



**DC
Rheum**

The Rheumatism Society of the District of Columbia

**The Rheumatism Society of the
District of Columbia**

Presents...

**The 14th Annual
Rheumatology Fellows Forum**

Saturday, May 21st, 2016

MedStar Washington Hospital Center

True Auditorium

Washington, DC

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Program Schedule

8:30-9:00 AM	Poster Placement/ Breakfast
9:00-10:00 AM	Keynote Speaker – Dr. Robert Inman, Edin Deputy Physician in Chief, Research University Health Network Professor of Medicine and Immunology, and University of Toronto Director of the Spondylitis Program at Toronto Western Hospital – <i>“Advances in the Treatment of Spondyloarthritis”</i>
10:00-11:00 AM	Poster Viewing/ Breakfast
11:00-noon	Podium Presentations

Award Winners

Podium Presentations

- Sara Alehashemi / NIAMS / *18F FDG PET-CT as a Diagnostic Test and Marker of Disease Activity in Large Vessel Vasculitis* (page 6)
- Asha Alex / GUH / *Exploring the Association Between Air Pollutant Exposure and Seropositivity in Rheumatoid Arthritis* (page 10)
- Kaitlin Quinn / GUH / *Can Exercise Echocardiography Predict Future Development of Pulmonary Hypertension in a High-Risk Cohort of Scleroderma Patients?* (page 28)
- Qianzi Zhao / CNMC / *B10 Cells may be involved in Controlling Disease Activity in Polyarticular Juvenile Idiopathic Arthritis Patients* (page 46)

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- Sara Alehashemi / NIAMS / *Clinical Response to JAK Inhibitor in a Case of Relapsing Polychondritis* (page 6)
- Robbins Rachel / WRNMMC / *Treatment of Primary Angiitis of the CNS with Rituximab* (page 31)
- Sam Serafi / GWU / *Long-term outcomes of Patients with Juvenile Dermatomyositis* (page 34)
- Kyawt Shwin / NIAMS / *Histopathologic and Immunologic Features of Skin Manifestations in Monogenic Autoinflammatory Disorders* (page 36)
- Rodger Stitt / WRNMMC / *Novel Use Of Rituximab In Macrophage Activation Syndrome* (page 38)

Title: *18F FDG PET-CT as a Diagnostic Test and Marker of Disease Activity in Large Vessel Vasculitis*

Authors: Sara Alehashemi, Mark A. Ahlman, Ali Cahid Civelek, Elaine Novakovich, Ashkan Malayeri, David Bleumke, Peter Grayson

National Institute of Arthritis and Musculoskeletal and Skin Diseases/NIH

Purpose: FDG- PET is reportedly useful to diagnose large vessel vasculitis (LVV) and to monitor disease activity; however studies of FDG-PET in LVV typically use oncology patients as a comparator group and often do not include follow up imaging during clinical remission. We assessed the utility of FDG-PET to differentiate between LVV and comparator diseases that mimic LVV. We studied FDG-PET as a longitudinal imaging biomarker of disease activity and determined clinical predictors of PET scan vascular abnormalities.

Methods: This prospective, observational cohort consisted of 39 patients with LVV and 50 comparators (systemic inflammation=15; atherosclerosis=35). All cases had at least one FDG-PET scan. Clinical and imaging assessments were performed blinded to each other. FDG-PET/CT was at 120min uptake time (256matrix, 1.5mm slice). Active vasculitis on PET scan was defined by agreement between two nuclear medicine experts. Multivariable regression adjusting for repeated measures was used to study associations between active FDG-PET and disease characteristics: vasculitis type, age, gender, disease activity and duration, acute phase reactants, and treatment.

Results: A total of 123 FDG-PET scans were performed in 89 patients, including giant cell arteritis (n=20; mean age 67.1 ±9.2; disease duration 1.9 ±1.3 years), Takayasu's arteritis (n=19; mean age 36.1 ±10.6; disease duration 15.5 ±10.4 years), and comparators (n=50; mean age 60.3 ±11.0). Among patients with clinically active LVV, the performance of FDG-PET as a diagnostic test was good (sensitivity 94%; specificity 90%). Strikingly, among patients with LVV in apparent clinical remission, findings on PET were consistent with active vasculitis in 22 of 45 scans (49%). In multivariable models, active clinical disease was associated with PET scan activity while no associations were found for type of LVV, age, gender, or acute phase reactants. Longer disease duration and glucocorticoid use were associated with a normal PET scan. The protective effect of glucocorticoids on PET scan activity was higher for patients on additional immunomodulatory medications.

Conclusion: FDG-PET is useful to distinguish active LVV from vasculitis mimics. Approximately half of patients with LVV who are in clinical remission have abnormal PET scans indicative of ongoing vasculitis. An inverse association between disease duration and PET scan abnormalities suggests that scan abnormalities observed during clinical remission are not simply due to accrued vascular damage. Inflammatory markers traditionally used to monitor disease activity (e.g. CRP) were not associated with PET abnormalities. Glucocorticoids and immunosuppressants were protective against an abnormal scan, suggesting that PET abnormalities are potentially modifiable by treatment.

Title: *Clinical Response to JAK Inhibitor in a Case of Relapsing Polychondritis*

Authors: Sara Alehashemi, Massimo Gadina, Wanxia Li Tsai, Anjali Takyar, Kenneth Olivier, James Katz, Marcela Ferrada

National Institute of Arthritis and Musculoskeletal and Skin Diseases/NIH

Background/Purpose: Use of Janus Kinase Inhibitor in a case of relapsing polychondritis with airway involvement and high dose steroid dependence

Case Description: A 36-year-old female with no prior medical history presented with fleeting pulmonary infiltrates on Chest CT scan, air trapping on pulmonary function tests, fever, inflammatory arthritis of bilateral knees and costochondritis. Bronchoscopy was negative for vocal cord dysfunction, subglottic stenosis or tracheal collapse. A diagnosis of Relapsing Polychondritis was confirmed using Damiani criteria based on costochondritis, arthritis, bronchial chondritis, recurrent laryngeal inflammation, and episodes of a painful red pinna.

Case Discussion: Patient required 150 mg prednisone daily to control respiratory and musculoskeletal symptoms and an attempt at tapering down the steroids resulted in reoccurrence of the symptoms. Multicolor flow cytometry and in depth immunophenotyping and Luminex technology was used to characterize cytokine and inflammatory cell involvement prior and after steroid sparing treatment initiation. The patient was found to have significant elevation of the Th17 cell population and related cytokines: IL-22 and IL-26. Serum levels of IFN-gamma a cytokine secreted by plasmacytoid dendritic cells (pDC) were elevated during a flare. Based upon these immunophenotyping results, tofacitinib was suggested as a small molecule agent to control disease. Following two weeks of treatment with Tofacitinib (10 mg twice daily) the patient's respiratory and musculoskeletal symptoms improved. Eventually, with the addition of weekly methotrexate (15 mg) and the reduction of tofacitinib to 5 mg BID, the patient was completely weaned off of the prednisone. Her course was complicated by only one episode of norovirus.

Significance: Currently, there is no standardized treatment approach for relapsing polychondritis. The decision to initiate treatment and the choice of initial therapy is guided by clinical acumen and often based on severity of disease and organ involvement. Severe cases historically treated with high dose corticosteroids and cyclophosphamide that carry significant side effects. Biologic agents have been used with inconsistent results. Tofacitinib is a JAK1/3 (Janus Kinase) inhibitor approved for treatment of rheumatoid arthritis. The clinical response to tofacitinib in our patient was impressive. Our patient had elevation of pDC. We theorize that tofacitinib increases the expression of indoleamine 2,3 –dioxygenase (IDO)-1 and IDO 2 and that appears to have an effect on pDC making them protective instead of pro-inflammatory. This appears to be the first report of successful intervention with a Jak inhibitor for this rare disease.

Title: *Multidisciplinary Approach to Blurry Vision*

Authors: Paloma Alejandro, Florina Constantinescu, Anastasia Markoupoulou

MedStar Washington Hospital Center

Background: Neuromyelitis Optica Spectrum Disorders (NMOSD) is often challenging to diagnose. It is an immune-mediated inflammation of spinal cord and optic nerve. Patients with connective tissue diseases, like Sjogren's are at high risk. Aquaporin-4 IgG antibodies (NMO-IgG) are present in 40-60% of the cases of patients who meet criteria. Of the NMOSD patients, 40% of them have SSA/SSB positive with no clinical symptoms of Sjogren's. NMO-IgG positivity is a marker of recurrent optic neuritis and longitudinal extended transverse myelitis in Sjogren's patients. The purpose of this vignette is to learn how to identify this challenging patients and how to effectively treat them in order to prevent permanent neurological damage.

Case Description: 28 y/o African-American Female patient with no significant past medical history presenting to the hospital with bilateral blurry vision. She noticed paresthesias below the breast area, dry mouth and bilateral knee stiffness but no swelling. Cold sensitivity in her fingers, turning white. Physical exam unremarkable. Eye exam: VA : 20/200 right, 20/200 left, VF: abnormal right, left. Fundi: bilateral optic nerve pallor. Light perception diminished, abnormal color plate differentiation with both eyes. Labs: CRP 0.31, ESR>85, RF 93, Hgb 10.9 g/dL Hct 35.2%, SPEP with M-spike. LP: WBC 2, RBC 0, protein 41, glucose 71 H, NMO IgG CSF positive. ANA 1:1280, speckled, SSA >8.0/ SSB >8.0, RF 9, NMO-IgG positive, C3 103, C4 27.4. MRI orbits with contrast: bilateral optic neuritis with bilateral chiasmitis. MRI thoracic spine with contrast: T2-T5 demyelinating disease. Final serology workup revealed Sjogren's. Patient received 5 days of IV solumedrol 1gm, and then she continued on oral prednisone 1mg/kg. M-spike likely related to Sjogren's. NMO positive, and started on plasmapheresis total 5 sessions. Patient received Rituximab, with recovery of vision 20/20 both eyes.

Discussion: Patient with Sjogren's with optic neuritis and longitudinal extended transverse myelitis often have NMO-IgG positive. Of the Sjogren's patients, 12% have NMO-IgG positive without symptoms. Rituximab is the first line treatment, with aims of preventing further neurological damage and possibly reversing it.

Conclusion/Significance: NMOSD is a newly recognized group of demyelinating diseases, often overlapping with patients with Sjogren's or SLE. This makes a diagnostic challenge; increase awareness about the disease has been seen. Rituximab is the first line treatment.

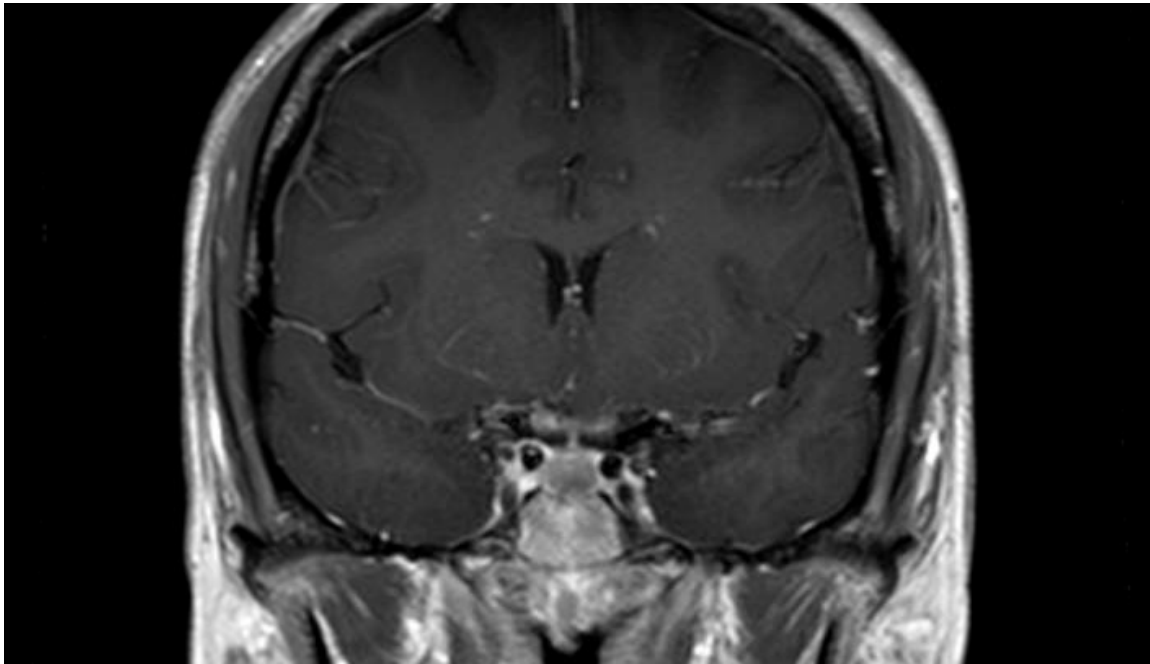


Figure 1: MRI Orbit Coronal T1 image, demyelination of bilateral optic chiasm.

Title: *Exploring the Association between Air Pollutant Exposure and Seropositivity in Rheumatoid Arthritis*

Authors: Asha Alex^{1,3}, Richard Amdur², Jorge D. Flautero Arcos^{3,4}, Gary Kunkel⁵, Gail S Kerr^{1,3,4}

¹Georgetown University Hospital, ²George Washington University School of Medicine and Health Sciences, ³DC Veteran Affairs Medical Center, ⁴Howard University, ⁵University of Utah Hospital and George E Wahlen VAMC

Background: The etiology of rheumatoid arthritis (RA) is multi-factorial, with expression of HLA-DRB1 shared epitope (SE) and smoking exerting influence. We evaluated the association of AP exposure with RA autoantibody status adjusting for socioeconomic status (SES), SE expression and tobacco exposure.

Methods: Patients from 7 sites of the Veterans Affairs Rheumatoid Arthritis (VARA) registry were included in the analysis. Socio-demographic, HLADRB1 SE status, tobacco exposure (never, former, current), and RA seropositivity parameters were available. Mean exposure levels for AP (NO₂, SO₂, PM_{2.5}, PM₁₀ and Ozone) was based on the patient's residence zip code air quality reports to the EPA. The pollution scores were standardized and the mean standardized scores used as a global pollution score for each subject. For SES, the mean standardized score of a composite based on zip code was used. Years of education served as a surrogate for SES. Generalized estimating equations (GEE) using the log of RF and ACPA titers with nested models based on location were used to determine independent associations of AP on RF and ACPA titers. SAS version 9.3 (Cary, NC) was used for all data analysis with p<0.05 considered significant.

