
UPDATE ON JUVENILE MYOSITIS
CARE AND RESEARCH
JUNE 29 - 30, 2018

CURE JM

**SUMMARY OF
SCIENTIFIC RESEARCH
POSTERS**



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VALIDATION OF PROMIS (PATIENT REPORTED OUTCOMES MEASUREMENT INFORMATION SYSTEM)

Kaveh Ardalan, M.D., M.S., is interested in understanding how JM affects quality of life. His expertise in patient-reported outcomes helps him incorporate the perspective of JM patients and parents into studies of quality of life. In order to study quality of life, aspects such as pain, fatigue, physical function, and emotional distress must be accurately measured. Dr. Ardalan's study examines whether a new approach to quality of life measurement, called PROMIS (Patient Reported Outcomes Measurement Information System), is a valid approach for JM patients. PROMIS was developed using Item Response Theory, a new statistical approach with the potential to measure quality of life more accurately than current approaches.

Dr. Ardalan's study has yielded some encouraging findings.

First, feedback from parents and children with JM resulted in similar PROMIS scores. However, he also found that patient and parent perspectives differ just enough that they should both be routinely assessed.

Secondly, some PROMIS scores correlate with strength assessments at clinic visits, suggesting PROMIS is a valid reflection of JM's impact on quality of life.

Lastly, parent PROMIS assessments correlated with physician assessments in clinics (e.g. strength testing), but correlation is less prominent in patient PROMIS self-assessments. This suggests that patient and parent perspectives differ enough that they should both be routinely assessed.

Thanks to Dr. Ardalan's work, the PROMIS assessment tool can help identify the most appropriate interventions, improve patient experience and most importantly, improve quality of life for children with JM, and their families.

Kaveh Ardalan, M.D., M.S., Attending Physician, Division of Rheumatology, Ann & Robert H. Lurie Children's Hospital of Chicago, Instructor of Pediatrics and Medical Social Sciences, Northwestern University Feinberg School of Medicine

STEPPING IT UP: THE USE OF PHYSICAL ACTIVITY MONITORS AS AN OUTCOME MEASURE IN JUVENILE MYOSITIS

Emily Brunner, D.O., is conducting a study to validate the use of Physical Activity Monitors using a type of Fitbit® as a measurement tool for physical function among Juvenile Myositis (JM) patients. The use of these may improve assessment of disease activity and supplement current core set measures (CSM) for disease activity. The study aimed to evaluate whether information provided by the Fitbit One® (average step counts per day) can measure disease improvement in patients with JM.

JM patients spanning the ages 4-17 years were enrolled from rheumatology clinics (enrollment is ongoing). Each patient was evaluated at baseline, one, three and six months using the following core set measures established by Pediatric Rheumatology International Trials Organization (PRINTO) and International Myositis Assessment and Clinical Studies Group (IMACS) including: Manual Muscle Testing (MMT), Childhood Myositis Assessment Scale (CMAS), Patient/Parent Reported Outcome measures (PRO), Patient-Reported Outcome Measurement Information System Mobility Short Form (PROMIS-SF) and Childhood Health Assessment Questionnaire (CHAQ); and functional tests: Sit-to-Stand (STS), Timed Up and Go (TUG), and Six Minute Walk Distance (6MWD). A waist-based Fitbit One® was worn by patients for seven consecutive dates every month for six months, average daily step counts were measured, and descriptive statistics were performed for demographic, clinical and patient reported data.

So far, the findings support the continued study of the Fitbit® as a tool for outcome measures in JM. The number of steps recorded by Fitbit® had a moderate to strong correlation with key JM CSMs except CMAS. The continued analysis of longer-term data will help determine any usefulness for Fitbit® in JM management.

Emily Brunner, D.O., Pediatric and Adult Rheumatology Fellow, University of Pittsburgh Medical Center, Division of Rheumatology and Immunology

RESEARCH PRIORITIES AMONG PARENTS AND FAMILIES OF CHILDREN WITH RHEUMATIC DISEASE

Colleen K. Correll, M.D., M.P.H., led a project for the patient-powered rheumatology research network, PARTNERS (Patients, Advocates, and Rheumatology Teams Network for Research and Service), to identify and prioritize research areas based on feedback from families and patients with JM and other rheumatic diseases. The goal of the project was to improve the quality and relevance of research.

