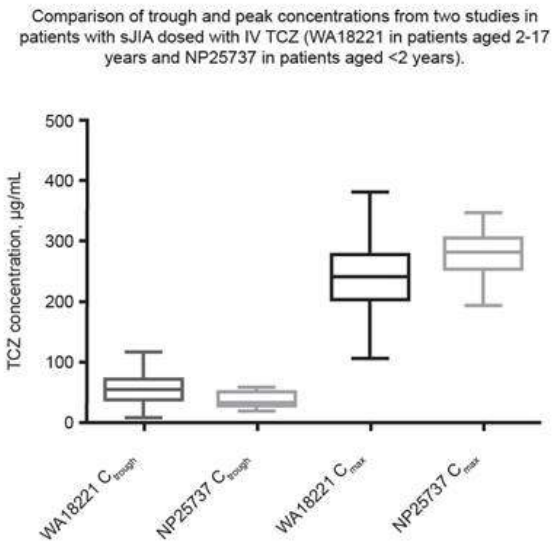
Background/Purpose: Tocilizumab (TCZ) is approved for the treatment of systemic juvenile idiopathic arthritis (sJIA) based on clinical trials in patients ≥2 years of age. This phase 1 study (NP25737), the first of a biologic in patients with sJIA <2 years of age, evaluated the pharmacokinetics (PK), pharmacodynamics (PD), efficacy, and safety of TCZ.

Methods: Patients with uncontrolled sJIA and symptoms for ≥1 month prescreening who failed treatment with corticosteroids and NSAIDs and had no history of allergy to TCZ or other biologics received open-label TCZ 12 mg/kg intravenously (IV) every 2 weeks (dose calculated at each visit based on body weight). Patients were treated up to week 12 and could continue until they reached 2 years of age or were treated for 1 year from baseline. End points included PK (primary) at week 12, PD and efficacy (exploratory), and safety. Comparison was made with exposures from a previous trial in sJIA patients ≥2 years of age (WA18221) that formed the basis for approval of TCZ in sJIA.

Results: Eleven patients were enrolled; median (range) age was 16 (10-22) months and weight was 10.40 (6.8-11.5) kg. Serum TCZ concentrations, estimated using population PK analysis, peaked immediately after infusion; median (range) maximum concentration was 282 (195-347) µg/mL (steady state reached by week 12) and median (range) trough concentration was 34.3 (19.2-59.7) µg/mL. Peak and trough exposures were within the exposure range in older children (244 [109-382] to 54.3 [10.9-117] µg/mL; Figure). Observed mean±SD soluble IL-6 receptor levels were 47.65±16.40 ng/mL at baseline and 927.83±148.07 ng/mL at day 71. CRP levels were 250.81±425.11 mg/L and 2.80±3.56 mg/L and ESR levels were 59.40±27.47 mm/h and 2.00±1.00 mm/h, respectively. Mean±SD Juvenile Arthritis Disease Activity Score-71 improved from 22.27±10.09 at baseline to 3.66±4.66 at day 71. By week 12, 10 patients had 32 adverse events (AEs); 4 withdrew due to AEs. Infections or infestations were the most frequently reported AEs (10 events, 9 patients). Five serious AEs (SAEs) occurred; 3 patients had SAEs of hypersensitivity that led to treatment withdrawal; 1 of these patients then experienced SAEs of foot and mouth disease and sJIA flare after study withdrawal. No actual cases of MAS were reported, but 2 patients had laboratory abnormalities indicative of MAS according to 2016 criteria (Ravelli A et al. *Ann Rheum Dis*. 2016;75:481-9). No deaths occurred during the study.

Conclusion: TCZ exposures achieved in this study fell within the exposure range of the previous trial in sJIA patients ≥2 years of age. This study provides evidence that TCZ is effective in sJIA patients <2 years of age and achieves PK and efficacy similar to those demonstrated previously in older patients. The safety profile was similar to that observed in patients ≥2 years of age in types of AEs observed, but there was a higher incidence of serious hypersensitivity events and suspected MAS.



Disclosure: N. L. Mallalieu, 1,3; **J. Hsu**, 3; **K. Wang**, 3; **S. Wimalasundera**, 3; **C. Wells**, 3; **I. Calvo Penades**, None; **R. J. Cuttica**, 5,8; **H. I. Huppertz**, None; **R. Joos**, None; **Y. Kimura**, 5; **D. Milojevic**, None; **M. Rosenkranz**, None; **K. Schikler**, 2; **T. Constantin**, None; **C. Wouters**, None.

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Abstract Number: 43

Tocilizumab Use in Pediatrics With Systemic Juvenile Idiopathic Arthritis: Single Center Data

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Background/Purpose: Tocilizumab is a humanized monoclonal antibody against interleukin-6 receptors and is indicated for the treatment of systemic juvenile idiopathic arthritis (sJIA) in patients 2 years old or older. The purpose of this project is to examine the clinical use of tocilizumab in a single-center sJIA patient population treated at a large academic free-standing children's hospital. Secondary aims included an evaluation of the safety profile and reasons for discontinuation.

Methods: This was a retrospective analysis of use of tocilizumab in patients treated at our institution over a 6 year period (October 1, 2010 – September 30, 2016). Patients were included if they were followed by the Texas Children's Pediatric Rheumatology Service, 18 years of age or younger, and received at least 1 dose of tocilizumab during the course of their treatment for sJIA. General demographic and dosing-related information were collected, as well as infections and

infection-related treatment information. All research methods were approved by the institutional review board of Baylor College of Medicine.

Results: Thirty-five subjects met inclusion criteria. Median age at initiation of treatment was 10.5 years (range: 1.3-18.5) with median weight of 28.8 kg. The mean number of doses per patient was 23 (range: 1-135). One patient received at least 135 doses safely with no reported complications. A confirmed discontinuation was found in 74.3% of patients; 22.9% due to adverse effects, 20% lost to follow up, 17.1% due to lack of response, 8.6% to disease remission, 2.9% were unable to go to the infusion center, and 2.9% discontinued therapy due to the cost of the drug. Adverse effects included - leukopenia (8.6%), fever (5.7%), and rash (5.7%). However, none of our patients experienced any infection or infection-related adverse effects.

For this patient population, 22 patients used steroids as first line therapy. Subsequent therapy included use of anakinra in 11 patients and tocilizumab use in 8 patients. Tocilizumab use was found to be first line treatment in 4 patients. Seven patients also used tocilizumab for symptom management.

Conclusion: The pattern of usage of tocilizumab in sJIA in a single center was described. Tocilizumab was most commonly used as a second line agent in our center. Observed adverse side effects associated with tocilizumab were minimal.

Table:

Patient Data		n = 35	
Median age at initiation, years (1.3-18.5)			10.5
Sex, n	Female	17	48.5%
	Male	18	51.5%
Median weight, kg (10.5-107.4)			28.7
Median Height, cm (38-176.4)			132.7
Race, n	White	24	68.5%
	Black	9	25.7%
	Asian	2	5.7%
Ethnicity, n	Hispanic	11	31.4%
	Non-Hispanic	24	68.5%
Mean number doses (1-135)		23	
Reasons for discontinuation	Adverse Effects	8	22.9%
	Lost follow up	7	20%
	Lack of response	6	17.1%
	Active Remission	3	8.6%
	Cost of drug	2	2.9%
	Could not attend infusion	1	2.9%
Adverse Effects	Leukopenia	3	8.6%
	Fever	2	5.7%
	Rash	2	5.7%
	Dyslipidemia	1	2.8%
	Post-infusion reaction	1	2.8%
	Pericardial infusion	1	2.8%
	Worsening Liver function	1	2.8%
Treatment Options	Steroids	22	62.9%
	Anakinra	11	31.4%
	Tocilizumab	8	22.9%
	Symptom Management	7	20%

Disclosure: S. Jain, None; **M. B. Bernhardt**, None; **A. A. Ramirez**, None; **A. C. Sagcal-Gironella**, None; **M. de Guzman**, None.

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Abstract Number: 44

Long-term Efficacy and Safety of Canakinumab in Patients With Active Systemic Juvenile Idiopathic Arthritis (SJIA): Results From a Phase III

Extension Study

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Background/Purpose: The management of SJIA with biological therapies is aimed to achieve and maintain clinical remission (CR), and accordingly taper corticosteroids (CS). Canakinumab (CAN) demonstrated high inactive disease (ID) rates in about 33% of patients (pts) on Day 15 and 30, respectively in previous studies.[1]However, little is known about high level response rates in SJIA pts using CAN long-term. The objective of this study was to evaluate the long-term treatment response in terms of safety and efficacy in CAN treated pts with active SJIA.

Methods: This was an open-label, non-comparative study of CAN-naïve SJIA pts (age ≥2–<20 yrs) receiving subcutaneous CAN 4 mg/kg every 4 weeks. Efficacy was assessed every 3 months by the aACR (30/50/70/90/100) responses compared to baseline (BL), ID or CR (ID for >6 months) and changes in JADAS10-CRP scores over time. Safety was assessed by adverse events (AEs) and serious AEs (SAEs). The results are based on the observed data with imputations to carry the last observation forward.

Results: Of 123 pts with active SJIA, 70 (57%) had fever and 71 (57.7%) used corticosteroids at BL. Mean C-reactive protein (CRP) was 117.8 mg/L (normal: 0-10 mg/L), and, on average, pts had 9.9 active joints and 8.9 joints with limited motion. A rapid response was observed at Day 15: 59 (51%) and 27 (26%) pts had aACR ≥70 and aACR 100 responses, respectively. These responses were maintained at subsequent time points (Table). At Month 6, CR was achieved in 52 (42.3%) pts. Overall, 33 (26.8%) pts had CR for at least 12 months. At BL, the median JADAS10-CRP score was 22.3, with median changes from BL of −12.0 at Day 15 and −16.8 at last assessment, respectively. At the last assessment, 59 (48.4%) pts had ID (JADAS10 ≤1); 14 (11.5%) had low disease activity (JADAS10 >1 and ≤3.8), while 14 (11.5%) had moderate and 35 (28.7%) had high disease activity. Overall, 24 (33.8%) pts were steroid-free at last assessment. In total, 108 (87.8%) pts had at least 1 AE. Overall, exposure adjusted AE and SAE rate was 8.22 and 54.8 events/pt-years (pyr) respectively, with 183.56 pyr exposure and 40 (32.5%) pts had SAEs; most commonly reported SAEs were disease flares or worsening of SJIA in 13 (10.6%) pts, macrophage activation syndrome in 6 (4.9%) pts, and fever in 4 (3.3%) pts. No deaths occurred in this study.

Conclusion:

Canakinumab treatment was associated with rapid response and sustained therapeutic effect over the long-term in the naïve patients with active SJIA. The safety profile is consistent with other canakinumab studies.

Reference:

1. Ruperto et al. *N Engl J Med*. 2012; 367:2396-406.

Table: ACR responses achieved in the cohort by time point			
Time point	**CAN N=123**		
	Minimum adapted ACR pediatric response	**n (n/m%)**	**Patients with Inactive disease (n/m)%**
Month 12	m	85	(52/88) 59.1
	Non-Responders	4 (4.7)	
	aACR ≥30	81 (95.3)	
	aACR ≥50	77 (90.6)	
	aACR ≥70	73 (85.9)	
	aACR 100	49 (57.6)	
Month 21	m	65	(48/65) 73.8
	Non-Responders	3 (4.6)	
	aACR ≥30	62 (95.4)	
	aACR ≥50	58 (89.2)	
	aACR ≥70	54 (83.1)	
	aACR 100	39 (60.0)	
Last Assessment	m	121	62/122 (50.8)
	Non-Responders	28 (23.1)	
	aACR ≥30	93 (76.9)	
	aACR ≥50	89 (73.6)	
	aACR ≥70	81 (66.9)	
	aACR 100	62 (51.2)	
n= number of patients who satisfy the criteria, m = number of patients with an assessment in the time period.			

Disclosure: H. Brunner, 5,8; **N. Ruperto**, 2,8; **P. Quartier**, 2,5,8; **T. Constantin**, None; **E. Alexeeva**, 2,8; **I. Koné-Paut**, 2,5; **K. Marzan**, 2; **N. Wulffraat**, 2; **R. Schneider**, None; **S. Padeh**, None; **V. Chasnyk**, None; **C. Wouters**, 2; **J. B. Kuemmerle-Deschner**, 2,5; **T. Kallinich**, 2,8; **B. Lauwerys**, None; **E. Haddad**, None; **E. L. Nasonov**, None; **M. Trachana**, 2,5; **O. Vougiouka**, None; **K. Leon**, 3; **E. Vritzali**, 3; **K. Lheritier**, 1,3; **A. Martini**, 2,8; **D. Lovell**, 2,5,8.

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Abstract Number: 45

Safety of Adalimumab in Pediatric Patients with Polyarticular Juvenile Idiopathic Arthritis, Enthesitis-Related Arthritis, Psoriasis, and Crohn's Disease

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Background/Purpose: Adalimumab (ADA) is a tumor necrosis factor (TNF) inhibitor used for treatment of chronic immune diseases. The safety of ADA treatment in pediatric patients (pts) is particularly important since prolonged treatment for these conditions is often required. The objective of this study is to evaluate the safety of ADA, alone or in combination with concomitant therapy, in pediatric pts with polyarticular juvenile idiopathic arthritis (pJIA), enthesitis-related arthritis (ERA), psoriasis (Ps), and Crohn's disease (CD).

Methods: Safety data from 6 clinical trials and their open-label extension studies were analyzed. Pts treated for pJIA (NCT00048542, NCT00775437, and NCT00690573) and ERA (NCT01166282 [interim week-52 data]) received ADA 24 mg/m^2 body surface area every other week (eow) or 20 mg eow (<30 kg) to 40 mg eow (≥30 kg). Pediatric pts treated for Ps (NCT01251614) received ADA 0.4 mg/kg (up to 20 mg) or 0.8 mg/kg (up to 40 mg) at week 0, then eow from week 1. Pediatric pts treated for CD (NCT00409682) received open-label ADA induction therapy (160 mg and 80 mg at weeks 0 and 2, respectively, if ≥40 kg; 80 mg and 40 mg if <40 kg), followed by double-blind maintenance dosing (high dose: 40 mg eow if ≥40 kg or 20 mg eow if <40 kg at week 4; low dose: 20 mg eow if ≥40 kg or 10 mg eow if <40 kg at week 4); weekly dosing was allowed for disease flare at week 12 or later; pts received high-dose eow or weekly ADA during an open-label extension (NCT00686374). Events (E) per 100 pt-years (PY) were calculated using adverse events (AEs) reported after the first ADA study dose through 70 days after the last study dose.

Results: The analysis included 577 pediatric pts, representing 1440.7 PY of ADA exposure **(Table)**. Over 90% of pts across indications reported treatment-emergent AEs. Common AEs were headache (13.6, 46.9, and 23.4 E/100 PY for pJIA and ERA, Ps, and CD, respectively), nasopharyngitis (12.4, 58.4, and 15.2 E/100 PY, respectively), and upper respiratory tract infection (30.2, 24.7, and 14.8 E/100 PY, respectively). The rates of serious AEs (E/100 PY) were 13.5 for pts with pJIA and ERA, 7.4 for pts with Ps, and 32.2 for pts with CD. One death was reported from an accidental fall (pt with Ps). There were no reports of malignancies, demyelinating disorders, pulmonary embolism, reactivation of hepatitis B, Stevens-Johnson syndrome, or erythema multiforme.

Conclusion: The safety profile of ADA in pediatric pts with pJIA, ERA, Ps, or CD was similar across indications, and no new safety signals specific to the pediatric population were identified.

Table. Treatment-Emergent Adverse Events Occurring in ≥1% of Patients in Pediatric Adalimumab Clinical Trials

Treatment-Emergent Event	pJIA and ERA N=274 Exposure, PYs=806.9		Pediatric Ps N=111 Exposure, PYs=121.5		Pediatric CD N=192 Exposure, PYs=512.3	
	N (%)	Events (Events/100 PY)	N (%)	Events (Events/100 PY)	N (%)	Events (Events/100 PY)
Any AE	267 (97.4)	4239 (525.3)	100 (90.1)	630 (518.5)	189 (98.4)	2902 (566.5)
Serious AE	67 (24.5)	109 (13.5)	8 (7.2)	9 (7.4)	92 (47.9)	165 (32.2)
AE leading to discontinuation of ADA	24 (8.8)	31 (3.8)	3 (2.7)	3 (2.5)	61 (31.8)	77 (15.0)
Severe AE	45 (16.4)	67 (8.3)	17 (15.3)	24 (19.8)	67 (34.9)	114 (22.3)
Drug-related† AE	200 (73.0)	1536 (190.4)	48 (43.2)	176 (144.9)	115 (59.9)	621 (121.2)
Infection	224 (81.8)	1216 (150.7)	82 (73.9)	205 (168.7)	145 (75.5)	676 (132.0)
Serious infection	21 (7.7)	22 (2.7)	1 (0.9)	1 (0.8)	25 (13.0)	34 (6.6)
Opportunistic infection (excluding tuberculosis and oral candidiasis)	0	0	0	0	4 (2.1)	4 (0.8)
Oral candidiasis	2 (0.7)	2 (0.2)	0	0	4 (2.1)	7 (1.4)
Tuberculosis	3 (1.1)	3 (0.4)	2 (1.8)	2 (1.6)	1 (0.5)	1 (0.2)
Active	1 (0.4)	1 (0.1)	0	0	0	0
Latent	2 (0.7)	2 (0.2)	2 (1.8)	2 (1.6)	1 (0.5)	1 (0.2)
Parasitic infection	3 (1.1)	5 (0.6)	0	0	1 (0.5)	1 (0.2)
Allergic reaction‡,§	41 (15.0)	62 (7.7)	7 (6.3)	9 (7.4)	19 (9.9)	25 (4.9)
Intestinal perforation	0	0	0	0	3 (1.6)	3 (0.6)
Intestinal stricture	—	—	—	—	6 (3.1)	6 (1.2)
Worsening/new onset of psoriasis‡	5 (1.8)	6 (0.7)	10 (9.0)	11 (9.1)	6 (3.1)	7 (1.4)
Hematologic disorders‖	10 (3.6)	16 (2.0)	2 (1.8)	3 (2.5)	27 (14.1)	36 (7.0)
Liver event¶	5 (1.8)	5 (0.6)	0	0	1 (0.5)	1 (0.2)
Injection site reaction‡	101 (36.9)	844 (104.6)	11 (9.9)	17 (14.0)	42 (21.9)	104 (20.3)

—, analyzed only in the CD population; ADA, adalimumab; AE, adverse event; CD, Crohn's disease; ERA, enthesitis-related arthritis; pJIA, polyarticular juvenile idiopathic arthritis; Ps, psoriasis; PYs, patient-years.

*The ERA study includes interim week-52 data.

†Investigator assessed as possibly or probably related to study drug.

‡None were serious.

§Events included hypersensitivity (n=36), urticaria (n=27), asthma (n=16), eye pruritus (n=3), rash (n=3), bronchospasm (n=2), generalized pruritus (n=2), injection site urticaria (n=2), drug hypersensitivity (n=1), eyelid edema (n=1), generalized rash (n=1), and wheezing (n=1). One event of anaphylactic reaction was reported as an immune system disorder.

‖Events included anemia (n=24), leukopenia (n=17), neutropenia (n=10), lymphopenia (n=1), macrocytic anemia (n=1), microcytic anemia (n=1), and pancytopenia (n=1); 10 events were serious (leukopenia, n=2 and neutropenia, n=2 [JIA]; anemia, n=6 [CD]).

¶Events included liver disorder (n=3), hepatotoxicity (n=1), and hepatocellular injury (n=1) in the pJIA and ERA group, and 1 serious event of hepatitis in the CD group.

Disclosure: G. Horneff, 2; **M. M. B. Seyger**, 2,5,8,9; **D. Arikan**, 3,1; **J. Kalabic**, 1; **J. K. Anderson**, 1,3; **A. Lazar**, 1,3; **D. A. Williams**, 1,3; **C. Wang**, 1,3; **R. Tarzynski-Potempa**, 1,3; **J. S. Hyams**, 2,6.

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Abstract Number: 46

Long-term Efficacy and Safety of Adalimumab in Pediatric Patients with Enthesitis Related Arthritis

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Background/Purpose: Enthesitis-related arthritis (ERA) is a JIA category primarily affecting entheses and peripheral joints but can involve the axial skeleton. Disease activity and structural change can adversely affect long-term physical function and quality of life of ERA patients (pts)**.** Adalimumab (ADA) has been previously demonstrated to be effective in children with polyarticular JIA and ERA. Objective of this study is to evaluate the persistence of efficacy and long-term safety of ADA compared to placebo (PBO) in children and adolescents with ERA.

Methods: This is a phase 3, multicenter, randomized, double-blind (DB) study in ERA pts aged ≥6-<18 years (yr) at baseline (BL). Methods have been previously described. Pts were randomized 2:1 to receive blinded ADA (24 mg/m^{2}BSA up to 40 mg every other week (wk) [eow]) or PBO for 12 wks followed by open-label (OL) ADA eow for up to an additional 192 wks. Primary endpoint was % change from BL in number of active joints with arthritis (AJC) at wk 12. Secondary variables assessed included enthesitis count (EC), tender (TJC) and swollen joint (SJC) counts, and American College of Rheumatology (ACR) Pediatric (Pedi) 30/50/70 responses. Kaplan Meier analysis was used to determine time to achieve SJC=0, TJC=0, and EC=0 from time of first ADA injection. **Results** are summarized through 156 wks of treatment for efficacy and 204 wks for safety. Safety was assessed in terms of adverse events (AE).

Results: 46 pts were randomized (ADA, n=31; PBO, n=15). No pts discontinued during DB period; 7 pts early escaped to OL ADA. 17 pts discontinued from OL period prior to wk 204 including 4 pts achieving remission. Percentage change from BL at wk 12 in AJC was greater in ADA group vs. PBO (-62.6±59.5 vs -11.6±100.5, *P*=0.039) with response maintained with continued ADA therapy through 156 wks (-88.3±27.7). During treatment with ADA 95.7%, 89.1%, and 89.1% of pts achieved SJC=0, TJC=0 and, EC=0, respectively. Median time from first dose of ADA to achieving SJC=0, TJC=0, and EC=0 was 41, 108, and 56 days, respectively. At wk 12 ACR Pedi70 was statistically significant in favor of ADA while EC, TJC, SJC, and ACR Pedi30/50 showed numerically greater, but not statistically significant improvement in favor of ADA with responses maintained through wk 156. During DB period AE incidence rates were similar [ADA/PBO (%)]: any AE (67.7/53.3), serious AE (3.2/0), and infectious AEs (29.0/20.0). Among pts who received at least 1 dose of ADA, any AE, serious AEs, infectious AEs, and serious infections were reported in 100%, 21.7%, 89.1%, and 8.7% respectively. Ten pts reported a total of 19 serious AEs through 204 wks of treatment. No deaths or malignancies were reported.

Conclusion: ADA reduced the signs and symptoms of ERA at wk 12 and efficacy was sustained through 156 wks. Safety profile observed through 204 wks of treatment in pediatric pts with ERA was consistent with that observed in children

aged ≥2 yrs treated for polyarticular JIA.

Weeks	% Change from BL in AJC[a], mean		Change from BL in EC[a], mean		Change from BL in SJC[a], mean		ACR Pedi 70 Responder[b], n (%)	
	PBO N=15	ADA N=31	PBO N=15	ADA N=31	PBO N=15	ADA N=31	PBO N=15	ADA N=31
12	-11.6	-62.6	-2.7	-4.4	-2.4	-3.5	3 (20.0)	17 (54.8)
	Any ADA (N=46)		Any ADA (N=46)		Any ADA (N=46)		Any ADA (N=46)	
24	-85.2		-6.8		-5.2		34 (73.9)	
52	-88.7		-6.6		-5.7		35 (76.1)	
108	-90.5		-6.3		-5.7		36 (78.3)	
156	-88.3		-6.0		-5.5		35 (76.1)	

[a]LOCF. [b]NRI.

Disclosure: R. Burgos-Vargas, 2,5; **S. M. L. Tse**, 2,5; **G. Horneff**, 2,8; **K. Unnebrink**, 1,3; **J. K. Anderson**, 1,3.

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Abstract Number: 47

Baseline characteristics of the first 123 patients enrolled in the Childhood Arthritis and Rheumatology Research Alliance Start Time Optimization of Biologic Therapy in Polyarticular JIA comparative effectiveness study

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Background/Purpose: Many new effective treatments for polyarticular JIA (p-JIA) are available, but there is significant variation among pediatric rheumatologists in the timing of when biologic medications are started. Three consensus treatment plans (CTPs), reflecting the most commonly used current treatment strategies, were developed by the Childhood Arthritis and Rheumatology Research Alliance (CARRA) using consensus methodology. The CARRA Start Time Optimization of Biologic Therapy in Polyarticular JIA (STOP-JIA) study aims to compare the effectiveness of the different CTPs in 400 patients using a prospective, observational study design. This abstract describes baseline characteristics, CTP

choices, and reasons for CTP choice for the initial patients enrolled in STOP-JIA.

Methods: P-JIA patients who had not yet received systemic glucocorticoid, DMARD or biologic therapies were enrolled into the CARRA Registry. Providers and patients chose one of the CTPs to follow: 1) Step-Up treatment (initial therapy with DMARD and biologic added later if needed); 2) Early Combination (initial therapy with both DMARD and biologic); and 3) Biologic First (initial treatment with biologic monotherapy). Providers had the option of prescribing glucocorticoids at baseline per their usual practice and were provided with tapering options.

Results: One hundred and twenty three patients were enrolled at 37 sites in the US and Canada between 11/1/15 and 1/27/17. Patient characteristics are summarized in Table 1. The most commonly chosen CTP was Step-Up (n=79; 64%). Early combination was the next most common choice (n=27; 22%). Thirty (24%) of patients received oral steroids at baseline. Providers indicated physician preference (89%) as the most common reason for choosing a specific CTP. Six adverse events were reported: influenza A (CTCAE Grade 2), septic shock (CTCAE Grade 3), other infection (CTCAE Grade 1), new onset uveitis (CTCAE Grade 2), hepatitis (CTCAE Grade 1), and seizure (CTCAE Grade 1).

Conclusion: Patients were enrolled into all 3 CTP choices during the first 14 months of enrollment, with the Step-Up option being the most common. Ongoing, prospective data collection from these patients will allow for a comparison of the effectiveness of the strategies.

Table 1. Baseline Patient Characteristics

Characteristic	Total Cohort (n=123)	Step-Up (n=79)	Early Combination (n=27)	Biologic First (n=17)
Female N (%)	88 (72)	58 (73)	19 (70)	11 (65)
White N (%)	80 (65)	58 (73)	12 (44)	10 (59)
Age in yrs – mean (range)	10 (1-18)	9 (1-18)	11 (1-17)	12 (2-18)
JIA Category N (%)				
Extended Oligoarticular	1 (1)	1 (1)	--	--
Polyarthritis (RF-)	83 (68)	61 (78)	13 (48)	9 (53)
Polyarthritis (RF+)	17 (14)	7 (9)	10 (37)	--
Psoriatic	7 (6)	4 (4)	1 (4)	2 (12)
Enthesitis-related	11 (9)	5 (6)	1 (4)	5 (30)
Undifferentiated	3 (2)	--	2 (7)	1 (6)
Number of Active joints – mean (range)	13 (5-49)	12 (5-35)	17 (5-49)	9 (5-16)
Physician Global Assessment of Disease Activity – mean (range)	6 (0-10)	5 (0-10)	7 (3-10)	6 (1-10)
Juvenile Arthritis Disease Activity Score – mean (range)	18 (7-29)	17 (7-29)	21 (9-28)	19 (14-25)
CHAQ score- mean (range)	1 (0-3)	1 (0-3)	1 (0-2)	1 (0-2)
Oral steroids prescribed at baseline – N (%)	30 (24)	17 (22)	12 (44)	1 (6)

Disclosure: S. Ringold, None; **G. A. Tomlinson**, None; **P. F. Weiss**, None; **L. E. Schanberg**, 9,9,9; **B. M. Feldman**, None; **M. E. Riordan**, None; **A. C. Dennos**, None; **V. Del Gaizo**, None; **K. Murphy**, None; **Y. Kimura**, None.

Abstract Number: 48

Methotrexate use and route of administration in JIA: Results from the Childhood Arthritis & Rheumatology Research Alliance Registry

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SESSION INFORMATION

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Background/Purpose: The Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry began enrolling children with juvenile idiopathic arthritis (JIA) in July 2015. The large number of children with prevalent JIA in the Registry provides a unique opportunity to study longitudinal medication use in clinical practice, including the use of methotrexate (MTX).

Methods: Participants were enrolled at 55 centers in the US and Canada. Children with the following characteristics were eligible for enrollment in the Registry: 1) new diagnosis JIA; 2) systemic JIA; 3) history of ≥ 5 joints involved during disease course; 4) children newly starting or re-starting MTX or biologic. Data were obtained from Registry medication logs that contain the patient's complete medication use history, including start and stop dates. Children were included in this analysis if they were ≥ 12 months since JIA diagnosis and treated with MTX. Patient date of diagnosis and medication start and stop dates were imputed if month or day were missing. Median and IQR for time to initiation of biologic therapy was calculated for those patients who started a biologic >= 60 days after MTX, in order to exclude those who were intended to have initial therapy with combination biologic and MTX therapy.

Results: Nine hundred and three children were included in the analysis (Table 1). Median time between diagnosis and initiation of MTX was 61 days (IQR: 0-461) and was similar for those initially started on oral (PO) and those initially started on subcutaneous (SQ). Forty-four percent of children received their initial MTX as PO. Children with extended oligoarthritis had the lowest proportion of initial PO MTX (26%) and children with polyarticular JIA RF+ had the highest percentage (56%). Among children started on initial PO MTX, 31% switched to SQ during their follow-up. Among children started on initial SQ MTX, 25% switched to PO. Median time to initial biologic therapy among those receiving initial PO MTX was 304 days (IQR: 142-731) and 250 days (IQR: 122-813) for those receiving initial SQ MTX.

Conclusion: Among this large cohort of children with JIA, route of initial MTX therapy was relatively evenly divided between SQ and PO and switching between routes was common. Patients started on SQ MTX had a somewhat shorter time to initiation of biologic therapy. Additional analyses will evaluate the associations between initial route of MTX, patient characteristics, and clinical outcomes.

Table 1. Methotrexate use and route of administration

Characteristic	Any methotrexate	Initial PO methotrexate	Initial SQ methotrexate
All eligible patients – n (%)	903	400 (44)	503 (56)
ILAR category – n (%)			
Oligoarthritis - persistent	121	43 (36)	78 (64)
Oligoarthritis - extended	45	12 (26)	33 (74)
Polyarthritis, RF-	457	208 (46)	249 (54)
Polyarthritis, RF+	88	49 (56)	39 (44)
Psoriatic arthritis	41	19 (46)	22 (54)
Enthesitis related arthritis	45	21 (47)	24 (53)
Systemic arthritis	91	40 (44)	51 (56)
Undifferentiated arthritis	13	8 (62)	5 (38)
Switched MTX Route – n (%)	250 (28)	125 (31)	125 (25)
Elapsed time to start MTX – days; median (IQR)	61 (0-461)	63 (0-435)	59 (0-474)
Elasped time to switch MTX route – days; median (IQR)	456 (169-1038)	273 (118-761)	666 (349-1312)
Elapsed time to start biologic if not initial combination therapy – days; median (IQR)	271 (133-745)	304 (142-731)	250 (122-813)

PO: oral; SQ: subcutaneous

Disclosure: S. Ringold, None; **F. Xie**, None; **Y. Kimura**, 2,9; **L. E. Schanberg**, 9,9,9; **T. Beukelman**, None.

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Abstract Number: 49

Perceptions of Methotrexate Intolerance in School-aged Children With Juvenile Idiopathic Arthritis

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Background/Purpose: Methotrexate (MTX) remains an effective and commonly used disease modifying anti-

rheumatic drug (DMARD) for the treatment of Juvenile Idiopathic Arthritis (JIA). Approximately half of the children taking MTX will experience MTX intolerance, that is nausea, vomiting, anticipatory or associative nausea/vomiting. While we have information about MTX intolerance from the perspective of parents and older children, to date there are no studies focused on school-age children's perception of MTX intolerance and its impact on daily life. School-age children have decisions made for them, however they remain experts of their own care and their input is essential for collaborative care and management. The purpose of this study was to explore school-age children's perceptions of MTX intolerance, how MTX intolerance impacts their daily lives and how they manage MTX intolerance.

Methods: An interpretive descriptive design was used with purposive sampling to explore the perceptions of school-age children with JIA experiencing MTX intolerance. All children were interviewed using semi-structured interviews that incorporated a storyboard technique. The storyboard was in the shape of a house with 4 rooms. Children were provided with a variety of felt pieces depicting family members, pets, toys and furniture. Medical play items were also provided, including a syringe, needle, alcohol swab and pill bottle. The storyboard activity allowed the participants to begin to tell their stories about MTX intolerance by visually setting up and displaying their home environment, including the room in which they took their MTX, and to describe who was involved in their MTX administration. The storyboard facilitated the semi-structured interview in which children continued to describe their experience of MTX intolerance. Interview and observational data were collected and analyzed using qualitative inductive content analysis.

Results: Twelve children, aged 6-12 years participated in the study. Interviews lasted an average of 35 minutes. All children enjoyed using the storyboard. Three themes were identified that captured the children's experiences: (1) Children's perceptions of methotrexate intolerance (including descriptions of anticipatory and associative nausea): "No kid likes taking methotrexate". (2) Children's strategies for managing MTX administration: "When I'm going to take my MTX...I'm going down the stairs in slow motion". (3) Working hard to live with MTX intolerance: "The next day, I'm happy because it's another week" [before MTX again].

Conclusion: School-age children are able to clearly articulate their experience of MTX intolerance. Findings highlight the importance of exploring young children's perceptions of intolerance when developing clinical strategies to manage care. Results will be used to explore more effective ways to prevent and manage MTX intolerance.

Disclosure: C. Hopper, None; **S. Khan**, None; **J. Mancini**, None; **J. Rennick**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/perceptions-of-methotrexate-intolerance-in-school-aged-children-with-juvenile-idiopathic-arthritis

Abstract Number: 50

Tumor necrosis factor-α (TNFα) inhibitor-induced psoriasis in juvenile idiopathic arthritis (JIA) patients

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Background/Purpose:

Occurrence of psoriasis while on TNFα antagonists is a paradoxical effect of agents that treat psoriasis, and is described in larger cohorts of inflammatory bowel disease (IBD), pediatric IBD, and rheumatoid arthritis. However, there is a paucity

of data available in JIA. The objective of this study is to determine the prevalence of anti-TNFα-induced psoriasis in JIA patients in one pediatric rheumatology center, and to characterize these patients with an analysis of their treatment course.

Methods:

A retrospective chart review was performed on current pediatric rheumatology patients with JIA on anti-TNFα agents (including infliximab, etanercept, and adalimumab), who developed TNFα inhibitor-induced psoriasis at our center. Information such as patient demographics, personal/family history of psoriasis, specific biologic agent(s), drug class change, discontinuation of agent, time until psoriasis onset from initiation of biologic therapy, concomitant therapies, and response to therapy were collected on affected patients. The prevalence of TNFα inhibitor-induced psoriasis was calculated in JIA patients on TNFα inhibition and in pediatric rheumatology patients on TNFα inhibition who do not have JIA.

Results:

Six of 100 (6%) JIA patients on anti-TNFα therapy at our institution were diagnosed with TNFα inhibitor-induced psoriasis. Pediatric rheumatology patients on anti-TNFα therapy for non-JIA indications such as uveitis, psoriasis, and inflammatory bowel disease (IBD) (n=15) did not experience psoriasis aside from 1 patient (6.7%). Therefore, the prevalence for all pediatric rheumatology patients on TNFα inhibition in our center is 6% (7/115). Of the JIA cases with anti-TNFα-induced psoriasis, all were female, with a median age of 14 (range 2-18) yrs. Affected patients did not have a family or personal history of psoriasis. Time from initiation of anti-TNFα agents to onset to psoriasis was a median of 16.5 (range 10 to 35) mos. 100% of patients with TNFα inhibitor-induced psoriasis experienced plaque psoriasis in two or more locations, including four with moderate to severe scalp involvement. Two patients achieved complete response following class switch while one patient had significant improvement following discontinuation of anti-TNFα therapy. Two patients who switched to different TNFα antagonists had no improvement in psoriasis, while two patients who continued their current anti-TNFα agents both had partial improvement with topical therapies.

Conclusion:

Our findings demonstrate the prevalence of anti-TNFα-induced psoriasis in JIA in a single center. In terms of response to therapy in JIA patients, a complete response (50%) occurred in those who underwent a class switch or discontinued TNFα inhibition.

Disclosure: D. Groth, None; **S. Lapidus**, 5; **S. Nativ**, 5; **M. Perez**, None.

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Abstract Number: 51

The real-world decisive reasons for drug-escalation and treatment results of synthetic and biological therapy in JIA

Joost Swart[1], Nico Wulffraat[2], Sytze de Roock[3] and Pieter van Dijkhuizen[4], [1]Pediatric Rheumatology/ Immunology, Wilhelmina Children's Hospital/ UMC Utrecht, Utrecht, Netherlands, [2]Wilhelmina Children's Hospital, Utrecht, Netherlands, [3]Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, [4]Istituto Giannina Gaslini, Genova, Italy

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Background/Purpose: We wondered if with our current physician based strategy we really do reach improvement within 3 months and inactive disease within 12 months in our JIA patients. We wanted to find out if we could find more objective criteria to guide the decision making for escalation to or switching anti-TNF.

Methods: We built a research data platform with which we extracted pseudonymized data from our electronic medical records. We included JIA patients in our center that started methotrexate, etanercept or adalimumab for the first time for their active JIA from 2008 till August 2015.

Results: Our RDP retrieved the data of 127 JIA-patients for the first time starting with methotrexate, 28 patients starting with adalimumab and 61 patients starting with etanercept. From these patients we could not always retrieve the JADAS-scores because of missing patient/parent VAS or ACR recommendation parameters. The number of active joints however was present at all visits. The baseline characteristics (table 1) showed as expected that the age and disease duration in the MTX-group is significantly lower compared to the anti-TNF groups. There was no significant difference between the ANA-status, JIA-subtypes, but when an anti-TNF agent was started in the presence of uveitis adalimumab was clearly favorite. Also the development of uveitis under anti-TNF therapy was significantly different. Following the intention-to-treat principle, 0 active joints in 12 months was reached by patients starting methotrexate, adalimumab and etanercept in 87.9%, 96.2% and 77.8% respectively. Figure 1 shows the percentage of patients reaching 0 active joints in time. The median time to reach inactive joint took 210 days for MTX, 95 days for adalimumab and 157 days for etanercept.

Table 1

	MTX		**Adalimumab**		**Etanercept**		**Total**	
N (%)	127		28		61		216	
Characteristics								
Sex, female (%)	88	(69,3)	21	(75,0)	38	(62,3)	38	(17,6)
Mean age at onset (sd)	7,2	(4,3)	6,8	(4,5)	5,6	(4,2)	6,7	(4,4)
Mean age at start (sd)	8,4	(4,8)	10,5	(5,3)	9,6	(4,8)	9	(4,9)
Mean disease duration at start (sd)	1,3	(2,2)	3,8	(4,0)	4,0	(4,0)	2,4	(3,3)
ANA+ (%)	21	(16,5)	5	(17,9)	14	(23,0)	40	(18,5)
HLA-B27+ (%)	9	(7,1)	4	(14,3)	3	(4,9)	16	(7,4)
Uveitis at medication start (%)	8	(6,3)	7	(25,0)	2	(3,3)	17	(7,9)
Subtype of JIA								
Oligo-articular (%)	62	(48,8)	12	(42,9)	26	(42,6)	100	(46,3)
Persistent (%)	*18*	*(29,0)*	*5*	*(41,7)*	*15*	*(57,7)*	*38*	*(38,0)*
Extended (%)	*44*	*(71,0)*	*7*	*(58,3)*	*11*	*(42,3)*	*62*	*(62,0)*
Poly-articular RF- (%)	51	(40,2)	12	(42,9)	30	(49,2)	93	(43,1)
Poly-articular RF+ (%)	9	(7,1)	1	(3,6)	4	(6,6)	14	(6,5)
Psoriatic Arthritis (%)	5	(3,9)	3	(10,7)	1	(1,6)	9	(4,2)
Medication history								
Previous DMARD usage (%)	41	(32,3)	28	(100,0)	60	(98,4)	129	(59,7)
IA steroids (%)	31	(24,4)	12	(42,9)	32	(52,5)	75	(34,7)
IA moments (mean, st dev)	1,5	(0,9)	2,9	(3,1)	2,6	(2,1)	2,2	(2,0)
MTX (%)	n/a		28	(100)	60	(98,4)	88	(40,7)
Duration in months (mean, st dev)			*24,6*	*(28,7)*	*23,9*	*(29,2)*	*24,2*	*(28,9)*
Leflunomide (%)	0	(0)	2	(7,1)	9	(14,8)	11	(5,1)
Duration in months (mean, st dev)			*9,7*	*(8,9)*	*21,2*	*(26,3)*	*19,1*	*(24,1)*
Sulfasalazine (%)	4	(3,1)	2	(7,1)	6	(9,8)	12	(5,6)
Duration in months (mean, st dev)	*5,5*	*(1,4)*	*6,6*	*(4,2)*	*11,7*	*(12,9)*	*8,8*	*(9,3)*
Prednisolon (%)	0	(0)	4	(14,3)	9	(14,8)	13	(6,0)
Duration in months (mean, st dev)			*11,3*	*(9, 5)*	*4,2*	*(3,0)*	*6,4*	*(6,4)*
Co-medication								
MTX (%)	127 (100)		21	(75,0)	41	(67,2)	62	(28,7)
Leflunomide (%)	0	(0)	2	(7,1)	3	(4,9)	5	(2,3)
Sulfasalazine (%)	0	(0)	1	(3,6)	0	(0,0)	1	(0,5)
Prednisolon (%)	3	(2,4)	2	(7,1)	6	(9,8)	11	(5,1)
Adverse event								
Uveitis developed under therapy (%)	6	(4,7)	0	(0)	5	(8,2)	11	(5,1)

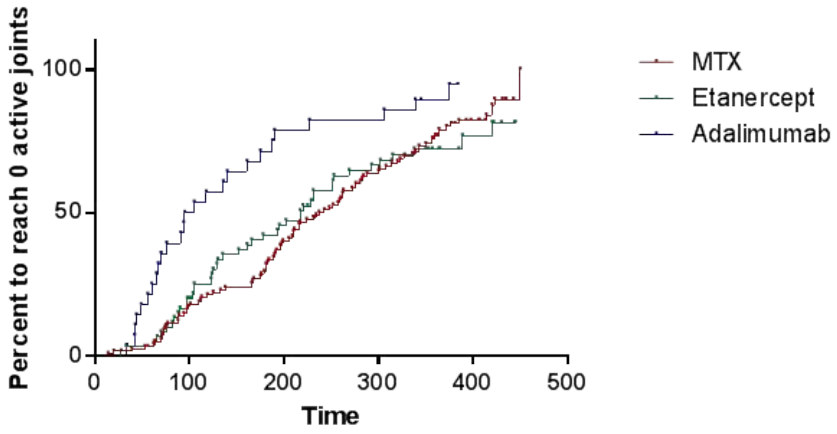

Figure 1.

Conclusion: On the basis of the results of this study, we can state that with the start of anti-TNF JIA improvement is indeed reached within 3 months and remission has been reached by 12 months in the majority. No significant difference is found between adalimumab or etanercept. MTX as concomitant medication is significantly less used with etanercept then with adalimumab. The reason for the physician-based decision to escalate to anti-TNF or not is now under analysis.

Disclosure: J. Swart, 2; **N. Wulffraat**, 2,5; **S. de Roock**, None; **P. van Dijkhuizen**, None.

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Abstract Number: 52

How Young People with Juvenile Idiopathic Arthritis and Their Caregivers Weigh the Risks of the Disease and its Treatment: A Mixed-Methods Study

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Background/Purpose: Prior research has examined factors important to clinicians in deciding whether to withdraw therapy for inactive JIA, but little is known about the perspectives of patients and families confronted with these decisions. We studied how patients with JIA and caregivers consider whether to continue or stop treatment for well-controlled JIA.

Methods: We conducted semi-structured telephone interviews of patients with JIA (age 13 years and older) and caregivers

of children with JIA in the US. Participants were purposively chosen among those who completed a preliminary online survey about demographics and medical history. Interviews included questions about experiences with JIA, medicines for JIA, and factors that influenced decision-making around treatment for active and inactive disease. Interviews were transcribed and independently coded by two researchers; coding was reviewed for consistency and accuracy by two other investigators. Another investigator conducted data triangulation for corroboration. Thematic analysis drew upon the common-sense model of self-regulation to categorize and compare emergent themes.

Results: We interviewed a diverse group of 20 patients (10 age under 18) and 24 caregivers (11 parents of children age under 11) (Table). Key themes revolved around perceived risks, fears, and threats. These concerns applied both to having JIA on the one hand and to taking medicines on the other hand: symptoms versus side effects; long-term damage (existing or feared); interference in school, work, and activities by disease, infusions, or side effects; and emotional burdens and behavioral problems from having JIA versus taking medicines. How participants balanced these competing risks related to past and ongoing experiences as well as concerns about long-term effects, the latter mainly among parents and adults with JIA. Coping strategies, disease state and duration, uncertainty and unpredictability, and trust in the rheumatology team were key modifying factors.

Conclusion: For patients and parents, decisions around withdrawing JIA medicines revolve around a trade-off between risks and fears of medicines and risks and fears of the disease itself. Balancing these risks and fears is influenced strongly by negative prior experiences and complications of JIA or its treatment as well as perceived threats of long-term damage. Clinicians' awareness of this trade-off may help improve shared decision-making around withdrawing treatment for inactive JIA.

Table. Characteristics of interview participants	
Self-reported characteristics	**N (%)**
Demographics and geography	
Group	
Patient, Ages 13-17 years old	10 (23%)
Patient, Ages 18 and older (range 18-38)	10 (23%)
Parent, Child 10 and younger	11 (25%)
Parent, Child older than 10	13 (30%)
Patient sex, female	35 (80%)
Latino ethnicity	10 (23%)
Non-white race	6 (14%)
Public insurance	10 (23%)
Maximum level of education of parent	
High school	4 (9%)
College	21 (47%)
Graduate school	19 (43%)
Region of US	
Midwest	9 (20%)
Northeast	8 (18%)
South	19 (43%)
West	8 (18%)
Disease and medication experience	
JIA category	
Oligoarticular JIA	11 (25%)
Polyarticular JIA	18 (41%)
Psoriatic JIA	4 (9%)
Enthesitis-related arthritis	5 (11%)
Systemic JIA	5 (11%)
Other	1 (2%)
Uveitis	9 (20%)
Methotrexate use	
None	7 (16%)

Prior	17 (39%)
Current	20 (45%)
Biologic use	
None	7 (16%)
Prior	5 (11%)
Current	32 (73%)
History of inactive JIA and treatment discontinuation	
Never inactive	10 (23%)
Never stopped, inactive before	2 (5%)
Never stopped, inactive now	11 (25%)
Stopped, now active	12 (27%)
Stopped, now inactive	9 (20%)

Disclosure: D. B. Horton, None; **J. Salas**, None; **A. Wec**, None; **T. Beukelman**, None; **A. Boneparth**, None; **K. Haverkamp**, None; **M. Kohlheim**, None; **M. Mannion**, None; **N. Moorthy**, None; **S. Ringold**, None; **M. Rosenthal**, None.

Abstract Number: 53

A Prospective Study to Assess for Changes in Mood with Initiation of Anti-TNF therapy: A Pilot Study

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Background/Purpose: Anti- tumor necrosis factor (anti-TNF) agents have been widely studied in the treatment of juvenile idiopathic arthritis (JIA) and inflammatory bowel disease (IBD). Although there are anecdotal reports of mood changes with anti-TNF therapy, these effects are not well described. Our aim is to prospectively evaluate mood changes in patients with JIA and IBD receiving anti-TNF therapy.

Methods: A single center, prospective, pilot study recruited patients with JIA, rheumatoid arthritis (RA), and IBD (8-17 years) who had never been treated with an anti-TNF agent. Each patient served as his/her own control. Formal rating scales were used to assess mood, pain and overall well-being (Table 1). Statistical analysis was performed using the paired t-test.

Results: We report a total of 10 patients (Table 2) who received anti-TNF therapy for the entire study period. Rating scales were completed before and during treatment with anti-TNF therapy. All 10 patients were evaluated between 1-4.5 months while 6/10 patients had a second evaluation between 4.5 and 9 months. Two had pre-existing psychologically - related diagnoses [1: depression/anxiety, 1: attention deficit hyperactivity disorder (ADHD)/oppositional defiant disorder (ODD)]. Baseline testing was abnormal in 5 patients including the 2 with known diagnoses [3: multiple abnormal results 1: ADHD/ODD, 1: school avoidance] and at risk for mood disorders in 2 patients [2: separation/panic]. At 1^{st} follow up (n=10), the scores for pain, performance/fears, separation/panic and school avoidance significantly decreased ($p= 0.014$, p: 0.008, $p= 0.012$, $p= 0.041$ respectively); no change was detected in the rest of the scores. At 2^{nd}follow up (n=6), a significant change was detected only in pain scores ($p=0.038$); no significant change relative to baseline was detected.

Conclusion: Mood disorders may be underestimated in patients with chronic conditions such as JIA and IBD and healthcare providers should consider screening their patients. Our results revealed a decrease in fears and in separation/panic, and an increase in school attendance in association with therapy. To our knowledge, this is the first study to evaluate mood changes prospectively in arthritis and IBD patients treated with anti-TNF therapy. Additional investigation in larger cohorts is required.

Table 1: Study Surveys

Rating Scales	Subcategories
Children's Depression Inventory (CDI)	Emotional Problems Negative Mood/ Physical Symptoms Negative Self-Esteem Functional Problems Ineffectiveness Interpersonal Problems
Multidimensional Anxiety Scale for Children (MASC)	Anxiety Disorder Physical Symptoms Harm Avoidance Social Anxiety Separation/ Panic
Screen for Child Anxiety Related Disorders (SCARED)	Panic Disorder/ Somatic Symptoms Generalized Anxiety disorder Separation Anxiety Disorder Social Anxiety Disorder Significant School Avoidance Anxiety Disorder
Childhood Symptom Inventory Parent Rating Scale (CSI)	Attention Deficit Hyperactivity Disorder Oppositional Defiant Disorder Conduct Disorder Generalized Anxiety Disorder Separation Anxiety Disorder Depression Autism Phobia/Tics Obsessions/Compulsions Schizophrenia Dysthymic Disorder
Visual Analog Scale (VAS)	Pain Overall Well-being
Childhood Health Assessment Questionnaire (CHAQ)	

Table 2: Sample Characteristics

	Number (n)	Percent (%)
Male Female	8 2	80 20
Age at Diagnosis Age at Enrollment	Mean = 14.5 years (SD = 2.46) Mean = 15 years (SD = 2.31)	
White Black Asian	7 1 2	70 10 20
Hispanic Not Hispanic	1 9	10 90
Juvenile Idiopathic Arthritis ERA Other Rheumatoid Arthritis IBD IBD Associated Arthritis	6 6 0 1 2 1	60 60 0 10 20 10
Known Mood Disorders Known ADHD	1 1	10 10
Adalimumab Infliximab Etanercept	6 3 1	60 30 10
Baseline 1st Follow-up 2nd Follow-up	10 10 6	100 100 60

SD: standard deviation, ERA: enthesitis related arthritis, IBD: inflammatory bowel disease, ADHD: attention deficit hyperactivity disorder

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Disclosure: K. Cetin Gedik, None; **H. Papaioannou**, None; **M. Marcus**, None; **C. Deutschman**, None; **B. Gottlieb**, 5.

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Abstract Number: 54

Treatment and 1-year outcomes of an inception cohort of Australian children with JIA

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Background/Purpose: Recent studies have provided insight into the short and intermediate term outcomes of cohorts of children with JIA managed with contemporary treatments in North America and Europe. There are no such data for Australasia.

The objective is to describe the treatment and 1-year clinical outcomes of an inception cohort of newly diagnosed Australian children with juvenile idiopathic arthritis (JIA) followed at a tertiary paediatric centre.

Methods: Retrospective review of prospectively collected clinical data from a specifically designed electronic rheumatology database on all patients newly diagnosed with JIA at the Royal Children's Hospital, Melbourne, between October 2010 and October 2014.

Results:

134 patients were included. Sixty two percent were female. The mean age at diagnosis was 8.3 years. The distribution of patients by subtype was:Oligoarticular 36%; RF + Polyarticular 2%; RF – Polyarticular 25%; Systemic 7%; Enthesitis Related 10%; Psoriatic 7% and Undifferentiated 13%. Ninety five percent of patients achieved a zero joint count at least once in the first year of follow-up, however, just 66% had a zero joint count at 1 year. The median time to a zero joint count was 4.1 months in patients achieving this outcome in the first year of follow-up. The systemic subtype had the shortest time to zero joint count at 1.7 months, psoriatic the longest at 7.6 months. For the 11% of patients who did not achieve a zero joint count in the first year of follow-up, the median time to this outcomewas 18.5 months.

Sixty two percent of patients were commenced on a conventional DMARD (cDMARD), most commonly methotrexate. The median time to commencement of a cDMARD was 0.9 months. 15% were commenced on a biologic DMARD (bDMARD). The median time to commencement of a bDMARD was 4.9 months. 55% were treated with oral corticosteroids. 17% were on oral corticosteroids at 1 year. 62% were treated with intra-articular steroids, most commonly the oligoarticular subtype, of whom 94% had at least one joint injection. 7% of children developed uveitis, with the highest incidence in the oligoarticular subtype, 17%.