Results: There were 1078 subjects of mean age 69.4 years (SD 10.4); 91.1% were male, 80.4% were Caucasian with mean disease duration of 12.5 years (SD 11.7). 73.3 % were positive for the HLADRB1 SE, while 80.6% and 75.1% were RF and ACPA positive respectively. In multivariate GEE models, former and current smoking (p< 0.001, p<0.0001), HLA-DR SE positivity (p<0.0001), lower education status (p<0.0001, p=0.015) were predictive of higher RF and ACPA titers, respectively. Univariate analyses of the individual AP scores revealed no association with either RF or ACPA positivity. In the multivariate nested GEE models, patients with the highest quartile of AP exposure had lower ACPA levels (p< 0.0001) and there were inconsistent associations of AP quartiles with RF (AP quartile 3 had higher RF, p< 0.0001).

Conclusions: In a predominantly male RA population with long standing disease, there was confirmation of the association of HLADRB1 SE and smoking with autoantibody seropositivity but an inverse relationship between higher amounts of air pollutant exposure and ACPA was found. The overall effect of air pollutants on RA autoantibody status appears to be a varied and complex relationship.

Title: *The Abdomen: Tomb of the Unknowns*

Authors: CPT Wayne T. Bailey, MAJ Christopher L. Tracy, LCDR Bruno A. Schmitz

Walter Reed National Military Medical Center

Introduction: The vasculitides are classically described as systemic inflammatory diseases with a predilection for vessels based on size. The gastrointestinal (GI) tract is commonly affected but may also occur as a single-organ vasculitis (SOV). When this occurs, excision is thought to be curative, although some cases progress to a systemic disorder. The differential typically includes the small and medium vessel vasculitides, inflammatory bowel diseases, and a very rarely described entity of localized vasculitis of the GI tract (LVGT). The differentiation is commonly made with pathological assessment. We present a case of LVGT presenting as abdominal pain and outline the differential diagnosis and treatment considerations.

Case: A 21 year old male presented to the hospital with worsening periumbilical abdominal pain of four days duration. He had been seen by multiple emergency rooms over the previous month with similar episodes. Imaging on admission showed jejunal wall inflammation with lymphadenopathy. Exploratory laparotomy was performed and showed small-to-medium vessel vasculitis with submucosal nodules and luminal narrowing within the 37 centimeters of the resected small bowel. Lymph node pathology was not consistent with lymphoma and the infectious evaluation was negative. Colonoscopy, pill endoscopy, mesenteric and renal angiograms were not suggestive of inflammatory bowel disease or systemic vasculitis. Anti-neutrophil cytoplasmic antibodies, antinuclear antibodies, and extractable nuclear antigens were negative and his erythrocyte sedimentation rate was normal. He was treated with prednisone tapered over a month with recrudescence of his symptoms three days following cessation. His manifestation at that time was his index abdominal pain and his C-reactive protein was again elevated. Methotrexate was added as a steroid sparing agent with achievement of remission.

Conclusion: LVGT is a rare disease that most commonly manifests as an acute abdomen with the diagnosis confirmed on exploratory laparotomy in the search for other etiologies. LVGT may be present in the setting of a normal angiogram given the lower sensitivity with small vessel vasculitis, requiring a biopsy with histopathological assessment for diagnosis. Case reports have described remission with as little as one month steroid taper. This case illustrates methotrexate as a reasonable treatment option for patients with LVGT who fail weaning from corticosteroids.

Title: *Infections, Medications and Other Possible Factors Associated With Onset of Myositis in MYOVISION, A National Myositis Patient Registry*

Authors: Nastaran Bayat¹, Payam Noroozi Farhadi¹, Jesse Wilkerson², Abdullah Faiq¹, Kathryn Rose², Lukasz Itert³, Anne Johnson³, Edward H. Giannini³, Hermine I. Brunner³, Richard Morris², Bob Goldberg⁴, Frederick W. Miller¹ and Lisa G. Rider¹.

¹Environmental Autoimmunity Group, NIEHS, NIH, ²Social and Scientific Systems, Inc., Durham, NC,

³Cincinnati Children's Hospital Medical Center, ⁴The Myositis Association, Alexandria, VA.

Background/purpose: Myositis is a rare systemic autoimmune disease with suspected environmental and genetic risk factors, but little is known about specific infections and medications and other factors that might be triggers.

Methods: 928 patients enrolled in MYOVISION were diagnosed with myositis after 2001 and met Bohan and Peter or Griggs criteria. Infections and medications received within 12 months of diagnosis were assessed. Significant univariable results were examined in multivariable logistic regression. Odds ratio point estimates with 95% confidence intervals and p-values were reported for each subtype pairwise comparisons, after adjusting for age of diagnosis, gender, and race. Responses to an open-ended question about what patients thought caused their myositis were also examined.

Results: Infections within 12 months of diagnoses were reported most frequently in Juvenile Dermatomyositis(JDM), and also more frequently in Dermatomyositis(DM) and Polymyositis(PM) patients than in Inclusion Body Myositis(IBM) (Table 1). These same trends were seen for fever/febrile illness, gastrointestinal infections characterized by nausea/vomiting/diarrhea, and respiratory infections, which included colds or upper respiratory infection, influenza, pneumonia and Strep pharyngitis. Among the respiratory infections, only pneumonia differed between subgroups and was reported more frequently in DM and PM patients than IBM. Urinary tract infections and skin infections were reported in ≤10% of patients in each subgroup and did not differ among subgroups. DM, PM and JDM patients reported higher number of infections within 12 months of diagnosis than IBM patients(p ≤0.05). Statins were used more frequently in DM and PM than IBM in the 12 months prior to diagnosis(Table 1), and diabetes medications and levothyroxine were reported more frequently in PM than IBM patients. NSAIDs were used most frequently in IBM, intermediate in DM and PM, and least frequently in JDM patients. Antibiotics, blood pressure medicines and other lipid lowering agents did not differ in usage by subgroup in the year prior to diagnosis. Among responses to the open-ended question about etiology of myositis, chemical exposures, including pesticides and solvents, were reported most frequently in DM, PM and IBM patients (30-39%) as the possible cause of their myositis. Stress was the second most frequently reported cause, seen in 44% of DM and 27% of PM patients.

Conclusion: Variations in infections and medications received within 12 months of diagnosis among myositis subgroups and patient thoughts about the etiology of their illness suggest possible risk factors

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for myositis. Controlled studies examining these factors may be helpful in elucidating their role in disease development.

Table: Prevalence of Reported Infections and Medications within 12 Months of Diagnosis in Myositis Subgroups*

Comparison	Adjusted Prevalence Rate		Adjusted Prevalence Rate		Adjusted Prevalence Rate		Adjusted Prevalence Rate	
	OR (95% CI) †		OR (95% CI) †		OR (95% CI) †		OR (95% CI) †	
Infections ‡ by Subgroups	Any Infection		Fever / Febrile Illness		Nausea/Vomiting/Diarrhea		Respiratory Infections §	
DM vs. IBM	46.6% vs. 31.8%	1.87 (1.19 - 2.92) ²	11.3% vs. 3.8%	3.20 (1.27 - 8.08) ¹	14.0% vs. 4.5%	3.46 (1.45 - 8.25) ³	32.7% vs. 21.6%	1.76 (1.07-2.90) ¹
DM vs. JDM	46.6% vs. 60.9%	N.S.	11.3% vs. 28.3%	0.32 (0.11 - 0.94) ¹	14.0% vs. 22.4%	N.S.	32.7% vs. 46.9%	N.S.
PM vs. IBM	42.6% vs. 31.8%	1.59 (1.01 - 2.52) ¹	12.3% vs. 3.8%	3.50 (1.38 - 8.89) ²	13.6% vs. 4.5%	3.35 (1.39 - 8.06) ²	33.4% vs. 21.6%	1.82 (1.10-3.01) ¹
JDM vs. IBM	60.9% vs. 31.8%	3.34 (1.22 - 9.13) ¹	28.3% vs. 3.8%	9.90 (2.17 - 45.1) ³	22.4% vs. 4.5%	6.16 (1.45 - 26.2) ¹	46.9% vs. 21.6%	3.21 (1.15-8.99) ¹
Medications ¶ by subgroups	NSAIDS		Statins		Diabetes Medications		Levothyroxine	
DM vs. IBM	36.6% vs. 45.8%	N.S.	17.1% vs. 8.6%	2.21 (1.32 - 3.68) ³	4.1% vs. 1.7%	N.S.	6.0% vs. 4.2%	N.S.
DM vs. JDM	36.6% vs. 16.6%	2.89 (1.20 - 6.97) ¹	17.1% vs. 0.0%	N/A	4.1% vs. 0.0%	N/A	6.0% vs. 6.4%	N.S.
PM vs. IBM	38.6% vs. 45.8%	N.S.	16.4% vs. 8.6%	2.08 (1.24 - 3.50) ²	5.1% vs. 1.7%	3.21 (1.32-7.80) ¹	8.7% vs. 4.2%	2.19 (1.03-4.64) ¹
PM vs. JDM	38.6% vs. 16.6%	3.16 (1.28 - 7.79) ¹	16.4% vs. 0.0%	N/A	5.1% vs. 0.0%	N/A	8.7% vs. 6.4%	N.S.
JDM vs. IBM	16.6% vs. 45.8%	0.24 (0.08 - 0.67) ²	0.0% vs. 8.6%	N/A	0.0% vs. 1.7%	N/A	6.4% vs. 4.2%	N.S.

Abbreviations: DM, dermatomyositis (n = 362); PM, polymyositis (n = 250); IBM, inclusion body myositis (n = 256); JDM, juvenile dermatomyositis (n = 60); NSAIDS, Nonsteroidal Anti-inflammatory Drugs; N.S., not significant; N/A, Not assessed because the prevalence was 0% in JDM.

* Values are adjusted for age of diagnosis, gender, and race. Medication outcomes are also adjusted for presence of infection. Patients diagnosed prior to 2002 were removed.

† Significant P-values: ¹p ≤ 0.05; ²p ≤ 0.01; ³p ≤ 0.005; ⁴p ≤ 0.001

‡ Among infections, urinary tract infection and skin infections did not differ in frequency among subgroups.

§ Respiratory infections include colds or upper respiratory infection, influenza, pneumonia and Strep pharyngitis.

¶ Among medications, Antibiotics, Blood pressure medications and Hormone Replacement Therapy/ Oral contraceptive pills did not differ in frequency among subgroups.

Title: *Unexplained Muscle Weakness: Dysferlinopathy as a Rare Cause of Muscular Dystrophy*

Authors: Delamo Bekele, Stefan Hemmings, Mehad Musbah, Ryan Rabilal, Farhan Khan, Feremusu Kamara, Mercedes Quñiones. Sharon Dowell, Gail Kerr

Howard University Hospital

Background: Dysferlinopathy is a hereditary condition caused by the deficiency or absence of the DYSF gene that has two main phenotypes: Miyoshi Myopathy or Limb-girdle Muscular Dystrophy-Type 2B. The rarity and difficulties posed in making a definitive diagnosis of Dysferlinopathy as a cause of muscle weakness is a challenge for the clinician.

Case Description: A 19 year-old female with multiple musculoskeletal complaints was admitted with an elevated creatine phosphokinase (CPK) level of 12,470 IU/L. Over the preceding 5 years, she had bilateral lower extremity pain and right-sided muscle weakness which progressed to difficulty getting up from a seated position, climbing stairs, and picking up objects from the floor. She had recurrent falls, increased fatigue, and weight gain. She was seen by different specialists with no clear diagnosis, and managed with physical therapy and steroid injections which yielded minimal improvement. Physical exam revealed globally decreased power involving both proximal and distal muscle groups including weak grip strength, difficulty performing tip-toe walking, and standing from a squatting position. There was no alopecia or skin rash. Cranial nerves, reflexes and sensory examinations were normal. Laboratory workup revealed aldolase 67 U/L (normal <8.1U/L) and myoglobin 403 ng/L (normal 23-72ng/L) with normal carnitine and lactate levels. CRP, ESR, thyroid function, HIV, rheumatoid factor, ANA, ACPA, and Anti-Jo-1 antibodies were negative. MRI of the pelvis showed edema of the bilateral hip adductor muscle and right gluteus muscles. EMG revealed myopathic potentials in the right gluteus and quadriceps muscles. Muscle biopsy of the right gluteus muscle revealed necrotic and regenerating myofibers; no evidence of metabolic, inflammatory, or immune-mediated myopathy; and complete absence of dysferlin immunostaining. Confirmatory gene testing revealed two pathogenic variants of the DYSF gene consistent with Dysferlinopathy.

Discussion: Dysferlinopathy presents with gradual onset of muscle weakness, typically during adolescence. Patients are often misdiagnosed as having an inflammatory myopathy due to clinical similarities with MD. Muscle biopsy and genetic testing should be considered in certain cases to avoid misdiagnosis and inadvertent immunosuppression, especially in the absence of findings supportive of inflammatory myopathy. No pharmacotherapy is currently recommended; the use of corticosteroids, Rituximab, and IVIG has not been effective in trials. In fact, corticosteroids may exacerbate symptoms. Management is challenging and requires a multidisciplinary approach including physical therapy and genetic counseling to improve quality-of-life.

Conclusion: Dysferlinopathy should be entertained in cases of muscle weakness, especially in the pediatric and adolescent age group with no other supportive findings of inflammatory myopathy.

Title: *An International Web Based Population Study on Relapsing Polychondritis*

Authors: Shubhasree Dutta Choudhury, Marcela Ferrada, Kam Newman, James Katz

National Institute of Arthritis and Musculoskeletal and Skin Diseases/NIH

Background and Purpose: Relapsing polychondritis is a rare connective tissue disorder characterized by recurrent episodes of chondritis. Variable clinical manifestations results in delayed diagnosis. Although auricular chondritis, is a specific diagnostic finding, patients can have involvement of other organs like nasal bridge, larynx, tracheobronchial tree, multiple joints, vasculature, heart valves and kidneys. We aim to evaluate different disease patterns by performing international survey of patients with RP and identify barriers to effective diagnosis and treatment.

Methods: Web-based survey methodology enabled us to capture a large study population. Prior to receipt of data from this survey (that was generated by the Relapsing Polychondritis Foundation), we obtained an exemption from OHSRP that use of this anonymous survey data is *Excluded from IRB Review* per requirements of 45 CFR 46 and NIH policy.