To understand the most important priorities of patients and families, Dr. Correll emailed a survey to members of the Cure JM Foundation, the Arthritis Foundation (AF) and the Lupus Foundation of America (LFA), and also posted to those organizations' social media profiles. Parents, patients thirteen-years and older, family and friends were included in the survey.

Common themes emerged from the open-ended survey responses and were distinguished further through focus groups. Using those themes, final surveys were made, distributed, and posted. Respondents ranked the themes most important to them, and the seven most important themes were identified.

There were 138 (77% parents), 57 (93% parents) and 47 (55% parents) respondents to the open-ended survey for Cure JM, AF and LFA, respectively. The open-ended responses were examined and 23, 28, and 16 research themes were identified for Cure JM, AF, and LFA, respectively. From those themes, 365, 44, and 32 respondents from Cure JM, AF, and LFA, respectively, ranked the seven most important priorities. The top seven priorities of Cure JM respondents from highest to lowest were: new treatments, flares (triggers, prevention, and treatment), medication side effects, standards to measure disease activity and/or remission, genetic/environmental causes, JM complications (i.e. rash, calcinosis, lipodystrophy), and risks of other autoimmune diseases. The survey results not only involved JM patients and families in more aspects of research activity, but also helped to frame the global JM research agenda.

Colleen K. Correll, M.D., M.P.H., Pediatric Rheumatologist and Assistant Professor at the University of Minnesota Masonic Children's Hospital

AUTO-IMMUNE DISEASE CLINICAL TRIAL

P rincipal Investigator Rodolfo Curiel, M.D., and co-investigator Gulnara Mamyrova, M.D., Ph.D., are conducting a clinical trial for the experimental therapy Abatacept. Abatacept is a drug used to treat auto-immune diseases. It works by interfering with the immune activity of T cells. It is meant for patients whose JDM has been difficult to manage.

To qualify, pediatric and adult patients with JDM must have moderately active disease, despite treatment with prednisone, and at least one other medication. They must be at least seven years old and weight at least 25kg.

Medical evaluations, study questionnaires, blood testing, and MRIs/x-rays will be performed at six visits over six months. Travel funds and compensation will be available.

This clinical trial is an important step toward getting more treatment options available for JDM patients.

Dr. Rodolfo Curiel, M.D., Program Director, Associate Professor of Medicine Director, Myositis Center, The George Washington University

Dr. Gulnara Mamyrova, M.D., Ph.D., Research Coordinator, Division of Rheumatology, Department of Medicine, The George Washington University

GENETIC RISK FACTORS IN JUVENILE DERMATOMYOSITIS

Claire Deakin, Ph.D., a Post-Doctoral Fellow at University College London is interested in the genetic components of Juvenile Dermatomyositis. The aim of Dr. Deakin's study was to gain insight into JDM - the symptoms and how they show up differently in different patients based on genetics, e.g. a patient's DNA. Specific goals of the study included linking genetic factors to specific features of JDM, linking age of disease onset to the likelihood of developing specific features of JDM, and also looking for a connection between genetics and cause of JDM in patients. This kind of information can lead the way to improved treatments for patients.

To accomplish these goals, JDM patients from North America and the UK were genotyped, i.e. their DNA sequences were examined and compared to a control group without JDM. The human leukocyte antigen (HLA) system is responsible for producing proteins that regulate the immune system in humans. Dr. Deakin's findings are very encouraging. They have confirmed the involvement of the HLA gene complex in JDM. And, specific locations in DNA sequences were identified that pinpoint the gene that is related to age of JDM onset. This knowledge regarding genetics in relation to JDM is key to developing the best suited treatments for each patient.

Claire Deakin, Ph.D., Post-Doctoral Fellow at University College London

THE GENETIC CONTRIBUTION OF RARE VARIANTS TO JUVENILE MYOSITIS

This study, led by Charlly Kao, Ph.D., and Hakon Hakonarson, M.D., Ph.D., aims to find mutations in genes that play a role in JM. By understanding how mutations in specific genes change its activity in a way that contributes to JM will enable development of therapies (such as new drugs) that can reverse the activity of the mutation, and thus treat the disease. In order to do this, Dr. Kao used Whole Exome Sequencing (WES). Since proteins encoded by genes play such a major role in our body functions, Whole Exome Sequencing is a more cost-effective and efficient way to identify genetic causes of disease because it gathers and analyzes only the ~1.5% of the genome containing protein-encoding genes (the exome).