Of patients with inactive arthritis at 12 months, 61% were on and 39% were off treatment.

Conclusion: This study demonstrates that children with JIA in Australia have demographic features and short term outcomes similar to those described in international cohorts. At twelve months, two thirds of the cohort had a zero joint count and over a third of these were on no medications. When compared to international cohorts there was some variation in management, with a higher proportion having intra-articular steroid therapy.

Disclosure: G. Tiller, None; **J. Buckle**, None; **J. Munro**, None; **A. Cox**, None; **P. Gowdie**, None; **R. Allen**, None; **J. Akikusa**, None.

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Abstract Number: 55

Celiac Disease in Children Diagnosed with Juvenile Idiopathic Arthritis

Alexandra Smith[1], Nicole Johnson[2], Nadia Luca[3], Dwaraka Veeramreddy[4] and **Heinrike Schmeling**[5], [1]Alberta Children's Hospital, University of Calgary, Calgary, AB, Canada, [2]Pediatrics, University of Calgary, Alberta Children's Hospital, Calgary, AB, Canada, [3]Pediatric Rheumatology, University of Calgary, Alberta Children's Hospital, Calgary, AB, Canada, [4]Department of Pediatrics/Alberta Children's Hospital, Alberta Children's Hospital, University of Calgary, Calgary, AB, Canada, [5]University of Calgary, Alberta Children's Hospital, Calgary, AB, Canada

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Background/Purpose: Celiac disease (CD) is a systemic autoimmune disease triggered by gluten. A higher incidence of CD in rheumatology conditions is reported. Joint pain and arthritis are also manifestations of celiac disease. Therefore, the aim of this study is to characterize the presentation of Celiac disease in children with juvenile idiopathic arthritis (JIA).

Methods: Celiac screening for children with JIA has become routine practice in our clinic over the last several years. Patients with JIA and celiac disease who initially presented to the rheumatology clinic were identified via an existing research database and clinic charts. Charts were reviewed to characterize the presentation of joint and celiac disease.

Results: A total of 10 children with JIA had confirmed celiac disease. All 10 had a positive anti-tissue transglutaminase antibody with 9 having greater than detectable levels. In 9 patients the diagnosis was confirmed via biopsy and 1* via genetic testing. Median age at JIA diagnosis was 8 years (3-16). The time interval between JIA diagnosis and subsequent celiac diagnosis ranged from 0-12 years (median 0.5). Median number of joints involved at celiac diagnosis was 2.5 (1-40), with greater than half being polyarticular pattern. 9 patients had no gastrointestinal complaints and were detected on routine screening (although after celiac diagnosis 4 retrospectively reported mild abdominal pain which was not severe enough to seek medical care). 1 patient[+]was tested due to chronic abdominal pain and family history. None had a classic presentation of celiac disease with diarrhea and poor weight gain. 6 of 10 patients were ANA positive. 1 of 10 was RF positive. 8 of 10 patients were tested for HLA-B27, 1 was positive. 4 patients were treated with disease-modifying anti-rheumatic drugs (DMARDs), while the remainder were treated with steroid joint injections and NSAIDs. 6 of 10 patients had joint symptoms improvement with initiation of a gluten free diet. Of these, only 1 was treated with DMARDs.

Conclusion: The presentation of celiac disease in children with JIA is varied. It can present at any age and with any number of joints. Importantly, there may be minimal or no gastrointestinal symptoms. Furthermore, our results suggest that for children with celiac disease and arthritis, initiation of a gluten-free diet may result in improved joint control. As untreated celiac disease can lead to significant morbidity, and treatment of celiac disease may improve joint disease, we recommend providers consider celiac screening in any child presenting with JIA.

Patient	Gender	Age at JIA Diagnosis	Time to celiac Diagnosis (years)	Pattern of Arthritis	Number of Affected Joints	GI Symptoms	Serology	HLA-B27	Celiac Serology
1*	Female	7	0	Oligo	1	Mild abdo pain	ANA - RF -	Not done	TTG >200 EMA +
2†	Femal	9	2	Poly	10	Constipation/ mild abdo pain	ANA + RF -	Negative	TTG >250 EMA +
3	Female	3	9	Poly	1	Mild abdo pain	ANA + RF -	Negative	TTG >200 EMA +
4	Female	4	4	Oligo	2	None	ANA + RF -	Negative	TTG 186 EMA +
5	Male	15	0	Oligo	1	None	ANA + RF -	Positive	TTG >200 EMA +
6	Male	9	1	Oligo	2	Mild abdo pain	ANA - RF -	Negative	TTG 122 EMA -
7	Male	16	0	Poly	40	None	ANA - RF +	Negative	TTG >200 EMA +
8	Male	11	0	Oligo	1	None	ANA + RF -	Not done	TTG >200 EMA +
9	Female	3	12	Poly	1	Diarrhea/ constipation	ANA - RF -	Negative	TTG >200 EMA +
10	Female	6	0	Poly	6	None	ANA + RF -	Negative	TTG >200 EMA +

Table 1. Clinical presentation of children with juvenile idiopathic arthritis and celiac disease.

Disclosure: A. Smith, None; **N. Johnson**, None; **N. Luca**, None; **D. Veeramreddy**, None; **H. Schmeling**, None.

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Abstract Number: 56

Prevalence of Serum 14-3-3η in Juvenile Idiopathic Arthritis

Iris Reyhan[1], Olga S. Zhukov[2], Robert J. Lagier[3], Robert Bridgforth[4], Gary J Williams[5], Joanna M. Popov[2], Stanley J. Naides[2] and Andreas Reiff[6], [1]Rheumatology, Children's Hospital of Los Angeles, Los Angeles, CA, [2]Immunology, Quest Diagnostics Nichols Institute, San Juan Capistrano, CA, [3]Research Support, Alameda, Quest Diagnostics Alameda, Alameda, CA, [4]quest diagnostics Nichols Institue, clemente, CA, [5]Nicolas Institue, Quest Diagnostics, San Juan Capistrano, CA, [6]Childrens Hospital of Los Angeles, Los Angeles, CA

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Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common pediatric rheumatic disease. Currently, diagnosis is based on clinical assessment defined by the International League of Associations for Rheumatology criteria. Disease specific laboratory biomarkers are limited to rheumatoid factor (RF) and cyclic citrullinated peptide (CCP) antibodies, which are associated with a poor JIA prognosis. The biomarker 14-3-3η (eta) is highly sensitive and specific for rheumatoid arthritis (RA) in adults. Elevated serum 14-3-3η levels improve the diagnostic sensitivity of RF and CCP in adult RA and 14-3-3η level is associated with a more severe RA phenotype [1,2]. The objective of this study was to evaluate the prevalence and clinical significance of serum 14-3-3η in children with JIA.

Methods: One hundred patients from the Pediatric Rheumatology Core at Children's Hospital of Los Angeles were divided into four groups: 31 with polyarticular JIA RF+ (PJIA RF+), 32 PJIA RF-, 25 oligoarticular JIA (OJIA), and 12 with psoriatic arthritis (PsA). OJIA patients served as a control group. RF, CCP, and 14-3-3η were measured via

immunoturbidimetry, immunoassay, and ELISA, respectively. Based on adult onset RA, a 14-3-3η serum level of >0.2ng/mL was considered positive. Association of PJIA with 14-3-3η positivity was performed by Fisher's exact test. Disease activity was assessed by Juvenile Arthritis Disease Activity Score-71 (JADAS-71), and correlation of 14-3-3η positivity with disease activity and with RF/CCP positivity by the Mantel-Haenszel statistics.

Results: RF, CCP, and 14-3-3η data are summarized in Table 1. Twenty eight patients had a positive 14-3-3η. Eight were single positive for 14-3-3η, 20 were positive for 14-3-3η and RF or CCP, and 15 were positive for all 3 markers. There was positive correlation between 14-3-3η and RF and CCP positivities (p=0.00001), but there was no correlation between presence and titer of 14-3-3η compared to JADAS-71 or age of onset.

Conclusion: All patient groups tested had levels of 14-3-3η above baseline. PJIA RF+ patients had the highest prevalence of 14-3-3η compared to all other groups. There was positive correlation between 14-3-3η and positive RF and CCP, but none with disease activity. Of note, 14-3-3η was positive in other forms of JIA, including OJIA where 25% of patients were positive. 14-3-3η may be a useful biomarker in diagnosis, prognosis and monitoring therapeutic response of children with PJIA RF+. However, its role in other forms of JIA remains to be determined.

References:

1. Maksymowych WP, Marotta A. 14-3-3η: a novel biomarker platform for rheumatoid arthritis. *Clin Exp Rheumatol.* 2014:32(suppl):S-35-9.

2. Maksymowych WP, Naides SJ, Bykerk V, et al. Serum 14-3-3η is a novel marker that complements current serological measurements to enhance detection of patients with rheumatoid arthritis. *J Rheumatol.* 2014;41:2104-2113.

Table 1: Prevalence of 14-3-3η, RF and CCP Across Patient Groups

	14-3-3η Positive	Odds Ratio	p-value	14-3-3η Positive RF and CCP Negative	14-3-3η Positive RF or CCP Positive	14-3-3η Positive RF and CCP Positive
PJIA	20/63 (32%)	1.2	0.80	1/63 (2%)	19/63 (30%)	15/63 (24%)
PJIA RF+	18/31 (58%)	3.5	0.03	-0-	18/31 (58%)	15/31 (48%)
PJIA RF-	2/32 (6%)	0.18	0.03	1/32 (3%)	1/32 (3%)	-0-
OJIA	7/25 (28%)	-NA-	-NA-	6/25 (24%)	1/25 (4%)	-0-
PsA	1/12 (8%)	-NA-	-NA-	1/12 (8%)	-0-	-0-
Total	28/100 (28%)	-NA-	-NA-	8/100 (8%)	20/100 (20%)	15/100 (15%)

Disclosure: I. Reyhan, None; **O. S. Zhukov**, 3; **R. J. Lagier**, 3; **R. Bridgforth**, 3; **G. J. Williams**, 3; **J. M. Popov**, 3; **S. J. Naides**, 3,1; **A. Reiff**, None.

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Abstract Number: 57

Quantification of Dynamic MRI examinations in Juvenile Idiopathic Arthritis

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Background/Purpose: In chronic inflammatory conditions, the need for a more objective measurement of disease activity has been identified, where dynamic contrast enhanced (DCE) MRI as imaging biomarker has been studied in RA. In children with juvenile idiopathic arthritis (JIA) similar knowledge is very limited. The purpose was to compare treatment related changes of clinical scores in patients with JIA and automated DCE-MRI quantitative parameters analyzed with a dedicated software Dynamika^{tm} also compared to clinical outcomes of the patients.

Methods: In patients with polyarticular JIA with insufficient (≥3 affected joints) response or intolerance to ≥3 months Methotrexate, Etanercept was started. Six Slice Axial DCE-MRI of the metacarpophaleangeal (MCP) 2-5 joints in the clinically most affected hand was performed at 3 time points: baseline (BL), month 3 and 6 of treatment using a 0.2 Tesla Esaote C-Scan. Clinical scores included active joint (AJ) counts. Clinical response was considered a state of ≤ 3 AJ. DCE-MRI was analyzed using regions of interest (ROI) covering synovium in slices where MCPs 2-5 were visible. Output parameters included dynamic MRI quantification scores (DEMRIQvol) corresponding to the volume of enhancing voxels within the synovial ROIs alone or multiplied with the mean of the maximum enhancement (ME) or the initial rate of enhancement (IRE) .

Differences in DEMRIQvol scores between visits were analyzed using t-test ($p<0.05$* = statistically significant, $p<0.25$** = clinically meaningful). Concordance between clinical and DEMRIQvol scores were described.

Results: 18 Caucasian patients (12 girls, median age 12,6 years, median disease duration 1,2 years) were included in the study. Two patients discontinued imaging after BL but continued treatment. In all but 3 of the remaining patients statistically significant and/or clinically meaningful changes were documented for DEMRIQ ME between visits.

In 4 patients clinical and DEMRIQvol scores showed corresponded changes. In all other patients clinical and DEMRIQvol scores were non-concordant.

Based on DEMRIQvol change (irrespective of the clinical scores) the outcome of the patient could be predicted:

- in 5 patients improvement of DEMRIQvol scores predicted response to treatment (within 2-6 months after last MRI examination)
- in 4 patients an increase or persistence of a high DEMRIQvol predicted non-response to treatment
- in 7 patients increase in DEMRIQvol (after initial decrease) or persistence of a high DEMRIQvol predicted flare (in 3 of the patients flare occurred after treatment discontinuation)

In all patients subclinical disease could be detected on MRI in clinically unaffected joints.

Conclusion: Dynamika based scores appear to be useful for depicting disease activity in JIA and seem to support clinical examination by detecting subclinical inflammation. More over, in the present study DEMRIQvol scores were predictive for the outcome of the patients and were able to “foresee” response to treatment, flare of disease, non-response to treatment in most patients possibly making DEMRIQvol scores supportive in research and clinical decision taking.

Disclosure: N. Tzaribachev, None; **R. Hagoug**, 3; **P. Louka**, 3; **J. Islam**, 3; **M. Hinton**, 3; **O. Kubassova**, 3; **M. Boesen**, 6.

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Abstract Number: 58

Analysis and Implications of Non-Invasive Knee Acoustical Emissions in Juvenile Idiopathic Arthritis

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SESSION INFORMATION
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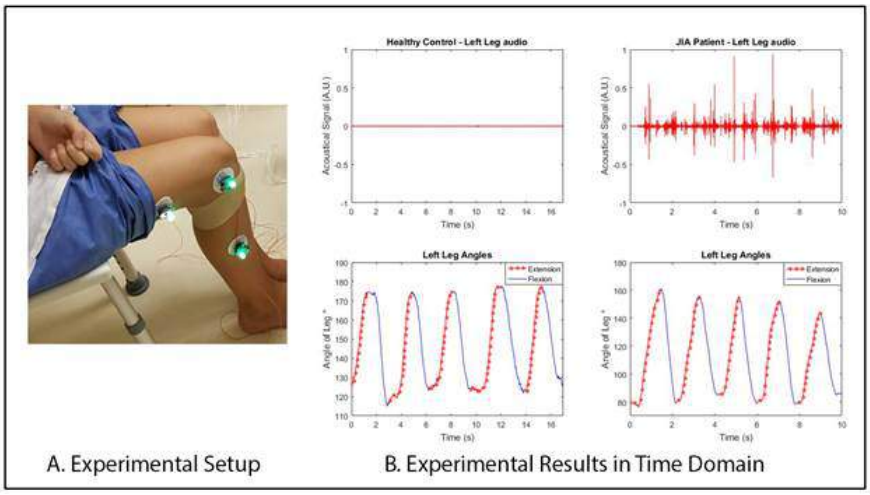
Background/Purpose: Juvenile Idiopathic Arthritis (JIA), the most common chronic rheumatic disease occurring in childhood, is an important cause of disability. Despite the persistence of disease activity in most patients, a marked improvement in functional outcome has been achieved recently - attributable to advances in diagnosis and new treatment regimens. Despite these improvements, 5-10% of patients still have serious functional disability five years post diagnosis. Advances in the standardization of clinical diagnostics and further refining of the treatment regimen will likely further improve outcomes. One principal difficulty in standardizing the diagnosis of JIA is the lack of specific biomarkers for the disease and its concomitant progression. We investigated measuring joint sounds as a non-invasive biomarker of joint health in JIA.

Methods: The advent of wearable technologies has ushered a new era of possibilities for continuous health monitoring. Joint acoustic emissions measured via contact microphones (i.e., accelerometers) are one unobtrusive method of capturing information regarding the underlying, physiologic processes of a joint. This information can readily be incorporated into a wearable platform. These emissions result from changes in the biomechanics of the joint. Internal friction between the articulating structures in the knee create various frequencies of vibrations that can be detected at the surface of the knee. The persistent inflammation in JIA provides opportunity for utilizing this technology to diagnose and monitor the condition. Proof of concept recordings were performed from two subjects with this device.

Results: The first subject was a 12-year-old male with systemic JIA; a healthy control subject was age and sex matched for comparison. The subjects' knee sounds were recorded using a custom hardware consisting of LED motion tracking and accelerometers for vibration detection (Figure 1A). Subjects performed five flexion/extension cycles with the recording apparatus in place. In Figure 1B, the bottom panels show oscillating graphs representing the angle of the knee, while the top panels show the filtered sound profile. The JIA subject's plot appears more chaotic with a periodicity to the sharp peaks.

Conclusion: Measuring acoustic emissions from joints affected by JIA shows promising differences which encourage further development and refinement of this acoustic recording system for the diagnosis and monitoring of JIA.



Disclosure: D. Whittingslow, None; **B. Semiz**, None; **L. Ponders**, None; **A. Wiens**, None; **O. Inan**, None; **S. Prahalad**, None.

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Abstract Number: 59

Six Minute Walk Test in Children with Juvenile Idiopathic Arthritis

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Background/Purpose:

The 6-minute walk test (6MWT) is a widely used measure of functional exercise capacity. It has not, however, been routinely used in pediatric rheumatology practice to date. There is little known about normative values for children with rheumatic disease, including juvenile idiopathic arthritis (JIA). The objectives of this study were to: 1) describe normative values for patients with JIA; 2) investigate which characteristics best predict 6-minute walk distance (6MWD) in this population and establish a prediction equation; and 3) compare 6MWD in patients with JIA to published values for healthy children.

Methods:

At the Glenrose Rehabilitation Hospital in Edmonton, AB, Canada, we have been administering the 6MWT to our JIA patients approximately every 6 months since June 2013. We performed a retrospective chart review of 116 unique patients with a total of 272 visits (6MWTs). Each 6 MWT was administered on a 25 m track by a therapy assistant. Sex, weight,

height, date of birth, testing date, JIA subtype, and lower limb involvement (active and chronic) were recorded. A mixed effects model was used to analyze the data. Univariate modelling of outcome (6MWD) vs. potential predictors was conducted. Variables with $p \leq 0.2$ were selected for inclusion in the final model (cross-sectional age, longitudinal age, height and weight). To address objective 3, predicted 6MWT distances were calculated according to established prediction equations for healthy children developed by Geiger et al. (2007) [6MWD (m)=196.72 + 39.81*age(years) − 1.36×age^2+ 138.28*height (m)] and Ben Saad et al. (2009) [6MWD (m)=56.32 + 4.63*height(cm) − 3.53*weight(kg) + 10.42*age(years)]. Percentage of predicted values were calculated using actual 6MWDs.

Results:

Normative values for children with JIA are presented in Table 1. The final prediction model for our population was 6MWD = 161.45 + cross-sectional age(years)*2.33 + longitudinal age *15.86 + height (m)*2.954 – weight (kg)*1.79; r^2= 0.62). All other factors, including sex, lower limb involvement, and JIA subtype were not significant and therefore were excluded from the model. The 6MWDs of children with JIA were lower than reported for typically developing children (Geiger =84%, range 59%-109% of predicted; Ben Saad = 78%, range 53% -107% of predicted).

Conclusion:

This study provides normative values and a prediction equation for the 6MWT for children with JIA. Reference values are clinically relevant as they provide a user-friendly method for the interpretation and prediction of functional exercise capacity. The characterization of functional exercise capacity in children with JIA could provide the basis for an outcome measurement in this population. The difference in 6MWD between children who are typically developing and the children with JIA shows that children with JIA have impaired functional exercise capacity.

Table 1: Six Minute Walk Results by Age

Age (years) (n)	Height, cm (,SD)	Weight, kg (,SD)	Mean 6MWD, m (,SD)
6 (15)	120 (3)	24 (4)	478 (61)
7 (18)	126 (6)	28 (8)	494 (56)
8 (17)	128 (8)	28 (8)	496 (79)
9 (22)	135 (7)	34 (9)	550 (75)
10 (23)	140 (7)	37 (8)	539 (60)
11 (24)	148 (7)	44 (10)	540 (70)
12 (39)	154 (9)	52 (14)	585 (70)
13 (25)	157 (7)	57 (14)	556 (71)
14 (21)	164 (6)	58 (12)	534 (69)
15 (20)	163 (8)	61 (14)	567 (80)
16 (30)	166 (8)	64 (14)	569 (83)
>16 (18)	166 (9)	65 (15)	602 (81)

Disclosure: D. G. Rumsey, None; **C. Kaup**, None; **M. Roy**, None; **L. Bourassa**, None; **E. Khodayari Moez**, None; **O. Verschuren**, None; **L. Pritchard-Wiart**, None.

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Abstract Number: 60

Paediatric Arthritis Rehabilitation Exercise Study

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Karine Toupin-April[9], Sarah Campillo[10], Gaëlle Chédeville[11] and Rosie Scuccimarri[12], [1]Pediatrics, Montreal Children's Hospital, Montreal, QC, Canada, [2]Montreal Children's Hospital, McGill University, Montreal, QC, Canada, [3]rehabilitaion medicine, co-PI, Montreal, QC, Canada, [4]rehabilitation, co-PI, Montreal, QC, Canada, [5]Kinesiology, Student, Montreal, QC, Canada, [6]medicine, research student, Montreal, QC, Canada, [7]pediatrics, research student, Montreal, QC, Canada, [8]research student, Montreal, QC, Canada, [9]Children's Hospital of Eastern Ontario Research Institute, Ottawa, ON, Canada, [10]Montreal Children's Hospital, Montreal, QC, Canada, [11]Rheumatology, McGill University, Montreal, QC, Canada, [12]Division of Pediatric Rheumatology, Montreal Children's Hospital/McGill University Health Centre, Montreal, QC, Canada

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JIA patients often require regular exercises to increase joint range of motion (ROM). Adherence is challenging; instruction by a physiotherapist (PT) / occupational therapist (OT) is often brief and can be done using standard sketch diagram reminders. Studies assessing the usefulness of video-based exercises among healthy adults and children, as well as adults with orthopaedic conditions show mixed results. These videos were found to be useful for self-reported knowledge, function and compliance. No studies were conducted among adults or youth with arthritis. **Background/Purpose:** To test the feasibility of bilingual home video exercises (video) in JIA, to describe adherence and accuracy of technique when using video vs sketch diagrams; Evaluate ROM improvement. **Methods:** 20 videos were developed for elbow & wrist & 30 videos for knee, ankle & subtalar ROM. Patients age 1-17.9 years with active joints were included if they received no prior media-based instruction. OT/PT demonstrated techniques then patients were randomized to password-protected videos (hospital website) or sketches. Therapists were blind to tool allocation. All joints in each patient were treated with same tool. Children ≤ 6 years did passive ROM & older patients did active assisted (active) exercises for next 35 days. Outcome measures: Ease of recruitment; Daily diary and validated questionnaires (CARQ/PARQ) for adherence; VAS for patient exercise accuracy vs ROM precision per OT/PT at study-end; ROM assessed by OT/PT using goniometry & metric measures pre & post-exercise. **Results:** 11 patients 3-17 years old (M4/F7) were enrolled, 2 withdrew since an extra visit required. 9 patients did 14 exercises: 5 video 9 sketches; 5 passive, 9 active; 3 upper & 11 lower limb. Exercise accuracy & adherence (daily diary) were better in the video group (Table 1). Median adherence to medication (maximum 5) on CARQ was 4.5 and PARQ was 5. Perceived adherence was considered higher by youth than parents and higher for participants who used the video from both parents and youth's perspectives. However, these differences were not statistically significant.

Conclusion: Families enjoyed easy access to videos via our hospital website. Patients found videos more detailed & exercises easier to do than with sketches. Patients not meeting inclusion criteria expressed interest in video-guided exercises. Greater patient enrolment possible if final visit is combined with physicians' at 3 months. Feasibility enhanced if more exercise videos are created for remaining joints. Passive exercises for children ≤ 8 years could improve adherence since 6-8 year olds struggled with active assisted exercises. Alternatives include self-produced images from family-owned smart phones during OT/PT visits or purchasing licenced OT/PT video programs. Our videos may be preferred as these show proper techniques, and how to correct for errors.

Table 1

Measures	Post-Intervention	
	Video	Sketch
Improved Joint Range of Motion	75% of patients	80% of patients
Exercise Accuracy Patients Perspective	100% of exercises with proper technique	78% of exercises with proper technique
Exercise Accuracy Therapist Perspective	100% of exercises with proper technique	78% of exercises with proper technique
Exercise Adherence (Daily diary)	31.5 /35 days 90%	23.5 / 35 days 67%

Disclosure: **C. LeBlanc**, None; **S. Laniel**, None; **M. Geoffrion**, None; **A. Sirois**, None; **S. Nene**, None; **S. Cloutier**, None; **Y. Gao**, None; **K. Toupin-April**, None; **S. Campillo**, None; **G. Chédeville**, None; **R. Scuccimarri**, None.

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Abstract Number: 61

Which Juvenile Idiopathic Arthritis patient is more likely to have Temporomandibular Joint involvement?

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Background/Purpose: Juvenile Idiopathic Arthritis (JIA) affects approximately 300,000 children in the United States. Temporomandibular joint (TMJ) involvement in children with JIA can lead to decreased mandibular growth. This may result in jaw asymmetry, malocclusion, and/or limited mouth opening. The purpose of this study was to characterize a population of patients with TMJ involvement and JIA in a single center cohort.

Methods: A retrospective analysis of patients diagnosed with JIA, who were concurrently enrolled in a study of uveitis in JIA at Children's Healthcare of Atlanta from 2012 to 2016. Children who also endorsed jaw symptoms in the past or during enrollment in the study were included. This study collected information regarding gender, race, JIA subtype, age at first jaw complaint, RF status, ANA status, HLA-B27 status, and involvement of all joints (in addition to TMJ).

Results: This cohort consisted of 470 patients. Of them, 60 patients (52 female, 8 males) with a mean age of 13 years (range, 5 to 18) met inclusion criteria. Patients were Caucasian (43, 71.7%), Hispanic (7, 11.7%), Black (4, 6.7%), or

other (6, 10%). Patients had Poly RF negative (19, 31.7%), Oligoarticular Persistent (15, 25.0%), Enthesitis Related (9, 15%), Oligoarticular Extended (7, 11.7%), Poly RF Positive (n, 6.7%), Systemic (3, 5%), Psoriatic (2, 3.3%), Undifferentiated (1, 1.7%). Of children with TMJ involvement, 38 (63%) had involvement of other joints. Patients were RF positive (9, 18.4 %), ANA positive (26, 43.3%), and/or HLA-B27 positive (9, 18.4%). In addition to TMJ, at the time of data collection, other involved joints were: none (22, 36.7%), fingers (18,30.0%), knees (18,30.0%), wrists (14,23.3%) and other (37, 61.6%).

Conclusion: In our cohort, sixty patients (12.8%) experienced TMJ symptoms either prior to or during their enrollment in the study. In this study population, patients who are female, white, RF negative, HLA-B27 negative, ANA negative, Poly RF negative subtype, and have involvement of other joints have a higher likelihood of having jaw symptoms.

Disclosure: S. abramowicz, None; **J. levy**, None; **C. Travers**, None; **S. Prahalad**, None; **S. Angeles-Han**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/which-juvenile-idiopathic-arthritis-patient-is-more-likely-to-have-temporomandibular-joint-involvement

Abstract Number: 62

Novel Approach to Quantifying Joint Pathology Via Musculoskeletal Ultrasound in Newly Diagnosed Juvenile Idiopathic Arthritis

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Background/Purpose: The pathology of inflammation in Juvenile Idiopathic Arthritis (JIA), including thickening and vascularization of the synovial membrane, joint effusion and bony erosions, can be detected by musculoskeletal ultrasound (MskUS). Previous studies measured joint effusion and synovial hypertrophy separately. However, it is often hard to distinguish between these two findings within an area of pathology as they are often overlapping and can have similar echogenicity. The objective of this study is to use a novel quantitative approach to characterize MskUS abnormalities in newly diagnosed JIA subjects.

Methods: Subjects underwent MskUS assessment of bilateral wrists (midcarpal and radiocarpal recesses) and bilateral knees (suprapatellar, medial and lateral recesses) by grey-scale and power Doppler. MskUS scans were performed by an experienced technician. Pathologic lesions were measured across the greatest dimension (mm) independently by two pediatric radiologists blinded to the clinical musculoskeletal exam. Subjects also underwent clinical evaluations including a joint assessment, and calculation of the clinical JIA disease activity score (cJADAS).

Results: Six subjects (5 oligoarticular and 1 polyarticular JIA) with newly diagnosed DMARD and corticosteroid-naïve JIA by ILAR criteria were evaluated in this cross-sectional study. The median age was 6.3 years (range 2.5, 7.1) and the median disease duration was 5.3 months, (range 2.5, 8.2). There was an equal proportion of male and female subjects. Total number of active joint counts ranged from 1 to 8. Of the 24 bilateral wrists and knees under study, 4 (17%) had clinical synovitis. 58% of the same joints under study had evidence of measurable MskUS pathology. Measurements of lesions ranged from 0.5 to 10mm. The interclass correlation between two independent raters for measurements of pathologic lesions in the suprapatellar recesses was 0.95. The Pearson correlation between cJDAS and total measurements of pathologic lesions was not significant.

Conclusion: Ultrasonography is a useful tool for joint assessment in JIA. Subclinical ultrasonographic abnormalities are common in this cohort of newly diagnosed JIA subjects. Quantitative measurement of total joint pathology is reliable and reproducible. It may be a useful tool to characterize ultrasonographic abnormalities in JIA when it is difficult to distinguish between synovial hypertrophy and joint effusion. Future longitudinal studies are necessary to determine if quantitative measures of ultrasonographic lesions are reliable in monitoring JIA disease activity across time.

Disclosure: L. Woolnough, None; **D. Wilkes**, None; **Y. Kanaan**, None; **T. Wright**, None; **H. Benham**, None.

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Abstract Number: 63

Performance of Disease Activity Measures in Pediatric Patients With Enthesitis-related Arthritis

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Background/Purpose: Enthesitis-related arthritis (ERA) is a category of juvenile idiopathic arthritis (JIA), with clinical features similar to those of adult spondyloarthritis (SpA). An unmet ERA need is the development of distinct disease activity measures and response criteria. The purpose of this analysis was to assess discriminatory aspects of several JIA and SpA clinical response criteria and disease activity measures for patients (pts) with ERA.

Methods: This post hoc analysis evaluated data from a 12-week (wk), randomized, placebo (PBO)-controlled trial of adalimumab (ADA) in pts 6 – <18 years of age with active ERA despite prior NSAID and DMARD therapy. JIA and SpA clinical response criteria were assessed categorically as the percentage of pts achieving response at wk 12. Continuous disease activity measures were assessed as mean change from baseline to wk 12. Categorical and continuous variables were analyzed by NRI and LOCF, respectively. Differences in categorical variables between ADA and PBO groups were assessed using chi-square values. Continuous variables were assessed for between group differences by Guyatt's effect size and standardized mean difference (SMD).

Results: At baseline, demographics and disease characteristics in ADA (n=31) and PBO (n=15) were balanced. Most pts were HLA-B27 positive males, with a mean age of 13 years; patients had experienced ~2.5 years of active disease, and exhibited a mean of 8 active joints with arthritis and 8 sites of enthesitis. Of the response criteria evaluated, the ASDAS-CRP disease states, ASDAS major improvement, BASDAI50, and higher levels of ACRPedi response appeared to discriminate best between ADA and PBO groups (**Table 1**), whereas ACRPedi30 did not discriminate well between treatments. The parent's assessment of pt's overall well-being appeared to perform the best of the disease activity measures in discriminating ADA from PBO (**Table 2**). Physician's global assessment, parent's assessment of pt's pain, BASDAI, ASDAS, and JADAS-10 also appeared to discriminate well.

Table 1. Discrimination Between Adalimumab and Placebo at Week 12 Using Clinical Response Criteria

Clinical Response	ADA (n=31)	PBO (n=15)	Chi Square Value	*P* value
ASDAS-CRP				
ASDAS <1.3	52	20		
ASDAS ≥1.3 – <2.1	13	20		
ASDAS ≥2.1 – ≤3.5	23	27	5.01	.17
ASDAS >3.5	13	33		
BASDAI50	61	27	4.85	.057
ACRPedi30/50/70/90/100	71/68/55/42/26	60/40/20/13/0	0.55/3.21/4.99/3.76/4.69	.46/.07/.03/.052/.03
ASDAS major improvement (≥2)	26	0	4.69	.03
JADAS-10 MDA (≤2)	36	13	2.45	.12
ASDAS clinically important improvement (≥1.1)	42	33	0.31	.58
BASDAI improvement ≥2	45	40	0.11	.74

ADA and PBO values are percentage of patients.

P value is from chi-square.

ADA, adalimumab; PBO, placebo; ASDAS, ankylosing spondylitis disease activity score; CRP, C-reactive protein; BASDAI, Bath ankylosing spondylitis disease activity index; ACRPedi American College of Rheumatology pediatric response criteria; JADAS10, 10-joint juvenile arthritis disease activity score; MDA, minimal disease activity.

Table 2. Discrimination Between Adalimumab and Placebo at Week 12 Using Disease Activity Measures

Outcome Variable	ADA (n=31)	PBO (n=15)	Guyatt's Effect Size	SMD	T-score
Parent's global assessment of patient's overall well-being, VAS	-29.2 (29.78)	-16.5 (10.53)	-2.77	-0.50	-1.60
Parent's assessment of patient's pain, VAS	-32.5 (28.98)	-19.9 (21.69)	-1.50	-0.47	-1.50
JADAS-10	-9.9 (7.30)	-5.7 (6.90)	-1.43	-0.59	-1.87
Morning stiffness (BASDAI inflammation)	-3.0 (3.06)	-1.3 (2.14)	-1.42	-0.60	-1.92
Physician's global assessment of disease activity, VAS	-31.4 (24.76)	-22.1 (23.27)	-1.35	-0.38	-1.22
BASDAI, 0-10	-2.5 (2.80)	-1.4 (2.18)	-1.17	-0.44	-1.39
ASDAS-CRP	-1.0 (1.26)	-0.6 (0.84)	-1.15	-0.30	-0.96
SPARCC enthesitis index, 0-16	-2.6 (3.30)	-2.4 (2.69)	-0.98	-0.08	-0.25
TJC, 0-72	-7.9 (8.25)	-4.5 (8.97)	-0.88	-0.40	-1.28
Number of sites of enthesitis, 0-35	-4.4 (6.20)	-2.7 (4.98)	-0.87	-0.28	-0.88
Number of joints with LOM, 0-66	-3.3 (3.89)	-1.1 (3.77)	-0.86	-0.57	-1.81
MASES, 0-13	-1.7 (2.61)	-0.7 (2.28)	-0.76	-0.40	-1.28
SJC, 0-68	-3.5 (5.61)	-2.4 (4.66)	-0.76	-0.21	-0.67
AJC, 0-72	-4.4 (6.08)	-2.5 (6.01)	-0.73	-0.32	-1.01
Patient's assessment of total back pain, VAS	-14.6 (24.18)	-9.5 (23.89)	-0.61	-0.21	-0.65
CHAQ, 0-3	-0.2 (0.56)	-0.1 (0.41)	-0.60	-0.36	-1.13
hsCRP, mg/L	0.4 (16.39)	-4.8 (23.12)	0.02	0.28	0.89
Number of digits with dactylitis, 0-20	-0.4 (1.54)	0.0 (0.00)	N/A	-0.28	-0.89

ADA and PBO values are mean change from baseline to week 12 (standard deviation).

Missing values are imputed using last observation carried forward.

Guyatt's effect size = mean ADA group/PBO standard deviation; SMD = difference between groups/standard deviation for difference between groups.

ADA, adalimumab; PBO, placebo; VAS, visual analog scale; JADAS10, 10-joint juvenile arthritis disease activity score; BASDAI, Bath ankylosing spondylitis disease activity index; ASDAS, ankylosing spondylitis disease activity score; CRP, C-reactive protein; SPARCC, spondyloarthritis research consortium of Canada; TJC, tender joint count; LOM, loss of motion; MASES, Maastricht ankylosing spondylitis enthesitis score; SJC, swollen joint count; AJC, active joint count; CHAQ, childhood health assessment questionnaire; hsCRP, high sensitivity C-reactive protein; mg, milligram; L, liter.

Conclusion: Of the JIA and SpA assessments, several response criteria and disease activity measures appeared to

discriminate active drug from placebo, suggesting candidate efficacy endpoints for future trials of pts with ERA. ACRPedi30, a typical endpoint in polyarticular JIA trials, did not perform well in this cohort, highlighting the differences in manifestations between ERA and polyarticular JIA.

Disclosure: R. Burgos-Vargas, 2,5; **G. Horneff**, 2,8; **S. M. L. Tse**, 2,5; **P. Quartier**, 2,5,6; **K. Unnebrink**, 1,3; **J. K. Anderson**, 1,3.

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Abstract Number: 64

Evaluating Levels of Activity and Health-Related Quality of Life in a Pilot Cohort of Youth Athletes with Juvenile Idiopathic Arthritis

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Background/Purpose: Children with JIA are increasingly being encouraged to be physically active and are participating in organized and competitive sports as youth athletes. These youth are at risk of experiencing pain and dysfunction related to their underlying rheumatic disease, as well as the sports-related injuries observed in the general population. Our objective was to describe the demographic characteristics as well as the physical activity level and health-related quality of life of a pilot cohort of youth athletes who have a diagnosis of JIA.

Methods: The JIA Sport and Exercise Medicine Clinic at Alberta Children's Hospital is a multidisciplinary clinic run by a pediatric rheumatologist, physiatrist, and physiotherapist. All practitioners have a special interest and experience in pediatric sport and exercise medicine. The clinic includes children with a diagnosis of JIA followed in the hospital's Pediatric Rheumatology Clinic, who self-identify as athletes and are interested in attending a Sport and Exercise Medicine clinic. Prior to the clinic visit, each child is asked to complete a series of questionnaires which includes validated measures of level of physical activity (Hospital for Special Surgery Pediatric Functional Activity Brief Scale (HSS Pedi-FABS) (scores 2-30) and Physical Activity Questionnaire for Adolescents (PAQ-A) (scores 1-5)) and health-related quality of life (Pediatric Quality of Life Generic Core Scale (Version 4.0, Adolescent) (PedsQL GCS-A) and Pediatric Quality of Life (Version 3.0) Rheumatology Module (PedsQL-Rheum)).

Results: A total of 11 youth with JIA participated in the JIA Sport and Exercise Medicine Clinic between October 2014 – April 2015. Children had a median age of 14 years (range 10-17) and 64% were male. The median time since diagnosis was 4 years (range 1-14). The sub-types of JIA included oligoarticular, 7, enthesitis-related arthritis, 3, and polyarticular RF negative, 1. All children took at least one arthritis medication, including NSAIDs (8), non-biologic DMARDs (5), and biologic DMARD (1). Children were involved in a variety of primary sports including ice-hockey, soccer, baseball, football, running, gymnastics, ringette, and dance. The children indicated that they were active a median of 13 hours per week (range 3-22). The measures of physical activity revealed moderate to high mean scores (SD) on the PAQ-A, 2.84 (0.84), and HSS Pedi-FABS, 22.45 (6.27). Health-related quality of life was found to be low with mean scores (SD) on the PedsQL GCS-A of 81.03 (11.08), (Physical Health, 73.58 (18.77), and Psychosocial Health, 85.00 (9.37)). The mean

scores (SD) on the PedsQL-Rheum were low to moderate for Pain and Hurt, 58.52 (24.25), Treatment, 76.62 (18.38), Worry 75.00 (23.86), and Communication, 71.97 (23.94). The score was high for Daily Activities, 95 (9.22).

Conclusion: Youth athletes with JIA are involved in a variety of sports. They are physically active for an above average number of hours per week but experience a significant degree of pain and have decreased scores of physical and psychosocial functioning. Additional support may need to be targeted to youth athletes with JIA to help them achieve their sports goals.

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Abstract Number: 65

Barriers at School for Children with Juvenile Idiopathic Arthritis (JIA) –A Patient Reported Outcome

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SESSION INFORMATION
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Background/Purpose:

Few studies in children with chronic illnesses/disability have reported challenges faced by patients at school. Therefore, the objective of this study is to identify barriers and their associated impact in Juvenile Idiopathic Arthritis (JIA).

Methods:

A cross-sectional observational study of children aged 8 to 17 diagnosed with JIA followed at the Rheumatology Clinic/Alberta Children's Hospital was performed between July and December 2016. Demographics, diagnosis and disease course were obtained from health records. A survey was administered to the child/caregiver to assess the barriers experienced by JIA patients at school. The questionnaire collected information about school attendance/performance, impact of JIA symptoms (e.g. pain, fatigue), challenges and accommodations, communication, participation/peers, and school support. Descriptive statistics were used to analyze the data.

Results:

A total of 66 children were recruited into the study. The median age of participants was 13 (range 8-17). The most common subtypes were rheumatoid factor negative polyarticular JIA (34.8%) and oligoarticular persistent JIA (31.8%) with a median disease duration of 5.3 years (range 0-12). The treatment included DMARDS (68.2%), NSAIDS (43.9%),

biologics (42.4%), steroids (4.55%) and no medication (9.1%).

Appointments, illness and JIA symptoms had a minor impact on school attendance and performance. However, physical challenges (e.g. gym, writing, sitting for long periods of time) at school were a barrier for 41.6% (sometimes 27.7%, often 10.8%, almost always 3.1%). 20.6% recorded using accommodations (e.g. accommodation letter, modified gym, computer access). Patients were unable to participate in activities in class/outside with their peers (37.5%; sometimes 32.8%, almost always 4.7%) and in gym (38%; sometimes 32.8%, often 5.2%). Patients told their teachers/gym teacher about their disease (82.0%) but most patients did not continue to update their teachers. 11.1% of participants reported that their teachers did not understand their illness compared to 19.2% of gym teachers. 84.3% of participants told their friends about their illness and 41.9% told their classmates. Social concerns included anxiety about being unable to participate in school related activities, being treated differently, and looking like they weren't trying. The majority reported that the school was supportive of their illness (92.3%). Barriers tend to be reported more often by patients with active disease.

Conclusion:

JIA had a minor impact on school attendance and performance. However, many patients experienced some impacting physical challenges. Additional barriers included teacher understanding, participation and social anxiety.

Disclosure: K. Chomistek, None; **N. Johnson**, None; **R. Stevenson**, None; **N. Luca**, None; **P. Miettunen**, None; **S. Benseler**, None; **D. Veeramreddy**, None; **H. Schmeling**, None.

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Abstract Number: 66

Feasibility Testing of An Internet-Based Psycho-Educational Game for Children with Juvenile Idiopathic Arthritis and Their Parents

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Background/Purpose:

Juvenile Idiopathic Arthritis (JIA) is a common chronic illness in childhood. The responsibility of JIA management during the younger years is shared among family members. However, many families do not receive comprehensive JIA education and coping skills training, which can negatively impact health-related quality of life (HRQL). Evidence supports psycho-educational treatments to improve health outcomes in children with JIA but no program has been developed to meet the needs of 7 to 12-year-old children. The aim of this research is to evaluate the feasibility of a bilingual (English and French) interactive, Internet-based psycho-educational game for children with JIA.

Methods:

A pilot randomized controlled trial (RCT) design with a usual care control group is underway (target n = 120). Recruitment is ongoing at four Canadian pediatric tertiary care centres and three additional centres will start upon completion of study setup. After informed consent is obtained and baseline questionnaires are completed, participants are randomized. Over the 8-week study period, participants in the experimental group are asked to download the game onto a personal device (i.e., computer or iPad) and interact with the game daily. Participants in the control group receive usual care and are offered the program after post-study. Parents of participants in both groups receive access to the 'JIA Resource Centre'. Post-study questionnaires are completed following 8-weeks. Implementation outcomes are analyzed using descriptive statistics.

Results:

To date, 57 participant dyads have enrolled in the study. Of these, 30 have completed the study, 24 are currently in progress, and 3 have dropped out. Reasons for dropping out included, failure to download the game due to technical difficulties (1 dyad) or lack of time (2 dyads). On average, dyads have taken 7.8 (SD = 6.5) days to download the game. Additional directions or prompts for families to download the game was required from the team for 61.3% (n = 19) of intervention participants and of these, the team contacted dyads an average of 5.4 (SD = 3.6) times before the download was successful. For 22.6% (n = 7), a change of device type was required for a successful download. On average, participants have gotten through 31.2% of game content at the end of 8-weeks. Participants were contacted at the 2-week mark (40.9%) and 5-week mark (78.9%) during the study period to follow-up on the lower than expected progress in the game. The response to the intervention has been mostly positive, however, some participants indicated that the level of difficulty was either "too easy" or "too hard" and some considered it too repetitive. Participants appreciated that a game had been developed for their disease population.

Conclusion:

The feasibility of this intervention would benefit from an easier distribution procedure as well as compatibility of the game across more platforms (i.e., older iPad versions). The level of difficulty could be better suited if tailored to the child's age. Next steps include development of a tutorial to assist younger participants. Upon completion of data collection, preliminary effectiveness outcomes will be analyzed.

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Abstract Number: 67

Relapse and Remission in Children with Chronic Non-Infectious Uveitis Treated with Methotrexate and Tumor Necrosis Factor-α Inhibitors

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Background/Purpose: Methotrexate (MTX) and tumor necrosis factor-α inhibitors (TNFi) are common treatments for children with chronic non-infectious uveitis (NIU). Optimal duration of treatment prior to taper and discontinuation is understudied. Our aim is to identify factors that predict successful medication discontinuation and sustained remission in children with NIU.

Methods: We reviewed records of 120 children with NIU and identified children who tapered and/or discontinued MTX or TNFi (infliximab or adalimumab). We recorded date of medication start, taper, and discontinuation, and time to relapse or remission. Comparisons between children with and without remission were made using Mann-Whitney tests or Chi-square tests.

Results: There were 28 children in whom we attempted to discontinue medication (MTX in 16 and TNFi in 12 (10 infliximab, 2 adalimumab)). They were mostly Caucasian (43%) females (79%), with JIA-associated uveitis (57%) (Table 1). Most common reason for drug discontinuation was remission/inactive disease (61%).

In 16 children, MTX was given for a median of 1.6 years (25^{th}- 75^{th}: 1.1 – 3.0) prior to taper. Four (25%) discontinued MTX without taper, and 12 (75%) tapered over a median of 8 months. Only 5 (31%) successfully discontinued medication and sustained remission for a median of 6 months as of last follow-up. The remaining 11 (69%) relapsed in approximately 8 months. Successful discontinuation of MTX was associated with longer duration of therapy (3.3 vs. 1.4 years; p =0.02) and fewer ocular complications (2/5, 40% vs.11/11, 100%, p= 0.02). Gender, race, NIU type, age at MTX start, duration of NIU before MTX, MTX route and dosing, and eye disease at taper/discontinuation were not associated with successful MTX discontinuation.

In 12 children, TNFi was given for a median of 1.8 years (25^{th}- 75^{th}: 1.4 - 2.9) prior to taper or discontinuation. Eight (67%) discontinued TNFi without taper. All 8 relapsed and needed to restart or switch therapy at a median of 3 months. Four (33%) attempted to taper medication, but only 1 discontinued but later relapsed after 1.3 years. The remaining 3 children restarted/switched therapy at a median of 10 months after starting taper.

In the 23 patients that relapsed, 9 (39%) relapsed within 3 months, 11 (48%) within 6 months, 17 (74%) within 1 year and 22 (96%) within 1.5 years of medication discontinuation/taper.

Conclusion: Most children were unable to discontinue MTX and TNFi. Our results suggest that longer duration of MTX treatment and fewer ocular complications may be associated with sustained remission. Patients requiring TNFi appear to require medication throughout their disease course. Factors leading to successful medication discontinuation and remission in children on TNFi need further study.

Table 1. Characteristics of Children with Uveitis Treated with Methotrexate and Tumor Necrosis Factor-α Inhibitor Medications		
Characteristics, N (%) or median (25^{th} – 75^{th})	**MTX** **N = 16**	**TNFi** **N = 12**
Demographics		
Gender, female	13 (81.3%)	9 (75.0%)
Race		
Caucasian	5 (31.3%)	7 (58.3%)
African American	6 (37.5%)	4 (33.3%)
Other	6 (31.3%)	1 (8.3%)
Uveitis Diagnosis		
JIA-Associated Uveitis	8 (50.0%)	8 (66.7%)
Other Types of Uveitis	8 (50.0%)	4 (33.3%)
Chronic Anterior Uveitis	2 (12.5%)	1 (8.3%)
HLA-B27 Uveitis	0 (0%)	2 (16.7%)
Idiopathic Uveitis	2 (12.5%)	1 (8.3%)
ACE+/Sarcoidosis	2 (12.5%)	0 (0%)
Pars Planitis	1 (6.3%)	0 (0%)
Unknown	1 (6.3%)	0 (0%)
Age at Uveitis Diagnosis, *years*	9.3 (4.6, 12.8)	4.8 (3.5, 6.0)
Duration of Disease To Date, *years*	6.5 (5.6, 7.1)	6.9 (5.5, 10.4)
Uveitis Characteristics		
Location		
Anterior	12 (75.0%)	11 (91.7%)
Intermediate	0 (0.0%)	0
Posterior/Panuveitis	3 (18.8%)	1 (8.3%)
Unknown	1 (6.3%)	0
Bilateral Disease	11 (68.8%)	11 (91.7%)
Complications		
Cataracts	9 (56.3%)	7 (58.3%)
Glaucoma	3 (18.8%)	3 (25.0%)
Synechiae	8 (50.0%)	8 (66.7%)
Keratopathy	4 (25.0%)	5 (41.7%)
Macular Edema	5 (31.3%)	4 (33.3%)
Medication Administration		
Taper/Discontinued Medication		
MTX Subcutaneous	11 (68.8%)	--
MTX Oral	5 (31.3%)	--
Infliximab	--	10 (83.3%)
Adalimumab	--	2 (16.7%)
Age at Start of Therapy, *years*	10.6 (5.0, 13.3)	8.0 (6.7, 12.7)
Duration of Uveitis Before Starting Therapy, *years*	0.47 (0.27, 1.66)	2.4 (2.1, 5.6)
Duration on Therapy until discontinuation or relapse, *years*	2.3 (1.3 , 3.1)	1.8 (1.4, 2.9)
Age at Start of Taper, *years*	11.9 (7.3, 15.4)	10.4 (7.6, 14.9)
Age at Discontinuation or Relapse During Taper, *years*	12.8 (8.8, 15.2)	10.4 (7.6, 14.9)
Reason for Discontinuation (>1 may apply)		
Remission/Inactive Disease	12 (75.0%)	5 (41.7%)
Patient/Parent Preference	4 (25.0%)	1 (8.3%)
Insurance	4 (25.0%)	3 (25.0%)
Allergic Reaction	0 (0%)	2 (16.7%)

Infections	0 (0%)	1 (8.3%)
Quick Taper/Discontinuation	4 (25.0%)	8 (66.7%)
Sustained Remission	5 (31.3%)	0 (0%)
Duration of Remission, years	0.5 (0.4, 0.8)	--
Relapsed/Restarted Medication	11 (68.8%)	12 (100%)
Time to Relapse/ Restarted Medication	0.7 (0.59, 1.53)	0.4 (0.20, 0.93)

Abstract Number: 68

HLA-DRB1 in Non-Hispanic African American Children with Juvenile Idiopathic Arthritis and Chronic Anterior Uveitis

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Background/Purpose:
HLA-DRB1*08, 11 and 13 are strong risk alleles for various juvenile idiopathic arthritis (JIA) subtypes. We reported that carriage of DRB1*11 and *13 increased the risk for uveitis in Non-Hispanic White children with oligoarticular and polyarticular rheumatoid factor (RF) negative JIA. HLA-B8, in linkage disequilibrium with DRB1*03, was reported in African American children with uveitis. Few studies have investigated the role of HLA-DRB1 alleles in Non-Hispanic African American (NH AA) children with JIA or uveitis. Our objective is to determine the association of HLA-DRB1 alleles in NH AA children with JIA and chronic anterior uveitis (CAU).

Methods:
We performed high-resolution HLA-DRB1 genotyping to determine the frequency of HLA-DRB1*08,11 and 13 alleles in our AA cohorts. Frequencies were compared among JIA and CAU (JIA-associated uveitis and idiopathic chronic anterior uveitis) groups using Chi-square tests and Exact tests. In addition, we compared the frequency of these alleles in our cohorts to 3734 AA healthy controls from the National Marrow Donor Program (NMDP) using two-sided Z-tests for proportions.

Results:
There were 35 NH AA children (21 JIA and 14 CAU) who were mainly female (51.4%). Of those with JIA, 12 (57%) had extended or persistent oligoarticular JIA, and 9 (43%) had polyarticular RF negative JIA. ANA was positive in 8 (38.1%) JIA children and 2 (40%) JIA-associated uveitis children.

Comparing children with JIA and CAU, there was a clinically significant difference in DRB1*13 (9.5% vs. 35.7%, p =

0.058). (Table 1)

Compared to AA controls, children with JIA had increased DRB1*08 (28.6% vs. 3.3%, p < 0.001) and DRB1*11 (38.1% vs. 13.4%, p <0.001). Children with CAU also had increased DRB1*08 (14.3% vs. 3.3%, p = 0.021) and DRB1*11 (42.9% vs. 13.4%, p = 0.001), which may be due to the JIA diagnosis. (Table 2)

Children with CAU had clinically significant increased DRB1*13 compared to controls (35.7% vs. 17%, p = 0.067). This was similar to the comparison with JIA children.

Conclusion:
We newly report that carriage of HLA-DRB1*08 or DRB1*11 may increase the risk for JIA and uveitis in NH AA children. Carriage of DRB1*13 may also increase the risk for uveitis, but may be specific to risk for eye disease, independent of arthritis. Further studies in NH AA children should be conducted to investigate the role of HLA-DRB1 in children with JIA and uveitis.