Results: We report descriptive statistics on 155 individuals.

1. Mean age 49.92 years. 88.3% were females and majority were White (93.5%). 32.5% smokers.
2. 51.3 % were diagnosed by rheumatologist and minority (17.6%) had a biopsy for diagnosis. 25.8% patients endured >1year effort to achieve diagnosis, and 8.4% patients were diagnosed by first physician visited. 43.2% patients had at least one ER visit.
3. Most common symptoms prior to, and after, diagnosis included nasal (45.2%), ear (85.5%) symptoms, voice changes (40%), shortness of breath (35.5) and musculoskeletal complaints 71.6%}. Raynaud's was reported in 20.6% subjects.
4. Popular treatments were prednisone (60%), methotrexate (32.9%), TNF inhibitors (12.9%), and azathioprine (11%). 18.7% were treated symptomatically. Dapsone, tocilizumab, and rituximab used less frequently.
5. 23.2% patients reported disability. Intubation/tracheomalacea reported by 13% subjects. Concurrent autoimmune disease rate was 48.4%.

Conclusion/Significance: We are reporting important data on RP symptomatology including high incidence of signs of tracheobronchial inflammation. Limitations of this study include inability to validate self-reported claims of diagnosis of RP and recall bias. But, anonymous web-based strategy enabled us to capture large population. In this study, majority are females. Time to diagnosis is commonly more than one year and characterized by frequent medical visits. In half the instances, diagnosis was established by non-rheumatologist. Voice changes and shortness of breath are common presenting symptoms. This study suggest that fruitful avenues for future research would include, identifying key points of entry into medical system for RP patients in order to target the health care providers for educational efforts towards earlier diagnosis, establishing standard laboratory practices to assess organ involvement to document inflammation and disease burden, and identifying best therapeutic interventions to minimize glucocorticoid exposure and prevent end organ damage.

Title: *Putting the Cart Before the Horse: Diagnosis of Sporadic Inclusion Body Myositis in a Patient with T-cell Large Granular Lymphocytic Leukemia*

Authors: Jeffrey Eickhoff, Hyun Park, Robert Jones, Christopher Tracy

Walter Reed National Military Medical Center

Introduction: Sporadic Inclusion Body Myositis (sIBM) is a myopathy characterized by onset generally after age 45, asymmetric proximal and distal muscle involvement, and characteristic histopathological findings. Muscle wasting is typically slow and unrelenting despite attempts at treatment. The underlying pathophysiology of this disease has not been completely elucidated. A recent study showed a much higher prevalence of T-LGL in sIBM patients than previously recognized, and it has been proposed that a subset of sIBM may be secondary to muscle invasion by LGL CD8+ T cells. We report an atypical presentation of sIBM in a young patient with preceding diagnosis of T-cell large granular lymphocytic (T-LGL) leukemia.

Case Description: The patient is a 41-year old male with T-LGL leukemia, which was diagnosed three years prior to onset of his clinical myopathy and subsequent diagnosis of sIBM. T-LGL leukemia was diagnosed via bone marrow biopsy and flow cytometry demonstrating T-LGL phenotype and clonality. He was treated with a course of cladribine but his leukemia proved refractory to chemotherapy. Eight months after his diagnosis of T-LGL, the patient noted onset of slowly progressive muscle weakness primarily in his hands and proximal extremities as well as mild dysphagia. This was brought to clinical attention three years after his T-LGL diagnosis. Further studies indicated elevated creatine kinase and aldolase levels, MRI findings consistent with myositis pattern of muscle involvement, and EMG with mixed myopathic/neuropathic pattern. Subsequent muscle biopsy was notable for CD8+ predominant T-cell endomyosial infiltrate with p62-immunopositive fibers and rimmed vacuoles. Serology was notable for negative myositis panel antibodies (PL-7, PL-12, Mi-2, Ku, EJ, OJ, SRP, U2 SNR, Jo-1) and positive NT5c1A antibody (>90% specificity for sIBM). He met all sIBM clinical and pathological diagnostic criteria by ENMC 2013 research diagnostic criteria with the exception of age at onset >45. The patient was treated with high dose corticosteroids with normalization of muscle enzyme levels and symptomatic improvement in his symptoms but relapsed upon steroid cessation. Steroids were restarted and methotrexate was added as a steroid-sparing agent, and he has thus far tolerated the therapy well without symptoms of dysphagia and near normalization of muscle strength.

Discussion: This case illustrates an unusual case of a relatively younger patient with T-LGL leukemia presumed related to treatment-responsive sIBM which was diagnosed years later. This demonstrates the indolent nature of an atypical case of sIBM, and highlights the importance of seeking out potential underlying etiologies of LGL leukemia.

Title: *Use of Kineret and IV Steroids for Refractory Kawasaki Disease*

Authors: Karen Ganacias, Nina Rodriguez, Katrina Fernandez, Meg Maultsby, Elizabeth Carter, Joseph May, Tiffany Stratton, Christopher Foster, Olcay Jones

Walter Reed National Military Medical Center

Background and Purpose: Kawasaki Disease (KD) is one of the most common childhood vasculitides associated with higher risk for mortality and morbidity if untreated, due to complications of coronary artery aneurysms. It is a systemic inflammatory and autoimmune disease with an acute onset of unknown etiology, and is characterized by 3 clinical stages about 2 weeks apart: Acute Phase (week 0 to 2), manifested with high and persistent fever, bilateral nonexudative conjunctivitis, erythema of the lips and oral mucosa, changes in the extremities, rash and cervical lymphadenopathy; Subacute Phase (week 2 to 4), associated with additional coronary artery changes; and Convalescence Phase (week 4 to 8), associated with wide spread desquamation and nail changes. There is no single test for KD, however, labs may be significant for CBC changes with leukocytosis, anemia, thrombocytosis, elevation of acute phase reactants (CRP, ESR), mild to moderate elevations in serum transaminases, and hypoalbuminemia. Although standard treatment comprises of intravenous immunoglobulin (IVIG) and aspirin, some children exhibit refractory disease necessitating the use of alternative therapies. This reports the case of a boy with IVIG resistant Kawasaki Disease successfully treated with Kineret and corticosteroids.

Case Description: A 2 y/o boy presented to an outside hospital with 5 days of high and persistent fever, Tmax 102+, bilateral conjunctival injection, hand/foot edema and erythema, right anterior cervical lymphadenopathy and a maculopapular rash along his forearms and legs. Mom also reports he had been irritable and fussy since onset of his fever. Initial ESR/CRP were significantly elevated (77/8.2), and the patient was noted to have normocytic anemia (10/32, MCV 81.7) thrombocytosis (497), and elevated AST/ALT/Alkaline Phosphatase (518/311/646). He was then admitted to the Pediatric Ward, WRNMMC (Day 0) for a diagnosis of KD, where a baseline ECHO was performed, without any abnormal findings of the coronary arteries. Upon admission, he (wt 15kg) was started on high dose aspirin (80mg/kg/day divided in q6h) and high dose IVIG (2 g/kg) with resolution of fevers and improvement of conjunctivitis for approximately 20 hours. However, by hour 21 of Day 0, he again developed fever Tmax 102.5, became fussy, irritable, and had worsening conjunctivitis. He was then treated with a 2nd round of IVIG (2g/kg) that subsided the fevers for the next 72 hours. However, his temperature started to rise, and by Day 6, his fever returned Tmax 101.4, along with bilateral conjunctival injection, returning irritability, fussiness, and refusal to bear weight, puffy hands/feet, and desquamation over the groin area. On labs, anemia and thrombocytosis were more significant (Hgb 10→7.8), (Plt 497→715), and albumin now became low for age (3.3). CRP although downtrending still remained elevated (18→7.7), and his ESR increased almost two-fold (>140). Findings were suggestive of his continuing KD at acute to early subacute stages (now refractory to IVIG), so he was then treated with three daily doses of Kineret (100mg →50mg→50mg) on Day 8-10 as an initial steroid sparing agent. However, he continued to have daily short lasting fevers Tmax 100.5, and continuing CBC changes (platelet count 715-990s) so he was also started on steroids consisting of three daily doses of IV solumedrol (50mg →100mg →100mg ; on

day 9 to 11) as well as daily oral steroids 15mg BID on Day 11. On this regimen, his presenting physical symptoms of edematous hands/feet, irritability, refusal to bear weight, and persistent fevers diminished. He was then discharged on Day 12, with a plan to continue with just oral steroids, after being afebrile for more than 48 hours. During his outpatient follow-up his CBC and CRP normalized by day 24. His daily steroids were weaned gradually to 15mg once a day. His aspirin was down to 81mg by day 16, and his repeat ECHO remained normal without coronary artery changes.

Case Discussion: Approximately 10-30% of patients fail to respond to initial IVIG, although the optimal treatment for IVIG-nonresponsive Kawasaki Disease remains controversial. Management options include further doses of IVIG, corticosteroids, TNF-alpha-blockade, cyclosporine A, and anti-CD20 therapy, anti-IL-1 therapy. However, few case reports have reported the use of Kineret in combination with IV steroids, and then a tailored fashion of oral steroids with successful resolve of symptoms.

Case Conclusion: This reports the case of a boy with IVIG resistant Kawasaki Disease whose symptoms and were resolved with Kineret, a fast but short-acting IL-1 receptor antagonist, and corticosteroids that were provided in a tailored fashion while under close observation. This suggests that a combination of alternative therapies could be considered in patients with refractory Kawasaki's Disease.

Title: *The Impact of Tobacco Smoking on Risk and Phenotypes of Polymyositis and Dermatomyositis*

Authors: Sara Faghihi Kashani, Frederick Miller, Adam Schiffenbauer

Environmental Autoimmunity Group, NIEHS/NIH

Background and Purpose: Polymyositis (PM) and dermatomyositis (DM) are related autoimmune muscle diseases influenced by both environmental and genetic factors. Tobacco smoking has been linked to the development, course and outcome of many autoimmune disorders; however, the role of smoking in influencing DM and PM risk and phenotype is not clear.

Methods: A total of 508 adult-onset myositis patients, who met probable or definite Bohan and Peter criteria for PM or DM were assessed. Race and smoking habits were collected. Diagnosis of interstitial lung disease (ILD) was based on physician chart review. Sera were tested for 28 myositis autoantibodies. Chi-square, student t-test and logistic regression models were applied.

Results: The cohort included 362 Caucasian, 106 African-American and 40 patients of other or mixed race. Most patients were female (70%) and were diagnosed had PM (57%). 171 patients were smokers with a median of 15.0 (range 0.14-140) pack years. In Caucasians, smokers were more likely to be diagnosed with PM than DM (OR=2.58, 95%CI: 1.62-4.11), whereas in African-Americans, no significant association between smoking history and diagnosis was observed (OR=2.81, 95%CI: 0.87-9.09) (Figure1-A). After adjusting for potential confounders, Caucasian smokers had a greater chance of being diagnosed with PM than DM (OR= 3.33, 95%CI 1.20-9.23).

In the total population, ILD was more frequent in smokers (41%) than non-smokers (32%), but did not reach the threshold of statistical significance (P=0.052). African-American patients were more likely to have ILD compared to Caucasian patients (OR=1.79, 95%CI: 1.13-2.83). In Caucasians, smokers had a 1.7 times greater risk of developing ILD compared to non-smokers (95%CI 1.06-2.78). In contrast, in African-Americans the frequency of ILD was higher in non-smokers, but not statistically significant (Figure1-B). Caucasian smokers were more likely to have antisynthetase and anti-Jo 1 autoantibodies than non-smokers (OR=1.74, 95%CI 1.02-2.96 and OR= 1.77 95%CI 1.01-3.11, respectively), and less likely to have anti-p155/140 and anti-ribosomal autoantibodies than non-smokers (OR=0.25, 95%CI 0.07-0.88 and OR=0.07, 95%CI 0.01-0.60, respectively). In African-Americans, there were no significant associations between smoking history and autoantibody status.

Conclusion: In Caucasians tobacco smoking is a risk factor for developing ILD and certain autoantibodies and also an independent risk factor for PM. Whereas in African-Americans smoking history is not significantly associated with diagnosis or autoantibody status and, while not significant, shows an opposite trend with development of ILD. These results suggest that smoking might have a differential impact on phenotypes in PM and DM patients in different racial groups.

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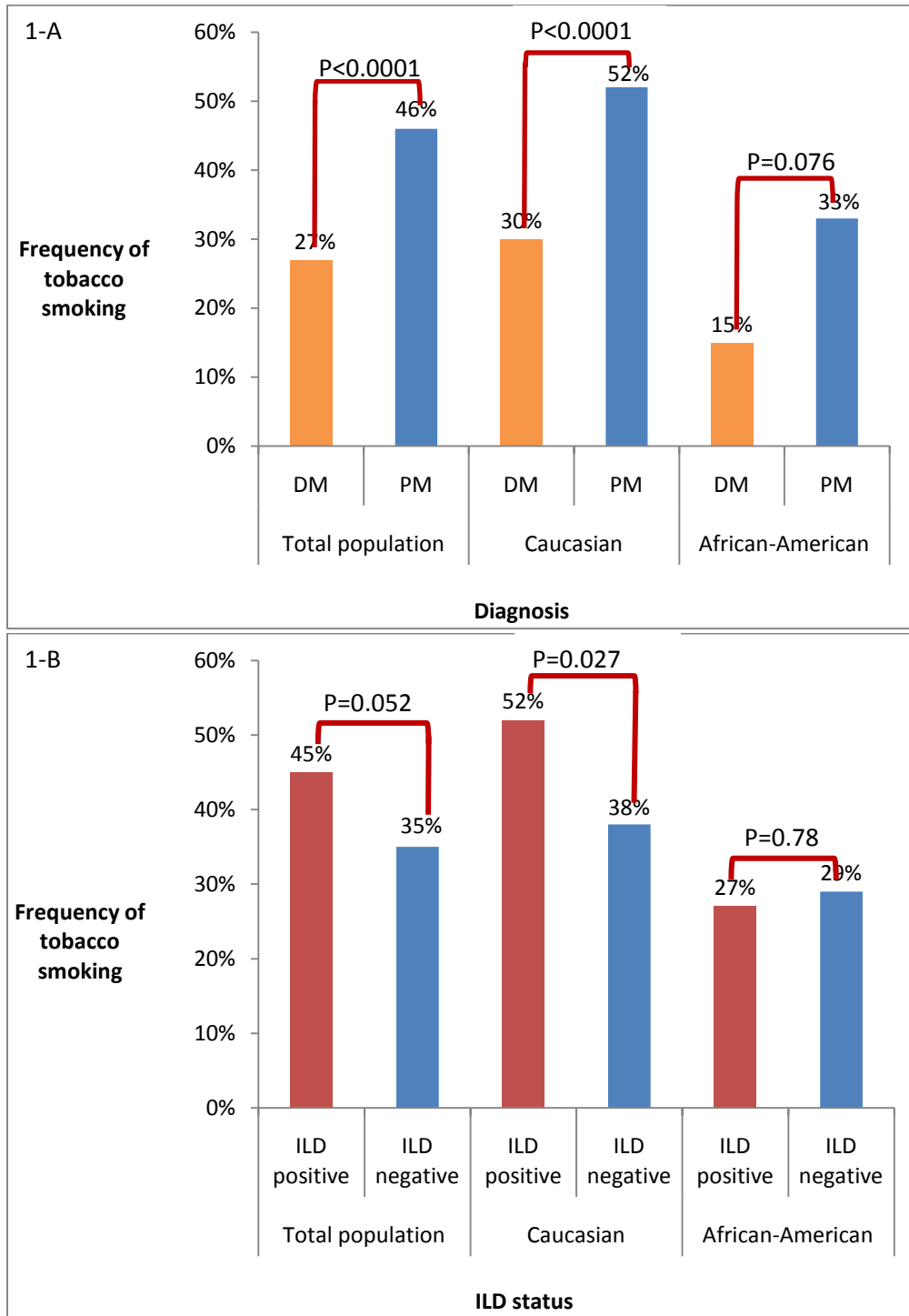


Figure 1. Frequency of tobacco smoking in total population, Caucasian and African-American cohorts A. Frequency of tobacco smoking based on ILD status of participants B. Frequency of tobacco smoking based on diagnosis.