Dr. Kao looked for rare genetic variants/mutations from DNA taken from blood or saliva of 79 subjects with suspected/confirmed incidence of JM, and compared the DNA from JM subjects to those without autoimmune/inflammatory disorders. For one Cure JM volunteer family, WES was performed on all family members, including the maternal grandfather and grandmother, to gather information on inheritance patterns.

The study yielded many encouraging findings. First, the discovery of possible new autoantigen epitopes, which may be triggers for myositis specific/associated antibodies (known to be important clinical markers in JM), and a variant in filaggrin (a type of protein), that may suggest a link between JM and anti-filaggrin antibodies. Additionally, new information was established about particular human leukocyte antigen (HLA) genes, an important set of genes used by our body to mount an immune response, which normally is directed to foreign, possibly dangerous materials such as infections, but is perturbed in autoimmune conditions like JM, that mounts an immune response to the body itself. Other important areas of discovery were related to metabolic activity as well as signaling pathways that can influence inflammatory responses. These results will guide relevant research and advance the genetic understanding of JM.

Dr. Charlly Kao, Ph.D., Senior Scientist, Center for Applied Genomics, Children's Hospital of Philadelphia

Hakon Hakonarson, M.D., Ph.D., Director of the Center for Applied Genomics, Children's Hospital of Philadelphia, Department of Pediatrics, Perelman School of Medicine, University of Pennsylvania

CROWDSOURCING AND IMPROVING ASSESSMENT OF SKIN DISEASE IN PEDIATRIC RHEUMATOLOGY

Susan Kim, M.D., M.M.S.c., works with children and adolescents with rheumatic diseases and specializes in juvenile dermatomyositis. She is also the Vice Chair of the juvenile dermatomyositis subcommittee in the Childhood Arthritis and Rheumatology Research Alliance (CARRA).

Skin disease plays a profound role in JDM, but measuring and monitoring it has been difficult for many reasons. Dr. Kim is leading a project that aims to develop an online platform (an APP) that collects and houses photos of JDM rashes. This type of tool will help physicians to learn, teach, and treat JDM better in the future. This project is in development; but, foundational steps have been made, including: Dr. Kim identified a secure place to store the data. Information will be collected and managed on a UCSF (University of California San Francisco)-approved, HIPAA (Health Insurance Portability and Accountability Act) and HITECH (Health Information Technology for Economic and Clinical Health) compliant, HITRUST (Health Information Trust Alliance) Amazon Web Services (AWS) server.

Second, she collaborated with pediatric rheumatologists and dermatologists from CARRA and the Pediatric Dermatology Research Alliance (PeDRA), and plans to expand her discussions with patients and families, through Cure JM to ensure that the APP is useable, useful and acceptable.

Ongoing and future work includes APP iteration, and ongoing discussions with CARRA and PeDRA members, as well as patients and families.

This crowd-sourced app will empower patients and families to capture the wide spectrum of skin disease in JDM, all in one place. A broad visual representation of skin disease in JDM will improve future identification and monitoring of disease activity and ultimately, improve future overall outcomes for JDM patients.

Susan Kim, M.D., M.M.S.c., Pediatric Rheumatologist and Associate Clinical Professor at UCSF, Benioff Children's Hospital

A PROCESS OF DRUG DISCOVERY FOR JUVENILE MYOSITIS

The National Center for Advancing Translational Sciences (NCATS) is a part of the National Institutes of Health (NIH) that focuses on developing new and repurposing existing treatments for diseases, particularly rare ones. In an effort to accelerate and improve the treatment of disease, a state-of-the-art screening system is used to expedite the drug development process. The network is called a 'high throughput system.' These systems use robots to screen and test compounds against assays. Assays are tools that measure the effects of compounds on cells and proteins related to a particular disease. The systems can quickly test hundreds of thousands of compounds that have the potential to be developed into drugs. Cure JM has partnered with an NCATS investigator, James Inglese, Ph.D., who leads the Assay Development and Screening Technology (ADST) program and a postdoctoral research fellow, Travis Kinder, Ph.D., with the ultimate goal of getting effective and safe treatments for JM patients.