Table 1. HLA-DRB1 alleles in Non-Hispanic African American Children with Polyarticular Rheumatoid Factor Negative or Oligoarticular JIA and Chronic Anterior Uveitis

HLA configuration	JIA[a] N = 21	CAU[b] N = 14	P-value
DRB1*03	5 (23.8%)	1 (7.1%)	0.200
DRB1*08	6 (28.6%)	2 (14.3%)	0.431
DRB1*11	8 (38.1%)	6 (42.9%)	0.778
DRB1*13	2 (9.5%)	5 (35.7%)	0.058
DRB1*08, 11 or 13	13 (61.9%)	12 (85.7%)	0.252
DRB1*11 or 13	9 (42.9%)	10 (71.4%)	0.097
DRB1*08/11	2 (9.5%)	0 (0%)	0.506
DRB1*11/13	1 (4.8%)	1 (7.1%)	1.00
DRB1*08/13	0	0	--
08/13 or 11/13	1 (4.8%)	1 (7.1%)	1.00

[a]JIA: juvenile idiopathic arthritis; [b]CAU: chronic anterior uveitis (9 idiopathic chronic anterior uveitis, 5 JIA-associated uveitis)

Table 2. Comparison of Allele Frequencies in Our AA Cohort to the General AA Population

N (%) P-value vs. control	Control N = 3734	JIA[a] N = 21	CAU[b] N = 14
DRB1*03	13.6%	5 (23.8%) P =0.172	1 (7.1%) P = 0.481
DRB1*08	3.3%	6 (28.6%) **P < 0.001****	2 (14.3%) **P = 0.021****
DRB1*11	13.4%	8 (38.1%) **P < 0.001****	6 (42.9%) **P = 0.001****
DRB1*13	17.2%	2 (9.5%) P = 0.350	5 (35.7%) P = 0.067

[a]JIA: juvenile idiopathic arthritis; [b]CAU: chronic anterior uveitis (9 idiopathic chronic anterior uveitis, 5 JIA-associated uveitis); ** p <0.05

Disclosure: L. H. K. Chan, None; **C. McCracken**, None; **K. Jenkins**, None; **S. Yeh**, None; **P. Patel**, None; **S. Prahalad**, None; **S. Angeles-Han**, None.

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Abstract Number: 69

The Disease Burden of Systemic Juvenile Idiopathic Arthritis for Patients and Caregivers: An International Health Related Quality of Life Survey and Retrospective Chart Review

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Background/Purpose: Systemic juvenile idiopathic arthritis (SJIA) is a severe autoinflammatory disease characterized by systemic features including high fevers, rash and arthritis. SJIA can impose high physical, psychosocial, behavioral and financial burden on patients (pts) and their families. The objective was to analyze the impact of the burden of SJIA by evaluating caregiver perspectives of disease burden in an international, real-world study.

Methods: SJIA treatment centers in France, Germany, Netherlands, UK and the US participated. Pts (aged 4-18 years) with confirmed SJIA received one of the following biologic treatments for ≥2 months: anakinra (ANA), canakinumab (CAN), or tocilizumab (TOC). SJIA burden in patients on biologics was assessed using a caregiver questionnaire and retrospective chart review. Validated measures included: Child Health Questionnaire Parent-Form 50 (CHQ-PF50), 36-Item Short-Form Health Survey (SF-36v2) and Work Productivity and Activity Impairment questionnaire: Specific Health Problem (WPAI:SHP). Caregivers completed function, treatment satisfaction and resource utilization questions.

Results: Sixty-one pts enrolled from June 2015- June 2016: 12 on ANA, 25 on CAN, 24 on TOC; 46% from the US; 48% female; mean age at survey was 11.3 years. Mean age at SJIA diagnosis was 6.4 years, mean age at start of ANA, CAN, and TOC treatment was 9.9, 9.1, and 7.5 years, respectively. Caregivers were 79% female, mean age 41.2 years, and 36% reduced or stopped working due to their child's SJIA. Of the pts enrolled on CAN and TOC, 72% and 46% respectively had previously been on ANA. Baseline CHAQ, CHQ-PF50, and WPAI scores were worse in CAN and TOC than ANA pts. Mean (±SD) CHQ-PF50 physical (PhS) and psychosocial (PsS) summary scores were significantly lower in SJIA patients than a normative population (PhS: 40.0±18.2 vs. 53.0±8.8; PsS: 46.6±11.3 vs. 51.2±9.1) as was caregivers' mean SF-36v2 mental component score (46.2±10.7 vs. 50.0+10). Highest caregiver stressors were worry over long-term SJIA impact on their child (45%) and uncertainty about the future (28%).

Conclusion: Treatment sequencing and patient-reported outcome measures indicate ANA is used as 1st line for less severe SJIA while CAN and TOC are used as 2nd/3rd line for severe SJIA. Caregivers expressed stress over the long-term impact of SJIA and fear for the future and had variable treatment satisfaction and resource utilization levels.

Disclosure: S. Shenoi, None; **G. Horneff**, 2; **M. Cidon**, None; **A. Ramanan**, None; **Y. Kimura**, 2,9; **P. Quartier**, 2,5,8; **I. Foeldvari**, 8; **A. Zeft**, 1,5; **K. G. Lomax**, 3; **J. Gregson**, 3; **A. Tineke**, None; **S. Campbell**, 5; **J. Weiss**, 5; **D. Patel**, 5; **N.**

Wulffraat, 2,5.

Abstract Number: 70

Impact of Systemic Juvenile Idiopathic Arthritis/Still's Disease on Adolescents as Evidenced Through Social Media Posting

Renee F Modica[1], Kathleen G Lomax[2], Pamela Batzel[3], Armelle Cassanas[3] and Melissa E Elder[1], [1]Department of Pediatrics, University of Florida, Gainesville, FL, [2]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [3]Treato, Princeton, NJ

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Systemic juvenile idiopathic arthritis (SJIA)/Still's disease is a rare form of chronic arthritis in pediatrics. The patient perspective of living with the disease is not well understood, particularly among adolescent age patients. The objective was to understand the adolescent SJIA experience as shown by their own social media posts.

Methods: English posts from SJIA patients were reviewed on public social media sites.

Results: 71 posts with a date range of 2009-2015 on 15 sites were reviewed in Nov 2015. 24 unique authors were identified: 17 SJIA patients (40 posts) and 7 mothers of SJIA patients (12 posts). Patients were aged 13-20 years. Several patients posted about similar diagnostic experiences marked by 5 stages: (1) misunderstood with their pain and fatigue being overlooked until a crisis occurs, (2) dismissed as 'fakers,' where their initial misdiagnosis is often 'growing pains' or 'fake pains', (3) misdiagnosis, often as cancer, when the symptoms acutely worsen (4) testing stage that leads to an SJIA diagnosis, and (5) focus on the difficulties of dealing with a chronic invisible disease where they feel ashamed of their arthritis and distressed at being different from their peers. Many adolescent patients, looking back at the onset of the disease when they were children, describe themselves as a "sleeping child" rather than the typical active, playing child. Patients describe trying to hide their illness from friends, but express their concerns more openly online. Patients also describe anger directed at SJIA which is described as a powerful external enemy attacking their body, using terms like "bulldozer," "dragon," and "monster." Many posters used superhero language or imagery in their social media posts to help them "fight" the disease and their struggle. Mothers of SJIA patients also used warrior-child imagery and language in their posts. Some SJIA patients also posted about the risk of death, or shared stories about other SJIA patients who died, which is a distinct difference from non-SJIA patients. Many patients also have adopted the term "spoonie" to describe themselves as living with a chronic disease, a term that originated in the autoimmune community to refer to how people with chronic conditions manage their energy throughout the day. Only the older teenagers used the term Still's.

Conclusion: Adolescent SJIA patients posted openly about the difficulties of their disease causing them to be different from their healthy friends, whereas in the real world they tried to minimize or hide the effects of their disease. They frequently used superhero words and images in posts in describing their fight for health. Physicians can use these insights when counseling adolescent SJIA patients to provide a narrative that meshes with the patients' worldview and perhaps, by speaking a similar language, could increase treatment adherence.

Disclosure: R. F. Modica, None; **K. G. Lomax**, 3; **P. Batzel**, None; **A. Cassanas**, None; **M. E. Elder**, None.

Abstract Number: 71

Consensus-based diagnostic approach to systemic juvenile idiopathic arthritis in Germany

Claas Hinze[1], Dirk Holzinger[1], Elke Lainka[2], Johannes Peter Haas[3], Tilmann Kallinich[4], Ulrich Neudorf[2], Helmut Wittkowski[1], Gerd Horneff[5], **Dirk Foell**[6] and PRO-KIND study group on SJIA, [1]Department of Pediatric Rheumatology and Immunology, University of Muenster, Muenster, Germany, [2]University of Essen, Essen, Germany, [3]Center for Pediatric and Adolescent Rheumatology Garmisch-Partenkirchen, Garmisch-Partenkirchen, Germany, [4]Charite, University Medicine Berlin, Berlin, Germany, [5]Asklepios Klinik Sankt Augustin GmbH, Sankt Augustin, Germany, [6]Pediatric Rheumatology and Immunology, University of Muenster, Muenster, Germany

SESSION INFORMATION
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Session Type: Abstract Submissions
Session Time: 5:30PM-7:00PM

Background/Purpose: Systemic juvenile idiopathic arthritis (SJIA) is currently classified by the International League of Associations for Rheumatology (ILAR) classification criteria. It is characterized by severe systemic inflammation and is associated with chronic arthritis in many, but not all, patients. Further guidance on the early diagnosis of SJIA is desirable, so that effective treatments can be initiated. The PRO-KIND initiative of the German Society for Pediatric Rheumatology (GKJR) aims to define consensus-based diagnostic and treatment protocols in order to harmonize diagnostic and treatment approaches in Germany. Within PRO-KIND, the first aim of this working group on SJIA was to generate a case definition to be used in the future development and application of consensus-based treatment protocols.

Methods: We retrieved and analyzed data on the clinical characteristics of patients diagnosed with SJIA from two national registries and one cohort in Germany. Subsequently, via online surveys and teleconferences among pediatric rheumatologists with an expertise in the management of SJIA, we identified current diagnostic approaches in Germany. These approaches were harmonized via the formulation of statements, supported by a search of the literature. Finally, a consensus conference using nominal group technique was held to further improve and consent the statements and GKJR case definitions.

Results: De facto only 47.8% and 54.3% (by imputation: 50.4% and 54.7%) of patients diagnosed with SJIA in the AID registry and the ICON-JIA cohort, respectively, fulfill the ILAR classification criteria for SJIA. Statements derived by harmonization indicate that chronic arthritis is not felt to be obligatory for the diagnosis and treatment of SJIA, and that certain biomarkers including S100 proteins are useful for the diagnosis of SJIA. Furthermore, the importance of ruling out competing differential diagnoses is emphasized. Our data support the notion that the Yamaguchi, the newly proposed “Martini classification criteria” and the herein developed GKJR case definition may perform better in classifying patients with SJIA since, in the AID registry and the ICON-JIA cohort, they de facto (by imputation) classify 55.1%/77.1% (69.3%/82.1%), 71.0%/71.4% (65.0%/77.7%) and 62.3%/65.7% (78.3%/68.0%) as SJIA, respectively.

Conclusion: We developed evidence-informed, consensus-based statements regarding the diagnosis of SJIA in Germany. These statements should prove useful for application in clinical practice and the implementation of consensus treatment protocols, which are developed in the PRO-KIND initiative. We developed case definitions rather than classification criteria since a delay of diagnosis may lead to delayed treatment and serious complications in case of SJIA. We therefore embrace the development of new classification criteria for SJIA to better reflect the entire spectrum of patients with SJIA and allow appropriate categorization of patients and access to clinical trials.

Disclosure: C. Hinze, None; **D. Holzinger**, None; **E. Lainka**, None; **J. P. Haas**, None; **T. Kallinich**, None; **U. Neudorf**,

None; **H. Wittkowski**, None; **G. Horneff**, 2,8; **D. Foell**, None.

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Abstract Number: 72

Systemic Juvenile Idiopathic Arthritis in a Colombian cohort: onset and clinical course

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose:

Juvenile idiopathic arthritis is the most prevalent rheumatic disease in children. The systemic form accounts for 10-15% of cases and is characterized by a dysregulation of the innate immune system. The prognosis of the disease is related to systemic involvement and complications such Macrophagic activation síndrome (MAS) and to the extent and severity of arthritis. The introduction of new drugs has changed the prognosis of these patients but continues to be a diagnostic and therapeutic challenge. This study presents the clinical and paraclinical characteristics of a cohort of Colombian patients with sJIA

Methods: Descriptive retrospective study of a cohort of patients from 1996 to 2016. Analysis of clinical records of patients with a definitive diagnosis of systemic juvenile idiopathic arthritis in 2 pediatric rheumatology clinics in Bogota,Colombia

Results: n=69. Mean age at diagnosis 6.7 years (SD 3,9 years), sex ratio F:M 1,37:1. The mean follow up time was 102 months (10-1080 months). Two patients (3%) died during follow up. Causes of death were MAS in one patient and multiple organ failure following gastrointestinal infection in the other. At diagnosis all patients present fever with a mean duration of 41 days (16-180 days). Rash was present in 93%, arthritis in 86% being polyarticular in most of the patients (56%), organomegaly in 50%, adenomegalies in 22% and serositis in 20% of patients. Laboratory features showed leukocytosis in 96%, anemia in 91% and thrombocytosis in 83% of patients. Increased levels of transaminases, ferritin, globular sedimentation velocity and C reactive protein were present in 19%, 97% and 100% (both) respectively. 48% patients had polyarticular course of arthritis and 44% systemic involvement. MAS occurred in 4 patients (6%) during debut and course of the disease. Regarding treatment, most of the patients were prescribed with nonsteroidal anti-inflammatory drugs (97%) and steroids (84%). Seven percent received Cyclosporine, 72,5% Methotrexate and 23% required biological treatment. At the last follow up 70% of patients were in functional class 1 or 2 and 7% were in class 4. There was a significant association between early disease onset (1-5 years) and functional class 3 and 4 (p=0,014). Also the worst functional class correlated with a polyarticular course (p=0,010). Patients with polyarthritis at onset had a worst functional class at the last follow up (p=0,003) and had a higher risk of continuing with polyarthritis at course of disease (p=0,000). Polyarticular course was more frequent in girls (p=0,016). Organomegalies at onset were more frequent in patients with a polyarticular course (p=0,007)

Conclusion: sJIA is a severe disease. Early onset and polyarticular involvement are prognostic markers. Aggressive treatment and periodic monitoring of complications may improve the prognosis of these patients

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Disclosure: A. Mosquera, None; **C. Malagón**, None; **C. Arango**, None.

Abstract Number: 73

Factors Associated with Etoposide Usage in Children with Macrophage Activation Syndrome Complicating Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION

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Session Time: 5:30PM-7:00PM

Background/Purpose:

Although macrophage activation syndrome (MAS) has been reported in association with almost all rheumatic diseases, it is by far most common in systemic juvenile idiopathic arthritis (sJIA). Reported mortality rates in MAS reach 10-20%. Standardized treatment guidelines for MAS are currently lacking, but management commonly includes high-dose corticosteroids combined with another immunosuppressive agent. Etoposide is a well established therapy in primary hemophagocytic lymphohistiocytosis. A recent systematic literature review on treatments of MAS in sJIA identified only a few patients who were given etoposide. We aimed to investigate etoposide usage among pediatric patients with MAS complicating sJIA and to identify predictors of etoposide administration.

Methods: Retrospective collected data from 362 patients included in the multinational study of the 2016 classification criteria for MAS in sJIA were examined to identify patients treated with etoposide and record potential predictors of etoposide administration. Variables significantly associated with etoposide usage in univariate analysis were entered in a multivariate regression model. Continuous variables were dichotomized according to the cut-off value obtained through ROC curve analysis.

Results:

Forty of the 362 patients (11 %) were treated with etoposide and 17 of those had information on all variables studied. Factors significantly associated with etoposide administration in multivariate analysis included multiorgan failure (OR 7.9, 95% CI 2.2-28.5), platelet count ≤ 132 x 109/liter (OR 5.8, 95% CI 1.8-18.2), triglycerides > 270.8 mg/dl (OR 3.7, 95% CI 1.3-10.4), aspartate aminotransferase > 389 units/liter (OR 3.7, 95% CI 1.3-10.3), and fibrinogen ≤ 1.53 gm/liter (OR 2.9, 95% CI 1.1-7.5). The AUC of the model was 0.86. In univariate analysis, there was no significant difference in mortality rate between patients given or not given etoposide.

Conclusion: Patients treated with etoposide were sicker than patients who did not receive this medication. However, mortality rate did not differ between the two treatment groups, suggesting that etoposide may be part of aggressive therapeutic interventions for severely ill children with MAS.

Disclosure: A. Horne, None; **F. Minoia**, None; **R. Q. Cron**, None; **A. Ravelli**, None.

Abstract Number: 74

Benefit of Anakinra in Treating Pediatric Secondary Hemophagocytic Lymphohistiocytosis

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SESSION INFORMATION
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Background/Purpose:

Familial, or primary, hemophagocytic lymphohistiocytosis (pHLH), is a rare but highly fatal condition due to mutations in lymphocyte cytolytic pathway genes. Secondary HLH (sHLH), termed macrophage activation syndrome (MAS) when associated with rheumatic disorders, affects children and adults with various disorders. sHLH can be associated with heterozygous defects in pHLH genes and usually the distinction between both forms is blurred. Both forms are routinely treated with etoposide-based protocols which are frequently limited by significant toxicity and mortality. Alternative less toxic therapies are currently being explored for sHLH. Anakinra is a recombinant interleukin-1 receptor antagonist that has been reported to improve survival in several cases of MAS.

Methods:

We performed a retrospective chart review of all anakinra-treated sHLH patients at Children's of Alabama from January 2008 to December 2016. The treating physician assigned diagnosis of sHLH was evaluated using 5 different sets of criteria: HLH-2004 and -2009, lupus (SLE) MAS, systemic juvenile idiopathic arthritis (sJIA) MAS-2016, and the H-Score. Demographic, clinical, laboratory, concurrent treatment, and outcome data were collected and analyzed by appropriate univariate statistical approaches.

Results:

44 (25 female) sHLH patients (mean age 10.3 years, range 1 - 19) were treated with anakinra. The underlying and associated diseases were sJIA (13), SLE/MCTD (8), infection (22), m

alignancy (3), gastroparesis (2), and other (6). Median duration of hospitalization was 15.5 days. The overall mortality was 25%. Earlier start of anakinra was associated with improved survival ($p = 0.008$).

Mean pre-treatment ferritin level was 33,316 ng/ml and dropped to 14,435 (43% decrease) within 15 days of starting anakinra. Mean duration to defervescence after anakinra was 1.7 days. Thrombocytopenia <100,000/µL was associated with increased mortality ($p=0.019$). sJIA associated MAS had 100% survival, whereas sHLH with underlying malignancy had 100% mortality.

Conclusion:

Anakinra appears to be effective for treating non-malignancy sHLH in children, particularly those with sJIA. The study is limited by its retrospective nature, non-uniform approach to therapy, lack of treatment controls, and variable follow-up period. Anakinra is currently being studied in a randomized, double-blinded, placebo-controlled trial to treat sHLH in children and adults.

	Total (*n*=44)	Survived (*n*=33)	Died (*n*=11)	P value
Demographics				
Male	19 (43.2%)	14 (42.4%)	5 (45.5%)	1[δ]
Female	25 (56.8%)	19 (57.6%)	6 (54.5%)	1[δ]
Mean age (years)	10.3 (SD=5.7)	9.7 (SD=5.3)	12 (SD=6.8)	0.252[#]
Presentation				
Persistent fever	43 (97.8%)	32 (97%)	11 (100%)	1[δ]
Hepatomegaly	13 (29.5%)	11 (33.3%)	2 (18.2%)	0.461[δ]
Splenomegaly	15 (34.1%)	13 (39.4%)	2 (18.2%)	0.282[δ]
Leucopenia	24 (54.5%)	16 (48.5%)	8 (72.7%)	0.294[δ]
Anemia	30 (88.2%)	21 (63.6%)	9 (81.8%)	0.456[δ]
Thrombocytopenia	31 (70.5%)	20 (60.6%)	11 (100%)	**0.019***
Hypertriglyceridemia	30 (73.2%) of 41	21 (70%) of 30	9 (81.8%)	0.463[δ]
Hypofibrinogenemia	19 (44.2%) of 43	10 (31.3%) of 32	6 (54.5%)	0.286[δ]
Hemophagocytosis	11 (31.4%) of 35	9 (34.6%) of 26	2 (22.2%) of 9	0.698[δ]
Low natural kill cells	13 (54.2%) of 24	10 (52.6%) of 19	3 (60%) of 5	1[δ]
Elevated serum sIL-2 Rα	31 (88.6%) of 35	23 (88.5%) of 26	8 (88.9%) of 9	1[δ]
Transaminitis	43 (97.8%)	32 (97%)	11 (100%)	1[δ]
Mean serum ferritin (ng/ml)	33,316	26,640	52,737	0.1810[#]
Underlying condition	**(56)**	**(41)**	**(16)**	
Infection	22 (39.3%)	15 (36.6%)	7 (43.8%)	0.763[δ]
sJIA	13 (23.2%)	13 (41.7%)	0	**0.0116*[δ]**
SLE/MCTD	8 (14.3%)	6 (41.6%)	2 (12.5%)	1[δ]
Malignancy	3 (5.4%)	0	3 (18.8)	**0.0191*[δ]**
Uveitis	2 (3.6%)	2 (4.9%)	0	1[δ]
Sjogren	2 (3.6%)	1 (2.4%)	1 (6.3%)	0.486[δ]
Gastroparesis	2 (3.6%)	1 (2.4%)	1 (6.3%)	0.486[δ]
Sarcoidosis	1 (1.9%)	1 (2.4%)	0	1[δ]
Crohn disease	1 (1.9%)	0	1 (6.3%)	0.281[δ]
Vasculitis	1 (1.9%)	1 (2.4%)	0	1[δ]
Enthesitis related arthritis	1 (1.9%)	1 (2.4%)	0	1[δ]
Multiple diagnoses	13 (29.5%)	10 (30.3%)	3 (27.3%)	1[δ]
Treatment analysis				
Hospital days before anakinra	12.1 (SD=22.9)	7 (SD=9.1)	27.5 (SD=40.5)	0.0084[#]
Anakinra monotherapy	14 (42.4%)	13 (39.4%)	1 (9.1%)	0.0759[δ]
Outcomes after anakinra				
Hospitalization (days)	30.1 (SD=39.5)	18.2 (SD=15.5)	65.6 (SD=63.9)	**0.0002*[#]**
Ferritin within 15 days	14,435	1,674	56,972	0.0569[δ]
Days to defervescence	1.7 (SD= 1.1)	1.6 (SD=1)	2.0 (SD=1.5)	0.1794[#]

t-test done between two means,[δ] Fisher exact text , * p value is statistically significant.

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Abstract Number: 75

Ferritin:ESR, A Predictor of MAS?

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SESSION INFORMATION

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Session Type: Abstract Submissions

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Background/Purpose:

Systemic onset juvenile idiopathic arthritis (SoJIA) is a rare autoinflammatory disorder comprising only 10% of JIA. Macrophage activation syndrome (MAS), an excessive and uncontrolled immune expansion, can develop within the setting

of SoJIA. MAS is often overt but can be subclinical in up to 40% of patients. Early recognition of MAS is imperative, as the mortality rate despite treatment is high. Unfortunately, there is no pathognomonic finding for MAS, which can lead to delayed recognition. Use of the ratio between ferritin and erythrocyte sedimentation rate (ESR) has been reported to discern between flares of SoJIA, other febrile illnesses, and MAS. The purpose of our project was to determine if utilization of the ferritin:ESR ratio at the onset of SoJIA could predict our patients with SoJIA who developed MAS.

Methods:

A single center, retrospective chart review of SoJIA patients was performed and data were extracted at the patientsÕ initial presentation. Patients presenting initially to an outlying facility with incomplete records were excluded. The 2016 Ravelli criteria were used to identify those patients with MAS. SoJIA patients with and without MAS were compared using descriptive statistics. Binary logistic regression analysis was performed to identify predictors of MAS.

Results:

Eight of 30 patients met criteria for MAS during initial presentation. Laboratory analysis can be found in Table 1. Patients with MAS had significantly higher AST, CRP, and triglyceride levels with lower fibrinogen levels. Binary logistic regression did not indicate any significant predictive variables for MAS.

Table 1: Laboratory Analysis

	SoJIA (median [IQR])	**SoJIA+MAS (median [IQR])**	***p***
AST (U/L)	40 [36,50]	67.5 [56,79]	0.048
CRP (mg/dL)	16.1 [11.9,24]	35 [33.7,36.4]	0.004
Fibrinogen (mg/dL)	558 [502,652]	380 [227,533]	0.039
Triglycerides (mg/dL)	93 [79.5,134]	123 [88,158]	0.032
Ferritin (ng/mL)	2898 [2165,4360]	8875 [4650,13100]	0.069
ANC (10^3/uL)	18.5 [10.1,22.8]	12.5 [0.6,14.4]	0.524
ESR (mm/hr)	80 [46,86]	60 [58,62]	0.709
Hemoglobin (g/dL)	10.4 [8.8,10.7]	9.9 [8.5,11.2]	0.701
Platelets (10^3/uL)	422 [399,514]	321 [177,465]	0.532
WBC (10^3/uL)	21.7 [16.1,25.9]	15 [13.3,16.87]	0.077
Ferritin:ESR	33.4 [28.4,50.4]	146 [80,211]	0.135
NK cell function	0.5 [0,3.4]	1.05 [0.1,2]	1
soluble IL-2R	1555 [1372,3844]	1990 [1859,2121]	0.133

Conclusion:

No single laboratory value, including the ferritin to ESR ratio, was associated with the development of MAS at the initial presentation of SoJIA. These findings highlight the need for a comprehensive clinical and laboratory evaluation in all SoJIA patients to identify MAS.

Disclosure: M. Gillispie, None; **M. DeGuzman**, None; **M. Gorelik**, None; **T. Vogel**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/ferritinesr-a-predictor-of-mas

Abstract Number: 76

Applying 2016 MAS Criteria to Systemic onset Juvenile Idiopathic Arthritis Patients with Diagnosis of Macrophage Activation Syndrome

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Background/Purpose: Macrophage activation syndrome (MAS) is the result of uncontrolled systemic inflammation, which can sometimes complicate systemic onset juvenile idiopathic arthritis (SoJIA). MAS classification criteria for SoJIA are recently developed. We aimed to apply the newly developed criteria to SoJIA patients with diagnosis of MAS.

Methods: We retrospectively analyzed our patients diagnosed with SoJIA between 1996-2015. Clinical features and laboratory parameters of patients who were diagnosed with MAS are reassessed according to 2016 criteria for MAS in SoJIA.

Results: 27 patients (32.1%, 13 boys and 14 girls) out of the 84 patients diagnosed with SoJIA, developed MAS. 7 patients had recurrent MAS episodes. Mean age of diagnosis for SoJIA was 5.8 ± 4.5 years and for the first MAS episode was 6.7 ± 5.2 years. 20 patients (22.9%) developed MAS at presentation of SoJIA while 7 patients developed it during the course of SoJIA. Among these 7, two patients were off treatment and the remaining patients were on biologic disease modifiying anti-rheumatic drugs (DMARDs) including infliximab, etanercept, anakinra, canakinumab and tocilizumab, in combination with classic DMARDs, except for one patient treated only with non-biologic agents. 14 patients fulfilled the 2016 criteria of MAS for SoJIA. Two patients did not have fever but met the lab criteria. Ferritin levels were not high enough in two patients. 11 patients had thrombocytopenia, 22 patients had increased AST, 9 had increased triglyceride and 10 patients had hypofibrinogenemia. No death occurred during the course of MAS.

Conclusion: Even if the criteria are not met, a high index of suspicion for MAS in SoJIA may be lifesaving. In addition to recently developed MAS criteria for SoJIA, following the trend of laboratory values can help to recognize a “developing MAS” and to treat accordingly early in the course.

Disclosure: E. Baris, None; **E. Anderson**, None; **F. Dedeoglu**, None.

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Abstract Number: 77

Effectiveness of Childhood Vaccinations in CAPS Patients Treated With Canakinumab: Results From an Open-Label Phase III Extension Study

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Canakinumab (CAN) has been shown not to impair antibody production following vaccination in children in an open-label phase 3 study (NCT01302860).[1] Here we present the results from the extension of this study. The objective of this study was to evaluate the presence of protective antibody levels following immunization with inactivated vaccines in patients with cryopyrin-associated periodic syndrome (CAPS) during extension study.

Methods: Patients who completed the core study were allowed to continue into the extension study on the standard dosing regimen of 2 mg/kg subcutaneous CAN every 8 weeks or on last dose/dosing regimen received in the core study. Vaccination response was evaluated using post-vaccination antibody titers at 4 and 8 weeks after immunization. Patients were considered assessable for an antibody response to a specific vaccination if they had a measurement of antibody titer 0-14 days post-vaccination (pre-vaccination assessment) and at least 1 subsequent measurement of antibody titer at 4 weeks and/or 8 weeks post-vaccination. However, for patients with adequate pre-dose antibody titers and maintained during the trial, the specific patient vaccination was deemed non-assessable.

Results: During the extension phase, of 17 patients (≤6 years), 4 received 8 types of vaccinations against *Corynebacterium diphtheria*, *Bordetella pertussis*, *Neisseria meningitidis*, *Clostridium tetani*, influenza type A and type B, *Haemophilus influenza* B, *Streptococcus pneumoniae*, or hepatitis B. Of 20 unique patient-vaccination cases, 17 were assessable for a vaccination response, whereas for the remaining 3, pre-dose antibody titer was not available. For 16 (94.1%) assessable cases, post-vaccination antibody titers increased above protective levels. For one patient who received Tetravec formulation (diphtheria, tetanus and acellular pertussis combination), the response observed for 1 (vaccination against *Clostridium tetani*) of the 3 vaccines included in Tetravac represented optical density rather than antibody concentrations and hence considered non-evaluable. For 19/20 patient-vaccinations, including those without pre-dose antibody titers, protective levels were observed during the study, which were maintained throughout the extension.

Conclusion: Canakinumab appeared to have no effect on post-vaccination antibody production following the administration of non-live vaccines in CAPS patients.

[1]Brogan P, et al. *Arthritis Rheumatol*. 2015;67:(S10).

Disclosure: P. Brogan, None; **M. Hofer**, 5; **J. B. Kuemmerle-Deschner**, 5,2; **B. R. Lauwerys**, None; **A. Speziale**, 3; **X. Wei**, 3; **R. Laxer**, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/effectiveness-of-childhood-vaccinations-in-caps-patients-treated-with-canakinumab-results-from-an-open-label-phase-iii-extension-study-2

Abstract Number: 78

Predictors of Outcome Following Tonsillectomy in Periodic Fever, Aphthous Stomatitis Pharyngitis, and Cervical Adenitis (PFAPA) Syndrome

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Tonsillectomy is considered curative in a majority of patients with periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome. Predictors of outcome following tonsillectomy are unknown.

Methods: Patients from Vanderbilt Children's Hospital and the National Institutes of Health (NIH) who met the diagnostic criteria for PFAPA and underwent tonsillectomy were recruited. Clinical and demographic features of patients who had complete resolution of symptoms and those who had continued symptoms after tonsillectomy were compared with the Chi-squared or Mann-Whitney U test.

Results: Fifty-five patients (38 from Vanderbilt and 17 from NIH) were followed after tonsillectomy for an average of 5.6 years. Following tonsillectomy, 63% of patients from Vanderbilt had complete resolution of episodes, while only 18% of patients from NIH had complete resolution. Of the 29 patients who continued to have episodes following tonsillectomy, 52% had less severe or less frequent episodes, 24% had a period of remission ranging from 9 months to 6 years followed by continued episodes, 17% had no change in episodes, and 3% reported feverless episodes. Patients who did not have complete resolution of episodes following tonsillectomy were more likely to have abdominal pain and limb pain (arthralgia or myalgias) during episodes (Table).

Conclusion: The majority of patients with PFAPA had improvement in the severity and frequency of episodes following tonsillectomy. Differences in outcome at Vanderbilt and NIH likely stem from referral bias in that NIH is a quaternary referral center and more likely to see patients refractory to conventional therapies. Patients with abdominal pain and limb pain may have lymphoid tissue outside the palatine tonsils that triggers systemic inflammation or may have illnesses distinct from PFAPA. Further analysis of tonsil immunology and imaging of lymphoid tissue outside of the pharynx in these two groups may help to resolve these questions.

Feature	Patients WITHOUT complete resolution after tonsillectomy	Patients WITH complete resolution after tonsillectomy	P value
Ulcer	82%	70%	0.30
Pharyngitis	93%	93%	0.97
Lymphadenopathy	82%	78%	0.69
URI symptoms	30%	22%	0.54
Headache	59%	48%	0.41
Abdominal pain	**70%**	**31%**	**0.004**
Vomiting	54%	33%	0.132
Diarrhea	20%	4%	0.19
Rash	30%	11%	0.18
Limb pain (arthralgia or myalgia)	**59%**	**30%**	**0.03**
Age at tonsillectomy	68 months	66 months	0.88
Age of episode onset	23 months	24 months	0.13
Duration of episode	4.6 days	5.1 days	0.10
Interval between episodes	28 days	28 days	0.92

Disclosure: K. Manthiram, None; **D. L. Kastner**, None; **K. Edwards**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/predictors-of-outcome-following-tonsillectomy-in-periodic-fever-aphthous-stomatitis-pharyngitis-and-cervical-adenitis-pfapa-syndrome

Abstract Number: 79

Predicting Colchicine Response in Patients with Undefined Autoinflammatory Diseases

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose:

Autoinflammatory diseases (AIDs) are a rare group of illnesses characterized by unprovoked episodes of fever and systemic inflammation. An understanding of their pathophysiology has led to the development of effective treatment guidelines. Unfortunately, many patients with recurrent fevers have symptoms that do not match any of the known AIDs. There is an unmet need to provide effective treatment to these patients with undefined AIDs (uAIDs). Colchicine, a treatment for patients with familial Mediterranean fever, is sometimes used to treat patients with uAIDs. We examined the efficacy of colchicine in patients with uAIDs and identified clinical factors that predicted a good colchicine response.

Methods:

We conducted a retrospective chart review of patients with a clinical diagnosis of uAIDs who tolerated colchicine from a large pediatric rheumatology clinic. Good colchicine response was defined as a decrease in the frequency, severity, and length of febrile episodes without requiring additional medications. Partial response was defined as decreasing the frequency, severity, or length of episodes; additional medicines may have been required.

Results:

184 patients with uAIDs were identified and 68 had used colchicine. Of these, 33 (48.5%) were good colchicine responders, 30 (44.1%) were partial responders, and five patients (7.4%) did not respond. Patient and disease characteristics are shown in Table 1. Ethnicity of colchicine responders is shown in Figure 1; ethnicity of partial and non-responders is shown in Figure 2.

Conclusion:

Colchicine was effective treatment for most patients with uAIDs, with 48% and 44% of patients having a good or partial response, respectively. Patients were more likely to have a good colchicine response if they had vomiting during flares; abdominal pain approached statistical significance. The presence of aphthous stomatitis predicted a partial response. Mutations in genes associated with AIDs, a family history of recurrent fevers, and age of disease onset did not predict colchicine response.

	Good colchicine responders, N=33 (n,%)	Partial and non-responders n=35 (n,%)	p-value
Patient characteristics			
Female	17 (52)	20 (57)	0.8078
Age at disease onset (in months)	50.0	49.9	0.9908
Family history of recurrent fevers	2 (6.1)	7 (20)	0.1510
Mean duration of follow-up while on colchicine (in months)	37.8	32.4	0.4782
Mean colchicine dose (in mg)	0.58	0.61	0.7184
Periodic fever syndrome panel test sent	24 (73)	29 (83)	0.3866
Patients with heterozygous MEFV mutations	8 (24)	9 (26)	1.000
Periodic fever syndrome panel negative	11/24 (46)	16/29 (55)	0.5857
Clinical characteristics of febrile episodes			
Aphthous stomatitis	6 (18)	18 (51)	**0.0054**
Fatigue	5 (15)	8 (23)	0.5415
Myalgia	6 (18)	8 (23)	0.7669
Headache	12 (36)	12 (34)	1.000
Lymphadenopathy	5 (15)	8 (23)	0.5415
Pharyngitis	2 (6)	2 (6)	1.000
Chest pain	2 (6)	2 (6)	1.000
Abdominal pain	21 (64)	14 (40)	0.0580
Vomiting	14 (42)	5 (14)	**0.0145**
Diarrhea	7 (21)	3 (9)	0.1809
Arthralgia	16 (48)	10 (29)	0.1341
Rash	6 (18)	8 (23)	0.7669

Table 1. Patient and disease characteristics.

Figure 1. Word cloud of ethnicity for good colchicine responders.

Figure 2. Word cloud of ethnicity for partial and non-responders.

Disclosure: J. S. Hausmann, None; **B. Guven**, None; **E. Anderson**, None; **F. Dedeoglu**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/predicting-colchicine-response-in-patients-with-undefined-autoinflammatory-diseases

Abstract Number: 80

Treatment of Blau Syndrome with Biologic Therapy: A Single Center Case Series of Seven Patients Over Two Decades

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose:

Blau syndrome is a rare autoinflammatory granulomatous disease that presents with fever, arthritis, dermatitis and uveitis. It results from mutations in *NOD2*, an intracellular pathogen sensor, with autosomal dominant inheritance. No therapeutic trials have been conducted in Blau syndrome and only limited case reports regarding treatment are available. The aims of this study were to review the disease course, clinical response, and safety of the prolonged use of biologic medications for seven patients with Blau syndrome.

Methods:

A retrospective chart review was completed with respect to the disease course, treatment regimens, side effects, and therapeutic response of seven patients with Blau syndrome cared for over two decades at Texas Children’s Hospital in Houston, TX.

Results:

Six of the patients are sibling pairs and all had either a sibling and/or parent with Blau syndrome. Six of the patients are male. Age range is 6-22 years. Mean age of symptom onset was 1.3 years and mean age at diagnosis was 5 years. Most of the patients were initially diagnosed as juvenile idiopathic arthritis. Arthritis was present in all patients. Other features varied in frequency: uveitis (n=4), recurrent fever (n=4), and cutaneous involvement (n=4). Initial medications for all patients included NSAIDs and corticosteroids. Additional therapies included methotrexate (86%), cyclosporine (29%), mycophenolate (14%), and azathioprine (14%). Biologic therapy was initiated in all patients and included etanercept (43%), adalimumab (86%), infliximab (57%), abatacept (14%), anakinra (29%), and tocilizumab (29%). Mean duration of therapy in years was etanercept 4.9, adalimumab 2.4, infliximab 3.3, abatacept 0.2, anakinra 3.6, and tocilizumab 0.2. Combined, our center has 43 patient-years of experience with anti-TNF medications in these patients (14.8 years etanercept, 14.6 years adalimumab, and 13.3 years infliximab). Adverse events included liver toxicity (n=2, resolved with stopping concurrent methotrexate), anemia (n=3), thrombocytopenia (n=1), and a benign lung nodule (n=1). Infectious complications occurred in 71%, leading to 4 hospitalizations (cellulitis, cutaneous varicella in two siblings, and bacterial pneumonia). None of these complications warranted a permanent discontinuation of the biologic therapy.

Conclusion:

Blau syndrome is a rare autoinflammatory granulomatous disease that results in significant morbidity if uncontrolled. In our center's experience with these patients, potent TNF inhibition with infliximab or weekly adalimumab was the most clinically efficacious biologic therapy. There were no serious adverse events warranting permanent discontinuation. These medications should be considered for the treatment of Blau disease.

Disclosure: J. Rammel, None; **P. Rosillo**, None; **T. Vogel**, None; **M. de Guzman**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/treatment-of-blau-syndrome-with-biologic-therapy-a-single-center-case-series-of-seven-patients-over-two-decades

Abstract Number: 81

Preliminary Consensus Treatment Plans for Periodic Fever, Aphthous Stomatitis, Pharyngitis and Adenitis: The Foundation for Capturing Treatment Responses in PFAPA from the CARRA PFAPA Subcommittee

Gil Amarilyo[1], Deborah Rothman[2], Kalpana Manthiram[3], Suzanne Li[4], Liora Harel[5], Kathryn Edwards[6], Gary Marshall[7], Simona Nativ[8], Kathleen Haines[9], Geraldina Lionetti[10], Julie Cherian[11], Yongdong Zhao[12], Patricia DeLaMora[13], Grant Syverson[14], Ian Michelow[15], Yuriy Stepanovskiy[16], Akaluck Thatayatikom[17], Cagri Yildirim-Toruner[18], Shoghik Akoghlanian[19], Lori Tucker[20], Katalin Koranyi[19], Hemaltha Srinivasalu[21], Fatma Dedeoglu[22] and Sivia Lapidus[8], [1]Schneider Children's Medical Center of Israel, Sackler School of Medicine, Tel Aviv University, Petach Tikva, Israel, [2]Albany Medical Center, Albany, NY, [3]National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, [4]Pediatrics, Joseph M Sanzari Children's Hospital, Hackensack Meridian Health, Hackensack, NJ, [5]Schneider Children's Medical Center of Israel, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, [6]Department of Pediatrics, Vanderbilt University School of Medicine, Nashville, TN, [7]Norton Children's Hospital, University of Louisville, Louisville, KY, [8]Pediatric Rheumatology, Goryeb Children's Hospital, Morristown, NJ, [9]Joseph M Sanzari Children's Hospital, Hackensack Meridian Health, Hackensack, NJ, [10]Pediatric Rheumatology, UCSF Benioff Children's Hospital Oakland, Oakland, CA, [11]Department of Pediatrics, Stony Brook University Hospital, Stony Brook, NY, [12]Seattle Children's Hospital, Department of Pediatric Rheumatology, University of Washington, Seattle, WA, [13]Weill Cornell Medical College, New York, NY, [14]Pediatric Rheumatology, Medical College of Wisconsin, Wauwatosa, WI, [15]Center for International Health Research, Alpert Medical School of Brown University, Providence, RI, [16]Shupyk National Academy of Postgraduate Education, Kyiv, Ukraine, [17]UF Health Shands Hospital, Gainesville, FL,

[18]Rheumatology, Nationwide Children's Hospital, Columbus, OH, [19]Nationwide Children's Hospital, Columbus, OH, [20]Pediatric Rheum/Rm K4-120, BC Childrens Hospital, Vancouver, BC, Canada, [21]Children's National Medical Center, Washington, DC, [22]Division of Immunology, Rheumatology Program, Boston Children's Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: PFAPA is the most common recurrent fever condition in children. A recent survey showed heterogeneity in physicians' management strategies. In order to evaluate the effectiveness of different treatments for PFAPA, standardized treatment plans are needed. The PFAPA Work Group of CARRA (Childhood Arthritis and Rheumatology Research Alliance) developed CTPs for PFAPA that will lead to improved characterization of a well-defined cohort and optimal treatment. We aimed to develop consensus treatment plans (CTPs) for periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome for future evaluation of treatment responses in PFAPA.

Methods: A core group of PFAPA experts including pediatric rheumatologists, infectious disease specialists and immunologists comprised the CARRA PFAPA Workgroup. After a literature review was conducted, a survey was distributed to pediatric rheumatology and infectious diseases physicians who treat PFAPA patients to query their management strategies. The CARRA PFAPA workgroup met monthly via teleconferences and in-person meetings from 2014-2016 to develop the CTPs. A modified nominal group technique was employed to create the proposed CTPs. Patient characteristics for enrollment were established through expert consensus.

Results: Based on these data, 4 preliminary CTP arms were created: anti-pyretic treatment, corticosteroids, prophylaxis arm and surgical management (Figure 1). This approach was approved by the majority of the PFAPA subcommittee.

Conclusion: CTPs with four treatment arms were developed for PFAPA. Coupled with data collection on patient outcomes at defined intervals, these CTPs will generate comparative effectiveness data in an observational setting to determine optimal treatment of PFAPA after the larger CARRA group is assessed for their willingness to follow at least one of the regimens in these CTPs.

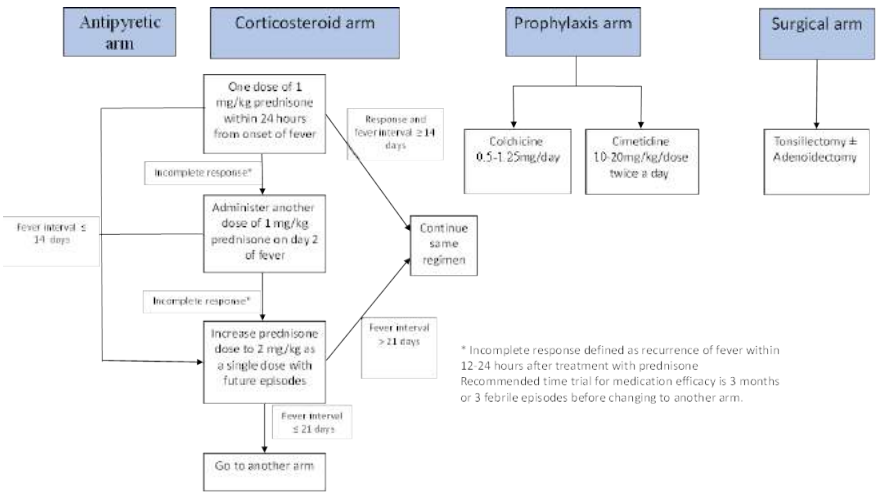


Figure 1

Disclosure: G. Amarilyo, 2,5; **D. Rothman**, None; **K. Manthiram**, None; **S. Li**, None; **L. Harel**, 2,5; **K. Edwards**, None; **G. Marshall**, None; **S. Nativ**, 5; **K. Haines**, None; **G. Lionetti**, None; **J. Cherian**, None; **Y. Zhao**, 2; **P. DeLaMora**, None; **G. Syverson**, None; **I. Michelow**, None; **Y. Stepanovskiy**, None; **A. Thatayatikom**, None; **C. Yildirim-Toruner**, None; **S. Akoghlanian**, None; **L. Tucker**, None; **K. Koranyi**, None; **H. Srinivasalu**, None; **F. Dedeoglu**, None; **S. Lapidus**, 5.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/preliminary-consensus-treatment-plans-for-periodic-fever-aphthous-stomatitis-pharyngitis-and-adenitis-the-foundation-for-capturing-treatment-responses-in-pfapa-from-the-carra-pfapa-subcommittee

Abstract Number: 82

Disease Burden and Social Impact of Chronic Nonbacterial Osteomyelitis on Affected Children and Young Adults

Melissa Oliver[1], Tzielan Lee[2], Bonnie Halpern-Felsher[3], Elizabeth Murray[4], Rebecca Gholson[5] and Yongdong Zhao[6], [1]Pediatric Rheumatology, Stanford University, Department of Pediatric Rheumatology, Palo Alto, CA, [2]Stanford University, Department of Pediatric Rheumatology, Palo Alto, CA, [3]Pediatrics, Adolescent Medicine, Stanford University, Department of Pediatrics, Adolescent Medicine, Palo Alto, CA, [4]CRMO Facebook Support Group, Seattle, WA, [5]CRMO Facebook Support Group, Asheville, NC, [6]Seattle Children's Hospital, Department of Pediatric Rheumatology, University of Washington, Seattle, WA

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose:

Chronic Nonbacterial Osteomyelitis (CNO) is a rare autoinflammatory bone disorder that can result in bone destruction, persistent bone pain, growth disturbances and pathological fractures. CNO is a diagnosis of exclusion; as such, families may experience obstacles before being diagnosed. Little is known about the impact of CNO on the daily lives of patients and their families. The objective of this study is to understand the disease burden and socioeconomic and psychological impact of CNO from the patients' and families' perspectives, with the goal of identifying areas of improvement for patient care and reduced disease burden.

Methods:

Population targeted were patients with a diagnosis of CNO made at <22 yrs of age and/or their parent/guardian if patient's age at time of study was <18 yrs. Participants were invited through the Facebook CNO support group and at clinic visits at Stanford Children's Health. The survey was administered and completed online through RedCap. Descriptive statistics were conducted with continuous variables reported as means/medians (SD/range) and categorical variables as frequencies and percentages.

Results:

A total of 284 consented and completed the survey. The median age at CNO diagnosis was 10 yrs (range 2-22+). Median time from first CNO symptom to diagnosis was 2 yrs with 48% first seeing a pediatric rheumatologist after 12 months of symptoms. Antibiotics, which are not an effective treatment for CNO, were used in 34.5% of patients prior to CNO diagnosis; of these, 24% received antibiotics for greater than 6 months (Table 1). Difficulty with obtaining MRI studies occurred in 26.7%. Between 25% and 61% reported a negative effect on relationships, school/work or finances; and 19% to 50% reported effects on psychosocial well-being. The majority agreed patients' performance with daily tasks and hobbies was challenged due to pain, fatigue and physical limitation related to CNO (Figure 1).

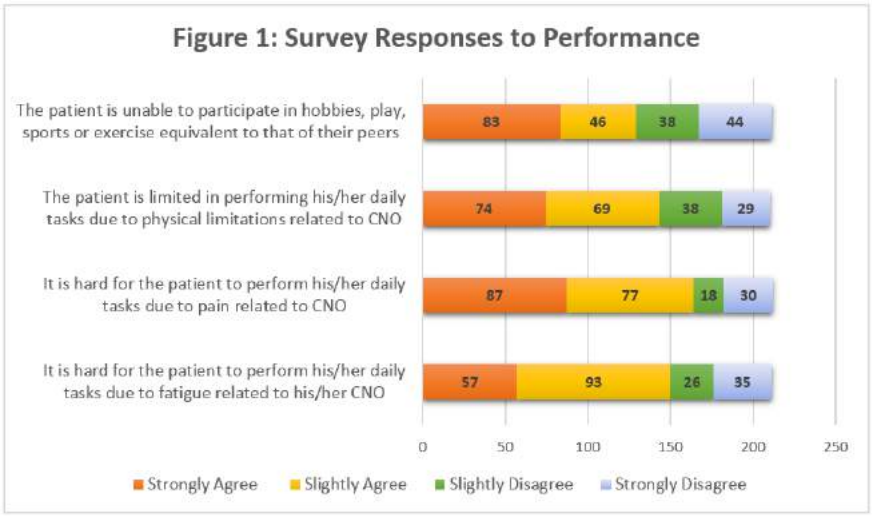
Conclusion:

This is the first study to understand the burden of CNO from the patients' and families' perspectives. Many experienced delays in diagnosis and seeing a pediatric rheumatologist, ineffective treatments, and problems with relationships, school, work, finances and well-being. Our findings emphasize the importance of educating the medical community about CNO, facilitating earlier referrals to rheumatology and assisting patients/families to cope with socioeconomic stressors and mental health issues. The findings will help develop specific patient reported outcome measures to be used for future clinical trials or comparative effectiveness studies.

Table 1: Baseline Characteristics and Patient Demographics

Characteristics	%	n*
Survey completed by parent	86.6	284
Gender, male	33.7	246
Race, white/Caucasian	91.8	245
Ethnicity, non-Hispanic/Latino	89.4	227
Country		247
North America	69.6	
Europe	22.3	
Other	8.1	
Time from symptom onset and 1st pediatric rheumatologist visit		239
< 6 mo	32.2	
6-12 mo	19.7	
> 12 mo	48.1	
Physicians seen prior to CNO diagnosis		284
PCP	76.8	
Orthopedic Surgeon	51.1	
Infectious Disease	30.6	
Biopsy performed	78.9	213
Received antibiotics prior to CNO diagnosis	34.5	284
Treated with antibiotics >6 mo	24.0	96
Associated Conditions		284
Acne	10.6	
Psoriasis	10.2	
IBD	9.2	
PPP	7.8	
JIA	6.3	
AS/ERA	2.8	
Uveitis	2.5	
Other	10.6	
Use of an assisted device	41.9	284

IBD= inflammatory bowel disease; AS/ERA= Ankylosing Spondylitis/Enthesitis related arthritis; JIA=juvenile idiopathic arthritis; PPP= Palmoplantar pustulosis
*= number of participants who responded to survey question



Disclosure: M. Oliver, None; **T. Lee**, None; **B. Halpern-Felsher**, None; **E. Murray**, None; **R. Gholson**, None; **Y. Zhao**, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/disease-burden-and-social-impact-of-chronic-nonbacterial-osteomyelitis-on-affected-children-and-young-adults

Abstract Number: 83

Feverprints: A Crowdsourcing Study of Temperature in Health and Disease

Jonathan S. Hausmann[1,2], Nitin Gujral[3], Soleh Al Ayubi[3], Jared B. Hawkins[3], John S. Brownstein[3] and Fatma Dedeoglu[2], [1]Rheumatology, Beth Israel Deaconess Medical Center, Boston, MA, [2]Rheumatology, Boston Children's Hospital, Boston, MA, [3]Innovation & Digital Health Accelerator, Boston Children's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Clinical and Therapeutic Poster Session
Session Type: Abstract Submissions
Session Time: 5:30PM-7:00PM

Background/Purpose:

Autoinflammatory diseases (AIDs) are a rare group of illnesses characterized by unprovoked episodes of fever and systemic inflammation. An understanding of their pathophysiology has led to the development of effective treatment guidelines. Unfortunately, many patients with recurrent fevers have symptoms that do not match any of the known AIDs. There is an unmet need to provide effective treatment to these patients with undefined AIDs (uAIDs). Colchicine, a treatment for patients with familial Mediterranean fever, is sometimes used to treat patients with uAIDs. We examined the efficacy of colchicine in patients with uAIDs and identified clinical factors that predicted a good colchicine response.