Title: *Unresolved Case of Cryoglobulinemia*

Authors: Deborah L. Kim, Florina Constantinescu

MedStar Washington Hospital Center

Background and Purpose: Cryoglobulinemia is defined as the presence of circulating immunoglobulins that precipitate below 37 degree Celsius which dissolve on rewarming. Here, we describe a case of cryoglobulinemia characterized by severe cutaneous manifestations due to hyperviscosity-related vasculopathy.

Case Description: We describe a 63 year-old Caucasian male with diabetes mellitus type II on insulin, chronic sinusitis and a recent onset of peripheral neuropathy who developed small palpable purpura in lower extremities, which over six weeks had progressed to full epidermal thickness sloughing and gangrene. The patient had no clinical response to high dose steroids. Extensive work up revealed 4% serum cryoglobulins, amorphous precipitates in peripheral smear consistent with cryoglobulins (see Figure1), and skin biopsy suggesting vascular occlusion. However, an infectious work up was unremarkable, repeat serum immunofixation studies showed inconclusive results, and the bone marrow biopsy was negative for lymphoma. In addition, no evidence of underlying autoimmune diseases was identified. Despite our best efforts to salvage the limbs with plasmapheresis, debridements and also with Rituximab treatment, the patient eventually had to undergo bilateral knee amputations.

Case Discussion: Type I cryoglobulinemia is associated with B-cell lymphoproliferative disorders characterized by single monoclonal immunoglobulin and hyperviscosity and vascular occlusion. In contrast, mixed cryoglobulinemia (type II and III) is mainly associated with chronic hepatitis C infection followed by lymphoproliferative diseases, systemic autoimmune diseases such as primary Sjogren's syndrome and systemic lupus erythematosus, and chronic infections. Type II and III manifest as immune-complex mediated vasculitis.

Conclusion/ Significance: Here, we report a case of cryoglobulinemia characterized by severe cutaneous manifestations due to hyperviscosity-related vasculopathy with uncertain type of cryoglobulinemia. The serum immunofixation was repeatedly abnormal, but non-specific and bone marrow biopsy offered no additional clue to its etiology. Although the possibility of cryoglobulinemia preceding lymphoproliferative disorders exists in this patient, this case still remains an unresolved case of cryoglobulinemia which would need further investigation.

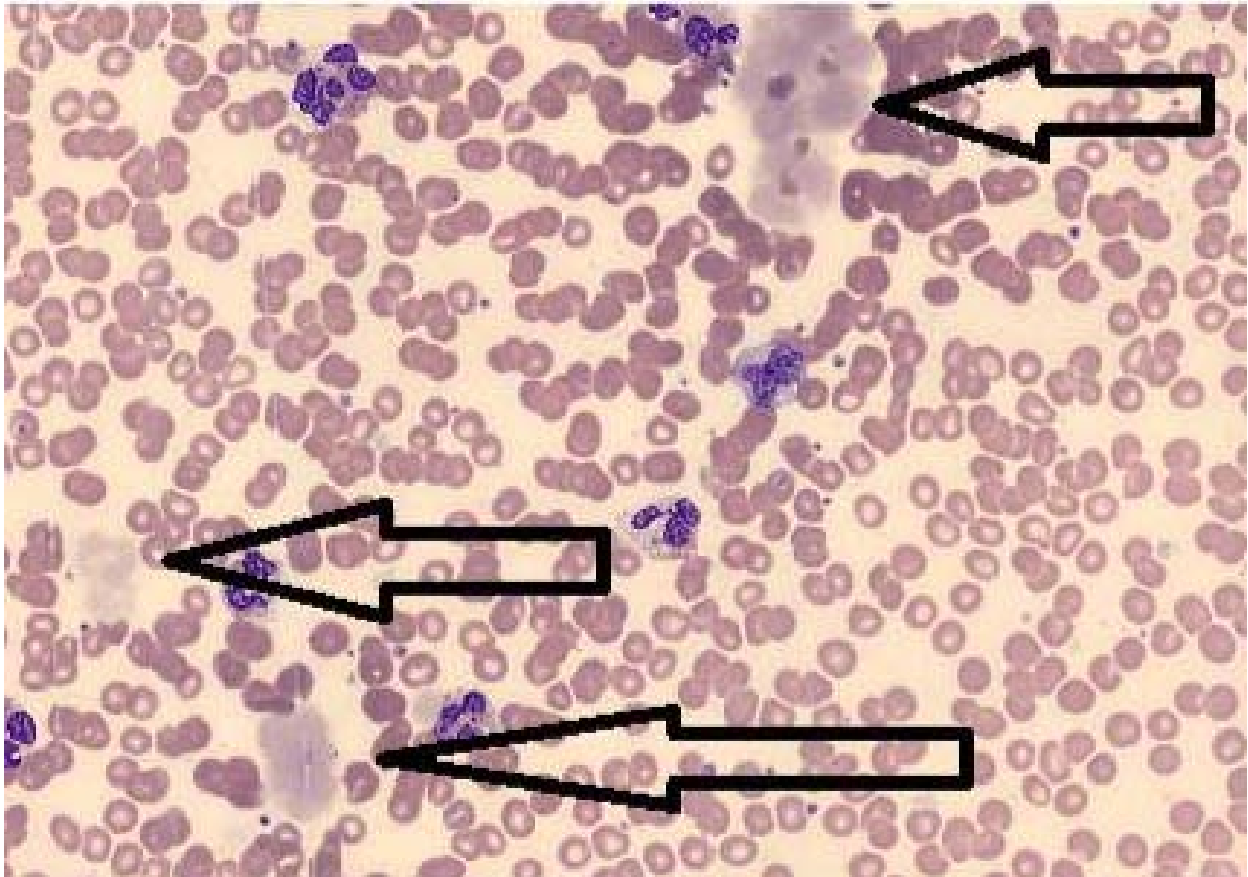


Figure1: Smear: Cryoglobulins appearing as precipitates of pale amorphous particles between the red blood cells (arrows).

Title: *Medication Usage in Patients with Juvenile Dermatomyositis*

Authors: Takayuki Kishi¹, Nastaran Bayat¹, Michael M. Ward², Adam M. Huber³, William Warren-Hicks⁴, Frederick W. Miller¹, Lisa G. Rider¹

¹Environmental Autoimmunity Group, NIEHS/ NIH, ²National Institute of Arthritis and Musculoskeletal and Skin Diseases/ NIH, ³Division of Rheumatology, IWK Health Centre and Dalhousie University, Halifax, Nova Scotia, Canada, ⁴Social and Scientific Systems, Durham, NC

Purpose: Juvenile dermatomyositis (JDM) is a systemic autoimmune disease with characteristic skin rashes and chronic muscle inflammation. Because of its rarity, most therapeutic choices are based on small open label trials or retrospective case series. The purpose of this study was to evaluate the change in therapy over time and factors modifying therapeutic choices.

Method: We performed a retrospective review of the treatment questionnaire for 334 JDM patients enrolled in the Childhood Myositis Heterogeneity Study. We examined year of diagnosis, onset severity, myositis autoantibodies (MSAs), number and type of medications received and their durations, as well as choice of medications as initial therapy and after first flare.

Results: Oral prednisone was the primary therapy used, seen in 97% of JDM patients in the initial 6 months of treatment. This decreased to 57% at 42-48 months after treatment ($p < 0.01$). In contrast, 90% of patients used oral prednisone in the initial 6 months after first flare, vs. 55% at 42-48 months after flare ($p < 0.01$). The median daily maximum steroid dose was 2.0 mg/kg/d [IQR 1.6-3.8], which decreased to 0.9 mg/kg/d [IQR 0.4-1.5] at 42-48 months. In contrast, patients after first flare received lower daily steroid dosage, 1.5 mg/kg/d [IQR 0.8-2.5], in the first six months ($p < 0.01$). The steroid dosage was greater in patients with severe disease onset, associated with more frequent use of pulse intravenous methylprednisolone (IVMP). Patients diagnosed after 1997 received lower initial doses of oral prednisone which were reduced faster compared to patients diagnosed before 1997 ($p < 0.01-0.018$). Methotrexate (MTX), Intravenous Immunoglobulin (IVIG), Hydroxychloroquine (HCQ), other DMARDs and Cytotoxic/ Biologic agents were used more frequently after 1997. Patients diagnosed after 1997 tended to receive a greater number of medications and longer duration of each medication than patients diagnosed before 1997. We examined factors for use of IVMP, MTX, IVIG and HCQ in the initial 6 months by multiple logistic regression. All four drugs had greater use after 1997 (OR 2.1-15.2). IVMP and IVIG were more frequently used in severe patients (OR 2.9-3.0), and HCQ was more frequently used in mild patients (OR 2.7). MTX was more frequently used in patients with anti-MJ Abs (OR 3.2) and IVMP was used more commonly in patients with anti-MDA-5 Abs (OR 4.0).

Conclusion: Prednisone is the mainstay of therapy in JDM, but there is increasing use of MTX, IVIG and other drug/biologic therapies after 1997. Diagnosis year, onset severity and MSAs are associated with medication usage in JDM.

Title: *A Resistant Case of Anti-Synthetase Syndrome*

Authors: Diman Raj Lamichhane, Christopher Collins

MedStar Washington Hospital Center

Background: Anti-synthetase syndrome is characterized by constitutional symptoms, Raynaud phenomenon, interstitial lung disease, myositis, non-erosive symmetric polyarthritis and mechanic's hand in the presence of anti-synthetase antibody. Not every patient with anti-synthetase syndrome has all of the manifestations. 30 percent of IIM patients present with this syndrome.

Case Description: 31 years African American female presented for progressively worsening bilateral symmetric joint pain involving upper and lower extremities for 10 months. She had lost 80 pounds over the period. She complained of Raynaud phenomenon, and weakness in shoulder and hip area. Laboratory tests ordered by the primary care physician revealed positive ANA, elevated SSA, RF and transaminase. Examination revealed symmetric synovitis involving upper and lower extremities. Muscle strength could not be tested due to pain. She was started on prednisone 60mg daily. Further lab result is in table 1. Hand x-rays were negative for erosion. She was started on methotrexate 15mg weekly after 6 weeks of prednisone 60mg. Then, prednisone dose was gradually. Joint pain and weakness resolved. After five months, she decided to stop prednisone abruptly. She started having synovitis and weakness again. She refused further steroid treatment so methotrexate dose was increased, but little improvement was achieved. She was given rituximab which improved symptoms for 2 days only. After 2 month, she was given IVIG at 2gm/kg every month. Symptoms improved after the first dose which lasted nearly 1 month. Second dose was not as effective as the first one. She was started on mycophenolate mofetil during the last visit. CPK had normalized within 1 month of steroid treatment, and it stays normal as long as she was on prednisone. It increased once she stopped prednisone. She had normal CT chest, Echocardiogram, and lung volumes in pulmonary function test. MRI of lower extremities revealed muscle edema. Muscle biopsy and electromyogram were not done.

Case Discussion: Presence of SSA in a patient with Anti-Jo-1 is associated with poor outcome. Those with both antibodies tend to have severe myositis, arthritis, symptomatic ILD and cancer. First line treatment for IIM is high dose steroid for 6 weeks, followed by gradual taper. methotrexate or azathioprine can be used as steroid sparing agent; methotrexate was chosen for the patient as it has better efficacy in controlling arthritis compared to azathioprine. She had clinical and laboratory evidence of improvement until she stopped steroid. For resistant cases, rituximab or IVIG is the drug of choice. Randomized double blind trials are ongoing for tocilizumab and abatacept.

Conclusion: Patients with anti-synthetase syndrome and SSA have worse prognosis and resistant disease.

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	Result	Reference
ANA	1:320 (homogenous)	<1:80
Anit-Jo-1	>8 AI	(0-0.9)
Anti-SS-A	>8 AI	(0-0.9)
Anti-SS-B	0.6 AI	(0-0.9)
RA Latex	102.8 IU/ml	0-13.9
Anti-DNA (ds)	<1 IU/ml	0-9
RNP antibody	0.5AI	(0-0.9)
Smith Antibody	0.4 AI	(0-0.9)
ESR	43 mm/hr	0-32
CRP	21.6mg/L	0-4.9
CPK	4391 U/L	24-173
C4	22 mg/dl	9-36
C3	123 mg/dl	90-180
AST	104 IU/L	0-40
ALT	82IU/L	0-32
Albumin	3.4 g/dL	3.5-5.5
Globulin	4.5	1.5-4.5
Creatinine	0.29mg/dL	0.57-1
WBC	14.3 x 10 ³ /uL	3.4-10.8
Hemoglobin	11.0 g/dL	11.1-15.9
Platelets	513x 10 ³ /uL	150-379

Table 1

Title: *A Complicated and Unusual Presentation of Systemic Amyloidosis in the Setting of Hepatitis C and IV Drug Use*

Authors: Sepehr Mesdaghinia, Weyman Lam, Emily Myers

MedStar Georgetown University Hospital

Background/ Purpose: Amyloid A (AA) amyloidosis is the most common form of amyloid disease worldwide. It is typically caused by chronic inflammatory processes including rheumatoid arthritis, spondyloarthropathies, inflammatory bowel disease, or chronic infections. We present an atypical case of amyloidosis in regards to the uncertain etiology and unusual presentation.