Biologists and JM experts are working to pinpoint molecular problems that occur in JM and identify how to correct those problems. A major focus of the NCATS project is the role of interferons and major histocompatibility complex (MHC). In JM, interferons are a type of inflammatory protein in the blood. The interferons cause MHC, another type of immune protein, to be overexpressed by the body's muscle cells. This overexpression activates white blood cells (called T cells), and causes muscle damage and weakness. Dr. Kinder is working on developing assays to search for compounds that inhibit the interferon-produced MHC expression in muscles. There are plans to develop a group of assays that will filter through many active compounds to identify drug candidates for use in animal studies, and eventually, into clinical trials with patients. Discovering already approved drugs with the assays could get a therapy to patients in a few years, but a novel compound could take around a decade to develop.

A PROCESS OF DRUG DISCOVERY FOR JUVENILE MYOSITIS, CONT.

One of the assays under development will use CRISPR/Cas9, a new technology for genome editing. A genome, made up of DNA, tells our body's cells and proteins what to do. CRISPR/Cas9 has generated a lot of excitement in the medical field because it enables geneticists and medical researchers to remove, add, and edit sections of DNA. Dr. Kinder will use CRISPR/Cas9 to cut the MHC gene in muscle cells and insert a gene called luciferase, in order to measure the level of MHC gene-expression. The cells will then be treated with interferon to activate the gene expression. Then, compounds will be screened to find those that can inhibit this pathway. Follow up assays will include measuring mRNA and protein from unedited cells to confirm the initial findings.

Once developed, these assays can also be used to determine if any chemicals in the environment can trigger increased MHC in muscle, which may contribute to the development of myositis. The Tox 21 library at NCATS, which consists of 10,000 environmental chemicals, can be screened rapidly with the robotic high throughput screening system. An additional NCATS siRNA library can also be screened to find other proteins and pathways that affect MHC expression. Dr. Kinder is currently developing the assays, with screening beginning this summer!

Travis B. Kinder, Post-Doctoral Research Fellow, Laboratory of Assay Development & Screening Technology, National Center for Advancing Translational Sciences, National Institutes of Health in Rockville, Maryland

James Inglese, Head, Laboratory of Assay Development & Screening Technology, National Center for Advancing Translational Sciences, National Institutes of Health in Rockville, Maryland

MENTAL HEALTH AND JUVENILE DERMATOMYOSITIS

Andrea Knight's, M.D., M.S.C.E., research focuses on the identification and treatment of mental health needs in children and adolescents with rheumatic diseases. Mental health conditions are common in youth with rheumatological disease, but there is little known about mental health and JDM. In this study, Dr. Knight's goal was to examine the mental health experiences, needs, and preferences, of patients with JDM.

Dr. Knight employed a patient-engaged approach to develop the anonymous electronic survey, and involved patient/parent advisors, the Childhood Arthritis and Rheumatology Research Alliance (CARRA) and the Patients, Advocates, and Rheumatology Teams Network for Research and Service (PARTNERS). JDM patients aged 14-24, and 153 parents were recruited through the Cure JM Foundation to participate in the survey. The survey assessed the impacts of disease on mental health, the prevalence of mental health problems, the comfort level with potential mental health care providers, and barriers to mental health care.

The results identified several aspects of JDM that affect mental health for patients. Concerns included worries about a flare, stress on the family, changes in appearance, physical limitations compared to peers, worrying about the future, limits on outdoor activities, and growing up too fast. In addition, depression, anxiety, and adjustment disorders were all prevalent in JDM patients, but many affected patients were not diagnosed. The participants identified several barriers to mental health services, including comfort level with mental health providers. Patients were much less comfortable with potential interactions with mental health care providers than were parents.

In conclusion, Dr. Knight found that youth with JDM have high rates of disease-related, clinician-diagnosed and self-reported mental health problems. The results from Dr. Knight's study can help develop the mental health education, screening, and treatment that is needed for JDM patients.

Andrea Knight, M.D., M.S.C.E., is an Attending Physician in the Division of Rheumatology at Children's Hospital of Philadelphia

ENVIRONMENTAL FACTORS ASSOCIATED WITH DISEASE FLARE IN JUVENILE AND ADULT DERMATOMYOSITIS

Gulnara Mamyrova, M.D., Ph.D., Lisa G. Rider, M.D., Rodolfo Curiel, M.D., James D. Katz, M.D., and Frederick W. Miller, M.D., Ph.D., conducted a study to assess environmental factors associated with disease flare in juvenile and adult dermatomyositis (DM).