Methods:

We conducted a retrospective chart review of patients with a clinical diagnosis of uAIDs who tolerated colchicine from a large pediatric rheumatology clinic in Boston. Good colchicine response was defined as a decrease in the frequency, severity, and length of febrile episodes without requiring additional medications. Partial response was defined as decreasing the frequency, severity, or length of episodes; additional medicines may have been required.

Results:

184 patients with uAIDs were identified and 68 had used colchicine. Of these, 33 (48.5%) were good colchicine responders, 30 (44.1%) were partial responders, and five patients (7.4%) did not respond. Patient and disease characteristics are shown in Table 1. Ethnicity of colchicine responders is shown in Figure 1; ethnicity of partial and non-responders is shown in Figure 2.

Conclusion:

Colchicine was effective treatment for most patients with uAIDs, with 48% and 44% of patients having a good or partial response, respectively. Patients were more likely to have a good colchicine response if they had vomiting during flares; abdominal pain approached statistical significance. The presence of aphthous stomatitis predicted a partial response. Mutations in genes associated with AIDs, a family history of recurrent fevers, and age of disease onset did not predict colchicine response.

	Good colchicine responders, N=33 (n,%)	Partial and non-responders n=35 (n,%)	p-value
Patient characteristics			
Female	17 (52)	20 (57)	0.8078
Age at disease onset (in months)	50.0	49.9	0.9908
Family history of recurrent fevers	2 (6.1)	7 (20)	0.1510
Mean duration of follow-up while on colchicine (in months)	37.8	32.4	0.4782
Mean colchicine dose (in mg)	0.58	0.61	0.7184
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Clinical characteristics of febrile episodes			
Aphthous stomatitis	6 (18)	18 (51)	**0.0054**
Fatigue	5 (15)	8 (23)	0.5415
Myalgia	6 (18)	8 (23)	0.7669
Headache	12 (36)	12 (34)	1.000
Lymphadenopathy	5 (15)	8 (23)	0.5415
Pharyngitis	2 (6)	2 (6)	1.000
Chest pain	2 (6)	2 (6)	1.000
Abdominal pain	21 (64)	14 (40)	0.0580
Vomiting	14 (42)	5 (14)	**0.0145**
Diarrhea	7 (21)	3 (9)	0.1809
Arthralgia	16 (48)	10 (29)	0.1341
Rash	6 (18)	8 (23)	0.7669

Table 1. Patient and disease characteristics.

Figure 1. Word cloud of ethnicity for good colchicine responders.

Figure 2. Word cloud of ethnicity for partial and non-responders.

Disclosure: J. S. Hausmann, None; **N. Gujral**, None; **S. Al Ayubi**, None; **J. B. Hawkins**, None; **J. S. Brownstein**, None; **F. Dedeoglu**, None.

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Abstract Number: 84

Predictors of Corticosteroid Discontinuation, Complete Clinical Response and Remission in Patients with Juvenile Dermatomyositis

Takayuki Kishi[1], William Warren-Hicks[2], Michael Ward[3], Nastaran Bayat[1], Lan Wu[1], Gulnara Mamyrova[4], Ira N. Targoff[5], Frederick Miller[1], **Lisa G. Rider**[1] and the Childhood Myositis Heterogeneity Study Group, [1]Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institute of Health, Bethesda, MD, [2]EcoStat, Inc., Mebane, NC, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [4]Division of Rheumatology, Department of Medicine, George Washington University School of Medicine and Health Sciences, Washington, DC, [5]VA Medical Center, University of Oklahoma Health Sciences Center, and Oklahoma Medical Research Foundation, Oklahoma City, OK

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Factors affecting treatment (Rx) responses in juvenile dermatomyositis (JDM) are not well understood. We examined a large JDM registry for predictors of excellent Rx responses, including final discontinuation of corticosteroid therapy (CS-DC), complete clinical response (CCR, clinically inactive disease for ≥6 continuous mths on Rx), and remission (inactive disease for ≥6 continuous mths off all Rx).

Methods: A retrospective review of Rx responses in 305 pts with probable or definite JDM was conducted. The median Rx duration was 30 mths [IQR 19-57 mths] and follow-up duration was 43 mths [IQR 22-74 mths]. We evaluated the probability of achieving CS-DC, CCR, and remission by Weibull time-to-event models. Significant univariable predictors of each outcome (Log rank $P<0.05$) were examined in multivariable time-to-event analysis using Markov chain Monte Carlo Weibull extension models. The conditional probability of each outcome was also evaluated using Bayesian network models.

Results: Fifty-two percent (159 pts) experienced final CS-DC and the probability of achieving CS-DC was 9.7% at 1 year, 35% at 3 years and 57% at 5 years after initial Rx. Thirty-three percent (99 pts) achieved CCR and the probability of achieving CCR was 7.9% at 1 year, 27% at 3 years and 44% at 5 years after Rx start. Twenty-six percent (80 pts) achieved remission, including 31 pts who achieved remission without CCR first. The probability of remission was 3.2% at 1 year, 16% at 3 years, and 31% at 5 years after Rx start. The probability of CCR or remission was found to be conditional: For CCR, the probability of attaining CCR given CS-DC was 47%; when CS-DC was not attained, the probability of achieving CCR was 19%. For remission, when CS-DC and CCR were achieved the probability of achieving remission was 66%. When CS-DC and CCR were not achieved, the probability of achieving remission was 3.5%. If either CS-DC or CCR were achieved in isolation, the probability of achieving remission was 27%.

The absence of calcinosis and infection within 6 months of illness onset were associated with shorter times to achieve these 3 outcomes in multivariable modeling (Table). The absence of GI, pulmonary or cardiac symptoms was associated with shorter times to achieve CS-DC and CCR. MDA5 Abs and lack of p155/140 Abs, but MJ Abs and lack of early flare were associated with shorter times to CS-DC and CCR, respectively. Achievement of CCR strongly predicted shorter time to remission, with CS-DC, absence of lipodystrophy and younger age at first Rx as other predictors.

Conclusion: A large proportion of JDM patients achieve positive Rx responses, including CS-DC, CCR, and remission, although timelines for these important outcomes are relatively long. Factors associated with shorter times to achieve these Rx outcomes include selected clinical features, MSAs, and environmental factors.

Table. Multivariable time-to-event analysis using Markov chain Monte Carlo Weibull extension models to examine predictors of shorter time to achieve corticosteroid discontinuation, complete clinical response and remission in JDM.

	CS-DC	CCR	Remission
Absence of calcinosis	0.63	0.65	1.10
Absence of infection within 6 months of illness onset	0.54	0.61	1.05
Absence of GI, pulmonary or cardiac symptoms	0.65	0.60	
Anti-p155/140 autoantibody negative	0.49		
No disease flare within 18 months from treatment start		0.83	
Anti-MDA-5 autoantibody positive	0.68		
Anti-MJ autoantibody positive		0.64	
Absence of lipodystrophy			1.65
Age at 1st treatment <7years old			0.97
CCR achieved			10.49
CS-DC achieved			1.55

The mean slope values are shown, which indicate the relative contribution to the overall model. For each variable, the parameter credible intervals did not overlap zero, and models with best fit based on lowest DIC values are shown.

Disclosure: T. Kishi, 2; **W. Warren-Hicks**, None; **M. Ward**, None; **N. Bayat**, 2; **L. Wu**, None; **G. Mamyrova**, 2; **I. N. Targoff**, None; **F. Miller**, None; **L. G. Rider**, 2.

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Abstract Number: 85

Characteristics of anti-MDA5 autoantibody-associated Juvenile Dermatomyositis (JDM) in North America

Gulnara Mamyrova[1], Takayuki Kishi[2], Ira N Targoff[3], Rodolfo V Curiel[1], Frederick W Miller[2], **Lisa G Rider**[1,2] and The Childhood Myositis Heterogeneity Collaborative Study Group, [1]Division of Rheumatology, Department of Medicine, George Washington University School of Medicine and Health Sciences, Washington, DC, [2]Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institute of Health, Bethesda, MD, [3]VA Medical Center, University of Oklahoma Health Sciences Center, and Oklahoma Medical Research Foundation, Oklahoma City, OK

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Anti-MDA5 Abs have been reported to associate with clinically amyopathic and classic dermatomyositis (DM), with severe progressive interstitial lung disease (ILD) and poor prognosis in Japanese pts. The aim of this study was to examine the frequency and characteristics of anti-MDA5 Abs associated with juvenile DM (JDM) in North America.

Methods: Demographic, clinical, laboratory and outcome features of 37 pts with anti-MDA5 Abs were assessed and compared to those of 60 MSA/MAA negative and 175 anti-p155/140 Ab+ JDM and JCTM/DM pts meeting probable or definite Bohan and Peter criteria. Differences were evaluated by Fisher's exact and Mann-Whitney tests. Kaplan-Meier and Log-rank tests were used for treatment analysis. Myositis Abs were tested by standard immunoprecipitation (IP) and MDA-

5 and p155/140 Abs tested by reverse IP-immunoblot. Significant univariable results were examined in multivariable logistic regression.

Results: Anti-MDA5 Abs were identified in 37 (7.9%) pts out of a cohort of 467 JDM and JCTM/DM pts. Characteristics of MDA5+ pts compared to MSA/MAA- and anti-p155/140 Ab JDM and JCTM/DM pts are shown in the Table. MDA5 Ab+ pts had lower serum CK levels. MDA5 Ab+ pts more frequently had fatigue, fever, weight loss, adenopathy, arthralgia, arthritis, abnormal PFTs, dyspnea, and ILD compared to Ab- and p155/140+ pts. The median skeletal, pulmonary and constitutional symptom scores at diagnosis were higher in MDA5 Ab+ pts, but the median overall clinical symptom score at diagnosis was lower compared to Ab- and higher compared to p155/140+ pts ($p<0.0001$). There were no differences in gender distribution, delay to diagnosis, and onset severity among the three groups. Anti-MDA5 Ab + pts did not differ in total number or types of medications received, or in frequency of remission compared to MSA/MAA- or p155/140 Ab+ pts. MDA5+ pts had fewer flares (48% vs. 73%, $p=0.014$), and shorter time to final steroid discontinuation (30 [IQR 16-66] vs. 53 mths [IQR 26-128], $p=0.009$) compared to p155/140+ pts. Multivariable analysis revealed weight loss, arthritis and lower serum CK level were significantly associated with anti-MDA5+ vs Ab – pts, whereas, weight loss, arthritis, arthralgia, dyspnea, fever, and slow disease onset speed were significantly associated with anti-MDA5+ vs. p155/140+. There were no differences in disease course, status at most recent evaluation, ACR functional class, and mortality of MDA5+ vs either group.

Conclusion: Anti-MDA5 Abs are seen in a distinct subset of juvenile myositis with JDM who have frequent arthritis, arthralgia, weight loss, adenopathy, and ILD, but lower serum CK. MDA5+ pts have comparable outcomes, but with the ability to discontinue steroids more rapidly and less frequent flares compared to p155/140+ pts.

Table. Characteristics of JDM patients with anti-MDA5 Abs compared to MSA/MAA negative and anti-p155/140 Ab

	Anti-MDA5+ Median [IQ range] or %	MSA/MAA Neg* Median [IQ range] or %	Anti-p155/140+* Median [IQ range] or %
Age at diagnosis (yr)	8.7 [6.4-12.9]	7.6 [5.3-11.4]	7.0 [4.2-10.9][1]
Slow onset speed (3-6 mo)	48.6	36.2	22.3[3]
ANA titer	40 [0-320]	40 [0-320]	320 [80-1280][4]
Fatigue	94.6	80.0	82.9
Weight loss	81.1	28.8[4]	32.0[4]
Fever	64.9	43.3	30.3[4]
Adenopathy	40.5	15.3[2]	20.8[1]
Constitutional System Score	0.5 [0.5-0.8]	0.25 [0.25-0.5][4]	0.25 [0.25-0.5][4]
Falling episodes	6 (16.7)	35.0	36.8[1]
Highest CK (≤ 252U/L)	182.0 [78.0-252.0]	745.5 [293.0-3029.0][4]	438.5 [189.5-2017.0][4]
Muscle System Score	0.29 [0.14-0.43]	0.29 [0.15-0.48]	0.29 [0.14-0.43]
Arthralgia	86.1	46.7[4]	53.7[4]
Arthritis	86.5	41.7[4]	39.4[4]
Skeletal System Score	0.5 [0.5-1.0]	0.0 [0.0-0.5][4]	0.5 [0.0-0.5][4]
Malar rash	62.2	65.0	89.7[4]
V-sign	16.2	25.4	39.7[2]
Periungual capillary abnormalities	83.8	63.2[1]	87.3
Cuticular overgrowth	27.0	17.2	46.5[1]
Cutaneous ulcers	29.7	16.7	20.0
Alopecia	5.4	0.0	1.7
Lipodystrophy	0.0	5.1	14.9[1]
Cutaneous System Score	0.28 [0.17-0.37]	0.24 [0.14-0.33]	0.31 [0.22-0.39]
Abnormal PFT	32.3	10.9[1]	22.3
Dyspnea on exertion	43.2	15.0[3]	17.3[3]
Interstitial lung disease	24.3	1.7[4]	1.7[4]
Pulmonary System Score	0.0 [0.0-0.2]	0.0 [0.0-0.0][1]	0.0 [0.0-0.0][1]
Dysphagia	16.2	35.6	35.4[1]
Gastrointestinal ulceration	8.1	5.0	0.6[1]
Gastrointestinal System Score	0.0 [0.0-0.1]	0.0 [0.0-0.0]	0.0 [0.0-0.11]
Overall/Total System Score	0.27 [0.22-0.34]	1.2 [0.87-1.8][4]	0.20 [0.11-0.28][4]
Chronic Disease Course	45.5	37.3	64.5
Mortality	2.7	3.3	1.1

*Significant differences from anti-MDA5 Ab: [1]p <0.05; [2] p<0.01; [3]p <0.005; [4]p < 0.001

Note that percentages may not reflect the number divided by the total number of subjects, if data missing

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Disclosure: G. Mamyrova, 2; **T. Kishi**, 2; **I. N. Targoff**, 5; **R. V. Curiel**, 2; **F. W. Miller**, None; **L. G. Rider**, 2.

Abstract Number: 86

The myositis-specific autoantibody and myositis-associated autoantibody phenotypes in Japanese juvenile idiopathic inflammatory myopathies

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Demographics,clinical features,and outcomes among myositis-specific autoantibody (MSA) and myositis-associated autoantibodies (MAAs) subgroups were assessed in children with juvenile idiopathic inflammatory myopathies (JIIM).

Methods: MSAs (anti-TIF-1, anti-MJ, anti-ARS , and anti-MDA-5), and MAAs were evaluated with above clinical information.

Results: Among 12 JIIM children,MSAs and MAAs were detected in 9 (anti-TIF-1 (n=3), anti-MJ (n=3), anti-MDA-5 (n=2), and anti-ARS (n=1))and 1(anti-Ku). The other two were

negative.Eleven except anti-Ku positive child were consistent with juvenile dermatomyositis.Three patients with anti-TIF-1 mainly had skin

manifestations, 2 of the 3 were diagnosed clinically amyopathic dermatomyositis.Typical skin manifestations and myositis were noted in another 3 patients with anti-MJ.Of the two children with anti-MDA-5, one developed interstitial pneumonia successfully treated intravenous cyclophosphamide pulse therapy,and the other had arthritis intractable to conventional treatments and improved by adalimumab.

Conclusion: The MSAs were highly detected in JIIM patients. Myositis was most severe in anti-MJ positive patients, whereas the skin and extra-skeletal muscles symptoms were mainly noted in patients with anti-TIF-1 and anti-MDA-5.

Disclosure: T. Miyamae, None; **T. Kishi**, 2; **H. Yamanaka**, None.

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Abstract Number: 87

Assessment of Endothelial Dysfunction and Atherogenic Risk Factors in Children with Juvenile Dermatomyositis

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session
Session Type: Abstract Submissions
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Background/Purpose: Endothelial pulse amplitude testing (Endo-PAT) measures changes in vascular tone by post-occlusive hyperemic response. A reduced hyperemic response suggests endothelial dysfunction and serves as a surrogate marker for subclinical atherosclerosis. Children with juvenile dermatomyositis (JDM) may be at increased risk of premature atherosclerosis due to risk factors including dyslipidemia, insulin resistance, obesity, systemic inflammation, high corticosteroid burden, sedentary activity and underlying vasculopathy. The aim of this study was to determine the prevalence of endothelial dysfunction and atherogenic risk factors in JDM patients compared to healthy controls.

Methods: Twenty patients with JDM and 20 age-, gender-, race-, and BMI- matched healthy controls were recruited. Atherosclerotic risk factor assessments included anthropometrics, family history, smoking history, lipid panel, lipoprotein A, apolipoprotein A1 and B, homocysteine, hsCRP, HOMA-IR, and hemoglobin A1C. JDM assessments included muscle enzymes, vWF antigen, Childhood Myositis Assessment Scale (CMAS), Disease Activity Score (DAS) for JDM, and Myositis Damage Index (MDI). The Endo-PAT reactive hyperemia index (RHI) was calculated, dichotomized using the adult cutoff of <1.67 and log-transformed to meet statistical assumptions.

Results: A summary of clinical and laboratory data are shown in Table 1. JDM patients had a median disease duration of 44 months [IQR: 27,75] with minimal evidence of active disease and damage (median CMAS=52, range 47-52; median DAS=0, range 0-5; median MDI (extent) =0, range 0-3). Among the JDM patients, 7 were currently on prednisone (35%), 13 on hydroxychloroquine (65%), 15 on methotrexate (75%) and 9 on IVIG (45%).

Table 1: Clinical and laboratory data in JDM patients and healthy controls (n=40)[a]

	Total (n=40)	Healthy controls (n=20)	JDM patients (n=20)	p-value
Age (years)	12.4 ± 4.1	12.7 ± 3.9	12.1 ± 4.4	0.651
Female gender	28 (70%)	14 (70%)	14 (70%)	>0.999
Race	14 (35%)	5 (25%)	9 (45%)	0.392
White, non-Hispanic	8 (20%)	4 (20%)	4 (20%)	
African American, non-Hispanic	18 (45%)	11 (55%)	7 (35%)	
Hispanic				
BMI	20.9 ± 5	20.9 ± 4.9	21 ± 5.1	0.950
BMI category	24 (60%)	12 (60%)	12 (60%)	>0.999
Healthy	16 (40%)	8 (40%)	8 (40%)	
Overweight/Obese				
Positive cardiac family history	23 (58%)	12 (60%)	11 (58%)	0.894
Systolic blood pressure (mmHg)	109.8 ± 10.8	106.9 ± 10.5	112.8 ± 10.5	0.081
Diastolic blood pressure (mmHg)	66 ± 7	63.7 ± 6.9	68.4 ± 6.6	0.035
Total cholesterol (mg/dL)	159.1 ± 32.9	163.1 ± 29.1	154.8 ± 36.7	0.441
LDL (mg/dL)	87.6 ± 25.5	92.8 ± 23.5	82.3 ± 27.0	0.203
HOMA-IR[b]	2.1 [1.4, 3.1]	2 [1.7, 2.8]	2.1[1.2, 3.3]	0.922
Hemoglobin A1c	5.5 ± 0.3	5.6 ± 0.3	5.4 ± 0.3	0.084
Lipoprotein A (nnmol/L)[c]	46 [14,87]	66 [24,91]	16.5 [10, 70]	0.055
Apolipoprotein B/A1 ratio	0.5 ± 0.1	0.53 ± 0.1	0.46 ± 0.1	0.082
hsCRP (mg/L)	0.2 [0.1, 0.7]	0.3 [0.2, 0.8]	0.2 [0.1, 0.4]	0.178
RHI	1.57 [1.2,1.9]	1.43 [1.2, 1.7]	1.72 [1.3, 2.4]	0.148
Abnormal RHI < 1.67	25 (63%)	15 (75%)	10 (50%)	0.103
Log RHI	0.45 ± 0.33	0.36 ± 0.24	0.54 ± 0.39	0.089

[a] Continuous variables expressed as mean ± standard deviation or median [IQR]. Categorical variables expressed as frequency (percentages).

[b] Homeostatic Model Assessment for Insulin Resistance (HOMA-IR): *HOMA-IR = fasting insulin x fasting glucose / 22.5* (43).

[c] Only evaluated in 31 participants (17 healthy controls and 14 JDM patients)

Although healthy controls show a higher proportion of endothelial dysfunction compared to JDM patients (75% versus 50%) and lower mean log RHI (0.36 ± 0.24 versus 0.54 ± 0.39 respectively), these results were not statistically significant. Healthy controls had relatively higher lipoprotein A levels (p=0.055). In a model adjusting for lipoprotein A,

JDM status became a significant predictor for increased log RHI (p=0.006).

Conclusion: This is the first study to evaluate for the prevalence of premature atherosclerosis in a pediatric population with JDM. In this study, patients with JDM did not appear to be at higher risk for endothelial dysfunction compared to healthy controls. Lipoprotein A, a traditional atherogenic risk factor, may be an important confounder in these results.

Disclosure: D. Wahezi, None; **E. Liebling**, None; **J. Parekh**, None; **M. Dionizovik-Dimanovski**, None; **J. Choi**, None; **Q. Gao**, None.

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Abstract Number: 88

Clinical Features and Frequency of Biologic use in Patients with Juvenile Dermatomyositis-associated Calcinosis

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SESSION INFORMATION

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Background/Purpose:

Calcinosis develops in an estimated 40% of patients with Juvenile Dermatomyositis (JDM). Conflicting studies have not definitively identified actionable risk factors or demonstrated that patients with calcinosis have unique clinical features. Diverse therapies are used to treat calcinosis, but there are limited data on the use of biologic agents apart from small case series. Using a large patient registry, we aimed to identify patients at risk for calcinosis, distinguish clinical phenotypes, and examine treatment history with biologic agents.

Methods:

The Childhood Arthritis and Rheumatology Research Alliance (CARRA) created a multi-site registry for pediatric rheumatologic diseases, enrolling patients from 2010 to 2015. We performed cross-sectional analysis of baseline data in all JDM patients. We compared those with any history of calcinosis to those with no history, in respect to demographics, disease features, patient-reported outcome measures and treatment with biologic agents. The difference of symptom onset date and first rheumatology visit was used to calculate duration of symptoms prior to treatment. Differences between patients with and without calcinosis were analyzed with t-test or Wilcoxon Rank Sum tests for continuous variables as appropriate, while comparisons for categorical variables used Chi-square or Fisher's Exact tests as appropriate. Statistically significant measures at the alpha level of 0.05 on univariate analyses were included in multivariate logistic regression modeling.

Results:

Of 652 JDM patients, 601 contained requisite data on calcinosis. Females accounted for 71% of patients. The majority (83%) were Caucasian, 13% African-American, while 15% identified as Hispanic. Mean age of JDM disease onset was 6.6 years. In total, 84 patients (14%) had a history of calcinosis. This history was associated with skin ulcerations

(p=0.0005), lipodystrophy (p<0.0001) and contractures (p<0.0001). Patients with cardiac, lung or gastrointestinal disease, individually or combined, did not show a significant association. Calcinosis patients also had higher CHAQ (p=0.0034), HRQOL (p=0.011) and global assessment scores, with the strongest correlation for parent/patient reported global scores (p<0.0009, 13.7%). In multivariate analysis, differences in the distribution of proportions retained significance in patients with calcinosis for measures of delayed time to treatment (OR 1.5, CI 1.3-1.8), male gender (OR 1.75, CI 1.02-3.03), and African-American race (OR 2.5, CI 1.3-4.8). Those with calcinosis were also more likely to have received IVIG (OR 1.9, CI 1.1-3.3), rituximab (OR 4.6, CI 1.8-11.4) and anti-TNF therapy (OR 2.7 CI 1.006-7.5).

Conclusion:

In this registry, one of the largest JDM and calcinosis cohorts, patients with a history of calcinosis are more likely to have received certain biologic agents than those without. Affected patients were also more likely to be male, of African ancestry and have longer symptom duration before treatment. These features should be considered risk factors and encourage screening measures. Patients with lipodystrophy, skin ulcerations or contractures should raise similar concern.

Disclosure: A. Orandi, None; **V. Dharnidharka**, None; **N. Al-Hammadi**, None; **K. Baszis**, None.

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Abstract Number: 89

Abatacept as Adjunct Therapy for the Calcinosis of Juvenile Dermatomyositis: A Single-Center Experience

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SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Clinical and Therapeutic Poster Session
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Session Time: 5:30PM-7:00PM

Background/Purpose:

Juvenile dermatomyositis (JDMS) is an autoimmune inflammatory myopathy which primarily manifests with skin, muscle, and blood vessel involvement. Dystrophic calcification or calcinosis has been associated with aggressive disease and/or chronicity. It is usually difficult to control and may be associated with poor wound healing, risk for secondary skin/subcutaneous infection, and adverse quality of life due to pain, joint contractures, and altered mobility. Currently, there is no standard of care for JDMS associated calcinosis. There are limited case reports and clinical trials in JDMS on the use of abatacept, a fully human soluble fusion protein that prevents the costimulatory signaling required in T-cell activation. We describe our center’s experience in the use of abatacept in the treatment of JDMS associated calcinosis.

Methods:

A retrospective chart review of JDMS patients with calcinosis treated with abatacept at our center was performed after IRB approval. Collected data include patient demographics, clinical presentation and course, and therapy. Onset, clinical characteristics, and course of calcinosis following therapy with abatacept were described.

Results:

Four patients were included (females: 3, Hispanic ethnicity: 2). Median age at diagnosis was 4 years. Three patients had disease duration of 1 to 5 months prior to diagnosis, while one patient was diagnosed 48 months following disease onset. All patients had severe disease on presentation, and all received both IV and PO glucocorticoids, IVIG, methotrexate, and hydroxychloroquine. Two patients received rituximab. Median onset of calcinosis from disease onset was 18.5 months. All patients had a combination of superficial, interfascial, interarticular, and tumorous calcinosis. The median time for abatacept use following clinical diagnosis of calcinosis was 13.5 months (range: 5-25). Median duration of follow-up while on abatacept therapy was 13.5 months (range: 10-32). Clinical and imaging improvement of calcinosis were noted within 6-12 months of abatacept initiation. All patients had resolution of pain, tenderness, and inflammatory changes at the sites of calcinosis. Joint contractures related to calcinosis in two patients resolved within 3-5 months of abatacept use. Ulcer formation in one patient resolved. Secondary skin/subcutaneous infection was not observed in all patients despite use of combination immunosuppressive/immunomodulatory therapies. All patients remained free of disease flare throughout therapy.

Conclusion:

We described the clinical course and response to abatacept as adjunct therapy for calcinosis in four patients with juvenile dermatomyositis in this single-center retrospective review. Our patient outcomes suggest that abatacept may be an efficacious and safe treatment option in JDMS associated calcinosis. Further study in larger patient cohorts is warranted.

Disclosure: M. DeGuzman, None; **S. Singla**, None; **M. Mizesko**, None; **A. C. Sagcal-Gironella**, None.

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Abstract Number: 90

Risk of Serious Infections in Juvenile Dermatomyositis patients treated with biological response modifiers including rituximab and abatacept

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SESSION INFORMATION

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Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Juvenile dermatomyositis (JDM) is a rare systemic auto immune disease in children. The risk of infection is increased with immunomodulation. There are no studies to evaluate the risk of serious infections with use of biological response modifiers like anti TNF agent- infliximab, anti B cell agent- rituximab or co stimulator inhibitor agent like Abatacept, in JDM.

Methods: We retrospectively analyzed records of 9 patients between the ages 5-17 years with JDM after obtaining IRB approval and informed consent from patients. All nine patients received treatment with chronic daily steroids, IV monthly pulse solumedrol and IVIG. These patients were on Infliximab or rituximab or on Abatacept along with other conventional medications. We retrospectively studied patients for two years on these medication. The infections during observational period were abstracted from the medical records.

Results:

Of the nine patients with JDM, one developed localized scleroderma during the treatment and one patient developed rheumatoid factor negative poly-articular JIA. Three patients each received infliximab, rituximab and abatacept.

Those who received Rituximab, got the infusion at a dose of 750 mg /m times two doses two week apart and then every three months for the next two years. They also received prednisone for average 4.5 months and oral weekly methotrexate during the entire study period. Infliximab and abatacept was given monthly as infusion.

Thirty three percent of patients had bacterial sinusitis six to nine months after the rituximab therapy was initiated. They were treated with oral antibiotics as an outpatient and 44% of patients in this group had skin infection and was treated with oral antibiotics.

The study population had no serious infections requiring hospitalization, deep tissue infection requiring IV antibiotics, infection requiring hospitalization, infections requiring oxygen or pressure support, invasive fungal infections or infection that requires surgical intervention or pneumonia requiring mechanical ventilation.

Conclusion: JDM patients in this cohort tolerated the medications with no risk of serious infections. We need further large multicenter studies to support this finding.

Disclosure: S. Sukumaran, None; **V. Vijayan**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/risk-of-serious-infections-in-juvenile-dermatomyositis-patients-treated-with-biological-response-modifiers-including-rituximab-and-abatacept

Abstract Number: 91

Peri-pubertal Onset of Systemic Lupus Erythematosus is Associated with Shorter than Expected Adult Height

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose:

Patients with childhood-onset SLE (cSLE) have a higher incidence of renal disease and may receive more intensive immunosuppression as compared to individuals with adult-onset SLE (aSLE). Growth failure, a proposed measure of damage in cSLE, may be associated with disease activity and steroid use. The goal of our study was to compare final height to expected height in adults with cSLE vs. aSLE.

Methods:

Data derive from telephone or online surveys from the 2002-07 cycles of the Lupus Outcomes Study (LOS) and the 2012-16 cycles of the Pediatric Lupus Outcomes Study (PLOS), two cohorts of adult SLE patients. SLE diagnosis was confirmed by chart review using the ACR SLE classification criteria. Participants diagnosed at age < 18 years were defined as cSLE (n=152). Respondents reported their height and both parentsÕ heights; participants with complete height data (n=648) were included in this analysis. Expected adult height was estimated from mid-parental height using the Tanner formula, a validated measure. Multivariate linear regression was used to compare the difference between expected and final height for cSLE and aSLE participants, adjusting for gender and ethnicity.

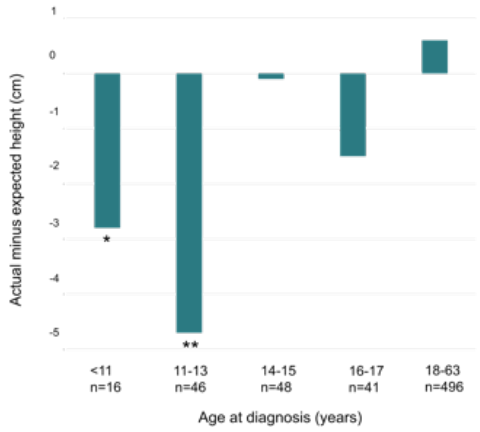
Results:

Participants with cSLE were younger (mean age 27±9 vs. 49±9 years; p<0.0001), more likely to be male (12% vs 6%; p=0.01) and less likely to be white (52% vs. 70%; p<0.0001). Mean age at diagnosis was 14±3 vs. 33±10 years (p<0.0001). Respondents with cSLE were more likely to have ever required dialysis (12% vs 7%; p=0.06). Nearly all cSLE participants reported a history of steroid use (99% vs. 94%; p=0.02) and were also more likely to have been exposed to cyclophosphamide (22% vs. 13%; p=0.001). Participants with cSLE were on average 1.4 cm shorter than expected before adjustment, and 2.1 cm shorter than expected after controlling for gender and ethnicity (95% CI -3.3, -1.0). This differed significantly from aSLE participants (p=0.0005), who were 0.6 cm taller than expected (95% CI 0.06, 1.1). Participants diagnosed at age 11-13 years showed the greatest difference between actual and expected height (Figure 1). This group was shorter than expected by 4.7 cm after adjustment (95% CI -6.5, -2.8), which differed significantly from the aSLE group (p<0.0001). Those diagnosed prior to age 11 years (n=16) were 2.8 cm shorter than expected after adjustment (95% CI -5.9, 0.3), which approached significance when compared with aSLE group (p=0.07).

Conclusion:

Onset of SLE in childhood appears to be associated with shorter than expected adult stature. Onset of SLE in the peri-pubertal period, a time of rapid linear growth, may have a particularly significant impact on final adult height. Further studies are needed to delineate the relative contributions of disease- and treatment-related risk factors, such as chronic inflammation, renal insufficiency and chronic steroid use, to shorter-than-expected adult height in cSLE.

Figure 1: Mean difference between actual and expected adult height by age at SLE diagnosis, adjusted for gender and race (n=648).



*p=0.07 as compared to adult-onset SLE group
**p<0.0001 as compared to adult-onset SLE group

Disclosure: M. Heshin-Bekenstein, None; **A. O. Hersh**, None; **E. von Scheven**, None; **E. Lawson**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/peri-pubertal-onset-of-systemic-lupus-erythematosus-is-associated-with-shorter-than-expected-adult-height

Abstract Number: 92

Mycophenolate Mofetil is an Effective Induction Therapy Agent in Childhood-onset Pure Membranous Lupus Nephritis

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017
Session Title: Clinical and Therapeutic Poster Session
Session Type: Abstract Submissions
Session Time: 5:30PM-7:00PM

Background/Purpose:

Treatment guidelines for childhood-onset class V membranous lupus nephritis (MLN) have not yet been established. The addition of mycophenolate mofetil (MMF) has shown improvement in the 5-year renal and patient survival rates in recent studies, but the role of early treatment with MMF remains unclear. We hypothesized that use of MMF as induction therapy in children is associated with good outcomes.

Methods:

We conducted a single-center retrospective observational cohort study of consecutively diagnosed children with pure MLN from 2002 to 2016 after obtaining an IRB approval. Patients treated with MMF on MLN diagnosis were identified. Clinical, laboratory measures, and treatment regimens were analyzed using descriptive statistics. Renal outcomes were documented before and after completion of 6 months of initial treatment. Numerical data was compared using paired t-test. Mean differences and 95% confidence interval were reported. All tests were considered positive with a p value <0.05. Renal response was defined using consensus definitions from the Childhood Arthritis and Rheumatology Research Alliance (CARRA).

Results:

Most patients prior to the year 2000 were treated with glucocorticoids alone. Introduction of MMF in addition to glucocorticoids for MLN patients was first prescribed in 2002, and became a regular practice after 2010. MMF usually started within 2 weeks of kidney biopsy. There was a total of 27 subjects with pure MLN treated with MMF in the cohort (85% females, 40% Hispanic, 37% African-American, 11% Caucasian, and 11% Asian) with a mean age of 14.0 ± 2.5 years and a median follow-up time of 2.8 years (IQR 1.5 – 4.6). Nearly half of the patients had hypocomplementemia (48%) and one-fourth had elevated anti double-stranded DNA (26%) on presentation. Nephrotic syndrome was seen in 81% and acute kidney injury in 11% on initial presentation. Mean initial prednisone dose was 0.5±0.3 mg/kg/day. Efficacy of MMF after 6 months of initial treatment was reflected by improvement in mean urine protein creatinine ratio (p=0.0047), increased serum albumin (p=0.0017), and SLEDAI score drop (p<0.001) (Table 1). Renal response rates at 6 months were: complete response in 31%, moderate in 31%, mild in 23%, and no response in 12% of the cohort. At 24 months, complete response was achieved in 67%, moderate in 5%, mild in 5% and no response in 22% of the patients.

Conclusion:

Favorable outcomes were reported with the early use of MMF on this single-center cohort of childhood-onset pure MLN.

Table 1. Differences in baseline variables before and after 6 months of mycophenolate mofetil treatment

Baseline Variable	Pre-MMF	Post-MMF	Mean difference (95% CI)	p value
Spot uPCR (g/g)	4.3 ± 5.0	1.0 ± 1.3	3.2 ± 4.9 (1.1 to 5.4)	0.0047
Urine protein (g/24h)	4.9 ± 6.5	1.0 ± 1.3	3.9 ± 6.7 (-1.3 to 9.1)	NS
Serum creatinine (mg/dL)	0.5 ± 0.2	0.6 ± 0.1	0.1 ± 0.2 (-0.06 to 0.09)	NS
Serum albumin (g/L)	2.9 ± 0.7	3.8 ± 0.5	-0.9 ± 0.8 (-1.2 to -0.3)	0.0017
GFR (mL/min/1.73m²)	135 ± 53	129 ± 29	6.2 ± 41 (-11.3 to 23.7)	NS
SLEDAI score (points)	12.8 ± 6.5	6.3 ± 4.4	6.5 ± 5.6 (4.2 to 8.8)	<0.001

uPCR, urine protein creatinine ratio; GFR, glomerular filtration rate;
SLEDAI, systemic lupus erythematosus disease activity index;

MMF, mycophenolate mofetil; NS, no statistical significance.

Disclosure: M. Pereira, None; **E. Muscal**, None; **M. DeGuzman**, None; **A. C. Sagcal-Gironella**, None; **S. E. Wenderfer**, None.

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Abstract Number: 93

Corticosteroid Regimen Use in the Pilot Study of Consensus Treatment Plans for Induction Therapy in Childhood Proliferative Lupus Nephritis

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SESSION INFORMATION
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Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose:

Comparative data in the pediatric lupus nephritis (LN) population are lacking. To reduce treatment variability and facilitate comparative effectiveness studies, the Childhood Arthritis and Rheumatology Research Alliance (CARRA) published consensus treatment plans (CTPs) for induction therapy in childhood proliferative LN. The CTPs recommend treatment with MMF or IV CYC and one of three corticosteroid (CS) regimens: primarily oral, primarily IV or mixed oral/IV. We describe CS regimen usage and report overall adherence and reasons for non-adherence in a multi-center pilot feasibility study.

Methods:

This observational cohort study enrolled 41 cSLE patients from 10 CARRA sites. Subjects had new-onset biopsy proven class III or IV active proliferative LN and were starting induction therapy with MMF or IV CYC and CS. Subjects were followed for up to 24 months. In addition to clinical parameters, providers were surveyed about reasons for CS regimen selection and overall adherence to the regimens. In addition, providers recorded prescribed medication use including CS taper schedule. Reasons for regimen selection, provider-reported adherence to regimens, adverse events, and weight gain (absolute and change in BMI percentile) were compared among the three regimens. To quantify the degree of deviation from the oral component of the CS regimens, the percent daily difference from the expected prednisone/prednisolone dose was calculated according to the assigned CS regimen.

Results:

CS regimen selection (9 primarily oral, 17 mixed oral/IV and 15 primarily IV) differed significantly by study site ($p=0.007$) and induction agent (oral CS regimens were more commonly prescribed with MMF and IV containing CS regimens were more commonly prescribed with CYC, $p=0.002$). Providers reported following the CS regimen as intended in 37% of patients at the 6 month visit (47% for primarily IV regimen, 33% for primarily oral regimen and 29% for mixed oral/IV regimen). Over the 24 week induction period there was a tendency to prescribe less oral CS in weeks 1-8 compared to published regimens (median -20% less, IQR -20,10). The most common reasons for not following the published regimen were subject non-compliance (20%) and intolerance (12%). There was one hospitalization for infection in a patient treated with the mixed oral/IV regimen. There were no reported cases of cataracts or osteonecrosis. The median baseline BMI was at the 84%ile. The 6 month median change in BMI %ile was 4 and from month 6 to month 12 the median change in BMI %ile was 1.2, this did not significantly differ among CS regimens.

Conclusion:

In this pilot there was substantial deviation from the CS regimens suggesting that revision may be needed to ensure implementation into clinical practice and to support comparative effectiveness research. No single regimen was superior in minimizing steroid-associated weight gain at month 6 or month 12. Patient-level adherence with oral CS tapers was not assessed by this study and warrants further investigation.

Disclosure: J. C. Cooper, None; **B. A. Eberhard**, None; **M. Punaro**, None; **S. P. Ardoin**, None; **H. Brunner**, None; **J. Hsu**, None; **L. Wagner-Weiner**, None; **M. Klein-Gitelman**, None; **K. A. Rouster-Stevens**, None; **L. E. Schanberg**, 9,9,9; **E. von Scheven**, None.

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Abstract Number: 94

Effects of Age and Gender on Reference Levels of Biomarkers Comprising the Pediatric Renal Activity Index for Lupus Nephritis (p-RAIL)

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SESSION INFORMATION

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Session Time: 5:30PM-7:00PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disease that disproportionately effects women and children of minorities. Renal Involvement (lupus nephritis, or LN) with SLE occurs in up to 80% of children with SLE and is a major determinant of poor prognosis. We have developed a non-invasive pediatric Renal Activity Index for Lupus (p-RAIL) that consists of laboratory measures that accurately reflect histologic LN activity. These markers are neutrophil gelatinase associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), monocyte chemotactic protein (MCP-1), adiponectin (APN), ceruloplasmin (CP) and hemopexin (HPX). A major gap in the knowledge base and a barrier to clinical utility is how these markers behave in healthy children. We set out to establish a reference range for for the p-RAIL markers in a population of healthy children, and to determine if levels of these markers fluctuate with age or sex.

Methods: : Urine was collected from 368 children from the Cincinnati Genomic Control Cohort (healthy kids presenting to Cincinnati Children's primary care clinic for well child visits) and assayed for NGAL, KIM-1, MCP-1, APN, CP and HPX using commercially available kits or assay materials.

Results: Specimens were grouped by age (0-5 years (n=94); 5-10 (n=89); 10-15 (n=93); 15-20 (n=91)) and sex (M = 184, F=184). For age and gender comparisons, values for log transformed prior to analysis. The 95% CI for the means of each marker in the combined population were as follows: NGAL (12.9-20.1 ng/ml), KIM-1 (474.6-558.4 pg/ml), MCP-1 (240.9-293.4 pg/ml), APN (7.6-10.0 ng/ml), CP (480-589.8 ng/ml), HPX (814.3-1163.5 ng/ml). All p-RAIL biomarkers but adiponectin had weak but significant positive correlations with age, with NGAL being the strongest ($r=0.33$, $p<0.001$). Adiponectin had a weak negative correlation with age ($r=-0.12$, $p=0.04$). For gender comparisons, CP and HPX were elevated in females vs males (CP = 3% higher log transformed mean in females, $p = 0.007$; HPX = 5% higher log transformed mean in females, $p = 0.0005$). Consistent with previous findings, NGAL was greatly elevated in females vs males (86% higher log transformed mean in females, $p<0.0001$). No other gender differences were found.

Conclusion: We have established a reference range for the p-RAIL biomarkers and have highlighted age and gender differences. This information is essential for rational interpretation of studies and clinical trials utilizing the p-RAIL algorithm.

Disclosure: M. Bennett, None; **Q. Ma**, None; **J. Ying**, None; **P. Devarajan**, 6; **H. Brunner**, None.

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Abstract Number: 95

Development of Cognitive Behavioral Therapy (CBT) for Childhood-onset Systemic Lupus Erythematosus (cSLE) Treatment

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SESSION INFORMATION
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Session Type: Abstract Submissions
Session Time: 5:30PM-7:00PM

Background/Purpose: cSLE can result in considerable decrements in health-related quality of life (HRQOL) for young patients. Youth with cSLE experience a myriad of symptoms, including fatigue, pain episodes, and depressive symptoms. While cognitive-behavioral (CBT) techniques for coping with pain, mood symptoms, and sleep problems have shown promise in treating youth with those respective conditions, there has not yet been a CBT approach developed to meet the *unique* needs of the cSLE population. Thus, the current study aimed to develop and pilot test a CBT protocol to meet the needs of adolescents and young adults with cSLE by addressing pain symptoms, depressive symptoms, and sleep difficulties. The goal was to develop a CBT intervention to improve pain levels, fatigue, depressive symptoms, and health-related quality of life (HRQOL).

Methods: The treatment involved 6 one-hour individual sessions held weekly with a doctoral level psychologist who specializes in CBT. Parent/caregivers were involved in 2 of the 6 sessions and participated in weekly check-ins. The goal of the sessions was to improve coping with pain symptoms, depressive symptoms, and fatigue. Content included psychoeducation (i.e., how fatigue, pain, and mood symptoms relate to cSLE), training in cognitive (i.e., problem solving, cognitive restructuring) and behavioral strategies (e.g., activity pacing, behavioral activation) aimed at improving symptoms. At baseline and post-treatment, participants completed self-report outcome measures on pain levels (Visual Analog Scale; 0-10 VAS), fatigue (PROMIS Pediatric Fatigue- short form), depressive symptoms (Children's Depression Inventory 2; CDI 2), and HRQOL (PedsQL Generic Core Scales).

Results: All participants were diagnosed with cSLE by their rheumatologist. Five of 8 participants (mean,range (years): 15.2/14-17) have completed the 6-session intervention, with 2 participants mid-treatment. At baseline, the average VAS score was 3.4, PROMIS Fatigue score was 18.8, and CDI score was 14.75. For treatment completers, PROMIS Fatigue reduced by 5 points (Z=-2.023, p>0.05), and CDI reduced by 3.5 points (Z=-1.841, p=.066). VAS and PedsQL scores did not change significantly post treatment.

Conclusion: Participants who completed CBT experienced significant reductions in symptoms of fatigue and depressive symptoms at post treatment. These preliminary results indicate that CBT may be a feasible and potentially beneficial self-management approach for adolescents who are experiencing mood, and/or fatigue symptoms associated with cSLE. Although there was not an immediate effect on pain or HRQOL at post-treatment, improving patient symptoms such as mood and fatigue may ultimately improve functioning and impact these domains over time.

Disclosure: J. Warner, None; **E. Moorman**, None; **N. Cunningham**, 2; **K. Wiley**, None; **A. Watts**, None; **S. Kashikar-Zuck**, 2; **H. Brunner**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/development-of-cognitive-behavioral-therapy-cbt-for-childhood-onset-systemic-lupus-erythematosus-csle-treatment

Abstract Number: 96

Correlation and Responsiveness of Cutaneous Lupus Disease Area and Severity Index and Skindex-29 with Cutaneous Childhood Lupus Erythematous

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Background/Purpose:

Characteristic inflammatory cutaneous lesions are common manifestations of children with systemic lupus erythematosus (cSLE); however they are among understudied areas of cSLE. The Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) allows for measuring active inflammation and chronic damage and, it has been validated to determine the impact of therapy on the activity of the cutaneous manifestations in adults. The Skindex-29 is a skin-specific Quality of Life Score (QoL). Their validation in cSLE has not been shown.

Methods:

Patients with cSLE from different three centers were enrolled in a prospective longitudinal cohort study. Inclusion criteria were (1) being diagnosed with SLE according to the American College of Rheumatology criteria for SLE, (2) being diagnosed before 18th birthday, (3) being under 18 years of age at the enrollment, (4) having active or chronic mucocutaneous involvement of lupus. In this ongoing study; CLASI, the PedsQL Generic Core scale and the Rheumatology Module, the Skindex-29, physicians-rated cSLE activity (SLEDAI) and completed the SLICC/ACR damage index (SDI) were achieved besides the clinical and laboratory data obtained from two routine visits 6 months apart.

Results:

The study cohort consisted of 48 patients (90% females) with a mean age at the first visit 14.5 years (ranges: 3-18). 62.5 % of patients completed their second visits. Patients had moderately active cSLE (total SLEDAI scores: 8.7±7.3) and 40 % had a SDI score >0. The mean mucocutaneous domain (MC) scores were 2.2±1.7 for SLEDAI-MC and 0.1±0.1 for SDI-MC at their baseline visits.

The average scores of patients were 6.7±7.6 for SLEDAI, 1.6±1.7 for SLEDAI-MC and 0.1±0.1 for SLICC-MC; 53 % had a SDI score >0 at their second visits. We found that SLEDAI, SLEDAI-MC, SDI-MC, the Skindex, CLASI activity and damage scores are strongly correlated with each other ($p<0.01$). In addition, cSLE activity (SLEDAI, SLEDAI-MC), damage (SDI, SDI-MC) and QoL are moderately associated with CLASI and the Skindex scores.

Conclusion:

We conclude that CLASI and the Skindex demonstrate a high validity and reliability when used in cSLE showing mucocutaneous involvement.

Disclosure: P. O. Avar Aydin, None; **A. AleEd**, None; **N. AlMutairi**, None; **S. Al-Mayouf**, None; **H. E. Sonmez**, None; **S. Ozen**, None; **J. L. Huggins**, None; **H. Brunner**, None.

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Abstract Number: 97

Bortezomib is Efficacious in the Treatment of Refractory Neuropsychiatric SLE with Psychosis

Renee F Modica[1], Kathleen M Vazzana[2], Natalie Jane Shiff[3], Akaluck Thatayatikom[3] and Melissa E Elder[1], [1]Department of Pediatrics, University of Florida, Gainesville, FL, [2]Pediatrics, University of Florida at Orlando Health Arnold Palmer Hospital for Children, Orlando, FL, [3]Pediatrics, University of Florida, Gainesville, FL

SESSION INFORMATION
Session Date: Thursday, May 18, 2017
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Session Time: 5:30PM-7:00PM

Background/Purpose: Neuropsychiatric systemic lupus erythematosus (NPSLE) with psychosis is challenging to treat with refractory cases often requiring prolonged hospitalization due to significant functional impairment and co-morbidities. Although plasma cells are the major source of pathogenic autoantibodies in SLE, current B-cell directed therapies for SLE do not target these cells. Both neoplastic and normal plasma cells are very susceptible to the proteasome inhibitor bortezomib. Bortezomib is approved for the treatment of multiple myeloma, a plasmacytoma, and has been shown to prevent and reverse antibody-mediated rejection in solid organ transplantation and in prevention of disease progression in lupus mouse models. Therefore, bortezomib may provide benefit to patients with treatment refractory NPSLE as well.

Methods: We describe the first pediatric case series of 3 patients with refractory NPSLE and psychosis who were treated safely and effectively with subcutaneous and/or IV bortezomib. All patients had persistent psychosis despite aggressive immunosuppression with repeated courses of IV methylprednisolone, cyclophosphamide, rituximab and plasmapheresis.

Results: All patients demonstrated rapid clinical improvement in their psychotic manifestations as well as reduction in steroid dose and need for plasmapheresis and anti-psychotic medications. No patient had recurrence of psychosis during a follow up period of 5 to 53 months. No severe side effects or adverse events were observed.

Conclusion: NPSLE with psychosis that is resistant to cyclophosphamide, rituximab and plasmapheresis is a potentially devastating complication of SLE. Plasma cell depletion with bortezomib when used as adjunct therapy to conventional immunosuppression may be effective in some patients with refractory NPSLE and psychosis. In our pediatric case series, after initiation of bortezomib, patients had demonstrable improvement in their psychosis within 1-2 weeks and were able to reduce concomitant SLE therapies and discontinue anti-psychotic medication over time. In this pediatric case series, bortezomib was well tolerated, in keeping with adult case reports of its use in refractory SLE. Further investigation is needed to determine the therapeutic role of bortezomib in pediatric-onset SLE.

Disclosure: R. F. Modica, None; **K. M. Vazzana**, None; **N. J. Shiff**, None; **A. Thatayatikom**, None; **M. E. Elder**, None.

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Abstract Number: 98

Contraceptive use, Counseling given and the Occurrence of Venous Thrombus Embolism in Adolescent Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Clinical and Therapeutic Poster Session
Session Type: Abstract Submissions
Session Time: 5:30PM-7:00PM

Background/Purpose:

According to the Center for Disease Control, 46.8% of high school students surveyed in 2013 have been sexually active. Of those surveyed 34% had sexual intercourse within the past 3 months; of whom 40.9% did not use a condom during their last sexual encounter. Reproductive health counseling is important for all teens, but is crucial for adolescents with active systemic lupus erythematosus(SLE) who may be prescribed teratogenic drugs and have an inherent risk for VTE. The current CDC medical eligibility for contraceptive use (MEC) provides guidance among different patient populations. Among antiphospholipid antibody positive (APLA) SLE patients, estrogen containing contraceptives are contraindicated. For this reason progestin only methods are typically utilized in sexually active adolescents with SLE and include the progestin only pill, injection, implant and intrauterine device. Although preferred, these progestin only methods are category 3, meaning the risk may outweigh the benefits. The occurrence of progestin only method risks has not been documented in the adolescent SLE population. A recent study demonstrated a 3.6 fold increase of VTE among those who used depo-medroxyprogesterone acetate (DMPA) compared to non-users of hormonal contraceptive methods, however this study only included women 18-50 years with other comorbidities and did not focus on adolescents with SLE.

Utilizing a large multi-ethnic single institution cohort we set out to: A) determine past contraceptive use and provision of contraceptive counseling among adolescent females with SLE, B) to identify the type/MEC category of medication use among SLE adolescents and if counseling was provided about potential medication teratogenic risks, C) determine if VTE or weight gain occurred while on a contraceptive method and D) identify human papillomavirus (HPV) immunization status in adolescent females with SLE.

Methods:

A retrospective chart review of ICD-9 code identified SLE in females <21 years between 2000- 2015 seen in both pediatric rheumatology and gynecology clinic. Descriptive statistics were reported.

Results:

We identified 87 menarchal females age 9-17. Sexual activity was reported in 46.51% of teens, with only 20% reporting consistent condom use. Twenty-four patients (28.24%) declined contraceptive hormones despite counseling. Two patients started on a combined estrogen-progestin contraception option. The remaining teens chose progestin only options. BMI increased an average of 2.68 one year after contraception was started. No VTEs were reported in any patients while using hormonal contraception, including DMPA. The HPV vaccine was completed by 66.3% of the teens, while 16.3% had never received the vaccine and the status of 17.4% was unknown.

Conclusion:

Sexual activity rates in our SLE cohort approximated national figures, while condom use was significantly lower.
No increase risk of VTE with progestin-only options in SLE patients irrespective of APLA. Although a significant average increase in BMI after one year on contraception, this was confounded by concurrent steroid. Only 66% received the HPV vaccine prompting our inclusion of reproductive health issues in QA projects.