Case Description: A 48 year old male with history of end stage renal disease on hemodialysis, Grave's disease, biopsy proven renal AA amyloidosis, Hepatitis C, and IV drug abuse initially presented to a community hospital with complaints of dyspnea on exertion and chest pain, with mild troponin elevation. He subsequently developed severe hypoglycemia with associated seizure-like episode. He was intubated for airway protection, and was transferred to MedStar Georgetown University Hospital for further workup for possible insulinoma. His examination was significant for hyperpigmented skin lesions on his forearms, which he confirmed were secondary to subcutaneous injection of drugs, and an indurated waxy plaque over his left lower abdomen. Upon further review of his history, a year ago he had a mediastinoscopy with biopsy done for workup of mediastinal lymphadenopathy in setting of weight loss. The pathology report noted "poorly differentiated granulomas" which led to suspicion for sarcoidosis. The slides were acquired by Georgetown pathology lab for a second opinion, but was reported no granulomas and clusters of epithelioid histiocytes, which were nonspecific for infection or sarcoid. Further workup of the extent of his amyloidosis revealed deposition in the liver confirmed by biopsy. Cardiac MRI and skin biopsy of abdominal plaque were negative for amyloid deposition. Further endocrine workup suggested against insulinoma as a cause for hyponatremia, and revealed insufficient cosyntropin stimulation test, low FSH, LH, TSH, free T4 and elevated prolactin, giving rise to suspicion for pituitary involvement. Brain MRI pending.

Significance: This is a case of renal amyloidosis that progressed to have systemic involvement with liver and likely pituitary involvement. Etiology of his amyloid remains elusive. HCV was a consideration, however though HCV has been associated with amyloid light chain amyloidosis (AL), our literature review did not uncover cases of HCV as an isolated etiology of AA amyloid. "Skin popping" drug use has been associated with renal amyloidosis, which remains a viable cause for this patients' amyloidosis. The subcutaneous deposition of multiple exogenous antigens can cause chronic immunologic inflammation. This case remarkably illustrates the multiple complications a patient with systemic amyloidosis can manifest with.

Title: *Neutrophil Dysregulation in ANCA-Associated Vasculitis During Clinical Remission*

Authors: Seema Patel, Jorge Irizarry-Caro, Carmelo Carmona-Rivera, Mariana Kaplan, Peter Grayson

National Institute of Arthritis and Musculoskeletal and Skin Diseases NIH

Objectives: There are no known biomarkers to reliably guide treatment decisions in ANCA-associated vasculitis (AAV). Majority of patients with AAV experience ≥ 1 disease relapse. Neutrophil extracellular traps (NETs) and low-density granulocytes (LDGs), a subset of pro-inflammatory neutrophils not seen in healthy subjects, have been demonstrated in AAV during active disease. Objective of this study was to measure degree of spontaneous NET formation and quantity of circulating LDGs in patients with AAV during clinical remission with the rationale that neutrophil dysregulation during remission may predict future relapse.

Methods: Patients with AAV, defined by existing classification criteria, were recruited prospectively from a single-center cohort at the NIH. Healthy controls were recruited from the NIH Healthy Volunteer program. All patients were in clinical remission defined as a Birmingham Vasculitis Activity Score of 0. Normal dense neutrophils were incubated for 4 hours. Resultant spontaneous NET formation was visualized by fluorescence microscopy and quantified by counting the percentage of neutrophils undergoing NET formation. LDGs were isolated by density gradient preparation and quantified by flow cytometry as CD10⁺/CD15⁺/CD14^{low}. Neutrophil data was analyzed in relationship to clinical data (historical ANCA subtype, ANCA titer, prednisone dose, age, and gender). A p-value of < 0.05 defined statistical significance.

Results: There were 62 visits from patients with AAV in clinical remission (median age 62, IQR 59-56; 78% female) and 13 visits from healthy controls (median age 49, IQR 39-65; 46% female). Among patients with AAV, historical ANCA subtype was MPO-ANCA (29%) and PR3-ANCA (71%). The majority (53%) had undetectable ANCA at time of study. All patients were on remission maintenance therapy (rituximab 74%, prednisone 50%, methotrexate 17%, azathioprine 11%, mycophenolate mofetil 6%, and cytoxan 4%). Significantly more spontaneous NET formation was seen in patients with AAV versus healthy controls (12% vs. 7%, $p < 0.01$), and 51% of patients with AAV had a degree of NET formation 2 standard deviations above the average percentage of spontaneous NETs observed in healthy controls. Degree of spontaneous NET formation correlated with younger age ($r = 0.31$, $p = 0.07$). Quantity of LDGs and percentage of spontaneous NET formation were not associated with prednisone use, and gender. There was a trend towards increased LDG levels in MPO-ANCA versus PR3-ANCA ($p = 0.16$) and in patients who were ANCA positive ($p = 0.07$).

Conclusions: The majority of patients have evidence of increased spontaneous NET formation during clinical remission. Prospective data is needed to determine whether degree of NET formation during remission is an independent predictor of future relapse in AAV.

Title: *Can Exercise Echocardiography Predict Future Development of Pulmonary Hypertension in a High-Risk Cohort of Scleroderma Patients?*

Authors: Kaitlin Quinn, MD Stephanie Wappel, MD; Tunay Kuru, MD; Virginia Steen

MedStar Georgetown University Hospital

Background: Pulmonary hypertension (PH) is the leading cause of scleroderma related deaths and is often detected late in the disease course. Early identification of patients will lead to earlier treatment and may improve survival. The purpose of this study is to evaluate if a positive exercise echocardiogram (EE) predicts future development of PH in a high-risk cohort of scleroderma patients.

Methods: This study included 90 scleroderma patients with features placing them at increased risk for pulmonary hypertension, including dyspnea on exertion, diffusion capacity of the lung for carbon monoxide (DLCO) <60% of predicted, FVC <60% of predicted, FVC%/DLCO% >1.6, or resting right ventricular systolic pressure (RVSP) 30-50 mmHg. In this prospective cohort study, all patients had baseline EE performed by the standard Bruce stress echocardiogram protocol with re-measurement of RVSP within 1 minute of stopping exercise. A positive EE was defined as an increase of at least 20 mmHg in the RVSP with exercise. All patients had at least one repeat echocardiogram at least one year after baseline EE. Patients were followed per standard of care and right heart catheterization (RHC) was performed in patients with a positive EE result.

Results: Table 1 shows the 43 patients who had a positive EE and the 44 who had a negative EE. There were no clinical demographic differences between these groups. In the positive EE cohort, 10 patients (23%) developed resting PH on RHC over time with a mean of 4 years (4 with pulmonary arterial hypertension (PAH), 5 with pulmonary venous hypertension (PVH), and 1 with pulmonary hypertension associated with lung fibrosis (PH-ILD) whereas in the negative EE group, only 3 (7%) patients developed pulmonary hypertension (1 PAH, 2 PVH) ($p=0.039$). Of the remaining 33 patients with positive EE exercise echocardiograms who did not develop resting PH, most (67%) patients continued to have a positive EE including 18 patients who had exercise induced pulmonary hypertension as documented on RHC over the mean of 5.3 years of follow up.

Conclusion: While a positive EE does predict the future development of resting PH, it is not necessarily PAH, even in high-risk scleroderma patients. PVH also is associated with a positive EE and many patients with a positive EE may have a persistently positive exercise echocardiogram without progression to pulmonary hypertension.

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Table 1:

	Positive ExEcho N=43 (48%)	Negative ExEcho N=44 (49%)	P-value
Age (years)	54.7 ± 12	50.6 ± 13	NS
FVC %	81 ± 21	85 ± 22	NS
DLCO %	66 ± 22	65 ± 20	NS
Baseline 6MWT (m)	435 ± 104	455 ± 102	NS
Baseline RVSP (mm Hg)	33 ± 7	31 ± 6	NS
Time to follow up (years)	5 ± 2.4	4.6 ± 2.4	NS
SSc type (limited scleroderma), %	60 %	68 %	NS
ANAs, %	Anti-centromere: 28% Anti-scl 70: 12% Anti-nucleolar ANA:26%	Anti-centromere: 32% Anti-scl 70: 20% Anti-nucleolar ANA:20%	NS
Developed PH	10 (23%)	3 (7%)	0.039

Title: *Coagulation Pathway Function in Ischemia/Reperfusion Tissue Injury in Autoimmune Prone Mice*

Authors: Robbins R, Tracy C, Edison J, Peng S, Moratz C

Walter Reed National Military Medical Center

Background: Impaired fibrinolysis in systemic lupus erythematosus (SLE) is a contributing factor in disease complications including hyper-coagulation, tissue ischemia, and an increased risk of thrombosis including stroke and deep vein thrombosis. Additionally, aberrant complement activation has been identified as a major factor in tissue injury in SLE. Previous work in the laboratory has focused on the role of complement activation in tissue injury due to ischemia in the MRL/lpr mice, an autoimmune prone mouse strain with a propensity to develop lymphadenopathy, glomerulonephritis, and polyarthritis. This work elucidated the role of complement activation in ischemia tissue damage and identified a C3b-independent mechanism of downstream complement C5a generation contributing to tissue injury subsequent secondary systemic inflammation. However, important interactive regulatory roles between the complement and coagulation pathway have been delineated in wild type mice. The C3b- independent pathway work indicated a role for thrombin, a coagulation component. The current work attempts to elucidate the mechanism by which the two pathway interact to contribute to hypercoagulability and increased risk of thrombosis in SLE. We hypothesized that the interaction between the two systems involves downstream mediators of C1q receptor activation and the extrinsic coagulation by altering the normal feedback regulatory loops that maintain homeostasis.

Methods: Using a superior mesenteric artery ischemia model, we compared the pathology of mesenteric IR induced tissue injury between immune competent (C57BL/6) and autoimmune prone (B6.MRL/lpr) mice after administration of complement or specific coagulation pathway inhibitors. The pathology was assessed by immunohistochemistry/ immunofluorescence analysis of tissue section, western blot analysis, or array analysis of secreted mediators of inflammation.

Results: The model utilized a complement C1q inhibitor and coagulation inhibitors targeting the intrinsic and extrinsic pathways (Tissue Factor Pathway Inhibitor and Anti-thrombin III) to evaluate and compare resulting tissue pathology, generation of secondary inflammatory mediators, extent of innate immune activation, and generation of breakdown products involved in regulating feedback regulatory loops after ischemic/reperfusion injury. Results indicate a close interaction between the complement system and the extrinsic coagulation pathway in the tissue pathology, generation of breakdown products and the recruitment of innate immune components.

Conclusion: The interaction between thrombin and the complement pathway in SLE has significant clinical implications. Especially in anti-phospholipid syndrome (APS) in which inflammation and hypercoagulability are known manifestations.

Title: *Treatment of Primary Angiitis of the CNS with Rituximab*

Authors: Robbins R, Tracy C, Edison J

Walter Reed National Military Medical Center

Introduction: Primary angiitis of the central nervous system (PACNS) is a rare autoimmune vasculitis of the central nervous system (CNS) that affects only about 2 in 1 million people, though its effects can be devastating leading to stroke, permanent neurologic deficits, seizures or death. Definitive diagnosis requires brain biopsy and once diagnosed, therapy must be started rapidly. Traditionally, therapy has hinged on long term, high dose glucocorticoids and induction with cyclophosphamide (CYC). Here we report two cases of definitively diagnosed PACNS treated with high dose glucocorticoids and rituximab (RTX).

Case Description: Patient A is a 31-year-old male who was diagnosed with PACNS in 2013 after presenting with neurologic deficits. The patient was worked up for his deficits and biopsy ultimately proved a diagnosis of PACNS. He was rapidly started on high dose glucocorticoids and started on induction therapy with CYC. Unfortunately despite rapid and aggressive therapy, his disease progressed through this treatment regimen with development of seizures and new enhancement on MRI. He was subsequently transitioned to RTX and responded very well. He relapsed after the initial induction, was re-induced and again responded well. With the second induction, he received three of four doses of RTX based on the traditional vasculitis protocol, but therapy was interrupted due to concern for JC virus after a positive antibody. A thorough work up for JC virus was negative. Despite only receiving three of four doses, the patient achieved remission and has been able to maintain it with mycophenolate mofetil (MMF) as a maintenance agent. Patient B is a 50-year-old male who presented with long standing headaches, new onset seizures and transient neurologic deficits. Head imaging revealed a discrete lesion concerning for possible mass with surrounding edema, though subsequent biopsy showed PACNS. He was immediately started on high dose glucocorticoids. A discussion regarding risks and benefits of treatment with CYC and possible therapy with RTX was had with the patient. Based on side effect profile and case reports showing efficacy of RTX, the patient chose to receive RTX. He tolerated the therapy very well, and was able to achieve remission based on regression of CNS lesions on MRI. He has been maintained in remission through preemptive dosing of RTX every 6 months.

Discussion: Rituximab has been well established as an important therapy in rheumatology particularly with respect to systemic vasculitides as proven by the RAVE and RITUXVAS trials among others. Though RTX is an important alternative to CYC in systemic vasculitis, aside from case reports, its efficacy has not yet been firmly established in PACNS due to the rarity of the disease and lack of randomized controlled trials. In our experience with two patients, RTX is an effective alternative to CYC that is able to induce remission in patients who are either refractory to CYC or naïve to CYC. Further, our patients have shown that maintenance can be achieved with either less immunosuppressing drugs or with preemptive dosing of RTX. These cases are important because the side effect profile of RTX is often preferable for patients and requires less frequent dosing and less frequent drug monitoring.