An online survey was distributed to juvenile and adult DM patients diagnosed between 1980 and 2011, from myositis clinics and patient support groups. The survey examined smoking, sun exposure, infections, medications, vaccines, stressful life events, and physical activity during the six months prior to flares, or in the past six months in patients without flares.

The following results were obtained:

Of 210 (103 juvenile, 31 adult) participants, 63.8% experienced a flare and 36.2% (61 juvenile, 15 adult) did not. There were no differences in gender, race distribution, or in myositis medication reduction in the prior three months between those who did, and did not, flare.

Participants more often reported a disease flare after sun exposure (44.4% of those who flared reported unusual sun exposure vs. 28.6% of those who did not flare). Use of photoprotective measures did not differ between those with and without flare.

In those who flared, urinary tract infections (10.2% vs. 0.0%) and gastroenteritis (16.5% vs. 5.8%) were more frequent in the preceding six months.

Subjects who flared recently used non-steroidal anti-inflammatory drugs (NSAIDs) (63.4% vs. 36.8%), blood pressure medicines (12.7% vs. 3.9%), or medication for depression or mood changes (7.5% vs. 0.0%).

ENVIRONMENTAL FACTORS ASSOCIATED WITH DISEASE FLARE IN JUVENILE AND ADULT DERMATOMYOSITIS, CONT.

Subjects who flared were more likely to have received the human papilloma virus (HPV) vaccine within six months of the flare compared to those who did not flare (8.2% vs. 0.0%). Nine subjects reported flare (six JDM and three DM) with HPV vaccine. But of these, only five were under the age of 20.

Stressful events were more frequent among the patients who flared, including moving to a new house (6.0% vs. 0.0%) and experiencing financial difficulties within six months of the flare (17.2% vs. 7.9%).

Subjects who flared tended to be more physically active (17.2% vs. 7.9%; exercising 1-5 times/week).

This data shows that sun exposure, certain infections, medications, and vaccines that have been associated with illness onset, may also play a role in disease flare for juvenile and adult DM patients. This data will be useful for future research as well as understanding and predicting disease flares.

Gulnara Mamyrova, M.D., Ph.D., Research Coordinator, Division of Rheumatology, Department of Medicine, The George Washington University

Lisa G. Rider, M.D., Deputy Chief and Senior Research Physician, Environmental Autoimmunity Group, National Institute of Environmental Health Sciences

Rodolfo Curiel, M.D., Program Director, Associate Professor of Medicine Director, Myositis Center, The George Washington University

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Frederick W. Miller, M.D., Ph.D., Deputy Chief, Clinical Research Branch and Head, Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health

FEATURES DISTINGUISHING CLINICALLY HYPO- AND AMYOPATHIC JUVENILE DERMATOMYOSITIS FROM JUVENILE DERMATOMYOSITIS

Gulnara Mamyrova, M.D., Ph.D., Lisa G. Rider, M.D., and Rodolfo Curiel, M.D., conducted a study that examined certain features of clinically amyopathic juvenile dermatomyositis (CAJDM). CAJDM patients have characteristic DM rashes with little to no evidence of muscle involvement. The goal of the study was to determine any distinguishable features that make CAJDM distinct from JDM.

Clinically amyopathic dermatomyositis (CADM) is a subgroup of dermatomyositis (DM) and includes patients with amyopathic dermatomyositis and hypomyopathic dermatomyositis, where patients have characteristic rashes, but no muscle weakness, and have evidence of myositis solely in their laboratory testing.

The demographic, clinical, laboratory, and outcome features and therapies of nine hypomyopathic and three amyopathic CAJDM patients were examined. Several tests were used to evaluate differences between CAJDM and JDM patients. The study yielded several important findings:

Compared to JDM, CAJDM patients were younger at the time of diagnosis (~4.1 y/o for CAJDM patients vs. 7.3 y/o for JDM), and more frequently had mild illness severity at onset (75% vs. 11.7%).

FEATURES DISTINGUISHING CLINICALLY HYPO- AND AMYOPATHIC JUVENILE DERMATOMYOSITIS FROM JUVENILE DERMATOMYOSITIS, CONT.

Several key serum muscle enzymes (CK, aldolase, LDH, AST, and ALT) were lower in CAJDM patients compared to JDM patients.

83.3% of CAJDM patients had Myositis Specific Autoantibodies (MSA); 75% had anti-p155/140 (a blood protein highly specific to JDM and DM), and 8.3% had anti-MDA5 antibody. Two patients (16.7%) were myositis antibody negative.