Disclosure: M. Curry, None; **J. Kurkowski**, None; **J. Geyer**, None; **J. Hakim**, None; **H. Sangi**, None; **M. deGuzman**, None.

Abstract Number: 99

PILOT STUDY MEASURING HEPCIDIN AND ARTERIAL STIFFNESS IN CHILDREN WITH SLE AND LUPUS NEPHRITIS

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose:

Cardiovascular disease (CV dz) is common in SLE and lupus nephritis (LN), but premature atherosclerosis risk does not appear to be linked to classic CV risk factors like hypertension. Up to 80% of children with SLE develop kidney dz, which is also associated with increased risk for CV dz and death compared to those without renal involvement. Hepcidin (Hp) is an iron-regulatory protein which may contribute to atherosclerosis and is elevated in autoimmune dz. Pulse wave velocity (PWV) is a validated indicator of arterial stiffness, an early marker of CV risk, in children and is increased in children with SLE vs. healthy controls. Our objective was to quantify Hp and PWV in children with SLE and to determine if those with biopsy-proven lupus nephritis (LN) have higher Hp levels and higher PWV compared to those without kidney dz.

Methods:

Cross-sectional analysis with Hp measured via ELISA assay. Arterial stiffness quantified by carotid-femoral PWV. Pearson chi2/paired t testing or Wilcoxan rank sum test for comparison of proportions, means, or median.

Results:

The cohort (n=16) was 93.8% female and 68.8% black with mean (SD) age of 15.2 (3.6) yrs. 37.5% (n=6) had LN. Overall mean (SD) Hp was 53.9 (47.8) ng/mL, median (IQR) 34.4 (18.9, 91.9) ng/mL. Both Hepcidin levels and PWV were higher in the subjects with LN.

	Nephritis (n=6)	No Nephritis (n=10)	p-value
Age (yrs)	16.5 (1.6)	14.5 (1.2)	0.32
% Black	100%	50%	0.23
Hepcidin, median (IQR)	71.55 (26.4, 116.4)	27.9 (18.7, 59.7)	0.19
Arterial Stiffness			
On BP meds, % (n)	83.3% (5)	0% (0)	<0.001
SBP (mmHg)	121 (10.9)	111 (17.5)	0.26
DBP (mmHg)	67 (19.3)	62 (8.2)	0.34
PWV (m/s)	4.9 (0.95)	4.1 (0.47)	0.05

Conclusion:

In this pilot analysis, serum Hp and PWV were both elevated in subjects with LN compared to those with SLE alone. No significant differences in blood pressure, a traditional CV risk factor, were noted. This suggests Hp may be a mediator of

morbid CV changes in LN and warrants further study.

Disclosure: S. Sule, None; **S. Joo**, None; **M. Atkinson**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/pilot-study-measuring-hepcidin-and-arterial-stiffness-in-children-with-sle-and-lupus-nephritis

Abstract Number: 100

Improvement of Salivary Gland Ultrasound Findings in Juvenile Sjögren's Syndrome after Systemic Corticosteroid Treatment

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Juvenile Sjögren'sSyndrome (jSS) is a rare systemic autoimmune disease affecting predominantly salivary glands (SG) in children who do not meet criteria for SLE or MCTD. Currently, no specific criteria for diagnosis or study of the disease are available. Salivary gland ultrasonography (SGUS) in adults with primary Sjogren's Syndrome (pSS) has proved to be a promising tool in detecting typical structural abnormalities for diagnosis and prognostic stratification of the disease; however, studies of its utility in jSS have been limited. SGUS is a non-invasive, inexpensive and non-irradiating procedure; therefore, further studies in children with jSS for potential usefulness of SGUS are needed.

Methods: Patients with jSS diagnosed between 2011-2016 at Shands Children's Hospital, University of Florida, were studied. Clinical examination, diagnostic tests and SGUS were obtained during clinic visits. SGUS studies of major salivary glands using a Sonosite Edge with a linear high-frequency transducer 6-15 MHZ were performed by a RhMSUS certified pediatric rheumatologist. Based upon previous SGUS studies in pSS, the sonographic findings including parenchymal echogenicity, inhomogeneity, hypoechogenic areas, hyperechogenic reflections and borders were evaluated.

Results: Three patients with jSS were studied. The age at onset of symptoms was 7, 8 and 12 years, and the age at diagnosis of jSS was 11, 11 and 15 years respectively. All patients had active parotitis and constitutional symptoms with abnormal laboratory findings including highly elevated anti-SSA, anti-SSB Ab, rheumatoid factor and immunoglobulins (IgG>2,500) with negative anti-Smith and anti-DNA Ab. Abnormal findings on SGUS were found in all patients, however, two patients treated only with hydroxychloroquine showed more severe parenchymal changes (grade 3). After adding systemic corticosteroids, the severity of the parenchymal findings improved to grade 1-2 associated with clinical improvement.

Conclusion: The improvement of SGUS after steroid treatment in children with jSS has not been previously reported. SGUS findings may be a useful tool for monitoring disease activity and response to treatment. Further long-term investigations of SGUS including correlation of pathologic findings and development of a consensual scoring system in large jSS cohorts are warranted.

Disclosure: A. Thatayatikom, None; **R. F. Modica**, None; **D. S. Hammenfors**, None; **N. J. Shiff**, None; **M. E. Elder**, None.

Abstract Number: 101

Defining Active Features of Juvenile Localized Scleroderma

Suzanne Li[1], Xiaohu Li[2], Elena Pope[3], Katie G. Stewart[4], Gloria Higgins[5], C. Egla Rabinovich[6], Kathleen O'Neil[7], Kathleen Haines[8], Ronald Laxer[9], Marilynn Punaro[10], Heidi Jacobe[11], Knut Wittkowski[12], Themba Nyirenda[13], Ivan Foeldvari[14] and Kathryn S. Torok[15], [1]Pediatrics, Joseph M Sanzari Children's Hospital, Hackensack Meridian Health, Hackensack, NJ, [2]Mathematical Sciences, Stevens Institute of Technology, Hoboken, NJ, [3]Dermatology, The Hospital for Sick Children, Toronto, ON, Canada, [4]Pediatric Rheumatology, Texas Scottish Rite Hospital, Dallas, TX, [5]Pediatrics, Nationwide Children's Hospital, Columbus, OH, [6]Pediatric Rheumatology, Duke University Medical Center, Durham, NC, [7]Pediatrics, Indiana University, Indianapolis, IN, [8]Joseph M Sanzari Children's Hospital, Hackensack Meridian Health, Hackensack, NJ, [9]Div of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, [10]Texas Scottish Rite Hospital for Children, Dallas, TX, [11]Department of Dermatology, University of Texas Southwestern Medical Center, Dallas, TX, [12]Rockefeller University, New York, NY, [13]Hackensack University Medical Center, Hackensack, NJ, [14]Kinder- und Jugenrheumatologie, Hamburger Zentrum Kinder-und Jugendrheumatologie, Hamburg, Germany, [15]Pediatric Rheumatology, Univ of Pittsburgh Med Ctr, Pittsburgh, PA

SESSION INFORMATION
Session Date: Thursday, May 18, 2017
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Session Time: 5:30PM-7:00PM

Background/Purpose:

Juvenile localized scleroderma (jLS) is the most common form of childhood scleroderma. Because of its chronicity and association with extracutaneous involvement, children are at risk for major morbidity including hemiatrophy, arthritis, and seizures. A sensitive clinical disease activity assessment tool is essential to optimize treatment of inflammation and thereby reduce the risk of fibrosis and associated damage. Several clinical tools have been developed; all include skin thickening and at least one other feature. No study has been done to evaluate the relative importance of scored features. Our Localized scleroderma Clinical and Ultrasound Study group (LOCUS), based in the Childhood Arthritis and Rheumatology Research Alliance (CARRA), conducted a longitudinal study to evaluate the specificity and relative importance of lesion features for disease activity.

Methods:

We conducted a multicenter prospective observational cohort study of jLS patients with either active or inactive disease (minimum ratio 2:1). Using a standardized evaluation form, we scored 1 specified study lesion per subject for defined features, at 3 visits over 6 months. Physicians scored global assessments for this lesion's activity and damage (PGA-A, PGA-D, respectively). Wilcoxon test, 2-sample t-test, correlation and regression analyses were used to evaluate assessed variables and their correlation with PGAs.

Results:

Of the 103 subjects enrolled, 66 were classified as active, 24 as inactive, and 13 were excluded from analysis because of incomplete data. Active and inactive patients had similar age of onset, gender, and lesion subtypes. The most common subtype was linear scleroderma (62% in active, 58% in inactive). Erythema, violaceous color, tactile warmth, new lesions, enlargement of lesion size, and abnormal skin texture were found to occur predominantly in active lesions. While skin thickening correlated with lesion PGA-A within the active group, neither presence nor level of skin thickening (at both

lesion edge and center) differentiated active from inactive lesions. No single variable was found to track tightly with PGA-A in all lesions, indicating that multiple lesion features need to be evaluated when assessing disease activity. Multiple regression analysis assigned highest weights to new or enlarged lesion and erythema.

Conclusion:

We identified several variables strongly associated with disease activity, and their relative contribution to physician scoring. Use of skin thickening as an activity variable is limited by its lack of specificity. These results aid development of a sensitive activity tool for comparative effectiveness treatment studies.

Disclosure: S. Li, None; **X. Li**, None; **E. Pope**, None; **K. G. Stewart**, None; **G. Higgins**, None; **C. E. Rabinovich**, None; **K. O'Neil**, None; **K. Haines**, None; **R. Laxer**, 5; **M. Punaro**, None; **H. Jacobe**, None; **K. Wittkowski**, None; **T. Nyirenda**, None; **I. Foeldvari**, 8; **K. S. Torok**, None.

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Abstract Number: 102

Duration of High-Dose Aspirin Therapy Does Not Affect Coronary Artery Outcomes in Kawasaki Disease

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Kawasaki Disease (KD) is an acute vasculitis targeting the coronary arteries. Prompt treatment with intravenous immunoglobulin (IVIg) reduces the occurrence and potentially the progression of coronary artery aneurysms (CAAs, defined in our study as Z-score $\geq$ 2.5). The role of high dose aspirin (HDA, 80-100 mg/kg/day) on the progression of CAAs is unclear, and the duration of HDA therapy varies widely.

Methods: We studied retrospectively all patients with KD presenting to our hospital over a 10-year period. Patients were categorized as having received one of three durations of HDA: 0, 1-7, or >7 days. The primary outcome was the maximum coronary artery Z-score measured by transthoracic echocardiography; secondary outcomes included C-reactive protein (CRP) and platelet count at diagnosis, 4-8 weeks, and at 9-15 months from presentation. Longitudinal data were analyzed using a linear mixed model.

Results: 103 patients with KD had HDA duration documented and were included in the analysis; 35 of those patients had CAAs at diagnosis. Within the overall study population, there was no difference in patient age, sex, race, KD status (classic versus incomplete KD), or CRP and platelet count at diagnosis between the three HDA groups. The 17 patients who received no HDA had longer duration of illness prior to diagnosis and were less likely to have received IVIg; twelve of these 17 patients defervesced prior to diagnosis. There was no difference in HDA duration between patients with and without CAAs at the time of diagnosis. Among patients with CAAs at the time of diagnosis, linear regression analysis adjusted for age, sex, and IVIg resistance revealed that HDA duration did not predict coronary artery dimensions at 9-15 months. Similarly-adjusted longitudinal analysis demonstrated no difference in the rate of decline of coronary artery Z-score, CRP, or platelet count between the three HDA groups. The only factors associated with higher coronary artery Z-scores at 9-15 months were higher coronary artery Z-scores at diagnosis and older age at diagnosis.

Conclusion: In patients with KD, a longer duration of illness before diagnosis and lack of administration of IVIg were clinical correlates associated with not administering HDA. This is a subset of patients in whom defervescence occurred prior to diagnosis as part of a prolonged illness course. Among all of the patients, the coronary artery Z-score at diagnosis and age at diagnosis were the only predictors of coronary artery Z-score at 9-15 months. The duration of HDA administration had no apparent effect on clinically-relevant outcome measures, particularly the persistence of CAAs.

Disclosure: K. Migally, None; **E. A. Braunlin**, None; **L. Zhang**, None; **B. A. Binstadt**, None.

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Abstract Number: 103

The Performance of a New Risk Assessment Scoring System in Detecting IVIG Resistance in Kawasaki Disease as Compared to the Kobayashi and Egami Scores in a Large Single Centre Canadian Cohort

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SESSION INFORMATION

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Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose:

We have shown previously that patients with Kawasaki Disease (KD) resistant to IVIG are at risk for the development of coronary artery abnormalities. Prediction of IVIG resistance with the Kobayashi and Egami scores has been successful in Japanese children. However, they lack sensitivity when applied to North American patients. There has only been one published North American score (San Diego), and it is not currently used in clinical practice. We aimed to develop a new risk assessment score to detect IVIG resistance in KD and compare its performance to the Kobayashi and Egami scores in this single centre multiethnic Canadian cohort.

Methods:

Data from our retrospective cohort of patients with KD treated with at least one dose of IVIG (2 g/kg) and low dose ASA (< 10 mg/kg/day) between 01/2004 and 12/2014 were used. IVIG resistance was defined as the requirement for further treatment after the first dose of IVIG. Using available laboratory data and clinical characteristics at diagnosis, we developed a new risk assessment scoring system. ROC (receiver operative characteristic) analysis was used to examine the predictability of individual variables based on their optimal levels of sensitivity and specificity. Only variables with a minimum AUC (area under the curve) of 0.5 were considered for the new scoring system. Score weights were allotted to each selected variable based on their strength of predictability; weight 1 was assigned if the AUC was between 0.5 and 0.6, and weight 2 or 3 was assigned if the AUC was >0.6. Scoring criteria was optimized after testing for various combinations of variables. Finally, logistic regression was carried out to verify the strength of association using the final model.

Results:

From our cohort of 269 patients, analysis was carried out in those with complete KD (n=206) with all the necessary

laboratory tests to construct the various scores (Kobayashi=129; Egami=120; New Score=137). Variables with AUC <0.5 were not included in the scoring system: fever duration at diagnosis, sodium and albumin. Variables with an AUC >0.5 were included: age, percent neutrophils, platelet count, CRP, AST and ALT. From these, we generated a 10-point score with an ideal cutoff of 4. Our new scoring system predicted IVIG resistance with a sensitivity of 70.8% (95% CI 55.9-83%), specificity of 62.9% (52.0–72.0), PPV of 50.7% (38.2-63.2), NPV of 80% (68.7-88.6) and AUC of 0.72 (0.63-0.81). After adjusting for age, sex, and fever duration in the logistic regression, patients with the positive new score (>=4) showed a strong, predictable association with IVIG resistance (OR=4.28; 95% CI=1.95-9.37). In our cohort, the sensitivity of the Kobayashi and Egami scores was relatively low at 38.6% and 29.7% respectively, but specificity was high at 87.1% and 87.6%.

Conclusion:

Our new risk assessment score performed better than the Kobayashi and Egami scores in predicting IVIG resistance in KD in this multiethnic Canadian cohort. However, it did not show additional utility compared to the San Diego score. Improvements are required to the proposed new score, and further analysis for this is currently underway.

Disclosure: D. Basodan, None; **A. V. Ramanakumar**, None; **R. Scuccimarri**, None.

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Abstract Number: 104

Rituximab Treatment for Chronic Steroid-Dependent Henoch-Schonlein Purpura

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SESSION INFORMATION
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Background/Purpose:

Henoch-Schonlein purpura (HSP) is a small vessel vasculitis characterized by non-thrombocytopenic purpura, abdominal pain, arthritis, and glomerulonephritis. Typically, HSP is self-limited, but more severe cases may require corticosteroid (CS) treatment. Rarely, a subset of patients has persistent rash, arthritis, abdominal involvement, or renal disease despite treatment with CS, or has disease recurrence on CS tapering. Although there is no consensus definition for refractory HSP, the 1-2 month timeframe is commonly used by many experts to determine refractoriness to daily oral CS treatment. Nevertheless, refractory HSP has been effectively treated with a variety of CS sparing therapies. For severe refractory HSP, the B cell depleting agent, rituximab (RTX), has been reported as beneficial for children with substantial renal or central nervous system involvement (J Pediatr 2009;155:136). However, RTX use for children with less severe HSP, but chronic CS dependent disease refractory to CS sparing immunomodulatory agents, has been less well explored. Herein, we describe 8 children treated with RTX for chronic refractory HSP and report a reduction in recurrent hospitalizations and

eventual CS discontinuation.

Patients and Methods:

Children diagnosed with HSP treated with RTX during the years 2008-2012 at a single institution were retrospectively identified through the electronic medical record. Clinical, laboratory, and therapeutic data were abstracted, including the presenting symptoms, the type and duration of treatment received, and the number of hospitalizations prior to and after RTX. Data were stored on an Excel spreadsheet and were subjected to the appropriate analyses and statistical tests.

Results:

Eight children (ages - 2 months to 16 years, 5 male), not previously reported, treated with RTX for chronic CS dependent HSP were identified (Table). In addition to palpable purpura (8), they suffered gastrointestinal distress/bleed (7), hematuria and/or proteinuria (7), and arthritis (1). Seven received long-term CS use, and 7 received various immunomodulatory therapies (methotrexate, azathioprine, mycophenolate mofetil, cyclophosphamide, and IVIg). All 8 received 1-6 rounds (two 750mg/m^2 doses, max. 1 gm/dose) of RTX with good B cell depletion. The incidence rate of hospital admission before and after receiving RTX was 1.78 vs. 0.68 per year, respectively, yielding an incidence rate ratio of 0.38 (confidence interval of 0.11 – 1.1, $p = 0.06$). Six achieved full remission off CS. The mean total oral steroid dose of RTX revealed a non-statistically significant reduction ($p = 0.668$). No serious adverse events were noted.

Conclusion:

RTX appears to be an effective and safe therapy for chronic CS dependent and immunomodulatory refractory childhood HSP. Future prospective analyses of RTX use for treatment of chronic CS dependent HSP will be worthwhile.

Patient #	1	2	3	4	5	6	7	8
Age at diagnosis	2 months	16 years	8 years	5 years	14 years	8 years	5 years	13 years
Sex	Male	Male	Male	Female	Male	Male	Female	Female
Ethnicity	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian	Caucasian	Hispanic	Caucasian
Palpable purpura	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hematuria and/or proteinuria	No	Yes	Yes	Yes	Yes	Yes	Yes	No
Arthritis	No	No	Yes	No	No	No	No	Yes
GI bleed /distress	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Long term CS use	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Immuno-modulators	MTX; MMF	MTX	AZA	CTX	None	MTX; MMF	MTX; MMF; IVIG	MTX
CD19 count after RTX (cells/mm^3)	<1	<1	<1	8	Not done	<1	<1	<1
# of rounds of RTX (2 doses/ round)	3	2	1	1	1	1	6	3
Hospitalizations for HSP prior to RTX	2	1	1	2	1	3	2	0
Hospitalizat-ions for HSP post RTX	0	1	1	0	0	0	0	0
Months in remission as of August 2014	47	50	26	37	43	68	N/A	N/A
Total oral steroid dose before RTX in mg	1,000	1,740	unknown	0	2,400	5,043	1,170	1,755
Total oral steroid dose after RTX in mg	0	1,370	2,400	1,700	5,459	742	1,005	0

Abstract Number: 105

Isolated Pediatric Pulmonary Capillaritis: A Comprehensive Single-Center Review of Disease Course, Management, and Prognosis

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SESSION INFORMATION

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Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose:

Pediatric diffuse alveolar hemorrhage (DAH) is a life-threatening disorder characterized by pulmonary hemorrhage and respiratory insufficiency. Histologically, DAH with capillary inflammation is known as pulmonary capillaritis (PC), and like DAH, can be secondary to autoimmune disease (SLE, systemic vasculitis) or an isolated condition. The latter is a rare condition and the disease course and prognosis has yet to be well described in children. We describe the clinical presentation, disease course, and outcomes of a pediatric cohort with biopsy proven isolated PC.

Methods:

After IRB approval, we reviewed the records of children with biopsy proven PC diagnosed between 2004 to 2015 who were evaluated by pediatric rheumatology. Inclusion criteria were capillaritis on lung biopsy and no diagnosis of systemic autoimmunity at presentation. We describe clinical features, imaging, bronchoscopy, immunomodulation, and outcomes.

Results:

Seven patients met inclusion criteria. Over half of the patients were female (57%), and 29% were Caucasian. The median age at diagnosis was 6.8 years (range 1.8 to 16.3 years). Most presented with an acute onset, 71% reported symptoms for less than 1 month. All presented with anemia, abnormal chest x-ray findings, and had a CAT scan consistent with DAH (including multi-focal ground-glass opacities). All patients had bronchoalveolar lavage showing hemosiderin laden macrophages. However, only 57% presented with frank hemoptysis. Eighty six percent required respiratory support at diagnosis: 14% nasal cannula, 57% conventional mechanical ventilation, and 14% high frequency oscillatory ventilation. At presentation, 86% had a positive ANA titer but no other classification criteria for SLE while 14% had a positive anti-RNP antibody but were never found to have systemic autoimmune disease. Induction regimen for all patients included intravenous (IV) pulse-dose steroids and IV Immunoglobulin (IVIG). Seventy one percent also received IV Cyclophosphamide, for a median of 6 months (range 3-6 months), 14% Rituximab and 14% Mycophenolate Mofetil (MMF). Plasmapheresis (6 sessions) was used in 14% as part of induction therapy. All patients received oral steroids (daily dose with taper) for maintenance therapy in addition to other medications. Seventy one percent received Methotrexate, 43% received IV steroids, 29% monthly IVIG, 14% MMF, and 14% Hydroxychloroquine. The median length of follow-up was 3 years (range 1-8 years), and in the majority of patients (71%), DAH did not recur. Twenty nine percent required supplemental oxygen after discharge (at night) and 29% had recurrent infections. One patient died which was likely related to a co-morbid condition (complications from congenital heart disease).

Conclusion:

Review of isolated PC at our institution indicates children present acutely and typically require ventilator support at

diagnosis. Despite ANA positivity, patients did not develop other antibodies or develop systemic autoimmune disorders. Mortality and morbidity rates were low with early, aggressive, multi-modal immunomodulatory regimens.

Disclosure: W. Lapin, None; **S. Singla**, None; **E. Muscal**, None; **M. Silva-Carmona**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/isolated-pediatric-pulmonary-capillaritis-a-comprehensive-single-center-review-of-disease-course-management-and-prognosis

Abstract Number: 106

Atypical manifestations and main misdiagnoses of Takayasu's arteritis in childhood: a multicenter study of 71 patients

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Takayasu's arteritis is a chronic inflammatory disease that affects the wall of large and medium-sized blood vessels. At the beginning of the disease, non-specific systemic symptoms predominate and in a more advanced phase of the disease, more characteristic signs and symptoms prevail. However atypical manifestations can occur, making the diagnosis difficult and leading to different misdiagnoses at the beginning of the disease. Therefore, our objective was to describe the main misdiagnoses and atypical manifestations in a multicenter study conducted on Brazilian children and adolescents.

Methods: This Brazilian multicenter retrospective study included 71 children and adolescents with Takayasu's arteritis diagnosed before their 19th birthday and followed up in 10 pediatric rheumatology centers. Patients' clinical, laboratorial and angiographic data were recorded.

Results: Of the 71 patients, 51 (72%) were girls. The mean age at onset was 9.2 years and the mean time to diagnosis was 1.2 years. Eleven (15.5%) patients had diagnoses other than Takayasu's arteritis at the beginning of the disease. The most common misdiagnosis was rheumatic fever, which was the initial diagnosis in 7 patients (2 of them had cardiac involvement). The other diagnoses before the correct diagnosis of Takayasu's arteritis were spondiloarthropaty, juvenile idiopathic arthritis (JIA), arteriovenous malformation and JIA with polyarteritis nodosa. We also found 10 atypical manifestations of Takayasu's arteritis, as follows: pyoderma gangrenosum (present in 2 patients), erythema nodosum, myositis, chorea, tendinitis, episcleritis, uveitis, hepatomegaly, splenomegaly and necrosis of extremities.

Conclusion: Our study demonstrated that there are a variety of misdiagnoses that can be made at the beginning of the disease and also there are some atypical manifestations that can contribute to the difficulty in diagnosing Takayasu's

arteritis.

Disclosure: G. Clemente, None; **A. P. Sakamoto**, None; **S. B. Sacchetti Sr.**, None; **V. Ferriani**, None; **F. Sztajnbok**, None; **S. Oliveira**, None; **B. Bica**, None; **A. Cavalcanti**, None; **T. Robazzi**, None; **M. Bandeira**, None; **M. T. Terreri**, None.

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Abstract Number: 107

Children with Relapsing Polychondritis are likely to be seen in the emergency room prior to establishing the diagnosis

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SESSION INFORMATION
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Background/Purpose:

Relapsing polychondritis (RP) is a rare immune-mediated disease characterized by recurrent episodes of chondritis. The pathogenesis of RP is poorly understood, and clinical manifestations can be variable resulting in a delay of diagnosis, especially in children. Auricular chondritis is a specific diagnostic finding but patients may also have life threatening involvement of multiple organs. We sought to explore the various patterns of early disease presentation in children by way of an international survey.

Methods:

A questionnaire based on known clinical symptoms and several possible clinical presentations associated with RP was developed. The Relapsing Polychondritis Awareness and Support Foundation administered the survey by posting the link to it on the Relapsing Polychondritis pediatric support group. The survey was anonymous and met criteria for exemption from IRB review per CFR 46 and NIH policy and was approved by the Office of Human Subjects Research Protections.

Results:

We had a total of 15 surveys completed; 2 patients were excluded from this analysis because they were older than 18 years of age at the time of diagnosis. The mean current age was 14.6 years (SD=6), with mean age at diagnosis of 9.9 years (SD=5). The majority of the patients were male 62% (n=8). 69% (n=9) of the patients saw more than 3 doctors prior to obtaining a diagnosis, and only 30% (n=4) were diagnosed by a rheumatologist. The most common symptom prior to diagnosis was ear pain or redness (85%; n=11). The most common painful joints were ankles and knees (each 38%; n=5). 46% (n=6) of the patients were diagnosed 1-3 years after onset of symptoms. 77% of the patients went to an emergency room due to RP symptoms prior to diagnosis with the top two reasons of ear pain 38% (n=5) and shortness of breath 31% (n=4). 38% (n=5) of the patients were diagnosed with asthma prior to establishing the RP diagnosis. The majority of the patients reported no association between symptoms and diet (67%; n=8). However, 62% (n=8) reported that weather

changes were symptom triggers. In females, 80% (n=4) had worsening of symptoms with menses. 77% (n=10) of the patients missed school for more than a week and 69% (n=9) missed more than a month of school due to their disease. The most common DMARD used to treat RP was methotrexate 46% (n=6).

Conclusion:

Here we report data from 13 pediatric patients with a rare disease. In this cohort, we found RP may adversely impact school attendance. We also found that there were possible environmental and personal triggers such as weather and menstruation. Our data suggest that establishing a diagnosis was difficult as evidenced by the fact that the majority of patients saw more than 3 doctors prior to establishing a diagnosis. The majority of doctors making the diagnosis were not rheumatologists. Although the most common symptoms were ear pain and redness, knee and ankle pain were also common. The data reported in this small cohort of patients provides important descriptions of presenting features and the burden of RP in children including missed school, emergency room visits, dependent joint arthritis, and pulmonary symptoms.

Disclosure: M. Ferrada, None; **N. Sinaii**, None; **K. A. Sikora**, None; **P. C. Grayson**, None; **T. Christie**, None; **R. Colbert**, None; **J. D. Katz**, None.

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Abstract Number: 108

Characteristics and long-term outcome of children and adolescents with initial diagnosis of Behçet's disease in a tertiary care center in Brazil

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SESSION INFORMATION
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Background/Purpose: Behet's disease (BD) is a rare systemic inflammatory disease with nonspecific clinical presentation that can mimic infections, tumors and other diseases. Diagnostic delay of several years is common. In 2016, classification criteria were published based on a prospective observational cohort (PEDBD[2]). The aim was to describe clinical characteristics and outcome of children and adolescents with initial diagnostic of BD attending a tertiary rheumatology center.

Methods: Retrospective analysis of medical records of patients under 18 years of age, attending Pediatric Rheumatology and Rheumatology Clinics, Ribeir‹o Preto Medical School Hospital, University of S‹o Paulo, from December 2000 to January 2015, whose initial diagnosis was BD.

Results: During the study period, a diagnosis of BD was suggested for 19 patients in the first evaluation, 11 female (57.9%), mean age 12 years (3 to 17 years). Thirteen of the patients (68.4%) maintained the diagnosis of BD until the last visit (mean follow-up 5 years - 1 to 10 years) and were on specific treatment: corticosteroid (77%), colchicine (30.8%), methotrexate (23%), cyclophosphamide (23%), azathioprine (15.4%) and chlorambucil (1%). Recurrent oral ulcers (89.5%), fever (84.2%), genital ulcers (63%), uveitis (21%), acneiform lesion/necrotizing folliculitis (37%), erythema

nodosum (10.5%) and optic neuritis (5%) were the main symptoms. Cranial angiography was performed in 8 (42%) patients, allowing the diagnosis of Neuro-Behet in 4 (21%). ANA and cANCA were negative in 17/19 and 12/19 patients respectively. aPL were detected in 6/13 patients (46%). Acute-phase protein levels were elevated in 79% of patients. Secondary antiphospholipid antibody syndrome was diagnosed in 2 patients – one with extensive dural venous sinuses and intracardiac thrombosis, other with ischemic stroke. Six patients (31.6%) with initial diagnosis of BD met diagnostic criteria for other diseases on the follow-up: two cases of periodic fever, adenitis, pharyngitis, aphtous stomatitis (PFAPA), and one case each of high-grade glioma, T-cell lymphoma, common variable hypogammaglobulinemia, ganglionar tuberculosis. The time for definitive diagnosis ranged from 2 months to 5 years, mean 17 months. At the time of presentation, PEDBD classification criteria were fulfilled in 7/13 patients (54%) that maintained BD diagnosis and in 3/6 patients with other diagnosis on follow-up.

Conclusion: Behet's disease is a challenging diagnosis and in some cases it can only be made after a follow-up period. The new pediatric BD classification criteria should be used with caution for clinical diagnosis.

1. *Criteria for diagnosis of Behcet's disease. International Study Group for Behcet's Disease.* Lancet, 1990. **335**(8697): p. 1078-80; 2. Kone-Paut, I., et al., *Consensus classification criteria for paediatric Behcet's disease from a prospective observational cohort: PEDBD.* Ann Rheum Dis, 2016. **75**(6): p. 958-64.

Disclosure: M. R. Tovar-Avila, None; **F. H. Gomes**, None; **L. Da Silva**, None; **V. Ferriani**, None; **L. Carvalho**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/characteristics-and-long-term-outcome-of-children-and-adolescents-with-initial-diagnosis-of-behcets-disease-in-a-tertiary-care-center-in-brazil

Abstract Number: 109

Clinical features of pediatric Behçet’s disease patients in Japan

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SESSION INFORMATION

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Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: To diagnose pediatric patients as Behçet’s disease (BD) is challenging. Sensitivity of four BD criteria, three BD criteria made for adult patients and Paediatric Behçet’s Disease study (PEDBD) criteria[1], are not high enough for Japanese pediatric BD patients (51%, 60%, 70%, 47%). The aim of this study is to clarify differences in clinical characteristics between Japanese pediatric BD patients (JP) and Japanese adult BD patients (JA) or pediatric BD patients in other countries (OP)[1].

Methods: We identified 51 cases of Japanese pediatric BD by questionnaire survey of pediatric rheumatologists in Japan. Then we compared their symptoms recognized at any time during disease course with those of other two groups.

Results: Oral ulcers were found with high frequency in all groups (JP 98%, JA 96%, OP 98%). Gastrointestinal symptom were higher in both pediatric groups (JP 45%, OP 40%) than adult group (JA 23%). In many of organ involvement, frequency of JP group were lower than other groups, Ocular (JP 24%, OP 33%, JA 61%), Central Nerve System (6%, 46%, 10%), Vascular (4%, 15%, 12%) respectively.

Conclusion: There may be differences in clinical features of BD due to onset of age or residential area. These differences could be a reason for difficulty to diagnose pediatric BD patient.

References

1. Isabelle Kone-Paut et. al. ：Consensus classification criteria for paediatric Behcet's disease from prospective observational cohort PEDBD. Ann Rheum Dis 2016;75:958-64

Disclosure: K. I. Yamaguchi, None; **S. Fujikawa**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/clinical-features-of-pediatric-behcets-disease-patients-in-japan

Abstract Number: 110

Risk Factors for Poor Health-Related Quality of Life in Children with Inflammatory Brain Diseases

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SESSION INFORMATION
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Session Type: Abstract Submissions
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Background/Purpose:

Inflammatory Brain diseases (IBrainD) are increasingly recognized causes of devastating neurological deficits in previously healthy children. Although the mortality has dramatically improved, disease and treatment related morbidity and impact on health-related quality of life (HRQoL) remain unclear. Therefore the purpose of this study was to determine the HRQoL in children with IBrainD and identify factors at diagnosis associated poor HRQoL.

Methods:

A multicenter, observational cohort study of children diagnosed with IBrainD at all participating sites of the BrainWorks network was conducted. Children age <18 years at time of diagnosis, who were followed for at least 12 months were included. HRQoL was measured using the Pediatric Quality of Life Inventory Version 4.0 (PedsQL) Generic Core Scales. The total PedsQL score and the physical and psychosocial subdomains were assessed. The relationship between the parent's perceived HRQoL of the child and the child's perceived HRQoL were explored. Independent variables evaluated included diagnosis, age at diagnosis, gender, time to diagnosis, presence of clinical symptoms at diagnosis, baseline disease activity as rated on the Physician's Global Assessment analog scale and neurological functioning at 1 year. The baseline clinical symptoms considered included seizures, hemiparesis and cognitive/behavioural dysfunction. Outcome: Impaired HRQoL as defined by PedsQL. Analyses of trends were performed using regression models adjusted for repeated measures.

Results:

140 patients were included in the study. The average age at diagnosis in this cohort was 9.8 years (Range= 0.4-18.4). Angiography-negative (small vessel) childhood primary angiitis of the CNS was the most common diagnosis. Statistically significant improvements in total PedsQL scores were associated with the absence of seizures ($p<0.01$) and the absence of cognitive and behavioural dysfunction at baseline ($p<0.01$). Increases in the physical functioning subdomain score ($p<0.01$) and the psychosocial subdomain score ($p<0.01$) were observed if seizures were absent. In the absence of cognitive and

behavioural dysfunction, improvement was seen in the psychosocial subdomain score ($p<0.01$). Gender ($p=0.36$) or presence of hemiparesis ($p=0.45$) showed no difference in the total PedsQL score. Identical prognostic factors were found in the parent PedsQl as for the child's PedsQL scores.

Conclusion:

Children with IBrainD presenting with seizures and cognitive dysfunction at time of diagnosis were at highest risk for poor HRQoL over time. Tight seizure control and early cognitive rehabilitation are mandatory. Additional resources should therefore be considered and allocated to children presenting with these symptoms, including extended rehabilitative services and counselling focused on improving psychosocial HRQoL.

Disclosure: E. Liu, None; **A. Dropol**, None; **M. Twilt**, None; **P. Tyrrell**, None; **S. Sheikh**, None; **S. Benseler**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/risk-factors-for-poor-health-related-quality-of-life-in-children-with-inflammatory-brain-diseases

Abstract Number: 111

Eosinophilic Fasciitis in Children: Clinical Course and Response to Treatment from Two Large Academic Centers

Suhas Ganguli[1], Meiqian Ma[2], Christine Lauren[3], Maria Garzon[3], Cassyanne L. Aguiar[4], Andrew Eichenfield[5], Amy Starr[6], Lisa F. Imundo[7,8], B. Anne Eberhard[9] and Joyce Hui-Yuen[10], [1]Pediatrics, Cohen Children's Medical Center of New York, Lake Success, NY, [2]Pediatric Rheumatology, Cohen Children's Medical Center of New York, Lake Success, NY, [3]Division of Pediatric Dermatology, Columbia University Medical Center, New York, NY, [4]Pediatric Rheumatology, Children's Hospital of The King's Daughters, Norfolk, VA, [5]Columbia University Medical Center, New York, NY, [6]Pediatric Rheumatology, Columbia University Medical Center, New York, NY, [7]Pediatrics, Columbia University Medical Center, New York, NY, [8]Assoociate Professor of Pediatrics in Medicine - Rheumatology, Columbia University Medical Center, New York, NY, [9]Cohen Children's Medical Center of New York, New Hyde Park, NY, [10]Cohen Children's Medical Center of New York, Lake Success, NY

SESSION INFORMATION
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Background/Purpose:

Eosinophilic fasciitis (EF) is a rare connective tissue disease characterized by a progressive inflammatory thickening of skin and soft tissues. The diagnosis is based on clinical features, imaging, and biopsy findings. Due to limited experience with pediatric disease, diagnosis and treatment are often challenging. We describe our longitudinal experience in treating children with EF.

Methods:

This is a retrospective study where data were collected on clinical features, laboratory results at diagnosis, disease course, and treatment response. Descriptive statistics were used where appropriate.

Results:

Our series includes 7 patients with EF, with a mean age at diagnosis of 12.4 (+/- 5.1) years and a mean follow-up of 45.1

months (Table 1). All patients had peripheral eosinophilia. Three patients had elevated serum aldolase, one had elevated creatine kinase, and two had abnormal thyroid function at diagnosis.

Six patients had typical biopsy features of eosinophilic infiltration of the fascial layer with inflammatory infiltrates. The remaining patient had non-specific inflammation on biopsy.

Table-1: Demographics and Clinical Presentation

Case	Age at Diagnosis (in years)	Gender	Race	Extent of Involvement	Pattern of Involvement	Raynaud's	Telangiectasia	Imaging Abnormalities on MRI
1	17	Male	Caucasian	Hands and forearms (morphea, extensive woody edema with groove sign in bilateral forearms)	Symmetric	Yes	Arms, legs	Fasciitis in right forearm flexor and extensor tendons. Subcutaneous edema in right hand
2	3	Female	Caucasian	Right arm, forearm, leg, Right side of back, Right side of face (morphea, woody edema, peau d'orange)	Asymmetric	Yes	Fingers	Right shoulder effusion with bursitis
3	14	Female	Caucasian	Left lower extremity (morphea)	Asymmetric	No	Fingers	Intramuscular fascial edema overlying left tibia
4	11	Female	Caucasian	Bilateral knees, toes, hands (morphea)	Symmetric	Yes	No	N/A
5	16	Male	Asian	Elbows, fingers, knees, toes	Symmetric	No	No	N/A
6	17	Male	Asian	Hands, fingers, legs (extensive woody edema)	Symmetric	No	No	Fascial edema and quadriceps edema
7	9	Female	African American	Right wrist, hand, fingers (peau d' orange)	Asymmetric	No	No	Perimuscular and peritendinous fascial edema of right forearm with dorsal radio-ulnar joint synovitis

Treatment induction in all patients consisted of high-dose intravenous solumedrol with subsequent oral prednisone or intravenous solumedrol. All patients required methotrexate (MTX) for disease control and 4 required addition of mycophenolate mofetil (MMF). Time to first improvement in any clinical symptom was 3.4 months. Improvement in skin findings and laboratory abnormalities was noted in all patients after treatment with intravenous solumedrol.

Two patients had disease flares. Case 1 had recurrent flares of arthritis at 4 months after steroid wean and after 2.5 months of MTX wean. Case 2 flared with skin lesions after 12 months of MTX wean. Chronic complications included lipodystrophy (3 patients), leg length discrepancy (1), and joint contractures (3) [elbows and ankles (1) and fingers (2)].

Conclusion:

Pediatric EF is challenging to diagnose and treat, mainly due to its rarity and lack of homogeneous clinical experience. This is the largest pediatric case series reported in the last 10 years. Our data show a higher prevalence of distal limb involvement, Raynaud's phenomenon and asymmetric disease in children, possibly exhibiting a phenotype distinct from classic adult EF. Systemic or visceral involvement was absent in our patients.

Our data confirm the efficacy of corticosteroid as first-line therapy, and suggest a role for MTX as a promising steroid-sparing agent. Our patients often experienced a more severe disease progression compared to adults, requiring escalation of therapy to include one or more steroid-sparing agents. In refractory cases, addition of MMF in our series showed optimistic results leading to remission of EF symptoms.

Disclosure: S. Ganguli, None; **M. Ma**, None; **C. Lauren**, None; **M. Garzon**, None; **C. L. Aguiar**, None; **A. Eichenfield**, None; **A. Starr**, None; **L. F. Imundo**, None; **B. A. Eberhard**, None; **J. Hui-Yuen**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/eosinophilic-fasciitis-in-children-clinical-course-and-response-to-treatment-from-two-large-academic-centers

Abstract Number: 112

Use of Rituximab and Risk of Re-hospitalization for Children with Neuromyelitis Optica Spectrum Disorder

Sabrina Gmuca[1], Amy T. Waldman[2], Pamela F. Weiss[3] and Jeffrey S. Gerber[2], [1]Pediatric Rheumatology, The Children's Hospital of Philadelphia, Philadelphia, PA, [2]The Children's Hospital of Philadelphia, Philadelphia, PA, [3]Division of Rheumatology, Center for Pediatric Clincial Effectiveness, Children's Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION

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Background/Purpose: First-line use of rituximab for neuromyelitis optica spectrum disorder (NMOSD) is common but the benefits of early immunosuppression remain unclear. We aimed to determine whether first-line administration of rituximab prevents re-hospitalization within 1 year.

Methods: We conducted a retrospective cohort study of subjects with NMOSD from November 2005 until December 2015 using the Pediatric Health Information System. We included subjects >1 and <25 years at time of initial documentation with ICD-9-CM code for NMO who received ≤1 course of glucocorticoids. We excluded subjects with ≥1 ICD-9-CM code for multiple sclerosis. The primary exposure was ≥1 rituximab dose during initial hospitalization. The primary outcome was first re-hospitalization within 12 months. Only the first re-hospitalization that occurred >30 days later was considered (given possibility of early re-admission for repeat dosing) with data censored at 12 months. The association between rituximab and re-hospitalization was analyzed using Kaplan-Meier survival curves, log-rank test and Cox proportional hazards models. Both univariate and multivariate Cox regression models (accounting for demographics, ICU status, first-line glucocorticoid exposure and MRI studies) were calculated. Secondary outcomes included time to first re-hospitalization and duration of re-hospitalization.

Results: We included 202 subjects (73% female, 38% Caucasian) with a median age of 13 years (IQR: 10.0, 15.0). Fifty-five subjects (27%) received rituximab at first hospitalization with an increasing trend in rituximab use over the study period ($p<0.01$). In unadjusted models, there was no statistically significant difference in risk of re-hospitalization between those exposed and unexposed (14.6% vs. 11.6%, respectively; $p=0.43$). Subjects exposed to rituximab were re-hospitalized a median of 60 days (IQR: 47, 121) after initial hospitalization, while subjects not exposed to rituximab were

re-hospitalized a median 125 days (IQR: 84, 187), but this was not statistically significant (p=0.06). Median duration of re-hospitalization was 2 days regardless of rituximab exposure (p=0.72). In multivariate analysis, the hazard ratio of re-hospitalization for exposed children was 1.73 (95% CI: 0.69, 4.38; p=0.25). Children exposed to glucocorticoids had significantly reduced odds of readmission (HR: 0.28, 95% CI: 0.09, 0.87; p=0.03). Additionally, subjects who had a MRI of the spine were approximately four times more likely to be re-admitted (HR: 4.29 [95% CI: 1.30, 14.13]; p=0.02).

Conclusion: Among children with NMOSD, first-line glucocorticoid exposure but not rituximab was associated with a significantly decreased risk of re-hospitalization. However, the possibility of residual confounding by indication cannot be entirely excluded. Spinal involvement was an independent predictor of re-hospitalization.

Disclosure: S. Gmuca, None; **A. T. Waldman**, None; **P. F. Weiss**, None; **J. S. Gerber**, None.

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Abstract Number: 113

Exploring the role of pediatric rheumatologists in the diagnosis and management of autoimmune encephalitis

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SESSION INFORMATION
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Background/Purpose:

Autoimmune encephalitis (AE) encompasses a spectrum of immune-mediated brain disorders that cause severe neuropsychiatric manifestations. These disorders often lead to protracted hospital stays, complex neurocognitive rehabilitation needs, and significant psychosocial strains on caregivers. Clinical outcomes are better with early recognition and prompt immuno-modulation. Pediatric rheumatologists may encounter children with AE while evaluating for NPSLE or CNS vasculitis, A survey of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) membership was conducted to assess the current roles of pediatric rheumatologists in caring for children with AE.

Methods:

Members of CARRA completed a Web-based survey (N=439 total members; 375 medical providers). 4 emails were sent over a 2 month period (June to August 2015). The study was submitted and exempted from review by Duke University's Institutional Review Board.

Results:

101 CARRA voting members (88% in US) responded to the online survey (26% response rate). 74% of respondents evaluated a patient with AE during the past year. Most respondents' divisions (57%) cared for less than 5 children with AE

per year, with 15% of divisions caring for over 10 patients/year. The AE subtypes most frequently encountered were NMDAR encephalitis (84%) and seronegative AE (clinical phenotype without an identified antibody) (80%). All respondents agreed that rheumatologists should rule out traditional rheumatic disorders affecting the CNS, with 60% also acknowledging a role in work up and diagnosis of AE. While 80% recommended a treatment protocol once a diagnosis was made, 20% of respondents stated that rheumatology was the primary service for AE patients. Of the 70 rheumatologists involved in a therapy role, 63% wrote for immunosuppressive medications. Most respondents became involved in care after 1st line therapy was already given (59%). Only 17% of respondents stated that their institutions had a standard protocol for children with AE (mostly for NMDAR). A collaborative relationship between rheumatology and neurology services was present in most locations (85%).Survey comments did reveal challenges in defining the roles of these two services. 32% (21/66) of respondents stated that their institutions had a neuro-immunology service/clinic). 76% of these neuro-immunology services included a pediatric rheumatologist. The most common challenges encountered in the care of children with AE included: inflammatory brain disease not covered in training (58%), lack of curricular development (42%), difficulty collaborating with neurology (41%), and lack of family resources (25%). 27% of respondents did not feel AE was part of rheumatology scope of practice.

Conclusion:

The majority of survey respondents are involved in caring for children with AE. Rheumatologists find work-up and management of AE challenging due to inadequate experience/training, absence of standardized protocols, absence of or challenges in collaboration with neurology and lack of educational resources. Survey results shaped subsequent multi-disciplinary sessions at both 2016 CARRA and ACR meetings that included neurology and rheumatology practitioners.

Disclosure: E. Muscal, None; **H. Van Mater**, None; **T. Cellucci**, None; **D. Co**, None; **J. Frankovich**, None; **M. S. Klein-Gitelman**, None; **M. Twilt**, None; **S. Benseler**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/exploring-the-role-of-pediatric-rheumatologists-in-the-diagnosis-and-management-of-autoimmune-encephalitis

Abstract Number: 114

Clinical Features and Treatment Outcomes in Down's Arthropathy

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Crude prevalence estimates indicate Down's Arthropathy (DA) is 3-8 times more common than juvenile idiopathic arthritis (JIA), however, DA is still largely under recognized at onset and has a 2 year average delay from onset of symptoms to diagnosis. The majority of DA presents with greater than 5 affected joints, more commonly affecting small joints, and treatment has historically been complex as many don't tolerate methotrexate (MTX) due toxicity. The objective of this study is to investigate the clinical features and treatment outcomes of DA at our institution.

Methods: In a retrospective chart review, potential DA patients were identified through electronic medical record system (EMR) from January 1, 1995 to December 31, 2015. ICD-9-CM codes were used to identify patients (less than 18 years of age) with both Down syndrome (758.0) and JIA (714.3, 714.31, 714.32, 714.33). Individual charts were then manually reviewed to confirm diagnosis of Down syndrome (DS) and JIA. Chart review included analysis of all documents included in EMR, including clinical visits, imaging studies and laboratory results.

Results: Of 26 identified patients, (3 did not have DS and 2 had incomplete records) 21 met inclusion criteria and were

analyzed with a mean follow-up period of 4 years (SD 4.2). Patients were 62% female, and 62% had a polyarticular, RF negative presentation at diagnosis. Within this cohort, there was a mean 19 months (SD 16) delay in diagnosis after symptom onset. At JIA diagnosis 71% reported morning stiffness, and on exam there was an average of 14 active joints (SD 10), and 57% of patients had small joint involvement. Mean physician global assessment of disease activity at diagnosis was 4.9 (SD 2.0). Of 18 patients with imaging at diagnosis, erosive changes were noted in 22%. All patients were started on NSAIDs at diagnosis with 33% simultaneously starting a disease-modifying antirheumatic drug (DMARD), and 5 % a biologic. Over the course of disease 62% used a DMARD (mostly MTX [58%]) and 48% used a biologic (mostly etanercept [90%]). Of those on DMARD therapy 54% were discontinued due to side effects and 56% had inadequate response to first-line biologic therapy. At last visit there was an average of 3 active joints (SD 4) and average MD global of 1.7 (SD 1.6).

Conclusion: Down's Arthropathy remains under recognized despite having a higher prevalence than JIA. There also remains a significant delay to diagnosis which likely contributes to poorer outcomes. Other barriers that inhibit optimal treatment and outcomes are DMARD toxicity and anti-TNF effectiveness, which appears different compared to those in JIA without DS. Earlier diagnosis through improved screening and more targeted treatment may allow for earlier disease control and better outcomes.

Table 1. Treatment and Response throughout course of Down's Arthropathy

Treatment	Patient (n/total)	Response* (n/total)
NSAIDs	21/21	5/21
Oral Steroid	5/21	1
Intra-articular Steroid	14/21	3
DMARDs	13/21	
Methotrexate	12/13	3/12
Leflunomide	3/13	0/3
Sulfasalazine	2/13	1/2
Hydroxychloroquine	3/13	2/3
Biologics	10/21	
Etanercept	9/10	3/9
Adalimumab	4/10	3/4
Infliximab	2/10	1/2
Abatacept	4/10	3/4

*Defined as tolerating and not requiring an increase in therapy

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Disclosure: J. T. Jones, 5; **L. Danawala**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/clinical-features-and-treatment-outcomes-in-downs-arthropathy

Abstract Number: 115

Anti-Phospholipid Antibodies in Children with Down Syndrome

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SESSION INFORMATION

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Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: The prevalence of anti-phospholipid antibodies **(**APL) in children with Down syndrome (DS) is unknown. Furthermore, it is unknown if an intermittent or persistent presence of APL in DS patients makes them at higher risk for thrombosis and strokes. Such knowledge may support the importance of routinely screening DS patients for APL. Our aim is to explore the presence of APL in children with DS compared with healthy children.

Methods: We screened 61 children with DS and a control group (CG) of 61 matched healthy children for anti-cardiolipin antibodies (aCL), anti-β2 glycoprotein-1 antibodies (anti-β2 GP 1), and lupus anticoagulant (LA) in the absence of recent infections. We repeated the positive tests any time after 12 weeks of the initial testing and counted the final APL-subtype as positive only if the repeated testing was positive. We then considered the participant to be APL-positive if any APL-subtype was positive. A retrospective review of medical records was performed for relevant medical conditions. The appropriate chi-square test was used to test for the difference in the number of participants in each group with positive APL.

Results: The number of APL-positive tests in DS patients was 12.1%, compared with 1.7% in the controls ($p = 0.03$), although the titers were generally in the low to moderate range. There was no difference between groups for APL subtypes; however, LA was a better predictor of the presence of APL ($p \leq 0.001$). Congenital heart disease was present in 57.1% of APL-positive DS patients. DS patients with known anti-thyroid antibodies or hypothyroidism ($n = 19$) were negative for APL. None of the DS patients had any history of stroke or thrombosis.

Conclusion: Our results suggest that APL antibodies, specifically using the LA test, may be found in DS patients. Larger confirmatory studies and long-term follow-up are needed to better understand the implications of our results.

Table 1. Demographics of the DS group and CG children.

	DS (n = 61)	CG (n = 61)	P value
Gender: n (%) Males / Females	29 (47.5) / 32 (52.5)	27 (44.3) / 34 (55.7)	0.85
Ethnicity: n (%) Arabic / Non-Arabic	54 (88.5) / 7 (11.5)	45 (73.8) / 16 (26.2)	0.06
Age: (mean ± SD)	9.73 ± 2.14	10 ± 2.14	0.71
Karyotype: n (%) Tri 21 Others *	59 (96.7) 2 (3.3)	NA NA	NA NA
Medical History: n (%) CHD Hypothyroidism Anti-thyroid ** Leukemia Celiac IDDM Moyamoya Neutropenia	28 (45.9) 19 (31.1) 19 (31.1) 2 (3.3) 1 (1.6) 1 (1.6) 1 (1.6) 1 (1.6)	0% 0% 0% 0% 0% 0% 0% 0%	NA NA NA NA NA NA NA NA

* One patient was 46, XY t (14, 21) and another was 48, XXY, +21

** Past presence of any anti-thyroid antibodies with or without thyroid disease

CHD: congenital heart disease, IDDM: Insulin dependent diabetes mellitus

Table 2. Presence of APL in DS group and CG children.

	DS (n = 61)	CG (n = 61)	P value
aCL positive: n (%)	2 (3.3)	0	0.49
Anti-ß2 GP 1 positive: n (%)	1 (1.6)	0	1.00
LA-positive: n (%)	4 (6.9) *	1 (1.7) **	0.20
Any APL positive: n (%)	7 (12.1)	1 (1.7)	0.03

* Number of Down syndrome patients with LA testing = 58

** Number of control subjects with LA testing = 59

Table 3. APL subtypes in DS patients with positive APL.