Title: A Randomized, Double-Blind, Placebo-Controlled Trial of Infliximab in Refractory Polymyositis and Dermatomyositis

Authors: Megha Sawhney¹, Galen Joe², Joseph Shrader², Frederick Miller³, Mark Gourley¹, Adam Schiffenbauer³

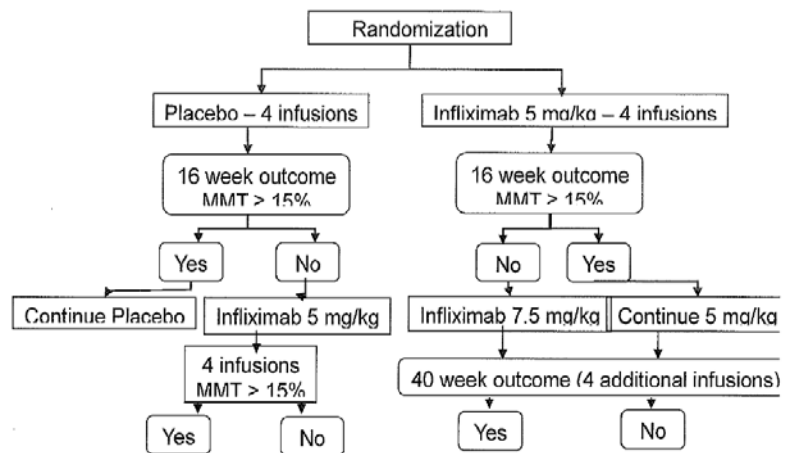
¹ National Institute of Arthritis and Musculoskeletal and Skin Diseases/ NIH, ²Rehabilitation Medicine Dept NIH, ³Environmental Autoimmunity Group, NIEHS, NIH

Purpose: To investigate in a pilot study the safety and efficacy of infliximab in patients with refractory dermatomyositis (DM) and polymyositis (PM).

Methods: A randomized, double blind, placebo-controlled trial included subjects with active DM or PM. A proximal manual muscle strength testing (MMT) score between 80-120 (out of 160) was required, as were stable prednisone ≤ 0.5 mg/kg/day and stable immunosuppressive drug doses for 4 weeks prior to participation. Participants received blinded infusions of either placebo or infliximab 5 mg/kg at 0, 2, 6 and 14 weeks. The primary outcome was a $\geq 15\%$ MMT improvement at week 16 compared to week 0. Secondary outcome measures were improvement defined by the International Myositis Assessment and Clinical Studies Group (IMACS) criteria. Subjects in the infliximab arm who did not meet the primary outcome (non-responders) were increased to infliximab 7.5 mg/kg at weeks 22, 30, 38. Non-responders in the placebo arm at week 16 received infliximab 5 mg/kg at weeks 16, 18, 22, 30, 38. At week 16, responders in each arm had the option of either continuing the same treatment or changing to the non-responder treatment for that study arm. Outcomes were reassessed at week 40.

Results: Twelve subjects completed the study to week 16. Infliximab treatment resulted in one subject responding at the dose of 5 mg/kg. Of the remaining five subjects, two crossed over to the infliximab 7.5 mg/kg dose and three withdrew because of no response. One of the two subjects that crossed over to the higher infliximab dosing responded. All 6 patients in the placebo arm crossed over to the 5 mg/kg dosing regimen after week 16 and 2 responded to infliximab. One death from stroke, thought unrelated to study drug, occurred during the study. Adverse events were uncommon.

Conclusions: Infliximab therapy for patients with refractory PM and DM was well tolerated and may benefit a subset of patients.



Title: *Diary Score Validation for the Assessment of Disease Activity in CANDLE (Chronic Atypical Neutrophilic Dermatosi s with Lipodystrophy and Elevated Temperature) and SAVI (STING Associated Vasculopathy with Onset in Infancy)*

Authors: Megha Sawhney, Gina Montele g are, Kost Bahar, Robert Wesley, Raphaela Goldbach- Mansky

National Institute of Arthritis and Musculoskeletal and Skin Diseases/ NIH

Background and Purpose: Daily diaries of prominent disease symptoms are accepted instruments to evaluate clinical disease activity in patients with a number of autoinflammatory diseases (AID) and have become standard in reporting treatment related outcomes in CAPS (Cryopyrin associated periodic syndrome) with acceptance as clinical outcome measures in CAPS by the FDA. For novel AID with distinct organ manifestations, disease-specific diaries need to be generated and validated. In pediatric inflammatory diseases the Childhood Health Assessment Questionnaire (CHAO), which measures physical function and the following patient and physician-derived outcome measures, patient global VAS (PATG) and physician global VAS (PHYG) are used to assess disease severity and response to treatment and have been used to validate patient related outcomes in the past.

Methods: The daily diary developed for NOMID was modified to reflect disease symptoms of CANDLE and SAVI. For CANDLE these include: fever, rash, joint pain, headache and fatigue For SAVI these also include respiratory symptoms and ulcerative lesions. Each symptom is rated on a scale from 0 to 4 for increasing severity. We validated the diary scores in CANDLE and SAVI patients against 6 validated outcome measures: Childhood Health Assessment Questionnaire (CHAO), which measures physical function, physician global VAS (PHYG), global pain assessment (PAINGL), parent global (PARG) the patient quality of life (PATOL), and parent OL (PAROL) by correlating each symptom and the summary of the diary score for all symptoms of the CANDLE (5 symptoms) or SAVI diary (6 symptoms) with CHAO, PHYG, PAINGL, PARG, PATOL and PAROL. We performed Pearson correlation and 1-sample t-test to assess whether these values PLAUSIBLY centered at 0 was performed. P-values were not corrected for multiple comparisons but p-values of <0.01 were considered significant.

Results: 11 CANDLE and 4 SAVI patients and 3 undifferentiated interfernopathy patients were included. Mean diary scores computed for all patients only correlated with CHAO($r=0.43$, $p<0.001$). For CANDLE patients the correlations were CHAO 0.45 ($p<0.001$), PAINGL 0.4 ($p=0.015$) PARG 0.35 ($p<0.01$) but the SAVI scores did not correlate with any of the measures. Individual symptoms like fever, rash etc correlated well with these outcome measures in both CANDLE and SAVI. However the SAVI specific parameters: respiratory symptoms and ulcerative lesions did not show any significant correlation with any of these measures.

Conclusion: Our study shows that diary score exhibit validity across other validated outcome measures in pediatric inflammatory diseases, but adjustments in assessing outcomes in SAVI need to be further refined.

Title: *Long-term Outcomes of Patients with Juvenile Dermatomyositis*

Author: Sam Serafi¹, Vladislav Tsaltskan¹, Anna Yakovleva¹, Heidi Sami¹, Rodolfo Curiel¹, Gulnara Mamyrova², Lisa Rider², Olcay Y. Jones³

¹George Washington University School of Medicine and Health Sciences, ²Environmental Autoimmunity Group, NIEHS, NIH, ³Walter Reed National Military Medical Center

Purpose: Juvenile idiopathic inflammatory myopathies (JIIM) are rare, autoimmune chronic muscle diseases of childhood. We present long term outcomes patients who have childhood onset JIIM (age <18 years) who are followed by GW Myositis Center and NIH and who are now over 18 years age. The purpose of this study is to review long term outcomes of disease activity and damage over time.

Methods: This is a retrospective chart review study approved by GWU IRB regarding a cohort of 49 JIIM patients. The analysis was done in GraphPad Prism.

Results: Demographics included 49 JIIM patients with a subgroup breakdown of 42 Juvenile Dermatomyositis, 5 Juvenile Polymyositis, and 2 JCTM with a median age of 22.5 years (range 18 to 49 years) and median disease duration of 11 years. Among those, 57% had a chronic continuous course, 28% had a polycyclic course and 11% with a monocyclic course. The parameters evaluated included MD global activity score at final visit was a median of 1.6 [IQR 1.0 - 3.7]. Myositis damage, by Myositis Damage Index, was present in 96% of patients with median score of 7 [IQR 4 - 9.9] (Table 1); The most frequent damage features included persistent muscle weakness in 71%, cutaneous scarring or atrophy in 61%, calcinosis in 57%, joint contractures 67%, and lipodystrophy 32%. The review of treatment revealed previous use of daily prednisone in 84% and current use of prednisone in 58%. Furthermore, 56.1% were on IV steroids at one time, and 15.9% still required IV steroids. Methotrexate was the most commonly used DMARD with 78.6% of patients receiving it in the past and 40.0% with continued use as adults. 32.5% of patients used biologics in the past, and only 7% remained on biologic therapies.

Conclusion: This is one of the largest cohorts of patients with JIIM evaluated for long term disease activity and damage outcomes. Our results showed the majority of patients have ongoing disease activity requiring continued use of prednisone and other immunomodulatory agents. It implies the need for new treatment modalities to improve disease outcomes. We will further examine predictors of illness complications in our cohort.

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	25th Percentile	Median	75th Percentile	Percent with score > 0
Muscle Damage (0-3)	1	2	3	77.6
Skeletal Damage (0-4)	0	1	2	65.3
Cutaneous Damage (0-5)	1	2	3	79.6
GI Damage (0-3)	0	0	0	12.2
Pulmonary Damage (0-4)	0	0	0	18.4
Cardiovascular Damage (0-4)	0	0	0	8.2
Peripheral Vascular Damage (0-4)	0	0	0	8.2
Endocrine Damage M:(0-4)F:(0-6)	0	0	1	30.6
Ocular Damage (0-2)	0	0	0	14.3
Infection Damage (0-2)	0	0	0	10.4
Malignancy Damage (0-1)	0	0	0	2.0
Total Damage Score M: (0-36), F:(0-38)	4	7	9.9	95.9

Table 1. Disease damage scores by system, as assessed by the Myositis Damage Index, in 49 adult patients with juvenile idiopathic inflammatory myopathies.

Title: *Histopathologic and Immunologic Features of Skin Manifestations in Monogenic Autoinflammatory Disorders*

Authors: Kyawt W. Shwin, Chyi-Chia Richard Lee, Adriana Almeida de Jesus, Carmelo Carmona-Rivera, Louise Malle, Yanfeng Hou, Gina A. Montealegre-Sanchez, Edward W. Cowen, Raphaela Goldbach-Mansky

National Institute of Arthritis and Musculoskeletal and Skin Diseases/ NIH

Background: Many genetically defined autoinflammatory diseases (AID) are caused by innate immune dysregulation and present with “neutrophilic dermatoses”. This study systematically assesses immune-cell infiltrates, and interferon (IFN) scores in skin biopsies of 2 IFN-mediated AID: STING-Associated Vasculopathy with onset in Infancy (SAVI) and Chronic Atypical Neutrophilic Dermatitis with Lipodystrophy and Elevated Temperature (CANDLE) and 2 IL-1-mediated AID, Neonatal-onset Multisystem Inflammatory Disease (NOMID) and Deficiency of IL-1 Receptor Antagonist (DIRA). We hypothesize that histopathologic and immunologic features present in skin lesions can distinguish IFN- from IL-1-mediated disorders.

Methods: Tissue from skin lesions of patients with NOMID (n=4), DIRA (n=4), SAVI (n=3), CANDLE (n=5) and other interferonopathies (UIFN) (n=7) were stained with H&E. Immunohistochemistry with antibodies to Myeloperoxidase (MPO/Neutrophil), CD163 (macrophage), CD123 (plasmacytoid dendritic cell (pDC)), CD3 (T cell), CD19 (B cells) was performed. The presence of Neutrophil extracellular traps (NETs, citrullinated histone H4) and IFN-inducible protein (Mx1) were assessed by immunofluorescence. An RNA IFN score was obtained. Inflammatory cells in skin regions were semi-quantitatively scored: 0=absent, 1=scant, 2=moderate or 3=abundant.

Results: Clinically, NOMID patients present with urticaria, DIRA with pustulosis, CANDLE with nodular rashes and SAVI with acral violaceous vasculitic plaques. Histochemically, epidermal MPO+ neutrophilic microabscesses were seen only in DIRA. In CANDLE, MPO+ and CD163+ cells were noted predominantly in the deep dermis and subcutis. SAVI had intravascular thrombi, fibrinoid necrosis of vascular wall with abundant perivascular MPO+ and CD163+ cells. Nuclear debris was seen in SAVI and CANDLE. Mild CD123+ cells were seen in dermis and perivascular areas in SAVI and CANDLE; but not in DIRA and rarely in one NOMID sample. CD3+ cells were seen predominantly in dermis and perivascular areas in SAVI, and in periadnexal areas in CANDLE. Dermal CD19+ cells were noted only in a patient with longstanding SAVI. The presence of NETs was evident in NOMID, DIRA and CANDLE, but not in SAVI. SAVI and CANDLE samples have positive Mx-1 staining and high IFN-response gene scores, but not in NOMID and DIRA.

Conclusion: A distinct histologic pattern of neutrophil and macrophage infiltration characterizes SAVI, CANDLE, NOMID and DIRA skin biopsies, while Mx-1 staining and the IFN score distinguish IFN- and IL-1 mediated AID. Thus, the histologic and immunologic assessment of skin biopsies may guide the diagnosis and identify dysregulated immune pathways in AID. Furthermore the skin can serve as a tissue model to evaluate molecular pathways that lead to the skin manifestations in genetically defined and undefined inflammatory diseases.

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Title: *70 Years of Progress: History of the Rheumatism Society of the District of Columbia, 1946-2016*

Authors: Sonia D. Silinsky Krupnikova¹, Victoria K. Shanmugam¹, Sean McNish¹, Joseph Croft², Christopher Collins³

²George Washington University School of Medicine and Health Sciences, ² MedStar Georgetown University Hospital, ³MedStar Washington Hospital Center

Background: In the aftermath of the Second World War, medical practice was at a turning point. Antibiotic therapy with penicillin and anti-inflammatory therapy with aspirin had just reached mainstream use. The National Institutes of Health had just been established, creating a place for young investigators to discover novel solutions to intractable problems in medicine. Multiple national societies appeared for the benefit of countless diseases, encouraging innovation and discovery. In the midst of this national engagement, a local special interest group, the Rheumatism Society of the District of Columbia (D.C. Rheum), became one of the first of its kind in the nation.

Methods: This paper uses primary sources gathered from PubMed, family archives, and the Society's archive of meeting minutes in order to characterize the historical contribution and development of D.C. Rheum. In addition to describing how the society evolved over time, this study contextualizes the activities of D.C. Rheum in the overall milieu of the science of rheumatology and aims to create a sense of the ways in which local professional societies interact with rapidly evolving scientific progress.