No differences in the frequency or type of exposures within the preceding six months were seen between CAJDM and JDM patients (infection, immunizations, unusual sun exposure/UV index of residential location, medications, or stressful life events). Also, most skin rashes were present in similar frequency but CAJDM patients had less frequent mucus membrane involvement, no documented calcinosis, cutaneous ulcers, widespread/intense reddening of the skin, inability to produce/maintain healthy fat tissue, or particular blood vessel disorder called Raynaud's phenomenon.

CAJDM patients had less frequent muscle pain (myalgia), arthritis, shortening/hardening of muscles, tendons, or tissue (contractures), joint pain (arthralgia), difficulty swallowing (dysphagia), abdominal pain, and fatigue than JDM patients, and they also received less medications/therapy.

The key data points that may be used to distinguish CAJDM from JDM are that, for CAJDM, patients are more likely to have a particular antibody (p155/140 (TIF-1)), fewer fundamental symptoms, and receive less therapy.

Rodolfo Curiel, M.D., Program Director, Associate Professor of Medicine Director, Myositis Center, The George Washington University

Lisa G. Rider, M.D., Deputy Chief and Senior Research Physician, Environmental Autoimmunity Group, National Institute of Environmental Health Sciences

Gulnara Mamyrova, M.D., Ph.D., Research Coordinator, Division of Rheumatology, Department of Medicine, The George Washington University

OVERVIEW OF THE GEORGE WASHINGTON MYOSITIS CENTER

The George Washington Myositis Center (GWMC), located in Washington D.C., is a national referral site for JM. The center opened in 2008 with the purpose of serving children and parents in need of comprehensive care. Its opening was supported by Cure JM and the George Washington Medical Faculty Associates (GW MFA).

GWMC's mission is to provide patients with a comprehensive and multidisciplinary consultation to either establish a diagnosis of JM or to provide expert opinion on the clinical management of JM. Additionally the GWMC offers:

- Expertise in transitional care for teens and young adults with JM
- Visits with the primary GWMC team free of charge
- Center-based research in JM and collaborative projects with the National Institute of Environmental Health Sciences (NIEHS) of the National Institutes of Health (NIH), and other myositis research centers
- Education of medical professionals and trainees on JM
- Review of patients not eligible for NIH studies and long-term consultation options

Annie Mitchell, Michelle Best, and Simonetta D'Onofrio are parent volunteers at the GWMC. They give support and guidance to patients and families by helping them to understand the illness, relieving any feelings of isolation, guiding patients in treatment options, and raising awareness.

Alongside parent volunteers, the GWMC team is made up of dedicated clinicians. Dr. Rodolfo Curiel, M.D., is the GWMC Director. He is the Principle Investigator of the ongoing Abatacept trial, a possible, new JM treatment. Dr. Curiel expanded the number of trainees attending the clinic, facilitates collaborations between the clinic and other investigators at George Washington University (GWU), and serves as an investigator in adult myositis clinical trials.

OVERVIEW OF THE GEORGE WASHINGTON MYOSITIS CENTER, CONT.

Dr. Gulnara Mamyrova, M.D., Ph.D., coordinates GWMC activities, conducts JM research and performs various statistical analyses related to research, prepares and submits regulatory forms and communicates with GWU IRB (Institutional Review Board), prepares and submits manuscripts to peer-reviewed journals, and abstracts for presentations to scientific meetings/conferences, works with GWMC research collaborators, and serves as co-investigator in JM research projects.

Dr. Lisa G. Rider, M.D., is the Deputy Unit Chief of the Environmental Autoimmunity Group at the Clinical Research Branch at the NIEHS of the NIH, a Clinical Professor at GW, and a world-known expert in JM with over 20 years of experience in the care and research of JM patients. She has led several of the largest national and international myositis studies resulting in over 140 publications. Dr. Rider sees all the patients in consultation who visit GWMC, helps oversee many research projects and facilitates collaboration with the NIH and other centers.

Dr. Olcay Jones, M.D., Ph.D., is involved in clinical work, facilitates trainees from the Walter Reed National Military Center (WRNMC), and serves as the Primary Investigator of the retrospective chart review study.