	N (%) with Positive APL-subtype:	N (%) with Negative APL-subtype:	P value
aCL	2 (28.6)	5 (71.4)	0.01
Anti-ß2 GP 1	1 (14.3)	6 (85.7)	0.12
LA	4 (57.1)	3 (42.9)	≤ 0.001

Disclosure: B. Al-Adba, None; **H. El Bashir**, None; **K. ZahrAldin**, None; **R. Thomas**, None; **M. Al-Khalifa**, None; **A. Al-Marwani**, None; **D. Al-Faridi**, None; **M. Al Dabbagh**, None; **B. Fathalla**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/anti-phospholipid-antibodies-in-children-with-down-syndrome

Abstract Number: 116

Arthritis as First Presenting Symptom of Inflammatory Bowel Disease: A Case Control Study

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SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Clinical and Therapeutic Poster Session
Session Type: Abstract Submissions
Session Time: 5:30PM-7:00PM

Background/Purpose:

Inflammatory bowel disease (IBD) is associated with extra-intestinal manifestations, the most common of which is arthralgia/arthritis. 4.1- 15% of patients with inflammatory bowel disease have arthritis[1]. There has been little to no published research indicating how frequently arthritis is the presenting manifestation of IBD. We performed a case-control study to investigate whether differences exist in initial laboratory values and body measurements in patients with arthritis who are ultimately diagnosed with IBD-associated arthritis compared to patients with juvenile idiopathic arthritis (JIA) without IBD.

Methods:

A retrospective review of children who presented to University Hospitals Rainbow Babies and Children's Hospital (UH RB&C) pediatric rheumatology clinic between 2010 and 2015 was performed. Children were identified who presented with arthritis without overt gastrointestinal symptoms and who were subsequently diagnosed with IBD. Age and gender matched controls were identified from children with oligoarticular or polyarticular JIA who were seen in the pediatric rheumatology clinic during the same time period. Controls and cases were matched at a 2:1 ratio. Body morphometrics (weight and height) and laboratory results (hemoglobin, platelet count, erythrocyte sedimentation rate, C-reactive protein, and serum albumin) were obtained at their first pediatric rheumatology visit. In all cases, the diagnosis of IBD was confirmed by endoscopy/colonoscopy with intestinal biopsy. Statistical analysis was performed using R software. The univariate analyses were obtained for all variables and if significant (p-value < 0.05) these variables were then included in the logistic regression.

Results:

We identified 12 patients who presented with arthritis and were subsequently diagnosed with IBD. Using the univariate analysis, patients with IBD associated arthritis had significantly lower weight, hemoglobin, albumin and total protein as well as higher CRP and ESR values. Compared to age and gender matched controls (n = 24), patients with IBD-associated arthritis were significantly more likely to have a lower weight percentile and lower albumin levels as compared to patients with JIA without IBD using odds ratios (OR=0.54, 0.023). Performing the multi-variate analysis showed that patients with IBD associated arthritis had significantly elevated CRP and lower weight (p-value= 0.034).

Conclusion:

These data suggest that in patients presenting with arthritis with elevated C-reactive protein in association with lower weight percentile (less than the 25th percentile), IBD should be excluded as the cause for arthritis.

Disclosure: K. Phillippi, 2; **T. Sferra**, None; **N. Singer**, None; **E. Brooks**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/arthritis-as-first-presenting-symptom-of-inflammatory-bowel-disease-a-case-control-study

Abstract Number: 117

The Effect of Bisphosphonate Use on Bone Density Measurements in Patients with Muscular Dystrophy

Simrat Morris[1,2], Syeda Maqsood[3], Christine Garapic[3], Andre Prochoroff[3] and Hulya Bukulmez[3], [1]Rainbow Babies and Childrens Hospital, Cleveland, OH, [2]University Hospitals Cleveland Medical Center, Cleveland, OH, [3]MetroHealth Medical Center, Cleveland, OH

SESSION INFORMATION
Session Date: Thursday, May 18, 2017
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Session Type: Abstract Submissions
Session Time: 5:30PM-7:00PM

Background/Purpose:

Individuals with Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy have impaired bone health and increased fracture risk due to several factors including immobility, abnormal calcium metabolism, low vitamin D levels, and the inability to perform weight-bearing activities. Most patients with DMD are treated with systemic steroids (prednisone 1mg/kg/day) starting around age five to improve muscle strength, preserve lung function, and help them maintain ambulatory status. However, chronic steroid use leads to increased fragility fractures and suppresses longitudinal bone growth.

Studies suggest that early recognition and preventive treatment of osteoporosis in DMD patients improves quality of life and prolongs life expectancy; thus, there is a need for studies that evaluate the effect of available osteoporosis treatments in this at-risk population.

Herein, we investigate the value of systemic bisphosphonate use in muscular dystrophy patients by reviewing their effects on bone density as measured by dual energy X-ray absorptiometry (DXA).

Methods:

We performed a retrospective chart review using data from the Muscular Dystrophy Association (MDA) clinic which

consists of DMD and Becker muscular dystrophy patients who undergo bone density screening using a GE Lunar DXA machine. Z-scores are based on the US standards for 5-26 year old healthy males as per protocol. Ninety five male MDA patients were identified. Those under 5 and over 21 years of age and those that did not undergo DXA scan after one year of therapy were excluded. Eleven patients on systemic bisphosphonate therapy (oral alendronate 1 mg/kg/dose weekly (n=9) or intravenous (IV) zoledronic acid 0.05mg/kg/dose (n=2) every 6 months) were used in our analysis. We followed the DXA scans of these patients for one year after which z-scores of the lumbar spine (L1-L4) before and one year after treatment were compared using paired sample t-tests.

Results:

Eleven patients underwent systemic bisphosphonate treatment while on chronic corticosteroid therapy. The mean pre-treatment lumbar DXA z-score was -2.5±1.9 (range -5.8 to 0). Subjects received systemic bisphosphonate therapy for a mean of 19.8±7.4 months (range 12-35 months) prior to re-evaluation with DXA. The mean DXA z-score increased by 0.37±1.5. However, a paired sample t-test revealed that there was no significant change in lumbar DXA z-scores in the subjects after bisphosphonate therapy (-2.5±1.9 versus -2.2±1.9, p=0.43). Of note, both patients on IV bisphosphonate therapy showed improvement in their lumbar spine z-scores (from -5.7 to -1.4 and from 0.0 to 0.5).

Conclusion:

There was no significant improvement in lumbar spine z-scores in patients treated with at least one year of oral bisphosphonates. However, oral bisphosphonates may still be involved in slowing the worsening of osteoporosis in this patient group, and our results may be underpowered. The limited subgroup of subjects receiving IV bisphosphonates demonstrated increased DXA z-scores, and further studies are needed to investigate the role of both IV and oral bisphosphonates in optimizing bone health in this at-risk population.

Disclosure: S. Morris, None; **S. Maqsood**, None; **C. Garapic**, None; **A. Prochoroff**, None; **H. Bukulmez**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/the-effect-of-bisphosphonate-use-on-bone-density-measurements-in-patients-with-muscular-dystrophy

Abstract Number: 118

Oxygen Saturation Recordings in Pediatric Rheumatology Patients At Risk For Lung Disease

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Pediatric rheumatology patients are at high risk for the development of pulmonary disease. Lung disease in these patients can go unnoticed for long periods of time, and carry significant morbidity and mortality. The importance of screening and monitoring for pulmonary manifestations in these patients is clear; however, many screening methods may be costly and difficult to administer. Pulse oximetry has been shown to be a useful screening tool for the ambulatory monitoring of COPD and certain types of interstitial lung disease. Despite this, pulse oximetry is rarely used as a routine measurement in the clinic setting. We therefore designed a pilot study to determine feasibility of in-clinic pulse oximetry to help determine when there is need for more in depth screening.

Methods: Baseline measurements of oxygen saturation (O2 sat) recordings were collected for all patients attending clinic at our institution. Measures were then implemented to improve these rates, including speaking with clinic nurses, clear signage, and working with information technology to include O2 sat in the vitals section in the electronic medical record system. This study was exempt from full review, and approved by the institutional IRB.

Results: As seen in figure 1, recordings of O2 sat increased from 1% to 94% during this period. Over the study period, O2 sat was also increasingly recorded as part of vital signs, where it could be easily accessed. As part of the intervention, one patient was found with abnormal pulse oximetry leading to further evaluation.

Conclusion: This study reveals that initiatives to increase O2 sat recordings in a clinic setting are effective and easily achieved. Research is ongoing about the best methods to screen for pulmonary disease in these patients who are at high risk.[i]The utility of post exercise and spirometry will be evaluated as ambulatory screening tools. Further research is needed to determine the efficacy of longitudinal O2 sat recordings as a screening tool for lung disease in pediatric rheumatology patients.

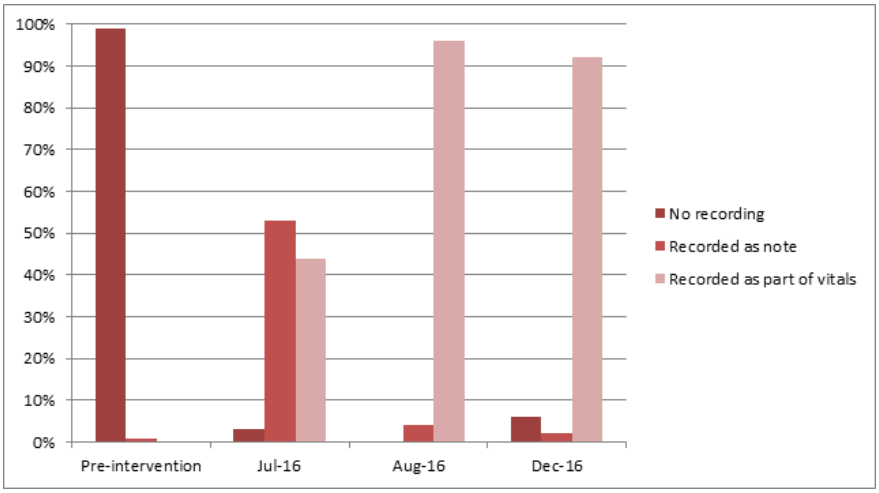

Figure 1. Oxygen Saturation Recordings

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[i] Gabor Kovacs et al., "Use of ECG and Other Simple Non-Invasive Tools to Assess Pulmonary Hypertension," *PloS One* 11, no. 12 (2016): e0168706, doi:10.1371/journal.pone.0168706; Suparaporn Wangkaew et al., "Correlation of Delta High-Resolution Computed Tomography (HRCT) Score with Delta Clinical Variables in Early Systemic Sclerosis (SSc) Patients," *Quantitative Imaging in Medicine and Surgery* 6, no. 4 (August 2016): 381–90, doi:10.21037/qims.2016.08.08; Benjamin E. Schreiber et al., "Improving the Detection of Pulmonary Hypertension in Systemic Sclerosis Using Pulmonary Function Tests," *Arthritis and Rheumatism* 63, no. 11 (November 2011): 3531–39, doi:10.1002/art.30535.

Disclosure: R. Trachtman, None; **A. Adams**, None; **N. Pan**, None; **S. Taber**, None; **K. Onel**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/oxygen-saturation-recordings-in-pediatric-rheumatology-patients-at-risk-for-lung-disease

Abstract Number: 119

Establishment of registry for pediatric rheumatic diseases in Japan: Pediatric Rheumatology International Collaboration Unit Registry (PRICURE) survey

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SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Clinical and Therapeutic Poster Session
Session Type: Abstract Submissions
Session Time: 5:30PM-7:00PM

Background/Purpose: To identify the number and characteristics of Japanese pediatric diseases, Pediatric Rheumatology International Collaboration Unit Registry (PRICURE) survey was established by Pediatric Rheumatology Association of Japan (PRAJ).

Methods: For the pediatric rheumatology specialist who belongs to PRAJ (68 hospitals and medical institutes), web-based registry system was constructed. After review and approval by the ethics committee of PRAJ and each hospital, PRICURE survey has started since January 2017. The survey covered juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), juvenile dermatomyositis (JDM), Sjögren's syndrome (SS), mixed connective tissue disease (MCTD), systemic sclerosis (SSc), Behçet's disease (BD), vasculitis syndrome and autoinflammatory diseases. Patient data included age, sex, date of disease onset, diagnosis, diagnostic criteria, treatment, complication and adverse effect.

Results: One medical institute and 3 hospitals were accepted by each ethics committee and had started to register patients. Sixty one patients were registered initially (JIA patients 25, SLE patients 8, JDM patients 3, Sjögren's syndrome patients 6, systemic sclerosis patients 3, Behçet's disease patients 6, vasculitis syndrome patients 3 and autoinflammatory patients 6). Planned number of enrollment is more than 500 in first year.

Conclusion: PRICURE survey is the exclusive survey by the pediatric rheumatologist in Japan. We hope to collaborate with other registry such as CARRA registry.

Disclosure: T. Imagawa, None; **K. I. Yamaguchi**, None; **Y. Inoue**, None; **H. Narasaki**, None; **Y. Nerome**, None; **Y. Itoh**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/establishment-of-registry-for-pediatric-rheumatic-diseases-in-japan-pediatric-rheumatology-international-collaboration-unit-registry-pricure-survey

Abstract Number: 120

Use Of Thalidomide From A Tertiary Level Pediatric Rheumatology Centre In India

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SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Clinical and Therapeutic Poster Session
Session Type: Abstract Submissions
Session Time: 5:30PM-7:00PM

Background/Purpose:

Thalidomide is an effective agent for several pediatric rheumatic diseases: Systemic onset Juvenile idiopathic arthritis(SOJIA), Behcet's disease and recalcitrant skin disease in cSLE to name a few.

SOJIA is a common subtype of JIA seen in India. Patients with SOJIA are often steroid dependent and relapse on dose reduction. Tocilizumab though available is prohibitively expensive for the majority. Thalidomide also has a role to play for the therapy of recalcitrant oral aphthae in Behcet's disease and can also be used for the calcinosis of Juvenile dermatomyositis.

Methods:

This study was a retrospective chart review of all children with pediatric rheumatic diseases who had been prescribed Thalidomide from 01/06/2009 to 15/01/2017.

Aims:

To study the usage, safety and efficacy of thalidomide in children with pediatric rheumatic diseases.

The Safety and side effects were studied for all patients(53/53). Efficacy was studied for patients with SOJIA(48/53).Systemic features of SOJIA recorded were: fever,rash,hepato and splenomegaly and lymphadenopathy.Articular features noted were the number of active joints.

Results:

Use: Thalidomide was taken by 53 children. SOJIA:48,SLE:1,Behcet's disease:2,Juvenile dermatomyositis with calcinosis universalis:1,Muckle wells syndrome:1

Safety and Side effects: Thalidomide was very safe in all patients at a maximum daily dose of 5.64mg/kg/day. No NCV screening was done in children prior to starting thalidomide.

11/53 children(20.75%) reported minor side effects, 2 had constipation that necessitated dose reduction , 9 had increased somnolence. No neurological adverse events were noted. Thalidomide was used as a single bedtime dose to decrease somnolence. Maximum dose used was 200mg/day.

Efficacy in SOJIA patients: Thalidomide taken by 48/170(28%)patients with SOJIA followed at our unit. There were 18 girls and 30 boys.

Table 1

Median age at disease onset	4.62yrs(0.7-13.5)	
Median age at disease diagnosis	5.45yrs(1-13.75)	
Median delay to diagnosis	4 months(1-48)	
Median age at thalidomide commencement:	7yrs(1.7-17.25).	
Median duration of therapy with thalidomide	16.5 months(1-93 months)	
Median dose of thalidomide	2.56mg/kg/day(0.8-5.64mg/kg/day	
Median dose of oral steroids prior to thalidomide	0.46mg/kg/day	
Median dose of oral steroids 6 months after thalidomide	0.01mg/kg/day(0-1.18)	P<0.001
Steroids stopped after Thalidomide	28/48(58%)	
Median time taken for response in systemic features	1 mth(0.5-18 months	
Median time taken to response for articular ds.	3.5mths(1-15mths).	
Response in systemic features	45/48(94%)	
Response in articular features	24/48(50%)	
No response to Thalidomide	3/48(6.2%)	
Longitudinal follow up		
No flare		19/48(40%)
Only articular flare		17/48(35%)
Both articular and systemic flare		12/48(25%)
Thalidomide stopped Disease remission No response/step up to Tocilizumab		21/48(44%) 14/21(67%) 7/21(33%)

Systemic flare was consequent to tapering/stopping Thalidomide. Articular flare was during ongoing Thalidomide therapy.

Conclusion:

1.Thalidomide is a safe drug with no neurological side effects noted in 53 children with a maximum daily dose of 5.64mg/kg/day over the maximum follow up period of 93 months.

2.It was used in 28% of total SOJIA patients followed at our unit

3.It was effective in 94% for systemic and in 50% for articular disease.

Disclosure: M. Agarwal, None; **A. Shivpuri**, None; **S. Sawhney**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/use-of-thalidomide-from-a-tertiary-level-pediatric-rheumatology-centre-in-india

Abstract Number: 121

Safety Of Biological Response Modifiers In Childhood Autoimmune Rheumatic Diseases From A Single North Indian Centre

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SESSION INFORMATION

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Session Title: Clinical and Therapeutic Poster Session

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Background/Purpose:

Biologic Response modifiers (BRMs) are sparingly used in India due to: cost & concern of infections. We are a tertiary level centre & have used BRMs since 2006,with stringent screening. This study was undertaken to add to the knowledge about the use of BRMs in children with rheumatic ds. from an area of high burden of infections.

Aims

1. To study the use of BRMs in pediatric rheumatic diseases at our centre.
2. To evaluate the safety of BRMS over a longitudinal follow up of 10 yrs.

Methods: All patients who received a BRM from 1st January 2006 to 15th January 2017 were included. The pre BRM screening, demographic details, diagnosis along with adverse events, were retrospectively collected till last review.

Results:

Demographics: Total 217 children received 268 BRMs. Male:female:125:92.

Median age at disease onset:8.91yrs(0.25-17.83),median age at disease diagnosis:9.66yrs(0.75-18.08),median delay to diagnosis:5 mths(0.5-84).

Median age at commencing first cycle of a BRM:11.37yrs(3.4-27.66).Median duration of follow up:25.9mths(1-124)

Diagnosis:**JIA**(ERA:102,SOJIA:42,PJIA:22,OJIA:8,UJIA:2,Extended OJIA:1,)
ChronicUveitis:12,**CTDs**(SLE:16,Overlap syndrome:1)**Vasculitis**(Kawasaki disease:4, Takayasu's aortoarteritis:1,Behcet's disease:1)**Others**(IBD associated arthritis:1,MAGIC syndrome:1)

Screening protocol: Chest X ray, USG abdomen, Mantoux test, HIV and HbsAg were done for all. Quantiferon gold(Q gold) was done for all since 2011.Contrast CT of chest &abdomen were done if Mantoux and/or Q gold were positive.

Table 1:Screening

Investigation	Normal	Abnormal	Not done
Chest X ray	215	2	0
USG abdomen	216	1	0
Mantoux test	201	16	0
Quantiferon Gold	162	18 Positive:10 Indeterminate:8	37
HIV	217	0	0
HbsAg	216	1	0
HCV	158	0	59
CECT thorax	107	3	107
CECT abdomen	19	4	194
Post biologic screening			
Screening for Tuberculosis with Mantoux test,Chest Xray,USG abdomen repeated after one year of TNFi exposure	Repeated	Not repeated	**Asymptomatic mantoux conversion without active TB disease**
No.	77	122	**7**

Table 2:Screening for Tuberculosis

Tuberculosis screening	
Mantoux positive and Q gold not done	3
Mantoux positive and Q gold negative	7
Mantoux positive and Q gold positive	6
Mantoux negative and Q gold indeterminate	7
Mantoux negative and Q gold positive	4

2 drug ATT given to 19 for LTBI,4 drug ATT:3 children for TB disease prior to commencing biologic

Table 3:Adverse event profile:

Drug (No of patients)	Side effects	Total
Infliximab N=58	Asymptomatic Mantoux conversion-6 Dengue fever-3 Tuberculosis disease-1 Varicella-1 Hepatitis A infection-1	12
Tocilizumab N=44	Prolonged upper respiratory tract infections-4 Dengue fever-3 Pneumonia-1 Gram negative septicemia-1 Herpetic keratitis-1 H1N1 infection-1 **Deaths-2** **(one Dengue fever with Macrophage activation syndrome, one H1N1 infection)**	11
Etanercept N=56	Uveitis-3 Dengue fever-2 Varicella-2 Autoimmune hemolytic anemia-1 Asymptomatic mantoux conversion-1 Malaria-1	10
Biosimilar Etanercept N=40	Skin cellulitis	2
Rituximab N=21	Herpes zoster-1 Enteric fever-1	2
Biosimilar Adalimumab N=40	Herpes zoster-1	1
Golimumab N=6	Urinary tract infection	1
Abatacept N=3	No adverse event	0
268 BRMs		39
Incidence of asymptomatic Mantoux conversion after TNFi exposure		**15.25/1000 patient years of TNFi exposure**

Incidence of TB disease after TNFi exposure	**2.176/1000 patient years of TNFi exposure**

Conclusion:

1. BRMs can be safely used for prolonged periods of time even in regions where there is a high background incidence of infections
2. 39 adverse events occurred on exposure to a BRM in 217 pts.95% recovered without sequelae.2/217 died**(0.92% mortality)**
3. Both Mantoux & Q gold should be done to screen for TB before TNFi, mantoux alone missed 11 latent TB patients that were detected by Q gold
4. Annual screen for TB should be done to detect asymptomatic Mantoux conversion to prevent dissemination of disease so that timely prophylaxis can be instituted. Asymptomatic Mantoux converters(n=7, 9.09% of tested patients)were picked up with this protocol.

Disclosure: S. Sawhney, None; **A. Shivpuri**, None; **M. Agarwal**, None.

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Abstract Number: 122

Presenting Manifestations of Amplified Musculoskeletal Pain Syndrome in Males versus Females

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Background/Purpose: Amplified musculoskeletal pain syndrome (AMPS) is a chronic non-inflammatory musculoskeletal pain condition. AMPS has a predilection for females but males can be affected as well and sex differences in this patient population are poorly understood. We aimed to describe the various phenotypes of pediatric AMPS in a large cohort and test for differences in presenting features based on sex.

Methods: We performed a cross-sectional cohort study of subjects diagnosed with AMPS (including complex regional pain syndrome (CRPS) and fibromyalgia) between February 2001 and October 2015 at two large tertiary care medical centers: The Children's Hospital of Philadelphia (CHOP) and Seattle Children's Hospital (SCH). Subjects were ≤ 21 years of age at diagnosis. Information collected included age; sex; race; ethnicity; past medical and psychological history; conversion symptoms; and primary pain diagnosis. Pain location, duration and functional disability measures were documented for a subset of subjects. Differences in demographic and clinical characteristics based on sex were tested using the Wilcoxon-Mann-Whitney, Fisher's exact or Chi-Squared test.

Results: This study included a total of 1598 subjects (66% from CHOP). The most common primary pain diagnosis was diffuse AMPS (47.6%) followed by localized AMPS (31.8%) and CRPS (20.6%) (Table 1). Subjects were predominantly non-Hispanic (96.5%), Caucasian (83.8%) and female (80.7%). The median age at presentation was 14.4 years (IQR: 12.0, 16.0). Boys were younger than females at diagnosis (median age 13.7 versus 14.5 years; $p<0.01$). Males were more likely to have localized AMPS (40.0% vs. 29.8%; $p<0.001$) and girls were more likely to have CRPS (22.2% vs. 13.9%; $p<0.01$). With regard to anatomical locations affected, males were more likely to have groin ($p<0.001$) and abdominal ($p<0.01$) pain. Females were more likely to have pain in the upper and lower extremities (all $p<0.05$). The presence of conversion symptoms was overall similar among the sexes ($p=0.27$) although visual disturbances appeared to be more common in females (12.5% vs. 8.8%; $p=0.07$). Preceding duration of symptoms (median 12 months; IQR: 7, 30), pain and Functional Disability Inventory (FDI) scores. Anxiety, depression and suicidality did not differ between the sexes (all $p>0.05$), while substance abuse was more common among males ($p<0.05$).

Conclusion: Significant sex differences exist in the presentation of AMPS. Males were younger and more likely to have localized AMPS whereas females had more CRPS. Males tended to have pain in the core whereas pain was located in the extremities in females. Psychological comorbidities were common with substance abuse more prevalent among males. Future studies should explore the biological and/or social constructs underlying these sex differences.

Table 1. Demographics, Pain Characteristics and Psychological Co-morbidities by Sex

	Total (n = 1598)	Female (n = 1289)	Male (n = 309)	P-value*
Demographics, N (%) or median (IQR)				
Race				
Caucasian	1339 (83.8)	1082 (83.9)	257 (83.2)	0.74
Black	75 (4.7)	59 (4.6)	16 (5.2)	0.65
Other	126 (7.9)	99 (7.7)	27 (8.7)	0.54
Ethnicity, non-Hispanic	1542 (96.7)	1249 (97.1)	293 (95.4)	0.15
Age (years)	14.4 (12.0, 16.0)	14.5 (12.3, 16.0)	13.7 (11.7, 16.0)	**<0.01**
BMI•	21.7 (19.0)	21.7 (19.3, 25.0)	21.3 (18.0, 26.1)	0.25
Amplified Pain Diagnosis, N (%)				
Diffuse AMPS	761 (47.6)	619 (48.0)	142 (45.9)	0.51
Localized AMPS	508 (31.8)	384 (29.8)	124 (40.1)	**<0.001**
CRPS	330 (20.6)	286 (22.2)	43 (13.9)	**<0.01**
Pain and Patient Reported Outcomes, median (IQR)				
Current pain (0-10)	6.0 (4.0, 8.0)	6.0 (4.0, 8.0)	6.0 (3.0, 8.0)	0.71
Most pain (0-10)	10.0 (9.0, 10.0)	10.0 (9.0, 10.0)	10.0 (8.0, 10.0)	0.26
Least pain (0-10)	4.0 (2.0, 6.0)	4.0 (2.0, 6.0)	3.0 (1.0,5.0)	0.07
Patient FDI (0-30)	22.0 (13.0, 32.0)	22.0 (14.0 ,32.0)	22.0 (12.0, 34.0)	0.90
Parent FDI (0-30)	22.0 (12.0, 32.0)	22 (12.0, 31.0)	22.5 (11.0, 33.0)	0.71
Duration of symptoms (months)	12.0 (7.0, 30.0)	12.0 (8.0, 32.0)	12.0 (6.0, 24.0)	0.15
Self-Reported Psychological Diagnoses, N (%)				
Anxiety	249 (23.8)	196 (23.9)	53 (23.5)	0.93
Depression	247 (23.6)	189 (23.0)	58 (25.7)	0.41
Substance abuse	8 (0.8)	3 (0.4)	5 (2.2)	**<0.05**
Suicidal Ideation	128 (12.2)	105 (12.8)	23 (10.2)	0.36
Suicide Attempt	21 (2.0)	16 (2.0)	5 (2.2)	0.80
Conversion±	657 (41.3)	522 (40.7)	135 (44.0)	0.27

Legend. *Differences in clinical and demographic characteristics by sex were assessed using Chi-squared, Wilcoxon-Mann-Whitney or Fisher's exact tests, as appropriate. $p<0.05$ is considered statistically significant. AMPS=amplified musculoskeletal pain syndrome. CRPS=complex regional pain syndrome. AMPS was defined as disproportionate pain to the stimulus without other medical explanation. CRPS was defined according to the International Association for the Study of Pain in 1994. Localized and diffuse pain were defined as ≤ 2 body parts and ≥ 3 body parts according to Malleson *et al*. Age was missing for 5 subjects (n=1593). •BMI = body mass index (n=1544). ±Conversion data missing for 8 subjects (n=1590). Race was unknown or missing for 58 subjects (CHOP = 2; SCH = 56). Most pain (n=1024). Least pain (n=1018). Current pain (n=1035). FDI patient (n=972). FDI parent (n=975). Duration (n=1040). Self-reported psychological diagnoses (n=1047).

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Abstract Number: 123

Acupuncture for Pediatric Chronic Pain Relief: A Review

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Background/Purpose: Acupuncture, a type of complementary and integrative therapy, has been widely used for pain relief in adults. However, evidence of the effect of acupuncture for pediatric chronic pain is scarce. We evaluate the effect of acupuncture on chronic pain in pediatric population.

Methods: We performed a comprehensive search of eastern and western databases in MEDLINE and Chinese databases: China Hospital Knowledge Database, China National Knowledge infrastructure, WanFang Data, and Traditional Chinese Medical Database System until January 2017. Selection criteria included clinical trials and observational studies of acupuncture in pediatric chronic pain patients, sample size ≥8, and outcome measures included pain evaluation.

Results: We identified 142 potentially relevant studies. Eight studies (total 493 participants) met eligibility criteria. Of the 8 studies, 1 was randomized controlled trial, 5 were nonrandomized controlled trials, and 2 were retrospective chart reviews. Four used traditional Chinese acupuncture, 1 Korean hand acupuncture, 1 Japanese style needle, and the other 2 unclear. **Table** summarizes the studies evaluating the effect of acupuncture on pain. More than 90% of subjects were able to complete all treatments. Acupuncture was associated with a significant pain reduction in 7/8 studies. All 8 studies reported improvement in pain related function after treatments. Four of 8 studies showed a reduction in pain by 3 to 5 points on pain scale; 3/8 studies reported either a high percentage of improvement in pain (70~96%) or a statistically significant reduction on pain scale (1.5 point, $P<0.001$). One study reported that patients with chronic fatigue improved function ($P<0.01$). None of the studies reported any adverse effects related to the acupuncture treatment, with 7 studies clearly stating that there were no adverse effects from the acupuncture treatment. Discordant trial designs, varying outcome measures, and methodological limitations precluded a pooled meta-analysis.

Conclusion: The current evidence suggests that acupuncture appears to be safe and helpful treatment for chronic pain in the pediatric population, but is insufficient for a definitive conclusion. Rigorous and well-controlled randomized trials are warranted.

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Table

Reference	Study Design	age (yr)	N	Indications	Intervention(s) and doses	Results	Author's Conclusions on Acupuncture
[1] Pintov, 1997 Israel	Randomized Controlled Trial	7-15	22	Migraine headaches	1) TCA[1] 2) needle in stratum corneum for placebo acupuncture group Weekly for 10 weeks	(1) Frequency of Headache reduced 9.3à1.4 in TCA[1] (2) VAS[2] reduced 8.7à3.3 in TCA[1] (3) Panopioid activity inhibition and Beta-endorphinlike immunoreactivity showed changes consistent with effective pain reduction in TCA[1]	Safe, efficient for migraine headaches in children
[2] Jodorkovsky, 1999 USA	Nonrandomized controlled studies	3.5-20	106	1. Traumatic pain 2. Musculoskeletal pain (10% chronic) 3. Non-painful conditions	Korean Hand Acupuncture, 1-4+ treatments per subject over 6 months	(1) Pain scale (1 to 10); 96% complete resolution or decrease pain by >50%, (2) >50% decrease in duration of symptoms in non-painful conditions	Safe, cost-effective and well accepted in children
[3] Kemper, 2000 USA	Retrospective case series	5-20	47	1. Migraine headaches 2. Endometriosis 3. Reflex sympathetic dystrophy	1) regular needle 98% 2) Moxibustion/heat 85% 3) Cupping 26%, Magnets 26% Median of 8 treatments over 3 months per subject	(1) 67% of patients (60% of parents) reported the treatments pleasant or relaxing; (2) 70% of patients (59% of parents) reported the treatments helpful	Pleasant and helpful in children with chronic pain
[4] Lin, 2002 USA	Nonrandomized controlled studies	2-18	53	1. limb pain 24% 2. Abd pain 24% 3. back pain 17% 4. Headaches 15%	TCA[1]; 112 treatments in 53 subjects	VAS[2] reduced by a mean of 3.1 points (P<0.01, average effect duration 3 days)	Reduced pain in pediatric patients significantly
[5] Zeltzer, 2002 USA	Nonrandomized controlled studies	6-18	33	1. Migraine headaches 46% 2. Abd pain 21% 3. Fibromyalgia 11% 4. CRPS[3] 11% 5. JRA[4] 4%	TCA[1] with a 20-minute hypnosis session, weekly for 6 weeks	(1) VAS[2] reduced 3.46à1.93 (P<0.001) (2) Total interference[5] reduced 30.48à23.13 (P=0.014)	Acupuncture is feasible with evidence of pain reduction in pediatrics
[6]	Nonrandomized	11-	8	Chronic fatigue and	Not otherwise	(1) VAS[2] 6.5à5.8	Improved

Lin, 2004 USA	controlled studies	18		pain	specified, at 9 acupuncture points weekly for 6 weeks	(P>0.5) (2) Function level (0-10) improved 4.5à7.0 (P<0.01)	functional level in patients with chronic fatigue syndrome
[7] Lin, 2002 USA	Nonrandomized controlled studies	9-18	50	Headaches	TCA[1], weekly for 6 weeks, elective bi-monthly treatment afterwards, mean of 6 treatment per subject	VAS[2] reduced 7.4à4.1 (P<0.01)	Well tolerated and beneficial treatment for pediatric headaches
[8] McDonald, 2015 USA	Retrospective chart review	0-21	174	1. Headaches 48% 2. back pain 28% 3. Neck, extremity pain 27% 4. Fibromyalgia 9% 5. Abd pain 9% 6. CRPS[3] 7%	1) Japanese style needle 96% 2) electroacupuncture 90% 3) Laser therapy 49% 4) Auricular acupuncture 32% 1090 treatment for 174 subjects over 3 years	VAS[2] reduced 5.5à2.2 (P<0.001)	Well tolerated, safe and effective for pediatric pain management

1. TCA: traditional Chinese style acupuncture 2. VAS: Visual analogue scale 3. CRPS: Complex Regional Pain Syndrome 4. JRA: Juvenile rheumatoid arthritis 5. Total interference: ratings of total pain-related interference in functioning

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Disclosure: Y. Zhang, None; **S. Hyon**, None; **C. Wang**, None.

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Abstract Number: 124

Underutilization of Social Workers for Mental Health Care of Adolescents in Pediatric Rheumatology: A Mixed Methods Study

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Background/Purpose: Mental health problems are common, but undertreated in adolescents with rheumatologic conditions. As social workers help manage medical and psychosocial aspects of illness, we examined their perspectives to identify opportunities for improving mental health care of these adolescents.

Methods: We surveyed social workers at pediatric rheumatology centers in the Childhood Arthritis and Rheumatology Research Alliance (CARRA). The online survey assessed demographics, beliefs, preferences, and practices for mental health care of adolescents with lupus, juvenile idiopathic arthritis, or juvenile dermatomyositis. Participants rated the frequency of 15 barriers to mental health screening and 18 barriers to treatment on a 4-point Likert scale. Survey participants were invited for semi-structured qualitative interviews to collect in-depth information to complement the survey data.

Results: One third of CARRA centers had no social worker. Of 44 social workers contacted, 37 (84%) responded to the survey. Excluding 5 incomplete responses, 32 were analyzed. Social workers were located mostly at US university-based (81%) and urban (75%) centers, spending a mean of 0.5 full-time effort (SD 0.3) in pediatric rheumatology. Most supported routine universal screening of rheumatology adolescents for depression (94%), anxiety (94%), and distress/coping (100%); none reported this as current practice. Willingness to administer screening was expressed by 88%. Of the 15 (47%) reporting screening of selected patients, only 4 had a protocol for handling the results. High accessibility of on-site psychologists and psychiatrists was reported by 32% and 19%, respectively. Forty-seven percent reported that follow-up by their center after mental health referral was inadequate. Although 94% had formal mental health training, only 6 (19%) provided psychological counseling/therapy to adolescents in rheumatology; of the 26 not providing therapy, 81% said it was not in their current scope of practice. Limited resources, lack of policy, and patient cost/time burden were among the most frequent barriers to mental health care (Figure 1). Interviews (n=15) revealed detailed information on barriers and facilitators (Table 1).

Conclusion: Almost all social workers at pediatric rheumatology centers have mental health training, and although willing, are underutilized to provide services. With adolescents facing many barriers to mental health care, social workers represent an untapped resource for routine mental health screening and timely intervention as part of comprehensive rheumatology care.

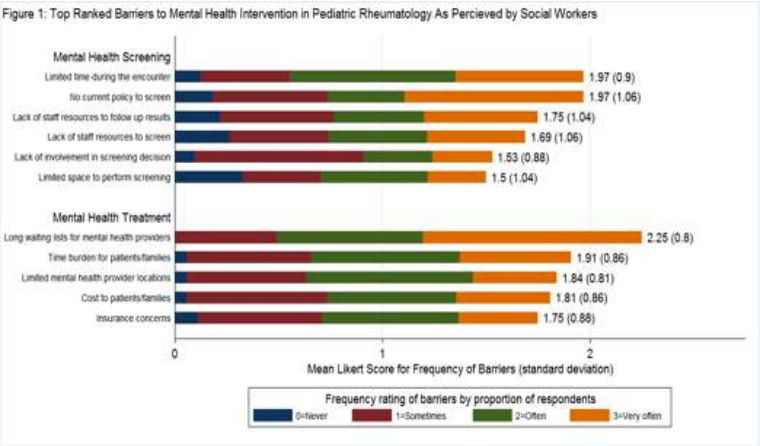

Table 1: Qualitative Analysis of Social Worker Perspectives on Barriers & Facilitators for Mental Health Care of Adolescents with Rheumatologic Conditions	
Barriers	**Illustrative Quotes**
1) Disrupted patient flow – limited time & space	*"We have such a jammed schedule and physical space… get in and get done and make the room available for the next person…it's a struggle sometimes if there's more time needed to find actually a physical place to go and have a private conversation."* *"If I want to provide more in-depth or more – you know deeper work, I think having appropriate space and time is really what I think will allow for that."*
2) Untapped potential for social worker mental health services	*"It is a role of social workers sometimes can be perceived as purely just a resource person…it would greatly benefit the families that we serve if we had either more time to provide more strict mental health services, whether it's counseling or it looks like a support group."* *"Underneath my licensure and my degrees, I can do counseling and bill for it…it would be easier to shift some of the school, paperwork stuff and utilize me more in the mental health/coping/ adjustment world."*
3) Lack of protocol for mental health intervention	*"So one of the things that I think might be in an ideal world, if we could have a more robust way of tracking and assessing the kids that we see in our clinic."*
4) Time and cost burden to families	*"And for families who have to work, trying to add to their stress of taking care of the physical illness, and take more time to take themselves or their kids to therapy – the burden of care is just too great. It should be a one-stop shop".* *"Our families come from far away… so it isn't actually practical for them to get any ongoing care in our facility"*
5) Limited access to psychologists/ psychiatrists	*"There are not a lot of places to refer people. Competency is unknown."* *"We have a pediatric psychology program, which is really great – except it's impractical for anyone that doesn't live in this county, they don't take Medicaid, there's a long waiting list, they don't work at night or on weekends."* *"Access to the resources that is the major challenge because when I do get people linked in…and able to put resources in place, I actually see change."*
Facilitators	
1) Integrated approach to medical & mental health	*"So I go in and it's just framed that I'm part of the clinic… allows me to ask questions and get a lot of information that they don't have to repeat then."* *"Because these kids get this diagnosis and then are followed for the rest of their lives…rheumatology needed much more of just a model where they had a social worker that was more available to them, part of the multidisciplinary team."* *"I've just noticed already families just having a lot more confidence in somebody they feel like is part of their child's medical team"*
2) Early & systemic approach to mental health intervention	*"I've been able to spend more time with our patients early on and build a relationship and rapport – kind of anticipate needs rather than react to needs."* *"I end up seeing families, and children and adolescents in crisis more than where we could maybe have avoided the crisis if I'd had the time to get involved when I should be getting involved, which is technically – I think – at diagnosis."* *"I feel like if we had uniform screening we would pick up a lot more. I can't tell you how many times I go into a clinic visit to talk about insurance or school and then I uncover suicidality in a patient. It's crazy."*
3) Strong relationship between social workers & rheumatologists	*"I think just having the time with the providers and them understanding the kinds of things that I'm working with families on, I think they started to use me more"*
4) Supportive divisional & institutional climates	*"My division chief advocated for me to be full-time on rheumatology."*
5) Partnership with foundations, schools & community agencies	*"I think following up with the school and getting the school aware and involved…the kid's there all the time…so that's really where we find our best allies."*

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Abstract Number: 125

How Do Health Literacy, Numeric Competencies and Patient Activation Impact Transition Readiness in Adolescents and Young Adults with Rheumatologic Diseases?

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Session Time: 5:30PM-7:00PM

Background/Purpose: Transition from pediatric to adult health care is a vulnerable time during which gaps in care may negatively affect disease outcomes. Validated measures including the Transition Readiness Assessment Questionnaire (TRAQ) measure adolescent and young adults' (AYA) readiness to transition to adult care. Although health literacy affects outcomes in many disease states, few published data address its impact on AYA's transition readiness. Numeracy reflects individuals' competency and comfort with numbers and is important in medical decision making. Little is known regarding parent/guardian (PG) literacy, numeracy and activation competencies influence AYA's transition readiness.

Methods: AYA ages 16-25 years were recruited from outpatient pediatric rheumatology clinics at a single academic institution in this cross-sectional study. Subjects provided demographic information and completed TRAQ 5.0 , Short Form Test of Functional Health Literacy in Adults (STOFHLA), Patient Activation Measure (PAM), Subjective Numeracy Scale, Objective Numeracy Scale and Symbolic-Number Mapping. In addition, when possible, parents/guardians (PG) of AYA completed the same self-report measures excepting TRAQ. Descriptive statistics were performed. Using TRAQ score as dependent variable, multivariable linear regression models were developed using backwards, step-wise regression. P values < 0.05 were considered significant.

Results: Ninety-one AYA and 54 PG completed the study. Participants' summary demographics and questionnaire scores are provided in Table 1. The majority of AYA (64/91; 70%) had juvenile idiopathic arthritis or rheumatoid arthritis; 4/91 (0.4%) had lupus or mixed connective tissue disease, 2/91 (0.2%) had JDM, and the remainder had other disorders. In a multivariable model, AYA female gender ($p<0.01$), age ($p<0.01$) and patient activation score ($p<0.001$) were independently associated with TRAQ score. The model $R^2=0.22$, suggesting that the included variables accounted for 22% of variability in TRAQ score. In a multivariable model, none of the PG demographic variables or competencies were independently associated with AYA TRAQ scores.

Conclusion: The majority of AYA (98%) and PG (100%) had adequate health literacy, defined as STOFHLA score> 22. AYA with chronic rheumatologic conditions had mean TRAQ scores of 4.0, reflecting an "I am starting to do this" stage of change. AYA older age and female gender predicted higher transition readiness scores which is consistent with the published literature. AYA health literacy and numeracy competencies were not independently associated with transition readiness. Higher patient activation scores predicted higher transition readiness scores which is not surprising as the TRAQ and PAM instruments measure overlapping domains. PG demographics and health competencies were not associated with AYA transition readiness.

Table 1: Demographic Information and Survey Results for Transitioning Adolescents/Young Adults and Their Parents/Guardians		
	Adolescent/Young Adult (n=91)	**Parent/Guardian (n=54)**
Age (years), mean (SD)	19 (1.3)	48 (7.9)
Gender, female n (%)	72 (80%)	45 (87%)
Race, n (%)	70 (78.6)	46 (88.5)
White	11 (12.4)	3 (5.8)
Black	8 (9.0)	3 (5.8)
Other		
Education, n (%)	1 (1.5)	0
10th grade	4 (5.8)	0
11th grade	18 (26.1)	9 (16.7)
12th grade	46 (66.7)	12 (22.2)
Some college/tech school	0	20 (37.0)
Graduated college/tech school	0	13 (24.1)
Graduate degree		
Annual household Income, n (%)	12 (18.5)	
<$25,000	11 (16.9)	2 (4.0)
$25,000-49,999	9 (13.6)	9 (18.0)
$50,000-74,999	7 (10.8)	10 (20.0)
$75,000-99,000	14 (21.5)	8 (16.0)
$100,000-150,000	12 (18.5)	13 (26.0)
>$150,000		8 (16.0)
TRAQ score, mean (SD)	4.0 (0.67)	Not done
STOFHLA score, mean (SD)	34.1 (3.5)	37.4 (1.7)
Patient Activation score, mean (SD)	3.2 (0.5)	3.3 (0.4)
Subjective Numeracy Score, mean (SD)	3.8 (1.1)	4.0 (1.0)
Objective Numeracy Score, mean (SD)	3.7 (1.7)	3.8 (1.7)
Symbolic Number Mapping, mean (SD)	-0.87 (0.2)	-0.85 (0.2)
Abbreviations: STOFHLA = Short Form Test of Functional Health Literacy in Adults; TRAQ = Transition Readiness Assessment Questionnaire.		

Disclosure: S. Lazaroff, None; **M. K. Tompkins**, None; **A. Meara**, None; **E. Peters**, None; **S. P. Ardoin**, None.

competencies-and-patient-activation-impact-transition-readiness-in-adolescents-and-young-adults-with-rheumatologic-diseases

Abstract Number: 126

Challenges in Transitioning Adolescents with Rheumatologic Diseases to Adult Care – The Brazilian Experience

Ana Paula Sakamoto[1], Catherine Anelli[1], Ana Luiza Amorim[1], Fabiane Osaku[2], Maria Teresa Terreri[1], Claudio A. Len[3] and Andreas Reiff[4], [1]Pediatric Rheumatology Unit, Federal University of São Paulo (UNIFESP - Universidade Federal de São Paulo), São Paulo, Brazil, [2]Pediatric Rheumatology, Federal University of São Paulo (UNIFESP - Universidade Federal de São Paulo), São Paulo, Brazil, [3]Pediatric Rheumatology Unit, Federal University of São Paulo (UNIFESP - Universidade Federal de São Paulo), São Paulo,, Brazil, [4]Division of Rheumatology MS 60, Children's Hospital Los Angeles, Keck School of Medicine, University of Southern California, USA, Los Angeles, CA

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Clinical and Therapeutic Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Due to the high survival rates in chronic pediatric rheumatologic diseases a well-structured and effective transition process becomes crucial to guarantee continuity of care and maintain an adequate health status. Recommendations in regards to transition guidelines are limited and best transition practices in young patients with chronic medical needs have been poorly studied. Our aim was to evaluate transition practices from pediatric to adult rheumatology care in Brazil.

Methods: Practicing pediatric rheumatologists registered in the Brazilian Society of Rheumatology were surveyed using a modified Childhood Arthritis and Rheumatology Research Alliance (CARRA) SurveyMonkey® questionnaire that had been used previously to evaluate transition practices of pediatric rheumatologists in the USA and Canada.

Results: Seventy-six of 112 (68%) pediatric rheumatologists responded. Only 13% of the respondents reported that they had a well-established transition program and only 14% were satisfied with their current transition process. 80% did not use any specific tools to assess transition readiness. 43% of respondents considered 18 as the ideal transition age, but only a third of patients transitioned at that age while 48% transitioned later. Major hurdles for a successful transition included emotional attachment to the patients (95%) insufficient knowledge about a transition team (87%), lack of devoted time for transition preparation and process (80%), lack of assistance by pediatric generalists (77%), and lack of available adult subspecialists (75%). 67% of respondents stated that their program would need more tools/resources to facilitate transition and 59% believed that the development of specific guidelines would be useful to standardize and help with the transition process.

Conclusion: Our study demonstrates that the identified challenges pertaining to transition in Brazilian patients are similar to those reported by American and Canadian pediatric rheumatologists. A comprehensive understanding of transition issues will support the development of transition guidelines and ensure better outcomes of adolescents transitioning patients.

Disclosure: A. P. Sakamoto, None; **C. Anelli**, None; **A. L. Amorim**, None; **F. Osaku**, None; **M. T. Terreri**, None; **C. A. Len**, None; **A. Reiff**, None.

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Abstract Number: 127

Description of first 40 patients from a Rheumatologic Transition Clinic in Chile

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Background/Purpose: Transition is the planned, coordinated and continuous process in which an adolescent with chronic rheumatic disease is transferred from the pediatric service to an adult service. This process should address the nature of the disease and also psychosocial, vocational, educational, sexual health issues and promote healthy habits, to finally result in an autonomous young adult. This process ends when patients are mature enough in all aspects of their lives and can be responsible for their own health. The purpose of this work is to describe the first 40 patients included in the Adolescent with Rheumatic Diseases Transition Program from the Department of Rheumatology of Pontificia Universidad Católica de Chile.

Methods: We included patients between 15 and 23 years old, transferred from Pediatric Rheumatology with diagnosis of a rheumatic condition of childhood onset. These patients were included in the Program between March 2015 and January 2017. First evaluation of all adolescents was in presence of the parent or the responsible adult, in next visits at least part of the interview was just between the young adult and the doctor. In some cases before the complete transfer, one alternate adult and pediatric clinic was scheduled. In every transition clinic the HEADDSS interview for adolescents was applied, besides address the particular issues concern to the specific disease. The time between controls was determined based on diagnosis and activity of the disease. Pharmacologic adherence treatment was defined as the follow up of instructions, asking parents and patients. Clinic adherence was defined as if the patients assist or not to their appointments at Transition Clinic.

Results: Mean age of patients was 18 years old (15-23 yo), 35/40 female gender and most of them form urban areas. 21/40 teenagers has Juvenile Idiopathic Arthritis, 9/40 Pediatric Systemic Lupus Erythematosus, 3/40 Undifferentiated connective tissue disease, 2/40 Uveitis, 1/40 Fibromyalgia, 2/40 Sjögren´s Syndrome, 1/40 Morphea and 1/40 Recurrent Polychondritis. 9/40 patients had active disease at the moment of transition, 4/40 was transfer to the adult team as inpatients because of the age at the moment of admission. The mean follow up time was 9,25 months (1 – 22 months). At first interview 8/40 adolescents were seen alone by the adult rheumatologist, in last visit of each adolescent, 14/40 came alone to the meeting. 10/40 could be seen in alternate way by the pediatric rheumatologist and the adult one at the Transition Clinic. Just 3/40 teenagers didn´t continue their attention at Transition Clinic and 4/40 were non adherent to therapy at some time during follow up.

Conclusion:

This is the first report of adolescents with rheumatic conditions at Transition Clinic in our Center and shows how a planned process to move teenagers and their parents from pediatric care to the adult care has allowed the continuity of treatment and attention in most of our patients.

Abstract Number: 128

Treatment Response in Polyarticular Juvenile Idiopathic Arthritis is Associated With Transcriptional Changes and Chromatin Reorganization in CD4+ T cells

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SESSION INFORMATION
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Background/Purpose: The polyarticular form of JIA is associated with well-documented transcriptional abnormalities in peripheral blood cells. The abnormalities can be observed in neutrophils, peripheral blood mononuclear cells, and whole blood gene expression profiles. The mechanisms underlying these abnormalities are incompletely understood. Furthermore we have little understanding of how commonly used therapies impact the observed transcriptional aberrations.

Methods: We isolated RNA from CD4+ T cells of children with 3 distinct phenotypes: children with active, treated polyarticular JIA (ADT, n=12), children on medication who fit criteria for clinical remission by the Wallace criteria (CRM, n=10), and 10 healthy children, a control group. RNA sequencing was performed using the Illumina HiSeq 2500 platform. In addition, we used the assay for transposase-accessible chromatin-sequencing (ATACseq) to survey open chromatin in a subset of these same patients (6 HC, and 5 ADT and CRM).

Results: Each of the 3 phenotypes was associated with its own its own chromatin accessibility signature as identified by ATACseq and its own transcriptional signature. We identified 16,039 accessible sites that were unique to HC, 38,451 that were unique to ADT, and 58,289 sites that were unique to CRM. Further analyses of the open regions unique to the HC cells showed that these regions were highly enriched (compared to genome background) for CCCTC-binding factor (CTCF) binding sites. These CTCF binding sites were absent in JIA CD4+ T cells. This finding suggests that aberrant 3D chromatin architecture (which is regulated by CTCF) may be a primary driver of the transcriptional aberrations observed in JIA. In contrast, open regions that were unique to the ADT state were highly enriched for NFIC and STAT4 binding sites. Both NFIC and STAT4 are known regulators of T cell activation, and the STAT4 locus has been identified as a region of genetic risk in JIA. Analysis of the combined RNAseq and ATACseq using BETA software demonstrated that the differences in chromatin accessibility had high regulatory potential for the differentially expressed genes, providing strong evidence that the chromatin changes and gene expression changes are causally linked. The CRM state was not associated with normalization of either the chromatin or transcriptional signatures of CD4+ T cells in children with JIA.

Conclusion:

Conclusion – Treatment response in JIA is associated with significant re-organization of chromatin and is accompanied by significant changes in transcription that can be attributed to the chromatin re-organization. Patterns of chromatin accessibility suggest important roles for chromatin regulators (e.g., CTCF) and transcription factors (NFIC, STAT4) in JIA. The achievement of CRM does not result in a normalization of either the transcriptome or the epigenome of CD4+ T cells.

Disclosure: E. Tarbell, None; **K. Jiang**, None; **Y. Chen**, None; **T. Liu**, None; **J. Jarvis**, None.

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Abstract Number: 129

Cell-bound Complement Activation Products Correlate with Disease Activity in Childhood-onset Systemic Lupus Erythematosus

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SESSION INFORMATION

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Background/Purpose: Elevated levels of cell-bound complement activation products (C4d deposition on erythrocytes [EC4d] and B lymphocytes [BC4d], CB-CAPs) have been demonstrated to be sensitive and specific for the diagnosis of systemic lupus erythematosus (SLE) and C4d deposition on platelets (PC4d) to be specific for the diagnosis of SLE. We sought to evaluate the usefulness of CB-CAPs as a biomarker for disease activity in childhood-onset SLE (cSLE).