Discussion: Founded in 1946, the Society aimed "to stimulate interest in and increase the knowledge of rheumatic diseases among physicians and laymen." Originally a collection of physicians from various fields of medicine (including cardiology, pediatrics, and orthopedic surgery), D.C. Rheum grew to be a meeting place for the capital's foremost intellectual contributors to the state of the art in the developing specialty of rheumatology. As therapies and understanding of rheumatic diseases improved, D.C. Rheum implemented multiple mechanisms to remain abreast of major developments, including CME accreditation and invitation of leading experts in clinical as well as basic science from across the country.

Significance: Over the last 70 years, the Rheumatism Society of the District of Columbia has grown and evolved in parallel to the field of rheumatology itself. From its origins as a physician interest group, it developed into an organization dedicated to continuing medical education for rheumatologists in the D.C. community, providing a forum for professional networking and knowledge dissemination.

Title: *Novel Use Of Rituximab In Macrophage Activation Syndrome*

Authors: CPT Rodger Stitt, CPT Zachary Junga, CAPT Michael Keith and MAJ Christopher Tracy

Walter Reed National Military Medical Center

Introduction: Macrophage activating syndrome (MAS), also known as secondary hemophagocytic lymphohistiocytosis syndrome (HLH), is a rare disease characterized by aberrant immune hyperactivation of T lymphocytes and macrophages driven by cytokine dysfunction. Clinical features include fever, hyperferritinemia, hepatomegaly, lymphadenopathy, cytopenias, and encephalitis. MAS differs from primary HLH in that it is triggered by an infection, autoimmune process, or malignancy whereas primary HLH is caused by an underlying genetic abnormality. Many providers consider the HLH-2004 protocol, which includes etoposide, cyclosporine, dexamethasone and intrathecal methotrexate, as standard of care in the treatment of MAS. However there are significant toxicities associated with this treatment regimen and it has been primarily studied in HLH associated with perforin gene mutations in children not MAS associated with autoimmunity. There is no consensus on alternative, less toxic treatments for MAS. We describe two cases of MAS caused by connective tissue diseases, both treated successfully with novel use of rituximab as part of their modified HLH-2004 protocol.

Case Description: Case 1 is a previously healthy 22-year-old African American female admitted for pancytopenia, constitutional symptoms, and arthritis. Evaluation resulted in diagnosis of systemic lupus erythematosus (SLE) based on inflammatory arthritis, cytopenias, positive anti-nuclear antibody, and high titers of anti-smith and anti-ribonucleoprotein antibodies. MAS was diagnosed based on the following HLH-2004 criteria: fever, markedly elevated ferritin >7500 ng/mL, pancytopenia, elevated liver associated enzymes, hypertriglyceridemia, and splenomegaly. She was started on the HLH-2004 treatment protocol and had significant side effects to etoposide and refused to continue with treatment. Etoposide was discontinued and she was treated with rituximab in addition to cyclosporine and dexamethasone. Her clinical symptoms, complete blood count, ferritin, and triglycerides all normalized and she remains in remission 6 months following last infusion. Case 2 is a 64-year-old Vietnamese female with a history of rheumatoid arthritis (RA) complicated by vasculitis was admitted with multiorgan failure requiring intubation. MAS was diagnosed based on fevers, cytopenias, elevated ferritin (highest 47,000 ng/mL), and hypofibrinogenemia along with a bone marrow biopsy showing hemophagocytes. She was initially treated with a modified HLH-2004 protocol to include etoposide, dexamethasone, and rituximab. Cyclosporine was held due to renal impairment. She has been without recurrence since finishing her treatment.

Case Discussion: The HLH-2004 treatment was designed for primary HLH and can have significant toxicities, mainly due to etoposide. There is a need for more tolerable and precise treatment options that target the pathogenic cytokines especially in the era with novel biologic therapy. Literature review found a single published case of rituximab successfully used in the treatment of MAS secondary to SLE. Our case series is unique in that both patients had underlying autoimmune diseases and responded very well to rituximab therapy as part of their treatment protocol. Rituximab has a more much more favorable side effect profile and if shown to work well in larger studies, may be a better therapeutic option in treatment of MAS. This case series highlights the importance for further research into the role of novel biologics, including rituximab therapy, in the treatment of MAS.

Title: *A Continuum of Disease, from Mevalonic Kinase Deficiency to Hyper-IgD Syndrome*

Authors: Ann Marie Szymanski, Lawrence Jung

Children's National Medical Center

Background and Purpose: To discuss the case of a female infant with mevalonic kinase (MVK) deficiency identified at birth, who ultimately underwent bone marrow transplant (BMT) with intent to cure. She relapsed and instead of her original, severe course of disease developed a milder, hyper-IgD phenotype. This conversion has not been reported before.

Case Description: A 3 month old female presented to our facility with a history of ascites diagnosed in utero. Initial workup revealed anemia, thrombocytopenia, and elevated liver enzymes. She was considered for liver transplant secondary to worsening hepatic disease. Diagnostic studies revealed elevation of urinary mevalonic acid and genetic sequencing demonstrated a previously undescribed homozygous mutation (c.889.C>A, L2971) thought to be related to her MVK deficiency. She was treated with IV steroids and eventually anakinra, with good results although she continued to have periodic fevers, rashes, and arthritis requiring frequent hospitalizations. She underwent 5/6 umbilical cord stem cell transplant (SCT) at the age of 15 months. Immediately following transplant, the patient's urine mevalonic acid was undetectable. Approximately 18 months following transplant she again developed fevers, rashes, and arthritis. Urine mevalonic acid returned as mildly elevated indicating a relapse. Concurrently, one hundred percent of her leukocytes were of donor origin. **Case Discussion:** Mevalonic kinase deficiency is a rare, autosomal recessive, autoinflammatory disorder. MVK deficiency and Hyper-IgD Syndrome (HIDS) represent a spectrum of the same disease. Both diseases are the consequence of mutations in the MVK gene, Those with HIDS exhibit less severe manifestations. Attacks are characterized by spiking fevers, rashes, arthritis, lymphadenopathy, and abdominal pain. In its more severe form, the clinical picture can include dysmorphism, growth inhibition, and developmental delay. Rarely, cholestatic complications occur. Patients may have some or all of these symptoms. Treatment usually includes NSAIDs, steroids, IL-1 blockade. When present in the neonatal period, the disease is much more severe and often fatal. Treatment of these type of patients include stem cell transplantation. There are a few reports which report that stem cell transplantation was curative. In this case, however, despite having full engraftment, she continued to be symptomatic, albeit less severe. Thus SCT did not fully correct her MVK deficiency.

Conclusion/Significance: While the original intent of our patient's BMT was to cure her disease, this case suggested that there exists the possibility of conversion into a milder phenotype of disease. Case reports to date have indicated that BMT can help to eradicate disease and avoid the neurologic complications associated with classic MVK deficiency. Our case illustrates the possibility that SCT may not be enough in certain cases. This conversion into a less severe phenotype has not been described before, but should be monitored for accordingly.

Title: *Fever of Unknown Origin: A Retrospective Review*

Authors: Ann Marie Szymanski, Hugo Clifford, Tova Ronis

Children's National Medical Center

Background & Purpose: Fever is a common complaint in medicine, especially in pediatrics. Cases of fever of unknown origin (FUO) where fever is prolonged and no source is easily identified can lead to hospital admission, multiple subspecialty referrals, and costly testing. Previous studies demonstrated infection to be the most common cause of FUO, particularly in children under 2 years; however few studies have examined the workup, diagnosis, and cost of hospitalization in older children. This study aimed to identify the most common etiology of patients hospitalized with FUO, and to assess the costs and resources used in diagnosing and treating these patients.

Methods: Charts of patients aged 2-18 years hospitalized at Children's National between September 2008 and April 2014 with a diagnosis code of fever (ICD-9 780.6) were reviewed. Patients with FUO, defined as a temperature $> 38.3^{\circ}\text{C}$ for at least 7 days were identified. Patients with underlying medical conditions were excluded. Charts were reviewed for final diagnoses, characteristics of admission, and cost. Descriptive statistics were used.

Results: Despite excluding children below 2 years of age, infection still proved to be the most common etiology with 45 (40.9%) of 110 patients diagnosed with infection. Even so, 38 children (34.5%) left the hospital without a diagnosis despite an extensive workup. On average, the mean length of stay for patients was 5 days. Mean number of subspecialty consults was 2 and mean number of imaging studies was 3. Mean total cost of hospitalization for all patients was \$38,191 (95% confidence interval \$30,113 to \$46,269). Highest average cost was associated with an oncologic diagnosis (mean \$183,629). Please see Table 1 for complete statistics.

Conclusions: This information, and in particular the cost associated with admission and the large number of children discharged without a diagnosis, draws attention to the concept of resource utilization and may influence clinicians to reconsider inpatient workup requirements for FUO.

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	Infectious n=45	Rheumatologic n=16	Oncologic n=5	Miscellaneous n=6	Unknown n=38	Total n=110
Age (yrs), <u>+SD</u>	6.5 (\pm 4.3)	6.6 (\pm 3.3)	4.2 (\pm 2.3)	8.7 (\pm 4.5)	6.2 (\pm 4.1)	6.4 (\pm 4)
Length of Stay (days)	4.1 (\pm 3.2)	4.3 (\pm 3)	21.8 (\pm 8.9)	8.7 (\pm 8.1)	3.8 (\pm 2.2)	5.1 (\pm 5.2)
Hospital Cost (USD)	27271 (\pm 22905)	39312 (\pm 31873)	183629 (\pm 53683)	77118 (\pm 64093)	25370 (\pm 13546)	38,191 (\pm 43,223)
Number of Imaging Studies	3 (\pm 3)	3 (\pm 3)	4 (\pm 2)	3.5 (\pm 2)	3 (\pm 2)	3 (\pm 2.7)
Number of Subspecialty Consults	2 (\pm 2)	3 (\pm 2)	4 (\pm 2)	4 (\pm 1.8)	2 (\pm 1)	2.4 (\pm 1.6)

Table 1: Mean Characteristics of FOU patients and hospitalization by diagnostic category

Title: *Application of Extra Corporal Membrane Oxygenation [ECMO] in patients with Diffuse Alveolar Hemorrhage in ANCA Vasculitis*

Authors: Rujtua Trivedi, Christopher Collins

MedStar Washington Hospital Center

Background and Purpose: Application of Extra Corporal Membrane Oxygenation [ECMO] in patients with Diffuse Alveolar Hemorrhage in ANCA vasculitis.

Case Description: 28 year old Caucasian female with no medical history presented to the outside hospital with hemoptysis , fever , exertional dyspnea and 5 week history of arthralgia and arthritis. At her initial presentation she was tachycardic [100-110] and hypoxic [85-90%]. Her Initial chest X ray showed peri bronchial cuffing and patchy infiltrates. Her ESR -81mm/hr, CRP-60.7mg/l were elevated. Her work up was negative for Infections [HIV, hepatitis, Fungal and TB] and toxin exposure. She had abnormal UA [Protein -100, RBC >50, WBC- 12], normal cr and her serology was positive for c ANCA- 1:1024 ,PR3 -6.2 [>1.0] , ANA 1:160 speckled and RF 62. Her CT chest was suggestive of Diffuse Alveolar Hemorrhage [DAH]. She was diagnosed with DAH associated with Granulomatosis Polyangitis. She was started on pulse steroid with weekly Rituximab protocol. Over the next 2 days her respiratory and cardiovascular status worsened. She required intubation and vasopressors. At this point she was transferred to WHC for ECMO. Patient had cardiac arrest of 15 mins , after resuscitation, she was placed on [Veno-Arterial] ECMO. This replaced her Heart and Lung. She was also started on plasma exchange. Her immunosuppression was changed to Cyclophosphamide 2mg/kg daily. She became conscious next day. Over the next few days her cardiac and respiratory status improved but she developed cannula site bleeding. Her repeat bronchoscopy showed improvement but no clearing. She required multiple transfusions for her bleeding. She had coagulopathy [low fibrinogen, low platelet], ECMO related complication. Eventually she was weaned off ECMO due to bleeding complication. Her immunosuppression was adjusted accordingly. She was discharge home 2 weeks later. At present she is fully functional.

Case Discussion: On reviewing the literature for ECMO in ANCA vasculitis we found abstract presented at ACR 2015 and few case reports. As per ELSO data base, 78 patients with DAH in ANCA vasculitis were treated with ECMO. Median duration for ECMO use was 8 days and ICU survival was 82 %.Major complication related to ECMO are bleeding [30-40%] or thrombosis of circuit in setting of conservative heparinisation.

Conclusion: ECMO is life saving procedure in Diffuse Alveolar Hemorrhage associated with ANCA vasculitis. Though bleeding is major complication and needs close monitoring, it should not prevent use of ECMO. ECMO provides cardio respiratory support while immunosuppression takes into effect.