Methods: This is a longitudinal study of 28 patients with cSLE (diagnosed prior to their 19th birthdays) who fulfilled ACR-SLE classification criteria, with a mean follow-up of 6 months. Clinical and demographic data were recorded. Venous blood was collected every 3 months and shipped overnight to the reference clinical laboratory for the multi-analyte assay. The assay evaluates a full panel of autoantibodies, including anti-dsDNA, aPLs (beta-2 glycoprotein antibodies, aCL, and/or aPS-PT) and conventional serum complement levels (C3 and C4), as well as CB-CAPs; CB-CAPs results are reported as net mean fluorescence intensity (MFI). SpearmanÕs correlation was used to evaluate the correlation between CB-CAPs and disease activity scores; t-tests to evaluate the presence of CB-CAPs in APL patients.

Results: Clinical and demographic variables are presented in the Table. Mean SLEDAI was 4.3±3.8 (range 0-16). Elevated CB-CAPs correlated with SLEDAI scores in cSLE patients (r^2 range 0.23-0.38, $p<0.05$ for EC4d, BC4d, and PC4d, respectively) at baseline, 3 and 6 months. Higher levels of EC4d (>75 net MFI) were found to have better correlation with disease activity scores at all time-points ($p<0.05$). Additionally, in 11 cSLE patients with positive aPLs CB-CAPs were significantly elevated with $p<0.05$ for EC4d, but $p=0.06$ for BC4d and $p=0.15$ for PC4d; of note, C3 and C4 did not correlate with the presence of aPL in these patients (p=NS). Interestingly, several patients had normal levels of C3 and C4, but elevated CB-CAPs, possibly indicating fluctuating complement activation that was not captured by C3 and C4 measurements.

Conclusion: These pilot findings suggest that CB-CAPs could provide a useful biomarker for disease activity in cSLE, and may be particularly important in the monitoring of SLE patients with anti-phospholipid antibodies. Further longitudinal data is needed to establish CB-CAPs as a biomarker in cSLE and APS.

Table: Patient demographics and results of CB-CAPs assays

	SLE (n=28)
Age (years)	18±2
Female %	75%
Duration of disease (years)	4.7±3.2
Mean SLEDAI	4.3±3.8 (range 0-16)
Low Complement	50% (14/28)
ANA (IFA: ³1:80)	93% (26/28)
Anti-dsDNA (confirmed with Crithidia)	54% (15/28)
Anti-Smith	18% (5/28)
EC4d>14 net MFI	57% (16/28)
BC4d>60 net MFI	63% (17/27)
PC4d>20 net MFI	29% (8/28)
Elevated CBCAPS (EC4d>14 net MFI, BC4d>60 net MFI, or PC4d >20 net MFI)	82% (23/28)

Disclosure: J. Hui-Yuen, None; **D. Barken**, 3; **J. Conklin**, 3; **T. O'Malley**, 3; **A. Eichenfield**, None; **A. Starr**, None; **L. F. Imundo**, None; **T. Dervieux**, 3; **A. Askanase**, 2.

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Abstract Number: 130

Validation of MRP8/14 serum levels as biomarker for the diagnosis of systemic juvenile idiopathic arthritis in fever of unknown origin

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SESSION INFORMATION

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Background/Purpose: The differential diagnosis of fever of unknown origin (FUO) is a major challenge in pediatrics especially for differentiation of systemic-onset juvenile idiopathic arthritis (SJIA) and infectious diseases. In a pilot study the analysis of MRP8/14 serum has been demonstrated as an excellent tool for the diagnosis of SJIA, allowing early

differentiation of patients with autoinflammatory diseases SJIA or Familial Mediterranean Fever (FMF) versus those with other diseases with a specificity of 95%. Based on our study published in 2009, the analysis of MRP8/14 serum levels has been offered to paediatric rheumatologists nationwide in the last years. Therefore, we aimed to validate the findings from our pilot study in samples from daily clinical practice and to evaluate their relevance in clinical practice.

Methods: The study was designed as a retrospective analysis. The study group comprised 984 patients from 44 centers who presented with FUO. Patients were selected from our database between January 2009 and October 2012. Data collected included signs (laboratory parameters CRP, BSG, leucocytes) and symptoms as well as the final diagnosis made by the caring physicians. In all samples, concentration of MRP8/14 was determined by sandwich enzyme-linked immunosorbent assay (ELISA) with a cut-off of 9200 ng/ml (for SJIA versus other diseases). A questionnaire about the relevance of the MRP8/14 result for the final diagnosis was completed.

Results: Final diagnoses made by physicians were SJIA (n=301), FMF (n=135) and other inflammatory diseases (including infections, vasculitis and other autoinflammatory diseases) (n=548). MRP8/14 serum levels of patients with SJIA or FMF (10.090±1.930 ng/ml, mean±SEM) were elevated compared to other diagnoses (3.140±570 ng/ml) irrespectively of the presence of fever and anti-inflammatory treatment. In the group of untreated patients with fever (n=213) MRP8/14 levels of SJIA patients (18.685±4.130 ng/ml) were even higher compared to other diagnoses (5.285±1.535 ng/ml). In this group, the sensitivity and specificity of MRP8/14 to differentiate between patients with SJIA vs. other diseases (excluding FMF) were 75% and 89% respectively. The sensitivity of the test increased to 83% in the presence of fever, joint pain and CRP>1mg/dl. There was a significant correlation (p<0,001) between MRP8/14 and CRP or leucocyte counts in the total group of patients with SJIA. The clinicians reported that MRP8/14 results were helpful (56%), decisive (11%), not important (32%) and distracting (1%) in the total cohort.

Conclusion: Measurement of MRP8/14 levels is a helpful tool for the diagnosis of SJIA in FUO. In daily clinical practice the marker has a sensitivity of 75% and specificity of 89% to detect SJIA in untreated patients with fever. These results have to be replicated in an independent cohort and additional markers might be useful to improve the detection of SJIA in patients presenting with FUO.

Disclosure: D. Holzinger, None; **C. Pretzer**, None; **M. Miranda-Garcia**, None; **H. Huppertz**, None; **G. Horneff**, 2,8; **J. P. Haas**, None; **G. Ganser**, None; **J. B. Kuemmerle-Deschner**, None; **M. Frosch**, None; **J. Roth**, None; **D. Foell**, None.

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Abstract Number: 131

Balancing JAK/STAT-signaling with tofacitinib may foster anti-inflammatory functions of human monocytes

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SESSION INFORMATION

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Session Time: 5:30PM-7:00PM

Background/Purpose: Monocytes are bridging natural and acquired immunity. Information about JAK signaling in monocytes is scarce especially in an inflammatory milieu. JAK-inhibition is a promising new anti-inflammatory treatment option. However, JAK/STAT activation may be involved both in pro- and anti-inflammatory monocyte programs.. We have shown that GM-CSF-activated regulatory monocytes (GMaM) induce Treg-differentiation in co-cultures with naive T-cells

in vitro. Inflammatory T-cells produce high amounts of GM-CSF *in vivo*, not leading to anti-inflammatory monocytes, likely because of pro-inflammatory cytokines in the environment. We used JAK-inhibitor tofacitinib to explore mechanisms that block such pro-inflammatory pathways and still allow anti-inflammatory functions in monocytes.

Methods: Primary monocytes from healthy human donors were isolated and phenotyped by FACS after inhibition with JAK-inhibitor Tofacitinib and subsequent treatment with GM-CSF. Monocytes were co-cultured with autologous naïve T-cells and differentiation of $Foxp3^+$ regulatory T-cells was evaluated. JAK1 activation (represented by IFNγ induced phospho-STAT1), JAK2 activation (represented by GM-CSF induced phospho-STAT5), and JAK3 activation (represented by IL-4 induced phospho-STAT6) was analyzed. Non-toxic dosages of 1-1000 nM of tofacitnib were used.

Results: We aimed to find the dose of JAK1 and JAK3 inhibition that keeps JAK2 activity (GM-CSF induced pSTAT5) intact. At 10 - 100 nM tofacitinib we detected GM-CSF-induced phospho-STAT5 while IFNγ induced phospho-STAT1 and IL-4 induced phospho-STAT6 were blocked. Phenotypic analysis showed inhibition of GM-CSF induced CD39-, CD206-, and CD209 expression with intact IL-10 expression and inhibited TNFα expression above 100 nM tofacitinib. Co-culture of GMaM and T-cells resulted in increased differentiation of $Foxp3^+$ Treg that was even enhanced when 10 nM tofacitinib was used, indicating GM-CSF-signaling through STAT5 is still intact, while JAK1 and JAK 3 are inhibited in monocytes simultaneously.

Conclusion: In summary, tofacitinib (10-100 nM) facilitates GM-CSF-induced reprogramming of monocytes to anti-inflammatory cells. Pro-inflammatory activation does depend on complex interplay of multiple factors and blocking JAK/STAT activation by tofacitinib can restore the GMaM phenotype by blocking pro-inflammatory pathways while still allowing anti-inflammatory signaling in monocytes.

Disclosure: F. Cordes, 2; **E. Lenker**, None; **T. Weinhage**, None; **G. Varga**, 2; **D. Foell**, 2.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/balancing-jakstat-signaling-with-tofacitinib-may-foster-anti-inflammatory-functions-of-human-monocytes

Abstract Number: 132

Influence of Juvenile Idiopathic Arthritis Fibroblast-like Synoviocytes and Mature Chondrocytes on Each Other in Culture: A Pilot Study

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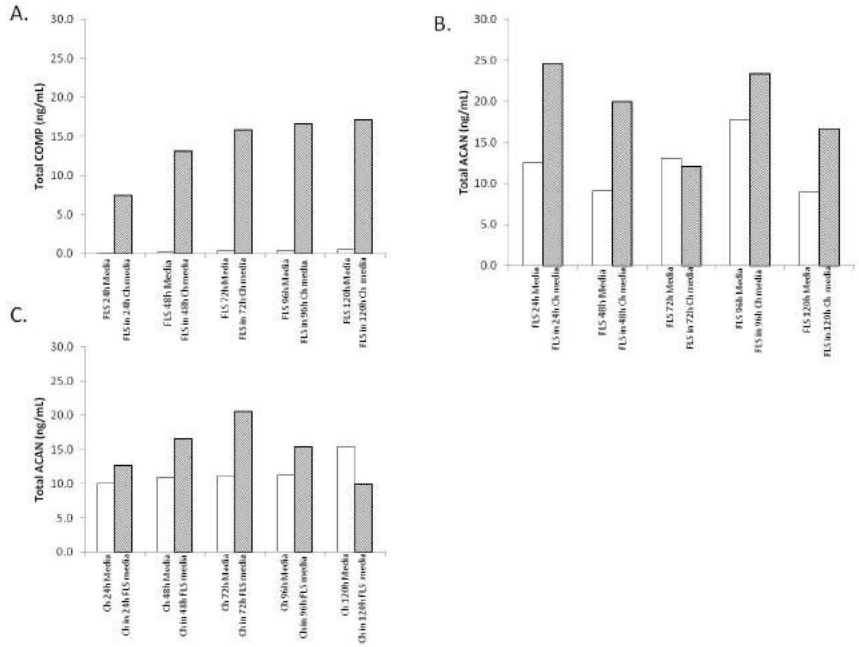
Background/Purpose: A chondrocyte-like phenotype has previously been described in pediatric fibroblast-like synoviocytes (FLS), which may contribute to bony overgrowth in juvenile idiopathic arthritis (JIA). The goal of this project is to study the influence that JIA FLS and chondrocytes (Ch) have on each other along the lines of chondrogenic differentiation.

Methods: As part of a separate ongoing IRB approved protocol, remnant synovial fluid (SF) was obtained from patients undergoing arthrocenteses. FLS were derived from SF of one patient with persistent oligoarticular JIA. Ch were obtained from Cell Applications Inc. Cell media samples were obtained every 24 hours over a five day course from both the JIA FLS and Ch lines. The JIA FLS were then treated for 72 hours with conditioned media from Ch from each of the time

points. Conversely, the Ch were treated for 72 hours with conditioned media from JIA FLS from the same time points. Samples were analyzed by ELISA for cartilage oligomeric matrix protein (COMP), aggrecan (ACAN) and type II collagen (CII). Differences in protein levels were compared to the levels secreted by the cultured cell types in 72 hours when exposed to non-conditioned media.

Results: JIA FLS untreated in culture did not produce significant levels of COMP. After 72 hours of exposure to Ch conditioned media, FLS display an increase in COMP production (Figure Panel A). By 72 hours, any COMP contributed by Ch into the conditioned media would be negligible (COMP half-life = approximately 7 hours). Conversely when Ch were treated with FLS conditioned media for 72 hours, there was no apparent increase in COMP production by Ch. In general we see an increase in ACAN production by FLS when exposed to Ch conditioned media (Figure Panel B). When Ch were exposed to FLS conditioned media for 72 hours there was also a dramatic increase in ACAN production by Ch (Figure Panel C). By 72 hours, any ACAN contributed by the other cell type into the conditioned media would be negligible (ACAN half-life = approximately 30 minutes). Due to the longer half-life of CII, there may be residual contribution of CII from Ch media after 72 hours in culture with FLS. Regardless of this contribution, it appears that there may be a modest increase in CII production by FLS when exposed to Ch media.

Conclusion: In this pilot study the JIA FLS are producing higher levels of COMP, an extracellular matrix (ECM) protein and marker of cartilage turnover, when exposed to Ch media in culture. JIA FLS and Ch may influence each other to increase production of ACAN, a major protein found in the ECM of cartilaginous tissues. Further studies are planned based on this pilot experiment to clarify and expand upon the influences that FLS and Ch have on each other in the inflamed joint.



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Abstract Number: 133

3-D Explant Method Facilitates the Study of Lymphocytes in Synovium and Reveals a Population of Resident Memory-Like T Cells in Rheumatoid Arthritis

Lauren Henderson[1], Deepak Rao[2], Nikola Teslovich[3,4], Sandra King[5], Fumitaka Mizoguchi[6], Sarah Ameri[6], Allyn Morris[7], Christopher Elco[5], Margaret Chang[8], Anais Levescot[9], James Lederer[10], Scott Martin[11], Barry Simmons[11], John Wright[11], Michael Brenner[2], Soumya Raychaudhuri[12,13,14,15,16], Robert Fuhlbrigge[17] and Peter Nigrovic[1,18], [1]Division of Immunology, Boston Children's Hospital, Harvard Medical School, Boston, MA, [2]Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [3]Program in Medical and Population Genetics, Broad Institute of Massachusetts Technical Institute and Harvard University, Cambridge, MD, [4]Divisions of Genetics and Rheumatology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [5]Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [6]Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [7]Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital, Boston, MA, [8]Division of Immunology, Boston Children's Hospital, Boston, MA, [9]Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Harvard Medical School, boston, MA, [10]Department of Surgery, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [11]Department of Orthopedic Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [12]Divisions of Genetics and Rheumatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [13]Program in Medical and Population Genetics, Broad Institute of Massachusetts Technical Institute, Harvard University, Cambridge, MA, [14]Partners Center for Personalized Genetic Medicine, Boston, MA, [15]Institute of Inflammation and Repair, University of Manchester, Manchester, United Kingdom, [16]Rheumatology Unit, Karolinska Institutet, Karolinska University Hospital Solna, Stockholm, Sweden, [17]Children's Hospital Colorado, Aurora, CO, [18]Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

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Background/Purpose: Tissue resident memory T (T_{RM}) cells survive indefinitely in barrier tissues and mediate swift immunologic memory responses at sites of microbe entry. T_{RM} cells have been implicated in recurrent site-specific inflammation in skin, intestine, and lung, but little is known about T_{RM} cells in synovium. We employed a highly efficient 3-dimensional (3-D) explant culture technique, developed to recover $T_{RM}$from skin, to investigate synovial infiltrating T cells.

Methods: Subjects with rheumatoid arthritis (RA) were identified by International Classification of Disease (ICD) codes, supported by medical record review by a board-certified rheumatologist. Synovial tissue samples were obtained from RA patients undergoing medically necessary joint surgery. Collagenase digestion and/or 3-D explant culture was used to isolate synovial T cells. In the 3-D explant culture system, 2mm x 2mm pieces of synovial tissue were placed on Cellfoam matrices, and cultured in T cell media enriched with IL-2 and IL-15 for 3 weeks. Multidimensional analysis of surface markers and cytokine production upon stimulation was performed by mass cytometry (CyTOF).

Results: Synovial samples were obtained from 13 women and 2 men with established RA. Treatment regimens varied (methotrexate, n=9; tumor necrosis factor inhibitors, n=6; prednisone, n=5; non-steroidal anti-inflammatory drugs, n=5). 3-D explant culture of RA synovium samples yielded 5-fold more mononuclear cells, on average, than collagenase digestion (mean number mononuclear cells per mg tissue ± SEM: 25,000 ± 17,000 vs. 5,600 ± 4,700). Approximately, 80% of cells collected by the 3-D explant culture method were $CD3^+$ T cells, with the majority being $CD4^+$ T cells (~80%). The ratio of $CD4^+$ to $CD8^+$ cells was not significantly different between the recovery methods. Multidimensional mass cytometry analyses demonstrated dramatic differences in phenotype between synovial and blood $CD4^+$ memory T cells, with significantly increased CD49d and MHCII and decreased CD27 on synovial T cells. A Th1 phenotype predominated in synovial T cells isolated by explant cultures, with ~35% of $CD4^+$ memory T cells expressing IFNγ and Tbet upon stimulation. Notably, memory $CD4^+$ T cells with a phenotype consistent with T_{RM} cells ($CD62L^-$, $CCR7^-$, $CD69^+$) were

identified in all tested synovial samples. While CD69 expression may be induced by recent activation, many of these potential T_{RM} ($CD62L^-$, $CCR7^-$, $CD69^+$) cells did not express two other markers of recent activation, CD25 and MHCII.

Conclusion: 3-D explant culture is a novel tool that can be employed to study lymphocytes that are resident in synovium. Memory T cells with T_{RM} features were identified in synovial samples from RA patients, supporting the hypothesis that this T cell subset may contribute to the persistence and recurrence of inflammatory arthritis. Further study will be needed to define the functional characteristics and pathophysiologic role of these cells.

Disclosure: L. Henderson, None; **D. Rao**, None; **N. Teslovich**, None; **S. King**, None; **F. Mizoguchi**, None; **S. Ameri**, None; **A. Morris**, None; **C. Elco**, None; **M. Chang**, None; **A. Levescot**, None; **J. Lederer**, None; **S. Martin**, None; **B. Simmons**, None; **J. Wright**, None; **M. Brenner**, None; **S. Raychaudhuri**, None; **R. Fuhlbrigge**, None; **P. Nigrovic**, None.

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Abstract Number: 134

Akkermansia Muciniphila May Be Permissive to Arthritis in the K/BxN Mouse Model of Arthritis

Matthew L. Stoll[1], Casey D Morrow[2], Pamela Weiss[3], Jennifer E. Weiss[4], Lennard W. Duck[5], Charles O. Elson[6], Randy Q. Cron[7], Elliot J. Lefkowitz[8], Ranjit Kumar[9] and Trenton R. Schoeb[10], [1]Pediatric Rheumatology, University of Alabama at Birmingham, Birmingham, AL, [2]Cell, Developmental, and Integrative Biology, University of Alabama at Birmingham, Birmingham, AL, [3]Division of Rheumatology, Center for Pediatric Clincial Effectiveness, Children's Hospital of Philadelphia, Philadelphia, PA, [4]Hackensack Univ Med Ctr, Hackensack, NJ, [5]Medicine, University of Alabama at Birmingham, Birmingham, AL, [6]Dept of Medicine, University of Alabama at Birmingham, Birmingham, AL, [7]University of Alabama at Birmingham, Birmingham, AL, [8]Microbiology, University of Alabama at Birmingham, Birmingham, AL, [9]Center for Clinical and Translational Sciences, University of Alabama at Birmingham, Birmingham, AL, [10]Genetics and Comparative Pathology Laboratory, University of Alabama at Birmingham, Birmingham, AL

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Background/Purpose: Studies have identified abnormalities in the microbiota of patients with arthritis. To evaluate the pathogenicity of human microbiota, we performed fecal microbial transplantation (FMT) from children with newly diagnosed enthesitis-related arthritis (ERA) and sex- and age-matched controls to germ-free KRN/B6xNOD (K/BxN) mice, a spontaneous arthritis model dependent upon an intact microbiota.

Methods: K/BxN mice were maintained under germ-free (GF) conditions and were gavaged with feces previously collected from children with ERA and healthy controls at 6 – 10 weeks of age, and maintained in isolators for 21 – 24 days following FMT. Additional controls included non-gavaged GF mice and mice transferred from the gnotobiotic to the conventional facility. Subsequent studies involved colonization with select cultured bacteria. Sequencing of the fecal microbiota was performed on the Illumina MiSeq device, and analysis was performed with the Quantitative Insight into Microbial Ecology program.

Results: 24 mice were gavaged with human microbiota (12 each of ERA and controls). 23 non-gavaged mice were maintained in the gnotobiotic facility, and 11 additional non-gavaged mice were transferred into the conventional facility. Among transplanted mice, ankle swelling assessed 21 – 24 days post transfer was equivalent in those that received ERA

(4.7 ± 0.5) vs control (4.4 ± 0.4) microbiota. Taken together, mice colonized with human microbiota had increased ankle swelling as compared to GF (3.5 ± 0.3, $p < 0.001$) and conventionally housed (4.0 ± 0.4, $p = 0.002$) mice. Principal coordinates analysis revealed incomplete uptake of the human microbiota, with clustering by species but not by donor-recipient dyad. This was due to substantial over-representation of two genera (Bacteroides and Akkermansia) at the expense of the Firmicutes phylum among the transplanted mice. Taken together, the microbiota as a whole predicted the extent of ankle swelling ($R2 = 0.185$, $p = 0.018$, adonis test). At the level of the individual genera, the abundances of *Bacteroides* ($r = -0.510$, $p = 0.010$) inversely and *Akkermansia* ($r = 0.367$, $p = 0.078$) directly correlated with ankle swelling. Although monocolonization of *A. muciniphila* did not impact ankle swelling, addition of A. muciniphila cultures to transplanted human microbiota resulted in increased ankle swelling as compared to mice that received transplanted human microbiota alone (median 4.5 mm, IQR 4.3 – 5.5 versus 4.1 mm, IQR 3.9 – 4.3, $p = 0.018$).

Conclusion: This study supports previous findings of a possible association between *Akkermansia muciniphila* and arthritis and opens up new avenues of research into the association between human microbiota and arthritis.

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Abstract Number: 135

Epigenetic Profiling Of Juvenile Idiopathic Arthritis (JIA) Synovial Fluid Monocytes Points Towards a Role For Monocytes In Bone Damage

Janneke Peeters[1], Arjan Boltjes[2,3], Stephin Vervoort[4], Paul Coffer[1], Bas Vastert[2,5], Femke van Wijk[2,3], Michal Mokry[3], Teun de Vries[6,7] and Jorg van Loosdregt[3], [1]Center for Molecular Medicine and Regenerative Medicine Center Utrecht, University Medical Center Utrecht, Utrecht, Netherlands, [2]Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, [3]Division of Pediatrics, University Medical Center Utrecht, Utrecht, Netherlands, [4]Peter MacCallum Cancer Centre, Melbourne, Australia, [5]Division of Pediatric Rheumatology, University Medical Center Utrecht, Utrecht, Netherlands, [6]Department of Oral Cell Biology and Functional Anatomy, Academic Centre for Dentistry Amsterdam, Amsterdam, Netherlands, [7]Department of Periodontology, Academic Centre for Dentistry Amsterdam, Amsterdam, Netherlands

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Background/Purpose: Juvenile Idiopathic Arthritis (JIA) is a multifactorial autoimmune disease characterized by the accumulation of various immune cells, including monocytes, in the joint synovial fluid (SF). Joint function is severely affected in JIA patients due to fluid accumulation and bone damage. The molecular mechanisms underlying JIA and other autoimmune diseases still remain largely elusive. We aimed to create more insight into disease pathogenesis by performing epigenetic and gene expression profiling of $CD14^+$ cells derived from the site of inflammation of JIA patients.

Methods: Chromatin immunoprecipitation sequencing was performed to determine the (super-)enhancer repertoire of JIA patient SF-derived monocytes. Gene expression of SF-derived monocytes was analyzed using RNA-sequencing. Osteoclastogenesis of monocytes was assessed by osteoclast differentiation assays followed by tartrate-resistant acid phosphatase (TRAP) staining and bone resorption measurements.

Results: The (super-)enhancer profile of JIA patient-derived monocytes demonstrated that osteoclast-related genes are

associated with an increased enhancer or super-enhancer in JIA compared to healthy control (HC) monocytes, suggesting that the osteoclast pathway might play a crucial role in JIA monocytes. This is in agreement with the observation that osteoclast-associated genes are enriched in genes that are upregulated in JIA SF-derived monocytes, indicating that osteoclast differentiation might be increased. Indeed, differentiation of HC monocytes in the presence of SF enhanced the formation of osteoclasts.

Conclusion: Our results indicate that monocytes obtained from the inflammatory site of JIA patients display increased osteoclastogenesis, resulting in more bone degradation. This enhanced osteoclast differentiation is likely to be the consequence of the inflammatory environment present in the joint. Altogether, therapies aimed at inhibiting the differentiation of monocytes into osteoclasts, for example by inhibiting inflammatory mediators present in the SF, might reduce bone loss and thus improve joint function in JIA patients.

Disclosure: J. Peeters, None; **A. Boltjes**, None; **S. Vervoort**, None; **P. Coffer**, None; **B. Vastert**, None; **F. van Wijk**, None; **M. Mokry**, None; **T. de Vries**, None; **J. van Loosdregt**, None.

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Abstract Number: 136

14-3-3π(eta) Protein in Juvenile Idiopathic Arthritis

Austin Dalrymple[1,2,3], Paul Tuttle IV[4], Lance Feller[5], Olga S. Zhukov[6], Robert J. Lagier[7], Robert Bridgforth[8], Gary J Williams[9], Joanna Popov[10], Stanley J. Naides[6] and Terry Moore[11], [1]Division of Rheumatology and Pediatric Rheumatology, Saint Louis University School of Medicine, St Louis, MO, [2]Division of Adult and Pediatric Rheumatology, Saint Louis University, St Louis, MO, [3]Division of Rheumatology and Pediatric Rheumatology, Saint Louis University, St Louis, MO, [4]Saint Louis University, Saint Louis, MO, [5]Former fellow, Saint Louis University, Watertown, ME, [6]Immunology, Quest Diagnostics Nichols Institute, San Juan Capistrano, CA, [7]Research Support, Alameda, Quest Diagnostics Alameda, Alameda, CA, [8]nichols Institute, Quest Diagnostics, San Juan Capistrano, CA, [9]Nicolas Institue, Quest Diagnostics, San Juan Capistrano, CA, [10]Immunology, Quest Diagnostics, San Jian Capistrano, CA, [11]Rheumatology, Saint Louis University, St. Louis, MO

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Background/Purpose: 14-3-3 proteins are chaperonins found in all eukaryotic cells. There are multiple isoforms which are thought to be involved in intracellular signaling and transcription regulation. Recent work has implicated the η (eta) isoform as having diagnostic potential in inflammatory arthritides. Its utility in JIA has not been established. Our preliminary prior investigation indicated positivity in some JIA patients. In this study, we investigated a much larger cohort of patients with JIA and disease and healthy controls.

Methods: Measurement of 14-3-3η protein was evaluated in 29 rheumatoid factor (RF) positive (pos) polyarticular (poly) JIA patients, 29 RF negative (neg) poly patients, 34 oligoarticular (oligo) patients, 12 systemic-onset (SO) patients, 19 adult rheumatoid arthritis (RA) patients, 60 patients with systemic lupus (SLE), and 20 healthy controls by the assay established at Quest Diagnostics. Comparisons were made to CBC, ESR, CRP, RF and anti-CCP isotypes, and ANA positivity.

Results: 14-3-3η at 0.2 ng/ml or higher was considered positive; values of 0.5 ng/mL or greater have been considered prognostic of poor outcome in adults. Ten of 29 (34%) RF pos polys were positive for the 14-3-3η protein; 8 (28%) had

values > 0.5 ng/mL. Nine of 29 (31%) RF neg polys were positive; 8/29 (28%) had values >0.5 ng/mL. Only 6/34 (18%) oligos were positive; 5/34 (15%) >0.5 ng/mL. Only 2/12 (16%) SO were positive; 1/12 (8%) >0.5 ng/mL. In the disease controls, 14/60 (23%) SLE were positive, but only 7/60 (12%) >0.5 ng/mL. 7/19 RA patients were positive, 4/19 (21%) >0.5 ng/mL. In the healthy controls, only 3/20 (15%) were positive, 1/20 (5%) > 0.5 ng/mL. The RF pos and RF neg polys positivity, especially at values >0.5 ng/mL compared favorably with the adult RA patient and were significant compared to disease and healthy controls. A weak correlation was noted between 14-3-3η positivity and CRP. Five of the 8 RF neg polys at original diagnosis that were 14-3-3η positive at >0.5 ng/mL have subsequently developed a positive RF and an anti-CCP antibody isotype. Also, the one SO positive for 14-3-3η >0.5 ng/mL also developed a positive RF.

Conclusion: Significant levels of 14-3-3η protein can be found in about 30% of RF pos and RF neg poly JIA patients. It may represent a new biomarker for RF neg poly JIA patients and a marker indicating the possibility of these patients becoming RF/anti-CCP antibody positive in the future. Further longitudinal studies are required to confirm these findings.

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Abstract Number: 137

Chromatin Landscapes and Genetic Risk For Juvenile Idiopathic Arthritis

James Jarvis[1], Lisha Zhu[2], Lai Ping Wong[3], Tao Liu[4], Kaiyu Jiang[3] and Yanmin Chen[3], [1]Pediatrics, SUNY Buffalo School of Medicine, Buffalo, NY, [2]Biochemistry, University at Buffalo, Buffalo, NY, [3]Pediatrics, University at Buffalo, Buffalo, NY, [4]Department of Biochemistry, University at Buffalo, Buffalo, NY

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Background/Purpose: The transcriptomes of peripheral blood cells in children with juvenile idiopathic arthritis (JIA) show distinct transcriptional aberrations that suggest impairment of transcriptional regulation. To gain a better understanding of this phenomenon, we studied known JIA genetic risk loci, the majority of which are located in non-coding regions, where transcription is regulated and coordinated on a genome-wide basis.

Methods: We examined the chromatin architecture in human neutrophils and CD4 primary T cells to identify genes and functional elements located within JIA-associated genetic risk loci.We analyzed RNA-Seq data, H3K27ac and H3K4me1 chromatin immunoprecipitation-sequencing (ChIP-Seq) data, and previously published chromatin interaction analysis by paired-end tag sequencing (ChIA-PET) data in CD4+ T cells to gain insights into cellular mechanisms that may contribute to genetic risk in JIA.

Results: In both neutrophils and primary CD4+ T cells, the majority of the JIA-associated linkage disequilibrium (LD) blocks contained H3K27ac and/or H3K4me1 marks. These LD blocks were also binding sites for a small group of transcription factors, particularly in neutrophils. Furthermore, these regions showed abundant intronic and intergenic transcription in neutrophils. In neutrophils, none of the genes that were differentially expressed between untreated JIA patients and healthy children was located within the JIA risk LD blocks. In CD4+ T cells, multiple genes, including HLA-DQA1, HLA-DQB2, TRAF1, and IRF1 were associated with the long-distance interacting regions within the LD regions as determined from ChIA-PET data.

Conclusion: These findings add insight into how genetic risk contributes to the aberrant transcriptional control observed in

JIA. Furthermore, the complex chromatin interactions identified here demonstrate the challenges of identifying the actual causal variants within complex genomic/chromatin landscapes.

Disclosure: J. Jarvis, None; **L. Zhu**, None; **L. P. Wong**, None; **T. Liu**, None; **K. Jiang**, None; **Y. Chen**, None.

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Abstract Number: 138

Modeling Transcriptional Rewiring in Neutrophils through the Course of Treated Juvenile Idiopathic Arthritis

Zihua Hu[1], Kaiyu Jiang[2], Mark B. Frank[3], Yanmin Chen[2] and **James Jarvis**[4], [1]Center for Computational Research, University at Buffalo, Buffalo, NY, [2]Pediatrics, University at Buffalo, Buffalo, NY, [3]Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, [4]Pediatrics, SUNY Buffalo School of Medicine, Buffalo, NY

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Background/Purpose: We have previously shown that neutrophils in children with polyarticular juvenile idiopathic arthritis (JIA) display abnormal transcriptional patterns linked to fundamental metabolic derangements. These transcriptional abnormalities include complex re-ordering of miRNA-RNA expression networks. In the current study, we sought to determine the effects of therapy of the reorganization of miRNA-RNA networks in polyarticular JIA.

Methods: In this cross-sectional analysis, we studied children with untreated, active JIA (ADU-n=35), 26 children with active disease on therapy with methotrexate + etanercept (ADT), and 14 children with inactive disease also on therapy (ID). We used Affymetrix exon and miRNA microarrays to identify expressed transcripts and compared results to findings from 35 healthy control (HC) children.

Results: Computational modeling demonstrated substantial re-ordering of miRNA-RNA networks after the initiation of therapy. Each of the 3 disease states, i.e., ADU, ADT, and ID, was associated with its own distinct transcriptional profile that showed only modest overlaps with the other 2. Gene ontology analysis corroborated this finding, as the genes showing differential expression between each of the disease states and HC were associated with different biological functions. Among the networks, the ADT state differed the most from HC while ID more strongly resembled HC. Computational modeling demonstrated complex interactions between transcription factors and miRNA that determine the gene expression signatures of each disease state.

Conclusion: Therapy for JIA induces substantial re-organization of neutrophil transcriptomes. It is interesting to note that each of the different treatment stages, which were derived from clinical observations (Wallace criteria), appear to be biologically distinct. These findings affirm the value of using the Wallace criteria for staging treatment response in JIA.

Disclosure: Z. Hu, None; **K. Jiang**, None; **M. B. Frank**, None; **Y. Chen**, None; **J. Jarvis**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/modeling-transcriptional-rewiring-in-neutrophils-through-the-course-of-treated-juvenile-idiopathic-arthritis

Abstract Number: 139

Dysregulation of miRNA in mononuclear cells of patients with enthesitis related arthritis

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Background/Purpose: Enthesitis related arthritis (ERA) is the most common category of JIA in Asia. Identifying dysregulated microRNA may help in understanding the pathogenesis of ERA. Thus we compared miRNA profile in PBMC from ERA subjects and healthy controls (HC) and further compared between PBMC with SFMC to understand the changes at the site of inflammation

Methods: MiRNA profile was determined using Agilent Human miRNA Microarray chips using PBMC from HC and ERA, and SFMC from ERA (n=8 each). The dysregulated miRNA were validated by qRT-PCR in 25 patients and 11 healthy controls. In silico target prediction and pathway analysis was also done for these miRNAs.

Results: Eight miRNAs were differentially expressed in the PBMC from ERA patients relative to HC ($p<0.25$). Moreover, 90 miRNA were dysregulated (38 higher and 52 lower; $p<0.05$) in SFMC compared to PBMC from ERA Patients qRT-PCR validated upregulation of miR-21, miR-126, miR-130a and downregulation of miR-150 ($p<0.05$) in ERA-PBMC (n=25) relative to HC-PBMC (n=11). In addition, expression of miR-155, miR-21, miR-34a, miR-210, miR-29b was upregulated and miR-146a, miR-150, miR-126, miR-130a and miR-26a was downregulated ($p<0.05$) in paired SFMCs relative to PBMC (n=9). Among the 4 dysregulated miRNAs in ERA-PBMC, relative to HC-PBMC, only miR-21 and miR-150 showed a positive association with their levels in SFMC ($p<0.05$). PDCD4, predicted target of miR-21 and miR-150, was up-regulated in SFMCs compared to ERA-PBMCs. In silico analysis revealed that the targets of differentially expressed miRNAs belong immune signaling pathways like MAPK signaling pathways, TLR signaling pathways, T cell receptor signaling pathways, mTOR signaling pathways, Wnt signaling pathways.

Conclusion: Differential expression of miR-21 and miR-150 in ERA may regulate T cell activation via PDCD4. Predicted target genes for other dysregulated miRNA found at the site of inflammation suggest a role of multiple immune pathways in ERA pathogenesis.

Disclosure: A. Aggarwal, None; **S. Singh**, None.

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Abstract Number: 140

Modular Gene Expression Discrimination of Juvenile Idiopathic Arthritis and Inflammatory Bowel Disease Subphenotypes in Peripheral Blood

Urko Marigota[1], Angela Mo[1], Jarod Prince[2], Lai Hin Kimi Chan[3], Subramaniam Kugathasan[2], Greg Gibson[1] and **Sampath Prahalad**[4], [1]Center for Integrative Genomics, Georgia Institute of Technology, Atlanta, GA, [2]Emory University School of

Medicine, Atlanta, GA, [3]Pediatrics, Emory University School of Medicine, Atlanta, GA, [4]Emory University School of Medicine and Children's Healthcare of Atlanta, Atlanta, GA

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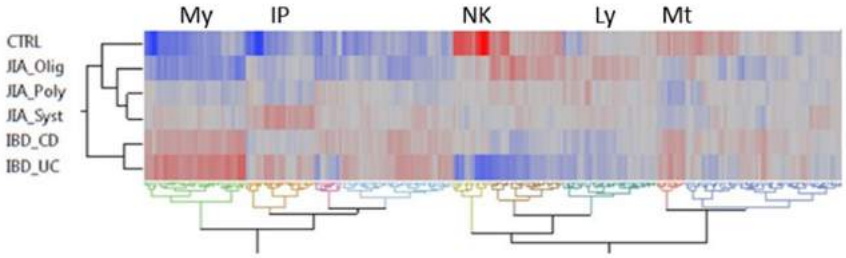
Background/Purpose: Juvenile idiopathic arthritis (JIA) is a heterogeneous group of diseases which have in common inflammatory arthritis, but distinct clinical and genetic associations. Using biological information to accurately classify JIA into subtypes will enhance our understanding of the molecular pathogenesis of JIA and allow for personalized therapeutic options. Gene expression profiling allows inspection of the entire transcriptome for patterns of gene activity that can be used to interpret signals from genome-wide association studies and elucidate the pathways that contribute to distinct disease subtypes.

Methods: We performed RNA-Seq transcriptome profiling of peripheral blood samples from 129 children with JIA (45 oligoJIA; 54 polyJIA; 30 systemic sJIA), as well as 12 healthy controls. For an inflammatory disease outgroup comparison we also included 76 inflammatory bowel disease (IBD) samples (61 Crohn's disease - CD; 15 ulcerative colitis - UC) samples. Pairwise differential expression analysis between cases and controls, and subtypes of disease was performed using edgeR software. We then extracted eigengenes representing 249 conserved Blood Transcript Modules (BTM), each capturing some aspect of immune gene expression, and characterized differences among phenotype categories.

Results: Overall peripheral blood gene expression in JIA shows a gradient (see Figure) of disrupted gene expression involving hundreds of BTM, from healthy controls to oligo to polyarticular then sJIA. IBD most resembles sJIA, although with some key differences. Myeloid gene expression tends to be elevated in IBD (My), and lymphoid suppressed (Ly), with JIA intermediate. In addition, UC has a specific deficit in NK cell gene expression (NK), sJIA has a unique signature including inositol metabolism (IP), and JIA in general shows reduced mitochondrial gene activity Mt).

Conclusion: Transcriptomic analysis of whole peripheral blood identifies hundreds of modules that are specific to individual categories of disease. These may represent cell-specific modification of gene expression, or specific depletion or elevation of cells such as NK cells from the circulating blood following migration to the gut mucosa or joints. Ongoing studies are examining the influence of drug treatment on the profiles, and relating the differential expression to mechanisms of regulation of transcription.



Disclosure: U. Marigota, None; **A. Mo**, None; **J. Prince**, None; **L. H. K. Chan**, None; **S. Kugathasan**, None; **G. Gibson**, None; **S. Prahalad**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/modular-gene-expression-discrimination-of-juvenile-idiopathic-arthritis-and-inflammatory-bowel-disease-subphenotypes-in-peripheral-blood

Abstract Number: 141

Expression of Siglec-10 on Synovial Fluid CD14dim Monocytes Was Decreased in Juvenile Idiopathic Arthritis Patients

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SESSION INFORMATION
Session Date: Thursday, May 18, 2017
Session Title: Genetics and Pathogenesis Poster Session
Session Type: Abstract Submissions
Session Time: 5:30PM-7:00PM

Background/Purpose: Monocytes plays a role in juvenile idiopathic arthritis (JIA). $CD14^{dim}$ monocytes have modulatory effects in innate and adaptive immune responses. Siglec-10, which is highly expressed on $CD14^{dim}$ monocytes, functions as an inhibitory receptor within the innate immune system. The interaction between Siglec-10 and its ligand CD24 could prevent tissue damage-induced immune responses. Siglec-G (murine Siglec-10 homolog) knockout mice developed increased clinical disease in mouse arthritis model, which suggests a role of Siglec-G/10 in pathogenesis of arthritis. IL-29 is a member of type III IFN family. Besides its antiviral and antitumor function, IL-29 also has immune-regulation function. In this study, we investigated the expression of Siglec-10 on $CD14^{dim}$ monocytes from synovial fluid (SF) and peripheral blood (PB) of JIA patients and assessed IL-29 as a candidate cytokine produced from the Siglec10-CD24 interaction.

Methods: A total of 42 patients, including 24 JIA, 10 systemic lupus erythematosus (SLE) and 8 controls were included. Siglec-$10^{+}CD14^{dim}$ monocytes were sorted by flow cytometry to culture with or without human CD24 fusion protein. The expression of Siglec-10 on PB and SF monocytes was measured by flow cytometry. IL-29 mRNA expression was assessed by quantitative real-time reverse transcriptase-polymerase chain reaction.

Results: The percentage of synovial Siglec-$10^{+}CD14^{dim}$ monocytes of JIA patients was significantly decreased compared with that from peripheral blood. Furthermore, the expression of Siglec-10 (Mean fluorescent intensity, MFI) was significantly lower on SF $CD14^{dim}$ monocytes when compared with PB $CD14^{dim}$ monocytes. Although the expression of Siglec-10 on PB $CD14^{dim}$ monocytes was similar in JIA, SLE and the control subjects, the percentage of Siglec-$10^{+}CD14^{dim}$ monocytes from PB was higher in JIA patients compared with SLE patients and controls. IL-29 mRNA transcript in Siglec-$10^{+}CD14^{dim}$ monocytes cultured with CD24 fusion protein in vitro was increased, relative to controls cultured without CD24 fusion protein.

Conclusion: Interaction between Siglec-10 and CD24 on $CD14^{dim}$ monocytes may trigger the production of IL-29 which may mediate immunoregulatory function. The reduction of SF Siglec$10^{+}CD14^{dim}$ monocytes in JIA patients and the reduction of Siglec-10 expression on these cells may have contributed to the pathogenesis of JIA.

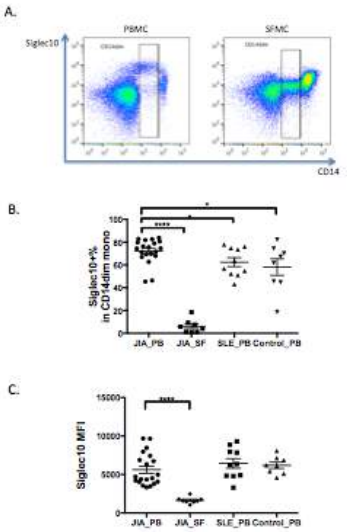

Figure. **A.** Representative staining of mononuclear cells with CD14 and Siglec-10 in PB (left) and SF (right) from the same JIA patient at the same day. **B.** The percentages of Siglec-$10^{+}$$CD14^{dim}$ monocytes in $CD14^{dim}$ monocytes in different groups. **C.** The MFI of Siglec-10 on Siglec-$10^{+}$$CD14^{dim}$ monocytes in different groups. **P*<0.05, **** *P*<0.0001. MFI, mean fluorescent intensity; JIA, juvenile idiopathic arthritis; PB, peripheral blood; SF, synovial fluid.

Disclosure: Q. Zhao, None; **Y. Liu**, 1,4,6,2; **P. Zheng**, 1,4,6,2; **L. Jung**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/expression-of-siglec-10-on-synovial-fluid-cd14dim-monocytes-was-decreased-in-juvenile-idiopathic-arthritis-patients

Abstract Number: 142

Neutrophils and monocytes in the early inflammatory cascade of systemic onset Juvenile Idiopathic Arthritis

Nienke M. ter Haar[1], Wilco de Jager[2], Rianne C. Scholman[1], Jenny Meerding[1], Bas Vastert[3,4] and **Sytze de Roock**[4], [1]Laboratory for Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands, [2]Dept Immunology, UMC Utrecht, Utrecht, Netherlands, [3]Division of Pediatric Rheumatology, University Medical Center Utrecht, Utrecht, Netherlands, [4]Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands

SESSION INFORMATION
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Background/Purpose:

Systemic onset Juvenile Idiopathic Artritis (sJIA) is an acquired systemic autoinflammatory disease characterized by spiking fever, arthritis and skin rash. Patients display high inflammatory parameters and high circulating levels of interleukin(IL)-18 and phagocyte-derived S100-proteins. The role of specific innate immune cells is still to be unravelled. Here, we aimed to dissect the role of monocytes and neutrophils in the early inflammatory cascade of sJIA.

Methods: We determined neutrophil activation *ex vivo* (cell surface markers) and after stimulation (ROS-production and degranulation) of sJIA patients with active disease or inactive disease, compared to healthy donors (HDs). To investigate the role of monocytes, we stimulated peripheral blood derived mononuclear cells (PBMC) from active and inactive sJIA patients and HDs with TLR4-stimulating S100-proteins or other TLR-ligands. Cytokine levels in serum and supernatant were measured by multiplex immunoassay.

Results: At disease onset, 37/47 sJIA patients had elevated neutrophil counts. Neutrophil-specific proteins elastase and neutrophil collagenase were significantly elevated in onset sJIA, compared to inactive sJIA. Neutrophils from active sJIA patients showed an activated phenotype, reflected by higher *ex vivo* expression of FC-gamma receptors (CD32, CD64) and degranulation markers (CD35, CD66b) and enhanced ROS-production and degranulation after stimulation, compared to HDs. Neutrophil phenotype normalized when patients had inactive disease. In contrast to the hyperactivated status of neutrophils in active sJIA, PBMC from active sJIA produced less IL-1beta, IL-18, IL-6 and TNF-alpha upon TLR-stimulation compared to inactive patients or HDs.

Conclusion: We show here that in active sJIA, neutrophils but not monocytes seem to be crucial in driving the systemic inflammatory response. Neutrophils show an activated phenotype, while monocytes display tolerogenic characteristics, possibly as a compensation to the high S100-levels *in vivo*. RNA-sequencing of FACS-sorted monocytes and neutrophils of sJIA patients is currently undertaken and will reveal pathways involved in the phenotype of these cells.

Disclosure: N. M. ter Haar, None; **W. de Jager**, None; **R. C. Scholman**, None; **J. Meerding**, None; **B. Vastert**, None; **S. de Roock**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/neutrophils-and-monocytes-in-the-early-inflammatory-cascade-of-systemic-onset-juvenile-idiopathic-arthritis

Abstract Number: 143

Influence of Age and Sex on Collagen-Induced Arthritis

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Genetics and Pathogenesis Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: Age and sex differences are found in certain subsets of juvenile idiopathic arthritis (JIA). Collagen Induced Arthritis (CIA) in rodents has utility in assessing pathogenic processes in arthritis. This study compared clinical, biomarker and imaging characteristics of CIA in male and female, adult and juvenile animals. The goal was to evaluate CIA as a model for studying age- and sex-related differences in inflammatory joint diseases.

Methods: Juvenile (5 wks old) and adult (13 wks old) male and female Lewis rats were immunized with bovine type II collagen/incomplete Freund's adjuvant. Naïve juvenile and adult, male and female rats served as controls. For each animal, the Maximum Daily Arthritis Score (MDAS) was recorded. 14 days after arthritis onset, paw swelling was measured, blood collected and paws imaged by micro-CT. Serum was assayed by enzyme immunoassay using a rat 27-plex cytokine/chemokine array. Micro-CT scans were scored on a 6 point scale to evaluate bone erosion and pathological ectopic bone/reactive bone formation. Statistical significance was determined by ANOVA and Holm-Sidak tests.

Results: Juvenile male CIA rats (JMC) had significantly higher MDAS ($p<0.0001$), Eotaxin ($p=0.0116$), Interleukin (IL)-4 ($p=0.0045$) and IL-12(p70) ($p=0.0236$) than juvenile female CIA rats (JFC). JMC also had higher MDAS than adult male CIA rats (AMC; $p<0.0001$) and corresponding higher levels of Granulocyte-colony stimulating factor (G-CSF) ($p=0.0160$), Eotaxin ($p=0.0058$), IL-4 ($p=0.0007$) and IL-12(p70) ($p=0.0500$) compared to AMC. JFC had higher MDAS ($p=0.0053$)

and macrophage inflammatory protein 2 (MIP-2; p=0.0434) than adult female CIA rats (AFC).There was no significant difference between MDAS of AFC and AMC. Two weeks after arthritis onset significant changes in serum C-X-C motif chemokine (CXCL) 10 (p<0.0001) and CXCL5 (p=0.0285) levels were specific to JFC; significant changes in serum IL-1β (p=0.0489) and IL-10 (p=0.0113) levels were specific to AFC; significant changes in serum IL-1a (p=0.0438), IL-13 (0.0286) and IL-17a (0.0356) were specific to JMC; and significant change in serum level of Leptin was specific to AMC (p<0.0001). No significant differences were observed in degree of bone erosion between groups. However, the majority of bone erosion was observed at the tarso-metarsal /metatarsal-phalangeal joints and, consistent with this finding, there were increases in paw thickness at the metatarsus in JFC (p=0.0021), JMC (p=0.0116) and AMC (p=0.0020). AMC had higher levels of reactive bone formation compared to JFC (p=0.0003), AFC (p=0.0003) and JMC (p=0.0006).

Conclusion: Results indicate age- and sex-related differences in arthritis incidence, severity and associated inflammatory biomarker profiling in the CIA model. Maturity of the immune system, rates of bone growth and changing hormonal levels are likely to contribute to these observed differences. These results indicate the importance of age and sex in CIA and the potential value of this model for studying the biologic basis for age- and sex-related differences in humans with arthritis.

Disclosure: T. Wilson-Gerwing, None; **A. Panahifar**, None; **D. M. L. Cooper**, None; **A. Rosenberg**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/influence-of-age-and-sex-on-collagen-induced-arthritis

Abstract Number: 144

Linear Discriminant Analysis of Cultured Fibroblast-like Synoviocytes Identifies 6 Candidate Genes Which Predict Extended Course in Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Genetics and Pathogenesis Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

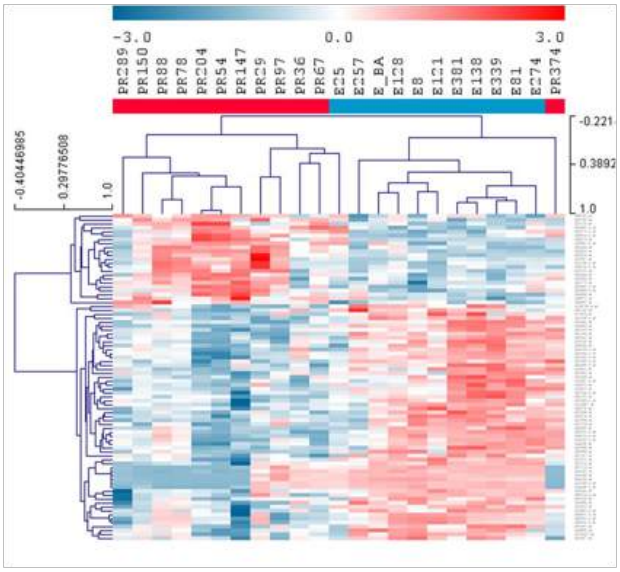
Background/Purpose: The goal of this project is the identification of informative synovial biomarkers to predict which children with oligoarticular juvenile idiopathic arthritis (JIA) will have a persistent course, with no more than 4 involved joints, vs those who will have an extended course, with a cumulative total of ≥5 affected joints after the first 6 months of disease.

Methods: As part of a separate ongoing IRB approved protocol, remnant synovial fluid was obtained from patients undergoing medically indicated arthrocenteses. All patients satisfied ACR classification criteria for JIA. Using our clinical database, JIA samples were separated into two groups: (1) oligoarticular JIA with persistent course (PR), (2) oligoarticular JIA with extended course (E). All samples were from steroid-na•ve joints and most samples from E were obtained prior to extension. Primary cultures of fibroblast-like synoviocytes (FLS) were established for each subject. RNA from cultured passage 3-6 FLS were isolated, amplified and hybridized to Affymetrix Human GeneChips using the Affymetrix protocol. Expression values were determined with GC-RMA. Global gene expression of FLS from 12 PR and 11 E samples were obtained. Data was filtered for log2 expression >4 in all samples of either E or PR, then for absolute value of 1.5-fold change. Bioconductor package Linear Models for Microarray Analysis (LIMMA) revealed 83 probesets

with statistically significant differential expression between E vs PR FLS (7% false discovery rate), shown in heatmap.

Results: Hierarchical clustering of the 83 probesets revealed samples from the different courses cluster together, with most of the PR to the left of the heatmap. Importantly, the all of the E were taken from the very first sample available, which preceded extension in the majority of patients, highlighting that there are detectible differences in the gene expression of the FLS early in the course in the patients whose disease is destined to extend. Of these 83 probesets, 9 corresponded to genes with secreted proteins. We performed mathematical modeling with linear discriminant analysis (LDA) on these 9 genes to reveal 6 genes (KLHL13, MAMLD1, ANKRD44, CD14, HSPBAP1, and MBP) which could correctly predict group, E or PR, 100% of the time using leave-one-out cross validation. ELISA was used to confirm expression of these secreted proteins in synovial fluids.

Conclusion: We were able to demonstrate differential gene expression in FLS from JIA patients who remained PR vs those who were destined to extend, demonstrating detectible difference early in disease which may be useful for prediction. The differentially expressed genes, especially for secreted proteins, provide a starting point for development of biomarkers to distinguish between PR and E JIA using aspirated synovial fluid.



Disclosure: A. Brescia, None; **M. Simonds**, None; **S. M. McCahan**, None; **T. Bunnell**, None; **K. E. Sullivan**, None; **C. D. Rosé**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/linear-discriminant-analysis-of-cultured-fibroblast-like-synoviocytes-identifies-6-candidate-genes-which-predict-extended-course-in-juvenile-idiopathic-arthritis-2

Abstract Number: 145

JAK Inhibition Rescues Novel PSMB8 Mutations

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Genetics and Pathogenesis Poster Session

Session Type: Abstract Submissions
Session Time: 5:30PM-7:00PM

Background/Purpose:

The proteasome associated autoinflammatory syndromes (PRAAS) are characterized by autosomal recessive mutations in the *PSMB8* gene. These mutations result in an early childhood overproduction of inflammatory cytokines due to dysregulation of the interferon gamma pathway with manifestations of recurring fever, nodular erythema, acute phase response and anemia. PRAAS entities include the chronic atypical dermatosis with lipodystrophy and elevated temperature (CANDLE) syndrome, Nakajo-Nishimura syndrome (NNS), and joint contractures, muscle atrophy, microcytic anemia and panniculitis-induced lipodystrophy (JMP). Various mutations of the *PSMB8* gene result in the overlapping clinical phenotypes seen in these syndromes. Common features of all PRAAS are skin eruptions, progressive lipodystrophy and muscular atrophy/myositis. We describe the clinical features and therapeutic response of a patient at our institution with novel compound heterozygous mutations in the *PSMB8* gene.

Methods:

We retrospectively reviewed the medical records of a 14 year old Caucasian female who developed recurring cutaneous eruptions of the face, neck and extremities starting at 3 weeks of age, initially thought to be Sweet's syndrome. She has maintained continuity of care by a single pediatric rheumatologist at our institution (MD) who has kept a journal of photographs and clinical data.

Results:

The patient was noted to have microcytic anemia from birth. Her rash was resistant to topical agents but responsive to oral corticosteroids. A skin biopsy was suggestive of interstitial granulomatous dermatitis. She had episodic fever and abdominal pain that led to multiple EGDs with only evidence of mild non-specific inflammation. Initial rheumatology evaluation at age 6 revealed an elevated acute phase response and pro-inflammatory analysis demonstrated elevated TNF and IL-8. She developed arthropathy at age 10 and a body MRI obtained due to bone pain demonstrated myositis and panniculitis in the extremities and body wall. She had calcifications in bilateral globus pallidi on MRI. She has been refractory to multiple immunomodulating agents and disease control has been exquisitely sensitive to oral prednisone. Whole exome sequencing revealed compound heterozygous variants in the PSMB8 gene: c.163C>T (p.Q55X) inherited from the mother and c.352T>C (p.S118P) inherited from the father, mutations not previously desribed. Studies elucidating the mechanisms underlying PRAAS have identified the type I interferon pathway as a potential target for therapy. Therefore, we prescribed the Janus kinase (JAK) inhibitor tofacitinib. Subsequently, the patient demonstrated clinical improvement and has successfully decreased oral prednisone to her lowest dose of 1mg daily with only intermittent mild disease flares, triggered by physical and psychoemotional stressors.

Conclusion:

We describe a patient with novel mutations in the *PSMB8* gene leading to a PRAAS phenotype, who has demonstrated excellent response to JAK inhibition. Insurance barriers have precluded increasing the dose, however we remain optimistic that titration of therapy will allow successful discontinuation of prednisone and maintain full clinical remission.

Disclosure: J. B. Shirley, None; **T. Vogel**, None; **M. de Guzman**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/jak-inhibition-rescues-novel-psmb8-mutations

Abstract Number: 146

Age-Related Differences in Neuronal High Mobility Group Box-1 and Resolvin D1 Receptors in Collagen-Induced Arthritis

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SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Genetics and Pathogenesis Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose: More thorough understanding of age-related molecular interactions that drive inflammation and inflammatory pain is required to help guide evidenced-based, age appropriate treatment strategies that improve arthritis care. Our earlier studies indicate that age is an important determinant of collagen-induced arthritis (CIA) progression and resolution. This study characterized age-related differences in an inflammatory pain pathway involving pro-inflammatory high mobility box 1 protein (HMGB1) and pro-resolution resolvin among different age groups of rats with and without arthritis.

Methods: Juvenile (5 wks old) and young adult (13 wks old) male Wistar rats were immunized with an emulsion of bovine type II collagen/incomplete Freund's adjuvant. Naïve juvenile and adult rats served as controls. For each animal, the Maximum Daily Arthritis Score (MDAS) was recorded. Fourteen days after arthritis onset, animals were euthanized and blood and tissues collected. Dorsal root ganglia immunohistochemistry assessed pro-inflammatory high mobility group box-1 (HMGB1), receptor for advanced glycation end products (RAGE) and the resolvin D1 receptors G-protein coupled receptor 32 (GPR32) and formyl peptide receptor 2 (FPR2).

Results: The MDAS for juvenile rats with CIA were significantly lower than the adult rats with CIA (3.96 + 0.17 and 5.25 + 0.16 respectively; $p<0.0001$). During the first week after onset of CIA, adult rats had a slightly higher MDAS than juvenile rats ($p=0.04$). During the second week of CIA, the MDAS for juvenile rats decreased ($p=0.03$) while the MDAS for adult rats increased significantly ($p=0.002$). At the end of the second week of CIA, adult rats had a significantly higher MDAS than juveniles ($p<0.0001$).

Adult naïve rats had significantly higher percentages of neurons expressing HMGB1 ($p<0.0001$) and RAGE ($p=0.02$) than juvenile naïve rats. Two weeks after CIA onset, percentage of neurons positive for HMGB1 ($p<0.0001$) and RAGE ($p=0.0002$) were significantly higher in the adult CIA group compared to the juvenile naïve group. In contrast, Juvenile naïve rats have significantly higher percentages of GPR32 ($p=0.02$) and FPR2 ($p=0.04$) expressing neurons than adult naïve rats. After two weeks, Juvenile CIA rats also had a higher percentage of neurons expressing GPR32 than the Adult CIA rats ($p=0.02$). No differences in the percentage of neurons expressing FPR2 were observed between Juvenile CIA and Adult CIA rats.

Conclusion: Results indicate age-related differences in arthritis severity are related to the balance between HMGB1 and resolvins and their respective receptors with the balance favoring promotion of inflammation in adults associated with higher levels of HMGB1 and lower levels of resolvin receptors. Juveniles have more available resolvin receptors that may impede transition from acute to chronic arthritis in this model. We postulate that anti-inflammatory effects of endongenous resolvins are mediated by impeding production of HMGB1 and/or HMGB1 binding to its receptors.

Disclosure: T. Wilson-Gerwing, None; **A. Rosenberg**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/age-related-differences-in-neuronal-high-mobility-group-box-1-and-resolvin-d1-receptors-in-collagen-induced-arthritis

Abstract Number: 147

Epigenetic and Transcriptomic Profiling of Primary Juvenile Idiopathic Arthritis Patient Cells: Better Understanding of Disease Pathogenesis

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SESSION INFORMATION
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Session Type: Abstract Submissions
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Background/Purpose:

For many autoimmune diseases, including Juvenile Idiopathic Arthritis (JIA), the molecular mechanisms remain elusive. JIA can be used as a model to study autoimmune disease as immune cells can be taken directly from the site of inflammation. To create a better insight into these mechanisms, we aimed to assess both the epigenetic and transcriptomic profile of JIA patient-derived cells. As both the CD4+T cells and monocytes are known to contribute to this disease ChIP-seq and RNA-seq were performed on both cell populations. We hypothesize that epigenetic and transcriptomic profiling can contribute to a better understanding of JIA pathogenesis, the identification of novel disease contributing cellular pathways and possibly new therapeutic targets.

Methods:

CD4+CD45RO+ T cells and CD14+ monocytes were FACS sorted from the blood of healthy controls and the blood and synovial fluid of five oligo JIA patients. Transcriptomic analysis was performed on both cell types using RNA-sequencing. To identify active enhancers ChIP-sequencing was performed for H3K27Ac, a marker associated with higher transcription.

Results:

Analysis of the active enhancer profile (ChIP-seq) of JIA patient cells demonstrated thousands of disease-associated differences, which corresponded to disease-associated gene expression (RNA-seq). Strikingly, arthritis-associated SNPs were significantly enriched in JIA enhancers, illustrating the importance of these non-coding regions for disease pathogenesis. Presently, we are genetically manipulating the top twenty of the target genes that we identified to further assess their role in JIA.

Conclusion:

These results demonstrate that active enhancers directly contribute to disease-associated gene expression, and identified many genes that could contribute to disease pathogenesis. Our data might provide novel therapeutic targets for the treatment of JIA.

Disclosure: L. Picavet, None; **J. Peeters**, None; **S. Coenen**, None; **A. Boltjes**, None; **F. van Wijk**, None; **P. Coffer**, None; **B. Vastert**, None; **J. van Loosdregt**, None.

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Abstract Number: 148

Oral Microbial Profile in Juvenile Idiopathic Arthritis

Sriharsha Grevich[1,2], Peggy Lee[3], Jeffrey McLean[3], Brian Leroux[3], Sarah Ringold[1,2], Kyle Hager[4], Mitchell Brittnacher[4], Hillary Hayden[4], Samuel Miller[4] and Anne Stevens[1,2,5], [1]University of Washington, Department of

Pediatrics, Seattle, WA, [2]Seattle Children's Hospital, Seattle, WA, [3]University of Washington, School of Dentistry, Seattle, WA, [4]University of Washington, Department of Microbiology, Seattle, WA, [5]Center for Immunity and Immunotherapies, Seattle Children's Research Institute, Seattle, WA

SESSION INFORMATION

Session Date: Thursday, May 18, 2017

Session Title: Genetics and Pathogenesis Poster Session

Session Type: Abstract Submissions

Session Time: 5:30PM-7:00PM

Background/Purpose:

Microbial communities in the mouth have been associated with the chronic inflammation of periodontitis and rheumatoid arthritis (RA), and there is higher prevalence of periodontitis in RA. Although periodontitis is rare in children, severe gingivitis, a chronic inflammatory precursor to periodontitis, is quite prevalent. We have found that children with juvenile idiopathic arthritis (JIA) have increased bleeding on probing, a marker of gingival inflammation, compared to controls. For this study, we hypothesize that kids with JIA have an altered microbiota presenting a link between gingivitis and JIA.

Methods:

Plaque samples were collected by dentists from 22 patients with JIA between the ages of 11 to 18 years who satisfied the International League of Association for Rheumatology (ILAR) classification criteria and 10 healthy adolescent controls. The JIA cohort included children with polyarticular JIA (8), oligoarticular JIA (10), and extended oligoarticular JIA (4). Samples were obtained by inserting a sterile endodontic paper point into the pockets or sulci of 6 teeth in each subject. Total genomic DNA was extracted from paper points containing oral plaque and amplicon libraries of the 16S rRNA gene were generated. Sequencing was performed on the Illumina MiSeq according to the manufacture's guidelines. Qiime (Quantitative Insights Into Microbial Ecology) software was used for microbial analysis of the raw sequencing data. For core diversity analysis, only samples with ≥2700 bp sequences were used. Diversity analysis was performed based on operational taxonomic units (open references using 20 sequences to OTU and clustering using 97% similarity in OTUs). A principle coordinate analysis plot was created using weighted unifrac distance between samples.

Results:

Higher microbial diversity (using rarefraction measure of observed OTUs) was observed in the JIA popuation compared to the healthy controls. Principle coordinate analysis showed the JIA cohorts clustering apart from the healthy controls, indicating that there is a potential difference in the oral microbial profile between the two groups. On further analysis, distinct operational taxonomic units classified as periopathogens were found to be enriched in the JIA cohort.

Conclusion:

This small study suggests that the dental plaque microbiota is distinct in JIA patients compared to healthy controls. Periodontal bacteria such as Prevotella and Porphyromonas have been suggested to play a pathogenic role in RA. In our study we found periopathogens to be higher in the JIA cohort, further supporting our prior finding of increased gingival inflammation in JIA and suggesting a possible mechanistic link between JIA and gingivitis.

Disclosure: S. Grevich, None; **P. Lee**, None; **J. McLean**, None; **B. Leroux**, None; **S. Ringold**, None; **K. Hager**, None; **M. Brittnacher**, None; **H. Hayden**, None; **S. Miller**, None; **A. Stevens**, 2,7.

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Abstract Number: 149

Deficiency of Complement C4A or Low Copy Number of Total C4 Genes,

HLA-DRB1*15 and HLA-DRB1*03 Are Strong Genetic Risk Factors for Pediatric SLE of European Descent

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Background/Purpose: A complete genetic deficiency of complement C4 almost always leads to the pathogenesis of systemic lupus erythematosus (SLE) with childhood onset, although its prevalence is extremely low. On the other hand, low gene copy number (GCN) of total C4 and genetic deficiency of C4A occur between 33 and 40% in adult SLE (aSLE) of European ancestry. Located centromeric to C4 on chromosome 6 is another SLE risk factor, specific alleles of HLA-DRB1. The objective of this study is to determine the effects of complement C4 gene copy number variations, C4A deficiency and HLA-DRB1 variants on the risk of pediatric SLE (pSLE).

Methods: Pediatric SLE patients and control subjects were recruited from Ohio and Atlanta, which included 105 Caucasian patients and 937 race-matched healthy subjects. The female to male ratio of pSLE was 5.7 to 1. GCNs of total C4, C4A, C4B, long and short C4 genes were determined by genomic Southern blot analyses, and/or TaqMan-based, quantitative realtime PCR using five amplicons. HLA-DRB1 variants were determined by 20 sets of specific PCR, and gel electrophoresis. Published data from 373 White aSLE were used for comparison.

Results: The copy number of total C4 genes varies from 2 to 8 copies in a diploid genome. Each of those C4 genes may code for an acidic C4A or a basic C4B protein. Low GCN of total C4 (C4T≤3) was present in 45.7% of pSLE, 42.9% of aSLE and 28.4% of healthy controls. The odds ratios and 95% confidence interval for C4T≤3 was 2.1 (1.4-3.2) in pSLE ($p=0.0004$), and 1.9 (1.5-2.5) in aSLE ($p=4.4\times10^{-7}$). Homozygous and heterozygous deficiency of C4A (C4A≤1) occurred in 39.8% of pSLE, 32.7% of aSLE, and 18.6% of healthy controls. The odds ratios for C4A deficiency were 2.9 (1.6-4.9) in pSLE ($p=2.6\times10^{-6}$), and 2.1 (1.6-2.8) in aSLE ($p=9.9\times10^{-8}$). HLA-DRB1*15 (DR2) has a frequency of 45.7% in pSLE, 31.7% in aSLE and 27.9% in controls. The odds ratios of DRB1*15 were 2.2 (1.2-4.0) for pSLE ($p=0.015$), but only 1.2 (0.89-1.6) for aSLE ($p=0.23$). Another DRB1 allele *03 (DR3) had similar frequencies in pSLE (37.0%) and aSLE (38.6%), but a significantly lower frequency in controls (26.7%). Subjects with a homozygosity of C4A deficiency, or HLA-DRB1*15, or HLA-DRB1*03 together are present in 6.0% of healthy controls, but 26.7% of pSLE [OR=5.7 (2.7-12.2), $p=4\times10^{-5}$] and 15.9% of aSLE [OR=3.0 (1.9-4.70), $p=2.5\times10^{-6}$].

Conclusion: C4A deficiency and low GCN of total C4 are significant risk factors for pediatric and adult SLE of European

ancestry, but their effect sizes are consistently larger for pSLE. HLA-DRB1*15 plays an important role on the risk of pSLE. C4A deficiency, HLA-DRB1*15 and HLA-DRB1*03 have strong effects on conferring high risk of pSLE.

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Childhood-onset Takayasu Arteritis Associated with Mutations in CBL

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Background/Purpose: Takayasu arteritis (TA) is an inflammatory large-vessel vasculitis of unknown etiology that rarely presents in childhood. No monogenic etiologies of TA have been identified.

Methods: We identified two unrelated cases of TA developing in children with Noonan-like syndrome and juvenile myelomonocytic leukemia (JMML) due to germline mutations in the *CBL* gene. We performed flow cytometry studies to assess T cell phenotype and function in one patient.

Results: Both patients were female. Patient 1 presented with massive splenomegaly and thrombocytopenia, being diagnosed with JMML at 1.5 years of age. She had delayed growth, developmental delay, optic atrophy, cardiomyopathy, hypertension, and was diagnosed with TA at 9 years of age. Angiography revealed severe stenoses of descending aorta and major branches. She underwent stenting of major arteries but died 9 months after diagnosis of TA. Genotyping showed a homozygous p.384C>R mutation in the *CBL* gene in granulocytes. Patient 2 had delayed growth, mild developmental delay, and congenital heart disease (atrial septal defect, patent ductus arteriosus, pulmonary stenosis). She was admitted at 14 months of age with massive splenomegaly, mild lymphadenopathy, bicytopenia, and fever. Extensive diagnostic studies showed normal bone marrow and liver biopsies, negative infectious disease work-up, hypergammaglobulinemia, and moderate T cell lymphopenia. She had mild positive anticardiolipin IgM antibodies, low C3 and C4, but negative ANA and ANCA. Lymph node biopsy showed interfollicular histiocytosis, but no malignancy or other specific diagnoses. Contrast-enhanced MRI revealed thickening of the thoracic aorta, suprarenal abdominal aorta, and proximal third of the celiac trunk and superior mesenteric artery, all of which had T2-hyperintensity and progressive contrast enhancement. PET-CT showed increased 18-F FDG uptake in the common carotid arteries, thoracic and abdominal aorta, celiac trunk, and superior

mesenteric artery. Whole exome sequencing revealed a p.396C>R mutation in the *CBL* gene of 88% of reads from blood DNA suggesting loss of heterozygosity of a germline mutation. The father is a heterozygote for this mutation. PHA-induced CD4+ T cell proliferation and PMA/Ionomycin-induced expansion of Th17 cells were increased in the patient compared to normal controls. Regulatory T cells and double-negative T cells were normal. The patient was started on prednisone and azathioprine and is currently in good state of health.

Conclusion: The E3 ligase CBL inhibits angiogenesis and cytokine and T cell receptor signaling. This negative regulation is lost in the case of germline loss-of-function *CBL* mutations and consecutive loss of heterozygosity, thereby resulting in JMML and autoimmunity. *CBL* mutations are associated with the development of childhood-onset TA, possibly mediated by increased T cell responses and Th17 cell expansion.

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Abstract Number: 151

Severe Phenotype of Mevalonate-kinase Deficiency in the Czech Republic

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Background/Purpose: Disease phenotype of mevalonate-kinase (MVK) deficiency (MKD) varies in relation to the extent of enzymatic activity reduction. It ranges from multi-organ involvement with fatal outcome in mevalonic aciduria to variably severe periodic fever of hyper-IgD syndrome (HIDS). Since the establishment of our fever clinic in 2004 eight patients were diagnosed with HIDS. In 5 out of them clinical course was severe enough to require biologic therapy. Such a disease severity in our cohort lead us to search for additional patients followed at other institutions in order to learn about potential specific disease features in the Czech population.

Methods: Only one specialized laboratory in the country provides urine MVA measurement and since 2012 also MVK gene analysis. All patients with positive MVA detected between Jan 2004 and Dec 2016 and/or those with 2 MVK gene mutations were retrieved and their electronic records reviewed by treating physicians.

Results: : Five patients from 2 other institutions were identified on top of the original 8 cases (11 females), all Caucasians.

Only patients with MKD phenotype and/or confirmed MVK mutations had positive urine MVA. Median age at onset was 15 (1-36) months, diagnostic delay was 8.2 (1-25.5) years. (Table) Gastrointestinal and joint symptoms were present in 54 and 62% of cases, respectively, 7 patients (54%) had cervical lymphadenopathy and 5 (38%) splenomegaly. "Severe" symptoms that lead to the introduction of biologics in 7 patients included high episode frequency interfering with daily activities (n=6), splenomegaly (n=3) and renal amyloidosis with onset at 5 years of age (n=1, patient 6). Patient 12 died in early infancy with the picture of fulminant HLH. When her younger sister presented with similar symptoms at 3 weeks of age she rapidly received HSCT for suspected unknown primary HLH. Only after her recovery results of the WES became available and confirmed MKD, which was then found also in her sister's stored DNA. Patient 5 had nearly complete resolution of symptoms without therapy during her uneventful pregnancy and gave birth to healthy twins. Her disease returned post-delivery in full severity and her treatment response remains unsatisfactory.

Conclusion: : Over the past 12 years 13 Czech patients were diagnosed with MKD. The genotype spectrum was similar to that reported with the p.V377I mutation being the most prevalent. Unlike other series, high proportion of patients (n=9, 69%) had severe or life-threatening phenotype requiring biologic therapy or HSCT. We learned that macrophage activation triggered by MKD may mimic primary HLH in neonatal period and that amyloidosis may complicate untreated MKD very early. Similarities with the more common and benign PFAPA syndrome have lead us to screen all suspected PFAPA patients for urine MVA.

Patient No.	Age at onset (months)	Diagnostic delay (years)	Episode duration (days)	Episode frequency prior to therapy (weeks)	Mutations	Severe symptoms	Therapy	Response to most recent therapy	Urine MVA (mg/g Cr)	IgD (U/ml) Reference range 0-100	IgA (g/l)
1	36	10	5	4-12	p.V337I + del	-	episodic CS	lost to F/U	7	939	3,4
2	11	7	3	4	p.V337I + p.R40L	episode frequency, GI, arthritis	enanercept	complete	7	28	4,6
3	12	7	5-7	2-4	p.V377I + del	episode frequency, GI, failure to thrive, hepatosplenomegaly, arthritis, vasculitis	CS, etanercept, anakinra, canakinumab	complete	10	418	3,2
4	4	15,6	6-7	3	p.V377I + p.R40L	episode frequency, splenomegaly, stroke, arthritis	anakinra	nearly complete	2	439	2,6
5	6	25,5	5	2	p.V377I + p.Y116H	episode frequency, aphtous stomatitis, arthralgia, arthritis	episodic CS, etanercept anakinra	partial	2	439	2,8
6	10	3,6	2-4	2-12	p.V377I + del	GI, arthritis, renal amyloidosis	colchicin, anakinra	partial	3	30,6	3,3
7	24	6	3	2-4 W	p.V377I + p.E93fs	-	episodic CS	satisfactory	10	36	4,8
8	12	1	2-3	1-12	p.V377I + p.E93fs	episode frequency, rash, splenomegaly, lymphadenopathy	etanercept, anakinra	nearly complete	13	NA	5,03
9	10	4,3	6	8	pending	-	episodic CS	NA	2	136	1,7
10	36	2	2-3	2-4	p.V377I + p.L29P	episode frequency, GI, arthralgia, rash, aphthous stomatitis	colchicin, CS, episodic anakinra	nearly complete	NA	NA	NA
11	6	NA	3-6	2	Netherlands*	-	episodic CS	lost to F/U	NA	NA	NA
12	1	-	-	-	p.R40L + p.R40L	hepatopathy, MAS, multiorgan involvement, death	-	death	127	NA	NA
13	1	-	-	-	p.R40L + p.R40L	hepatosplenomegaly, MAS, aphthous stomatitis, rash	HSCT	complete	NA	NA	NA

GI- gastrointestinal symptoms (abdominal pain, vomiting, diarrhea; CS – corticosteroids; HSCT- alogeneic hematopoietic stem cell transplantation; NA - not available; MAS - macrophage activation syndrome; *The first historical patient from other hospital with genetic analysis performed in Netherlands, complete report missing

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Characteristics of Patients With Juvenile Idiopathic Arthritis in a US Healthcare Claims Database

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Background/Purpose: Abatacept, the first selective co-stimulation modulator approved and used for the treatment of juvenile idiopathic arthritis (JIA), has a mechanism of action that is fundamentally different from that of other biologic (b)DMARDs. The purpose of this study was to describe the baseline characteristics of patients with a diagnosis of JIA in a US healthcare claims (HCC) database treated with abatacept and those treated with other bDMARDs.

Methods: Patients <18 years of age and diagnosed with JIA in the Truven Health MarketScan® database between July 1 2006 and September 30 2014 were eligible for inclusion in the analysis. Patients were required to have at least 180 days of continuous health plan enrollment prior to, and ≥1 day following, a diagnosis of JIA based on two International Classification of Diseases, Ninth Revision, Clinical Modification codes (714.3x) within 90 days. The abatacept cohort includes patients initiating abatacept or another bDMARD who may be initiating a biologic for the first time or switching from one biologic to another. Baseline characteristics including at least 15 co-morbid conditions and concomitant medications were captured within the 6-month period prior to the diagnosis of JIA. **Results:** A total of 13,602 patients with a diagnosis of JIA were identified in the US HCC database, with an average follow-up of 2.26 years (maximum 8.26 years); 343 abatacept users and 3507 users of other bDMARDs were identified. Overall, abatacept users were slightly older and more likely to have asthma and hypertension; other bDMARDs users were more likely to have uveitis reported in the 6-month baseline period. Corticosteroid use and outpatient visits were also higher in abatacept users.

	JIA patients N=13,602 n (%)	Abatacept-treated patients n=343 n (%)	Other biologic-treated patients n=3507 n (%)
Female, n (%)	9679 (71.2)	284 (82.8)***	2563 (73.1)
Age, mean (SD)	10.4 (4.6)	12.0 (3.8)	11.2 (4.4)
Asthma, n (%)	873 (6.4)	28 (8.2)*	187 (5.3)
Cardiovascular disease, n (%)	618 (4.5)	24 (7.0)	171 (4.9)
Hypertension, n (%)	83 (0.6)	8 (2.3)*	27 (0.8)
Uveitis, n (%)	1302 (9.6)	32 (9.3)	467 (13.3)*
Biologic DMARDs, n (%)	1732 (12.7)	168 (49.0)	1564 (44.6)
Non-biologic DMARDs, n (%)†	3321 (24.4)	156 (45.5)	1548 (44.1)
MTX, n (%)	2798 (20.6)	125 (36.4)	1382 (39.4)
IV antibiotics, n (%)	366 (2.7)	11 (3.2)	100 (2.9)
Corticosteroids, n (%)‡	1789 (13.2)	93 (27.1)**	731 (20.8)
NSAIDs, n (%)	5151 (37.9)	145 (42.3)	1551 (44.2)
Inpatient visits, mean (SD)	0.08 (0.36)	0.10 (0.45)	0.09 (0.38)
Outpatient visits, mean (SD)	8.70 (7.81)	11.66 (10.41)***	9.60 (8.54)

*p<0.05; **p<0.01; ***p≤0.0001 for the difference between abatacept-treated

patients and other biologic-treated patients. †Non-biologic DMARDs included

hydroxychloroquine, sulfasalazine, leflunomide, and cyclosporine;

‡Corticosteroids consist of prednisolone, methylprednisolone,

triamcinolone, prednisone, dexamethasone, budesonide, and

betamethasone

Conclusion: In this analysis, patients with JIA who were treated with abatacept were older and more likely to have asthma and hypertension than patients treated with other bDMARDs. The patients with JIA treated with abatacept in this US HCC database were slightly younger, with less uveitis at baseline, compared with a population of abatacept-treated patients in a worldwide JIA registry (mean age 13 years and 15% history of uveitis).[1,2]

References:

1. Lovell DJ, et al. *ACR/ARHP Annual Scientific Meeting*, 2015. Poster 1446. 2. *Abstract reprinted from the PreS 2016 Annual Meeting held September 27–October 1, 2016. The* Paediatric Rheumatology European Society *does not guarantee, warrant, or endorse any commercial products or services. Reprinted by Bristol-Myers Squibb.*

Disclosure: T. Simon, 1,3; **A. Baheti**, 5; **N. Ray**, 5; **S. Kelly**, 1,3; **Z. Guo**, 1,3.

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Training pediatric rheumatology fellows intra-articular injection techniques and skills using a cadaver based musculoskeletal curriculum

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Background/Purpose: Intra-articular injections are important to treat children with arthritis. Practice differences, comfort levels, and reimbursement can decrease fellow exposure to this skill. The purpose of this study is to develop a curriculum for intra-articular injections which increases pediatric rheumatology fellows' comfort and proficiency.

Methods: : At Texas Children's Hospital, a cadaver workshop was implemented in July 2016 to teach joint injection techniques to pediatric rheumatology trainees. Six pediatric rheumatology fellows participated. A tutorial on anatomy and technique was given by a faculty member or senior fellow. Fellows practiced injecting large and small joints with immediate feedback. Ultrasound was used to define landmarks and evaluate proper needle placement. Pre and post surveys assessing comfort level of performing intra-articular injections were administered. A six month follow up survey was given to reassess comfort in performing joint injections.

Results: The pre-survey showed that prior to participating in the workshop, comfort with joint injections ranged from "Nervous, but able to take it on" to "comfortable". Mode was "comfortable" with four participants. The post-survey showed comfort ranged from "nervous but able to take it on" to "comfortable". The mode was "comfortable" from five participants showing an overall increased comfort level. At 6 month follow up, comfort ranged from "nervous, but able to take it on" to "comfortable" with a mode of "comfortable" with 4 participants. Three trainees attempted injecting new sites not previously tried subsequent to the workshop. Each of them felt "nervous but able to take it on". Trainees felt the workshop was a favorable experience. Comments were "this was very helpful, good, no pressure environment to review/point out landmarks and technique, learned common pitfalls", "definitely more comfortable after today", and "became more comfortable with the approach and actual procedure". Five trainees wanted review material prior to the workshop.

Conclusion: Post workshop surveys showed improvement in comfort level. At 6-month follow up the comfort level was identical to the pre-cadaver workshop survey. This could reflect insufficient practice with live patients. Only 3 fellows performed untried joint injections after the workshop. Trainee comments were favorable. They appreciated the lower stress environment, practicing various approaches to joint injection and reviewing anatomy. Joint injections are a key therapy for children with arthritis. It is important to give trainees opportunities to improve their proficiency. Hands on workshops can provide practice for injections. This is necessary in the era of biologics, as fewer injections are performed. There is no published curriculum for teaching joint injections on cadavers. Our ultimate goal is to create a multi-modal curriculum incorporating simulation lab, cadaver workshop, and ultrasound education for proficiency in intra-articular injection training. This could be generalized for other pediatric programs, as well as adult rheumatology programs, or other specialties.

Disclosure: B. Goldberg, None; **A. Brown**, None; **M. Marcus**, None.

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"Celebrate Ability": Structured Art Workshop as a Therapeutic Coping Strategy for Patients with Juvenile Idiopathic Arthritis

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Background/Purpose: Juvenile Idiopathic Arthritis (JIA) affects nearly 20,000 Canadian children. Despite success with medications, managing "invisible" symptoms such as pain and fatigue and psychosocial limitations such as restricted participation in extracurricular activities remain challenging. Our objectives were to 1) create a Standardized Art Program to assess potential psychosocial benefits in JIA patients and to 2) engage the local Hospital, University and general community through the workshops.

Methods: A prospective cohort of children with JIA (ages 8-18 years) was referred to the Art and Arthritis Workshop from local pediatric rheumatology clinic. Full day (7 hour) workshops were led by established artists from the local and extended community on various techniques (painting, sculpting, and journaling). The principle behind the workshops was to focus on children's abilities. A reproducible standardized structure included: a focused theme for a session, demonstration by the leading artist on technique and individual guidance for each participant. Community engagement involved volunteers from the local University's Faculty of Art, hospital staff and parents/siblings of JIA patients, and a journalist. Pre-workshop psychosocial health was assessed by the Pediatric Quality of Life Inventory Communication and Worry subsections (PedsQL 3.0 Arthritis Module, a standardized instrument; best score 100, range 0-100). Anonymous participant evaluations were provided at the end of each workshop on workshop quality, location, time, and "favourite part".

Results: Eight workshops were held from January 2014 to November 2016. Twenty-eight individual participants (7M:21F) (8-12 per session) attended at least one workshop, with 84 participants in total. Mean [median] time from JIA diagnosis to first workshop was 51.4 [48] months (range=0-146 months). The mean pre-project PedsQL subscore for Worry was 82/100 (range 8-100) and for Communication 68/100 (range 0-100). Six parents, 5 siblings, 2 art graduates and several hospital staff volunteered for at least one workshop. The art workshops were featured in local and University newspapers and on Youtube. Post-work shop evaluations were provided by 64/84 participants (76%): 100% (64/64) of participants enjoyed the workshops and 98% (63/64) the location, 92% (58/63) reported time was convenient, and 95% (61/64) indicated intention to attend a future workshop. As "favorite part", participants responded: 'seeing my painting come to life'; 'learning how artistic I can be'; 'good time for relaxation'; 'the wonderful freedom of [the artwork]' and 'meeting kids my age with arthritis'.

Conclusion: We implemented a structured Art Program for children with JIA that involved artists from the local and extended community and volunteers. While limitations in "communication" and "worry" on PedsQL were identified pre-workshop, art creation allowed the patients to communicate in a non-verbal way and discover new strengths (art skills, engagement with peers). Our results suggest that such a Program can be a useful tool for patients coping with the burden of

chronic illness while improving community engagement and disease awareness.

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View Abstract and Citation Information Online - http://acrabstracts.org/abstract/celebrate-ability-structured-art-workshop-as-a-therapeutic-coping-strategy-for-patients-with-juvenile-idiopathic-arthritis

Abstract Number: 155

A Single Center Review of Health Related Quality of Life in Children with Systemic Lupus Erythematosus Using the Pediatric Quality of Life Inventory Version 4.0 Generic Core Scale

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SESSION INFORMATION

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Background/Purpose:

Systemic lupus erythematosus (SLE) can cause adverse effects in various aspects of daily functioning for pediatric patients. Measuring Health-related Quality of Life (HRQOL) provides additional yet critical information and data for provision of best care, and assists to define additional resources and interventions. The Pediatric Quality of Life Inventory Version 4.0 (PedsQL 4.0) Generic Core Scale is a measure used to examine HRQOL and encompasses physical, emotional, social and school functioning of patients and identifies functional areas of concerns. The PedsQL 4.0 is used to measure HRQOL in both healthy and chronically ill children.

Methods:

The PedsQL 4.0 child self-report survey was administered to pediatric patients (aged 8-18) diagnosed with SLE in a large children's hospital system over a 2 year period during outpatient clinical visits. The survey was given in both English and Spanish. Average scores were reviewed for each functional area as well as total averages. Patients received follow up surveys 3-12 months following their initial survey. Responses (ranging from 0-100) were scored by taking the average of each functional area, and a total scale score derived from the average of the combined functional area items. Higher scores indicated greater HRQOL.

Results:

The initial PedsQL 4.0 was completed by 48 pediatric SLE patients, of which 81% were female. The ethnic makeup of patients was: 88% White Hispanic, 8% White Non-Hispanic, 35% Black or African American Non-Hispanic with a median age of 13.81±2.45. One standard deviation below the mean (71.72-14.1) was identified as a cut-off point to identify patients at-risk of impaired HRQOL [1], resulting in a cut-off point score of 57.62. School was the functional area reported

as most problematic on the initial survey (61.67), with social functioning reported as least problematic (88.23). Follow up surveys were completed by 38 patients during this 2 year review. At follow up, the average of the self-reported school scores was 66.4, meeting the criteria of a 4.4 point score change for minimum clinically important difference established in the literature [1]. Total scale score rose 8.76 points to 80.48 indicating improved HRQOL for SLE patients overall.

Conclusion:

Measuring HRQOL through the administration of the PedsQL 4.0 provides clinicians with further information regarding patient functioning over the course of disease. This allows greater focus on areas patients are reporting as being negatively impacted by their disease. For pediatric SLE patients at Texas Children's Hospital this tool demonstrated improved HRQOL over a 1 year period.

1. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. Ambul Pediatr 2003; 3: 329–41.

Disclosure: J. Rogers, None; **A. C. P. Sagcal-Gironella**, None; **P. Rosillo**, None; **A. A. Ramirez**, None; **R. Banuelos**, None; **M. M. de Guzman**, None.

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Abstract Number: 156

Teaching High Value Musculoskeletal Care Through Online Simulation Cases

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Background/Purpose: Musculoskeletal (MSK) complaints comprise 6-15% of general pediatric visits.[1,2] Many MSK complaints can be diagnosed through simple history and physical with limited laboratory and imaging workup. With rapidly rising healthcare costs, there is an increased emphasis placed on high value care in graduate medical education. Our purpose was to create online MSK simulation cases to teach high value care and diagnostic evaluation of MSK complaints.

Methods: Five simulation cases of pediatric MSK complaints were developed for general pediatric residents, with online learner input allowing tracking of tests utilized to arrive at diagnosis, cost of workup, and the final diagnosis. An anonymous post-simulation survey was given to all subjects. All subjects received online feedback on the correct diagnosis and appropriate workup after each simulated case. Measured outcomes were presumed diagnosis, cost of evaluation, diagnostic testing utilized, and perceptions towards the learning platform and high value care. Simulation outcomes were assessed using Chi Square tests and survey data was assessed utilizing Wilcoxon sign-rank testing.

Results: 29 residents participated in the pilot and 27 completed the survey. Overall, only 46% of simulations were diagnosed correctly, and in 33% of cases, an antinuclear antibody was ordered unnecessarily. There was no difference in the frequency of correct diagnosis or cost of workup depending on order of case presentation: 93.3% and $103.67 versus 76.92% and $39.62 for a case of growing pains ($p = 0.22$ and 0.06), 42.9% and $244.29 versus 73.3% and $305.67 for a

case of leukemia with leg pain (p=0.10 and 0.47). Arrival at the correct diagnosis was not associated with a difference in the cost of workup of any of the 5 cases. 25/27 (93%) of learners ranked factoring cost into evaluation as somewhat important or very important. 23/27 learners reported feeling more comfortable post-simulation with their knowledge of costs of common diagnostic tools ($p < 0.0001$).

Conclusion: Regardless of the order of presentation of the cases, there was no increase in the correctness of diagnosis or decrease in the amount spent on workup. Secondly, correctness of diagnosis was not associated with cost of workup. Subjects expressed increased knowledge of costs and recognized high value care as an important component of patient care after the simulation. Further studies are warranted with a greater diversity of cases and larger study groups.

References:

1 deInocencio, J. Musculoskeletal pain in primary pediatric care: analysis of 1000 consecutive general pediatric clinic visits. Pediatrics 1998; 102(6): e63.

2 Vital and Health Statistics. Patient's reasons for visiting physicians: National ambulatory medical care survey, US 1977–78. DHHS publication 82-1717. Hyattsville, MD: National Center for Health Statistics; 1981

Disclosure: N. D. Patel, None; **M. Buchner**, None; **A. B. Robinson**, None.

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Utility of Mailed Reminders for Uveitis Screening Guidelines in Patients with Juvenile Idiopathic Arthritis

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Background/Purpose: Uveitis is a major complication in patients with juvenile idiopathic arthritis (JIA) and can be completely asymptomatic until vision loss develops. In order to prevent ocular complications, it is important to adhere to the recommended screening guidelines which range from every 3 to 12 months depending on JIA subtype, age of onset, duration since diagnosis and ANA status. A previous study within our institution found that barriers to uveitis screening in patients with JIA include difficulty with scheduling appointments and poor knowledge of the screening guidelines. The specific aim of this study was to assess the utility of a mailed reminder letter to patients.

Methods: Patients at Nationwide Children's Hospital with JIA who were behind on their screening eye exams were identified through the PR-COIN registry. A reminder letter with information about uveitis and the patient's specific uveitis screening guidelines was mailed to the patient's address listed in the EMR. The guardians of those patients or the patients if over 18 years of age receiving letters were called one to two months after the letter was sent and a semi-structured interview was completed. The interview included questions regarding the letter, previous information the family had received about uveitis and ways the family would like to receive reminder notifications in the future.

Results: 44 patients were identified as non-adherent with the screening guidelines. 24 guardians of these patients or patients older than 18 years old were interviewed. 6 of the interviewees (25%) were able to recall receiving the letter in the mail and 4 of these 6 stated that they had read the letter. Of the 4 participants who had read the letter, 2 had been seen

by ophthalmology at the time of the phone interview. Despite the low number of patients who remembered receiving the letter, 10 of the 24 interviewed indicated that mail would be the best way to communicate with them. Only 2 of the guardians interviewed (8%) did not know their child's recommended uveitis screening frequency. Families identified a variety of methods for future communication including mail, email, text message and messages through an online patient portal.

Conclusion: This qualitative study identified that a small percentage of families recalled receiving a mailed reminder regarding uveitis screening. Some of the families that stated they preferred mail for communication could not recall receiving the reminder letter. Other families identified other preferred methods for communication. Knowledge was less of a barrier than in our previous study. These results will be helpful in developing future tools for sending information and reminders to patients and their families.

Disclosure: L. Ballenger, None; **K. Driest**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/utility-of-mailed-reminders-for-uveitis-screening-guidelines-in-patients-with-juvenile-idiopathic-arthritis

Abstract Number: 158

Quality of Referral Letters to Pediatric Rheumatology and Its Impact on Access to Care

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Background/Purpose:

Delays in access to care in pediatric rheumatology (PR) are well known and may lead to significant morbidity. While barriers in accessing PR care are multifactorial, the literature suggests that incomplete referral letters may contribute to delays in subspecialist assessment. This study aims to describe the content of referral letters to PR at a tertiary care pediatric center, the impact of incomplete referral letters on time to PR assessment, and the proportion of referrals that resulted in a rheumatic diagnosis, all of which have yet to be described.

Methods:

All new referral letters to PR at our centre over an 8-month period were prospectively evaluated during weekly patient triage by 3 PR physicians. Using a validated referrals' checklist, letters were reviewed for 8 components of a high-quality referral as outlined by hospital policy: rheumatic diagnosis of concern; patient symptoms; investigations; physical examination (musculoskeletal and general); co-morbidities; current and past management; and medications. Referrals for patients >17 years old or previously followed by PR were excluded. Basic patient demographics and referring physician specialty were also collected.

Dates of triage decisions and resultant times to PR visits were recorded. Where incomplete referrals required additional information from referring physicians, we documented when this information was received and the resultant delay in triage time. Final diagnoses were recorded in retrospect.

Results:

Referrals (n=179, 63% female, median age 11.5 years) were received and analyzed from: family doctors (44%); pediatric providers, including subspecialists (43%); and others, e.g., pediatric ENT (13%). The frequency of specific components included in referral letters were: patient symptoms (94%); investigations (65%); diagnosis of concern (57%); medications (48%); musculoskeletal examination (46%); current and past management (41%); co-morbidities (34%); and general examination (27%).

Further information was requested from 33/179 (18%) referral letters regarding one or more of the following components: physical examination (91%); pertinent history (91%); diagnosis of concern (76%); and investigations (36%). Where missing information was requested, the median delay in time to triage was 1.3 weeks (IQR 0.1 – 2.3).

A final diagnosis was documented in 153 referrals, of which 53% had a confirmed rheumatic disease. The proportion of referrals resulting in a rheumatic diagnosis by provider was: 55% of those from pediatric providers; 51% from family doctors, and 52% from others. Referring physician specialty had no significant effect on the likelihood of a referral resulting in a rheumatic diagnosis.

Conclusion:

Pertinent history and physical examination were the most commonly omitted or inadequately described components of referral letters to PR. Requesting missing information resulted in delayed triage. Only about half of PR referrals from all referring physicians resulted in a rheumatic diagnosis. These findings can help guide medical education initiatives for referring physicians in their understanding of PR disease and facilitating access to timely PR care.

Disclosure: A. Rydz, 2; **F. Fu**, None; **M. Drew**, None; **D. Rumsey**, None; **Y. Yuan**, None; **M. Chan**, None.

View Abstract and Citation Information Online - http://acrabstracts.org/abstract/quality-of-referral-letters-to-pediatric-rheumatology-and-its-impact-on-access-to-care

Abstract Number: 159

Preferences and Satisfaction in a Pediatric Multi-specialty Infusion Center

Catherine McDermott &[1], Brian Sohl[1], Lisa M. McGregor[2], Lisabeth V. Scalzi[3] and Barbara E. Ostrov (does not meet authorship criteria)[4,5], [1]Penn State Hershey Medical Center, Hershey, PA, [2]Penn State Hershey Children's Hospital, Hershey, PA, [3]Department of Rheumatology, Penn State Hershey Children's Hospital, Hershey, PA, [4]Pediatrics, Penn State Hershey Medical Center, Hershey, PA, [5]Pediatrics, Penn State Hershey Children's Hospital, Hershey, PA

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Background/Purpose:

Many pediatric rheumatology patients receive infusions in multi-specialty infusion centers (MSICs). There is little data about pediatric patient satisfaction and preferences within MSICs and no data about their physicians' perceptions of these preferences. In order to better understand and improve the patient experience, we studied these concepts.

Methods:

We created and administered a survey containing free response and 5-point Likert scale questions to parents of children receiving infusion therapy and their respective physicians at our center. We compared means and sums of the scores using

t-tests and ANOVA analyses.

Results:

We surveyed 21 physicians (8 oncologists, 13 non-oncologists) and 174 parents of patients with oncologic (n=66) and non-oncologic (n=108) diagnoses who were receiving infusions in our MSIC. Our results showed significant differences between family satisfaction/preference and physician perception (Fig 1).

For all 3 questions, families responded positively towards the multi-specialty nature of the infusion center, though oncology families to a lesser degree than non-oncology families (respectively, mean=4.5 ±0.07 vs. 4.8 ±0.05; $p<0.009$).

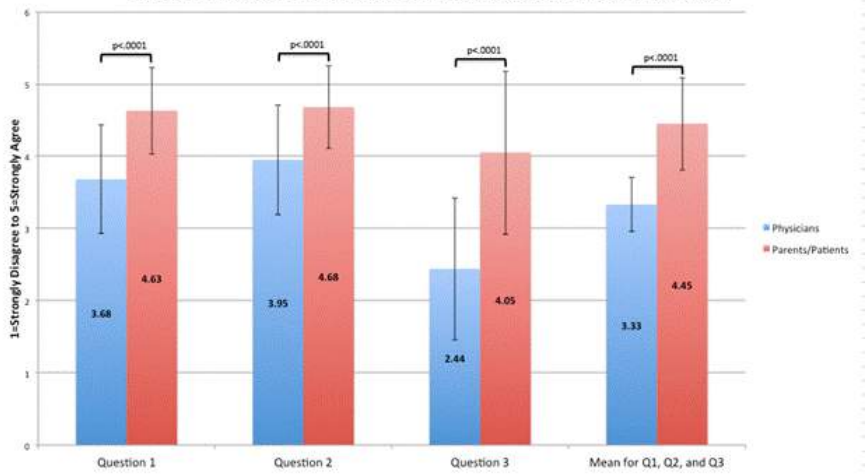
Rheumatologists had a greater discrepancy than oncologists did in their perceptions of their patients' preferences, predicting their patients would be less satisfied receiving care in an MSIC than patients reported (Fig 2). In addition, rheumatologists believed their patients would prefer to receive infusions in a center specific for children without cancer, despite families not having this preference (mean = 1.3 ± 0.58 vs. 2.7±0.90; $p<0.027$, respectively).

Lastly, the majority of families surveyed reported they had increased awareness and empathy from exposure to children with other diagnoses, reflected in their comments (Table 1).

Conclusion:

Pediatric rheumatology patients are satisfied with their experiences in an MSIC. Patients are significantly more satisfied than their physicians perceive. As infusion therapy for rheumatologic conditions increases, it is important to understand patient preferences as a crucial aspect of patient-centered care. Patients are content to receive infusions in an MSIC and find value in their experiences with families of children with other diagnoses.

Figure 1: Satisfaction and Preferences of Parents/Patients vs. Physicians' Perceptions



Question 1: My patients/I am content to have my child receive infusions in the same clinic as patients with/without cancer.

Question 2: My patients/I am content that the Penn State Children's Hospital Infusion Center treats children with a variety of diseases, both cancer and non-cancer related.

Question 3: My patients/I would not prefer my child to receive infusions in a center specifically for kids who have/do not have cancer.

Figure 2: Three Question Mean Score of Oncologists & Oncology Patients vs. Rheumatologists & Rheumatology Patients

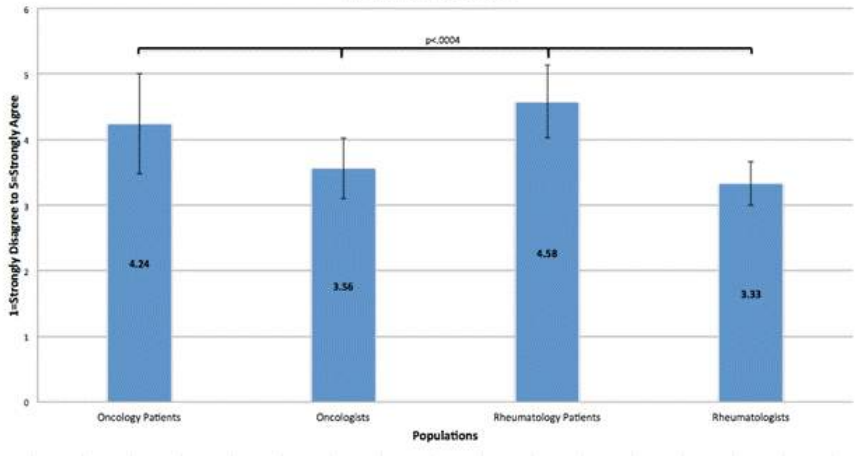


Table 1: Families find value in exposure received and connections made in a multi-specialty infusion center
"No one [illness] is 'harder' than another, I think being exposed to other 'issues' children are dealing with makes you a more educated person and also makes you appreciate what you have... [there] is always someone who is dealing with something that is harder..."
"I like the fact that this shows my daughter that there are many kiddos with differences, yet they're similar in that they like to play in the play area just like she does."
"Because some of these other diseases are some that we may have never heard of if we weren't in a situation like the clinic. And when you meet someone in this type of environment it makes you want to learn more..."
"[It] makes us more aware of how blessed we are to be where we are at"
"...to see other children with other diseases helps him understand that it's not only kids like him must endure treatment."
"Being around others with different diagnoses is almost like going to school. Awareness and learning of other diseases/treatments may one day link a cure."
"It was good to be able to show my son that there are children who have conditions/ diseases that have affected their lives far worse than his... he could have had it much worse."

Disclosure: C. McDermott &, None; **B. Sohl**, None; **L. M. McGregor**, None; **L. V. Scalzi**, None; **B. E. Ostrov (does not meet authorship criteria)**, None.

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Abstract Number: 160

Stepping Stones to Transition Smartly

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Background/Purpose:

Living with a rheumatic disease presents many challenges for adolescents. To help them meet these challenges and become healthy independent adults, teams need to foster an environment of comprehensive medical care which includes addressing transition. Transitioning adolescents to adult care is a complex process; which requires ongoing coordination and continuity of care. The Multidisciplinary team at a Midwest Rheumatology Center identified a need to develop a quality improvement initiative addressing transition to adult care to ensure a seamless transition for their patients.

Many childhood rheumatic conditions are lifelong; > 50% of youth with Juvenile Idiopathic Arthritis (JIA) will have active disease as adults, requiring complex aggressive therapies. National surveys show that adolescents, parents, and young adults are not prepared to meet the challenges essential for transitioning to adult health care. Often as a result of navigating the change to adult healthcare services unprepared the health care of the young adults is compromised. Data from surveys on transition shows that without education regarding transition young adults have declining health, less than optimal quality of care, resulting in increased health care costs. Prior to instituting a formal quality improvement transition program the staff found many adolescents were not prepared to transition as evidenced by missed adult appointments, poor adherence to medications, not calling for refills, and overall lack of knowledge on key issues needed for a successful transition to the adult health care environment.

Methods:

Using the Got Transition model the team developed a formal transition program, starting with drafting a transition policy. This policy outlined a comprehensive educational process for preparing adolescents and their parent's for the challenges in transitioning. All patients 16 years and older with a chronic rheumatic diagnosis were approached to participate. To begin they received a letter introducing the topic of transition. Next both the adolescent and parent were given a brief questionnaire assessing the teen's knowledge of their chronic condition/treatment plan and how the adolescent feels they learn best. This information was integrated into an individualized education plan for the adolescent. Each adolescent received a personal health care binder with general information on transitioning as well as individualized educational materials on their diagnosis, and medications/therapies past and present. Counseling for Transition was added to the medical problem list, and a educational transition check list was started in the EMR. A summary pamphlet was developed with pertinent web resources. To engage use of social media a free medical app that mirrored the summary pamphlet was piloted.

Results:

Early feedback has been positive; adolescents found the binders helpful and are using the medical app. Young adults who transitioned feel more prepared and confident at their first appointment.

Conclusion:

Transition is an ongoing process and taking small steps along the way helps ensure a seamless transfer to adult care.

Refernces: GotTransition.org

Disclosure: E. Roth-Wojcicki, None; **J. Lemke**, None; **S. Thomson**, None; **S. Liedtke**, None; **K. Cedars**, None.

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