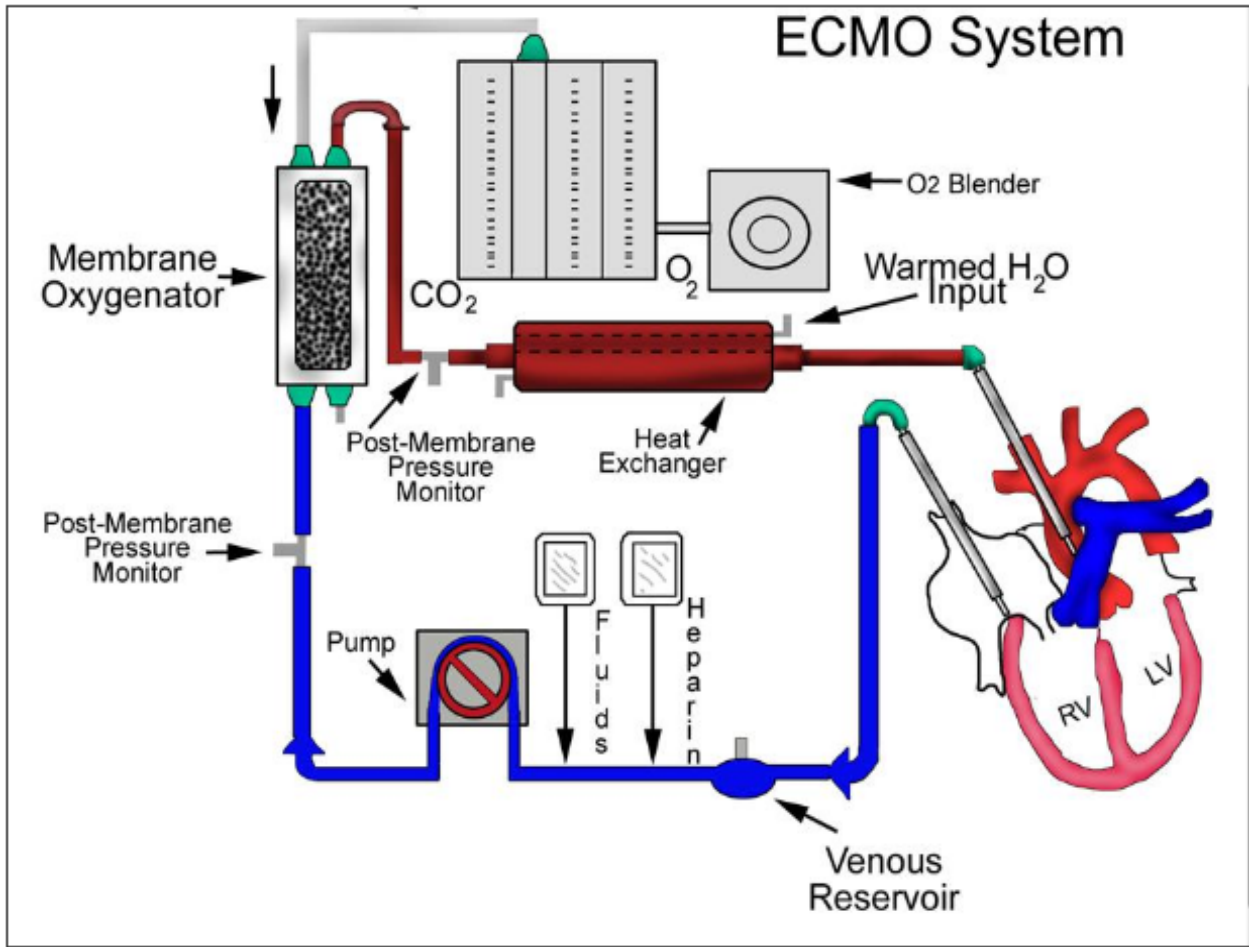


Figure 1

Title: *Juvenile Dermatomyositis with Catastrophic Gastrointestinal Vasculopathy: A Case Series*

Authors: Vladislav Tsaltskan, Sam Serafi, Rodolfo Curiel, Olcay Y Jones

George Washington University

Background: Juvenile dermatomyositis (JDM) is a rare autoimmune myopathy of childhood that most commonly manifests as a disease of the small proximal muscles. Gastrointestinal involvement in JDM is rare but can have severe consequences. Here, we report two cases of severe JDM leading to catastrophic GI illness.

Case Description: Case 1: A 17-year old male with a 4-month history of fulminant JDM treated with steroids, methotrexate, and IVIG presented to the hospital with acute abdominal pain. He was found to have a perforated duodenal ulcer requiring emergency surgery with a CT showing pneumatosis intestinalis. He was treated with methylprednisolone, cyclophosphamide, IVIG, and methotrexate, and was discharged. Two months later, he developed a new episode of vomiting, hematemesis, and hematochezia. Emergency surgery was again required, resulting in resection of a large portion of large bowel and colostomy placement. He was also found to have portal vein thrombosis on MRI, necessitating anticoagulation, bowel rest, and TPN. He improved after a course of cyclophosphamide, IV steroids, and methotrexate.

Case 2: A 21-year old male with a 5-year history of chronic stable JDM treated with steroids, mycophenolate mofetil, and IVIG presented with acute-onset abdominal pain for 48 hours. He was found to have ischemic colitis and required an emergency colectomy within 24 hours of admission. During the same hospitalization, the patient developed a small bowel perforation requiring resection of a large amount of small bowel and jejunostomy placement. He was treated with IV steroids, mycophenolate mofetil, and later started on cyclophosphamide without any subsequent recurrence of gastrointestinal symptoms, however he remained with persistent diffuse thickening of the small bowel on CT.

Case Discussion: Gastrointestinal involvement in patients with JDM is uncommon but can be severe. The occurrence of gastrointestinal disease in JDM patients appears to be correlated with overall disease severity, however it can occur at any point in the disease course. GI involvement ranges from dysphagia due to involvement of the laryngeal muscles to GI bleeding, intestinal perforation, or colitis due to vasculitis of the gut. Management generally involves controlling the underlying disease process with steroids, cytotoxics, DMARDs, or other agents as well as nutritional and surgical management if needed.

Conclusion/Significance: Due to the high morbidity and mortality associated with GI manifestations of JDM, the clinician should closely monitor patients for any evidence of gastrointestinal disease.

Title: *Recurrent Massive Pleural Effusion in Systemic Lupus Erythematosus*

Authors: Vanya D. Wagler, Stacy-Ann S. Comer, Michael P. Keith

Walter Reed National Military Medical Center

Background and Purpose: Pleuritis is the most common pulmonary manifestation of systemic lupus erythematosus (SLE) and may occur with or without a clinically apparent pleural effusion. The lifetime incidence of effusion in SLE patients is 30-50%, but autopsy studies show an incidence as high as 93%. SLE-related effusions are typically exudative by Light's criteria and have a total volume of less than 1,000 mL. Large volume effusion in SLE that persists despite repeat thoracentesis is uncommon. Recurrent massive pleural effusion in SLE is an uncommon condition for which there are no established treatment guidelines.

Case Description: A 24 year old African-American female with SLE and class III/V lupus nephritis presented with pleuritic chest pain. CT pulmonary angiogram revealed a large left-sided pleural effusion. Patient had a two year history of lupus nephritis treated with mycophenolate mofetil (MMF). Initial thoracentesis yielded 1400 mL of exudative fluid. Bacterial, fungal and mycobacterial cultures and cytology were negative; fluid antinuclear antibody (ANA) was strongly positive. Patient had increased proteinuria and serum double stranded DNA antibody titer. Prednisone dose was increased to 60mg daily and MMF to 1500mg twice daily for treatment of suspected lupus flare; hydroxychloroquine was continued and daily colchicine was added for potential benefit in reducing pleural inflammation. Despite initial therapy, effusion rapidly returned and expanded, and thoracentesis was repeated. Serial thoracenteses were required and a total of over 8,000 mL of fluid was removed during a 3 month period. Chemical pleurodesis or surgical pleurectomy was offered, but patient opted instead for repeat drainage and medical therapy.

Case Discussion/Conclusions: Differential diagnosis of massive pleural effusion in SLE includes heart failure, pulmonary embolism, bacterial pneumonia, tuberculosis, and malignancy; initial evaluation should focus on ruling out etiologies besides SLE that may be more immediately life-threatening. Only a small number of published case reports discuss management of SLE-associated massive pleural effusion, which makes it difficult to define best practices. Despite this limitation, a reasonable approach appears to be initial thoracentesis followed by systemic corticosteroids and steroid-sparing therapy with agents such as azathioprine, methotrexate, MMF, or cyclophosphamide. Colchicine may also have a role as an adjunctive treatment. Additional local therapy with pleurodesis or pleurectomy should be considered in refractory cases. Chemical pleurodesis with talc has been reported in multiple cases, though reporting bias is possible. Tetracycline pleurodesis and surgical pleurectomy have also been described with mixed results. Our patient demonstrated significant improvement with serial thoracentesis and medical therapy alone.

Title: *B10 Cells may be involved in Controlling Disease Activity in Polyarticular Juvenile Idiopathic Arthritis Patients*

Authors: Qianzi Zhao, Lawrence Jung

Children's National Medical Center

Background and Aims: The inhibitory function of B cells is partially dependent on the production of Interleukin-10 (IL-10), an anti-inflammatory cytokine. IL10-producing B cells (B10 cells) have been shown to ameliorate collagen-induced arthritis in mice. In humans, very little is known about the role of B10 cells in juvenile idiopathic arthritis (JIA). B10 cells are not restricted to a defined population. CD24^{hi}CD38^{hi} and CD24^{hi}CD27^{hi} have been described as phenotypes for B10 cells in human. In our study, we aimed to analyze the percentages and phenotypes of B10 cells in active and inactive polyarticular JIA (poly-JIA) patients and controls.

Methods: Twelve poly-JIA patients (7 active and 5 inactive) and 11 children with joint pain but excluded for JIA as controls were included. Inactive disease was defined as an active joint count of 0, absence of uveitis and a Physician Global Assessment <10 mm with normal erythrocyte sediment rate (ESR). B10 cells were generated from peripheral blood mononuclear cells stimulated with CpG and CD40L for 48 hours, and phorbol 12-myristate 13-acetate+ionomycin+brefeldin A (PIB) for the last 6 hours. Intracellular production of IL-10 in B cells and their surface markers were assessed by flow cytometry.

Results: The percentage of B10 cells was significantly higher in inactive poly-JIA patients than in active patients (11.87±1.56 vs. 5.05±1.31, P<0.01) and controls (11.87±1.56 vs. 4.56±0.71, P<0.001), while there was no significant difference of percentages of B10 cells between active patients and controls. Although the percentages of CD24^{hi}CD38^{hi} and CD24^{hi}CD27^{hi} B cells among the three groups were similar, the percentages of IL10+CD24^{hi}CD38^{hi} and IL10+CD24^{hi}CD27^{hi} B cells were significantly higher in inactive group compared with active patients and controls. The percentages of B10 cells were significantly higher in CD24^{hi}CD38^{hi} B cells subset (9.94±1.32 vs. 6.30±0.86, P<0.0001) and CD24^{hi}CD27^{hi} B cells subset (10.40±1.07 vs. 6.30±0.86, P<0.0001) than in total B cells. There was no significant difference of B10 cells percentages in CD24^{hi}CD38^{hi} B cells subset compared with CD24^{hi}CD27^{hi} B cells subset. There was no correlation between B10 percentage and ESR within active poly-JIA patients.

Conclusions: The ability of B cells to produce IL-10 might be suppressed in active poly-JIA patients and restored in inactive patients, which suggests a role of B10 cells in poly-JIA pathogenesis. More samples and longitudinal follow-up are needed to confirm the results next.

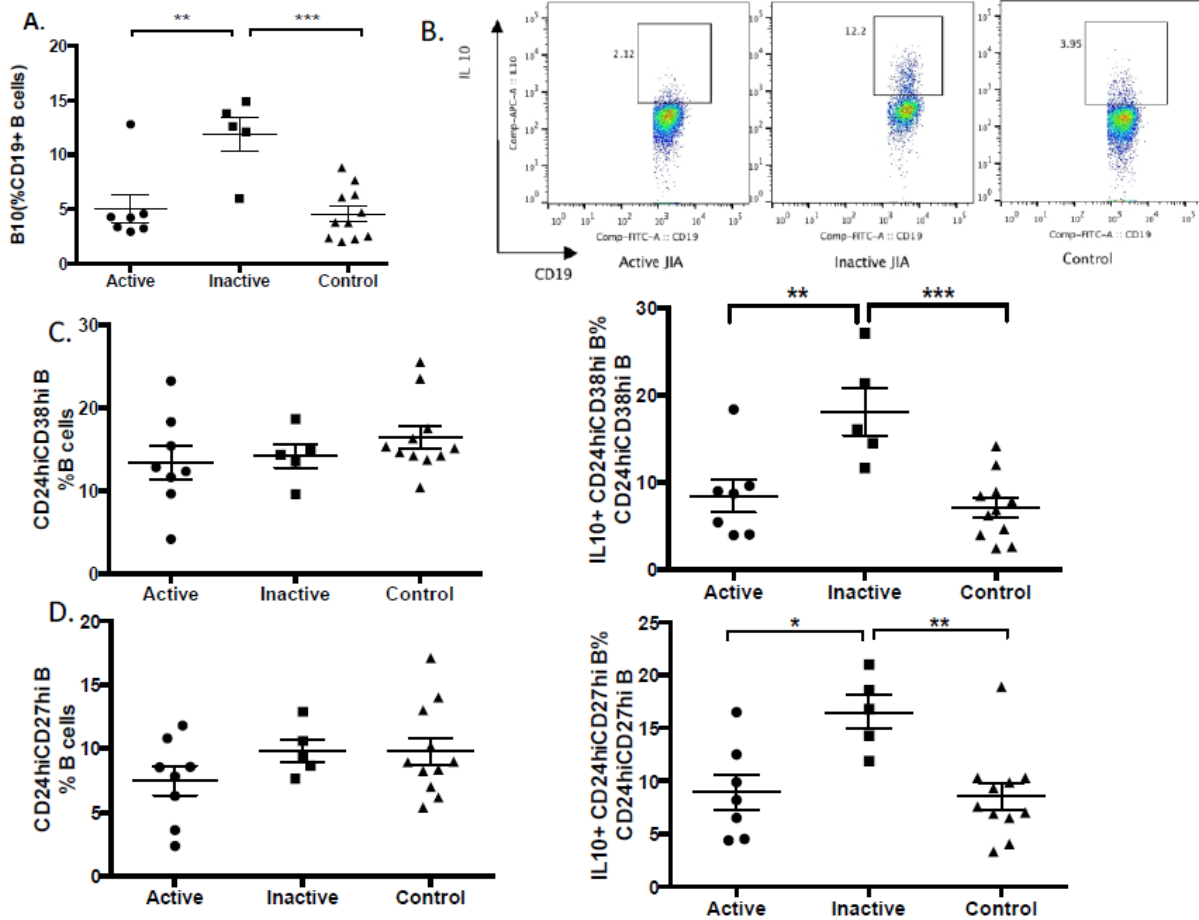


Figure. A. IL10-producing B (B10) cells percentages in total B cells after ex vivo CpG+CD40L stimulation for 48h and phorbol 12-myristate 13-acetate+ionomycin+brefeldin A (PIB) for the last 6h in 7 active, 5 inactive polyarthritis juvenile idiopathic arthritis (JIA) patients and 11 controls were compared. **B.** Representative intracellular IL-10 expression in B cells of active, inactive poly-JIA patients and control. **C.** The percentages of CD24hiCD27hi B cells and IL10+CD24hiCD27hi B cells in active, inactive poly-JIA patients and controls were compared. **D.** The percentages of CD24hiCD38hi B cells and IL10+CD24hiCD38hi B cells in active, inactive poly-JIA patients and controls were compared. *P<0.05, **P<0.01, *** P<0.001.

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