The GWMC team works alongside clinical consultants: Drs. Allison Ehrlich, M.D., Patience White, M.D., and Kathleen Brindle, M.D., research collaborators: Drs. Frederick W. Miller, M.D., Ph.D., Victoria Shanmugam, M.D., Derek Jones, Ph.D., Gurusher Panjra, M.D., Samuel Simmens, Ph.D., and Josh Woolstenhulme, D.P.T., Ph.D., and past/current trainees: Drs. Seema Agarwal, M.D., Dareen Almanabri, M.D., Anupam Chahal, M.D., Olena Guzhva, M.D., Heidi Hanna, M.D., Jonathan Miller, M.D., Shiraz Moinuddin, M.D., Sami Serafi, M.D., Geeta Navyar, M.D., Tina Shah, M.D., Mahsa Tehrani, M.D., Marc Phillpotts, M.D., and Erica McBride, M.D.

Gulnara Mamyrova, M.D., Ph.D., Research Coordinator, Division of Rheumatology, Department of Medicine, The George Washington University

TYPE I AND TYPE II INTERFERONS: INCREASED EXPRESSION IN MUSCLE BIOPSIES AND RELATED TO CLINICAL AND HISTOLOGICAL DISEASE FEATURES

Rebecca Nicolai, M.D., is a rheumatology clinician and her studies play an integral role in developing a more complete understanding of the inflammatory mechanisms of JDM and the contribution of interferons (IFNs) to JDM activity. The first aim of this study was to investigate muscle expression of genes controlled by type I and type II IFNs because these signaling proteins are thought to play a role in the development and activity of JDM. The term “expression” is used to describe the process that occurs when the genetic information carried by a gene produces a specific, corresponding protein. Proteins are essential to the cellular activity of muscles, organs, skin, and more. The second aim of this study was to investigate the correlation between type I and type II interferon-regulated genes (IRGs) and the clinical and histological (body tissues at a microscopic level) aspects of the disease.

Using muscle biopsies of JDM patients, Dr. Nicolai analyzed the expression of interferon-related genes and inflammation-promoting cytokines (another type of signaling protein involved in immune responses). Type I and type II IFN-regulated gene expression levels were measured and recorded and abnormalities in JDM muscle tissue were assessed. Dr. Nicolai performed group comparisons, developing a quantitative description of the relationship between gene expression levels and the severity of disease features.

Dr. Nicolai’s study rendered important data for understanding the immunologic processes leading to the development of JDM. The increased expression of IRGs found in the muscle biopsies of JDM patients and the association between IRGs and certain disease features attribute the cause of muscle damage and inflammation to interferons. From this information, potential biomarkers (a measurable indicator of disease activity and predictor of disease course and long-term outcomes) could be established which would allow for earlier interventions and the best-suited treatments.

Rebecca Nicolai, M.D., Rheumatology Clinician and Researcher, Bambino Gesù Hospital, Rome, Italy

INTERFERONS AND MUSCULAR DISEASE ACTIVITY IN JDM PATIENTS

Rebecca Nicolai, M.D., is a rheumatology clinician in Italy who researches the role of different inflammatory mediators in the biological mechanisms leading to the development of JDM. It is thought that one major contributor to the development of JDM is the increased presence of interferons in the body. An interferon (IFN) is a type of protein responsible for signaling immune responses in the body. The production of proteins, including interferons, is controlled by genes. Often high levels of interferons are seen in muscle biopsies and skin cells in patients with JDM. Because genes are responsible for regulating the production of proteins like interferons, studies that investigate gene expression in JDM patients are important for developing the best interventions for patients.

Dr. Nicolai collected 79 blood samples from 26 JDM patients. Using the blood samples, Dr. Nicolai recorded type I IFN scores based on measured activity levels of the interferon-regulated genes (IRGs). Other clinical data recorded included the Physician's Global Assessment (PGA) of disease activity on the Visual Analogue Scale (VAS), cutaneous (skin) activity using the VAS, Cutaneous Assessment Tool (CAT) activity and damage score, muscle function using the Childhood Myositis Assessment Score (CMAS), levels of creatine phosphokinase (an enzyme that can leak into the blood with muscle damage), as well as prednisone dose, and other immunosuppressive medication levels.

The study resulted in several important findings.

First, IRGs were over-active in untreated JDM patients compared to healthy blood samples. Second, IRG levels were lowered after introducing glucocorticoid and immunosuppressive therapy. Also, it was seen that the type I IFN score correlates with disease activity of the skin assessed by the CAT activity score, whereas there was no significant correlation between the type I IFN score and the skin VAS or CAT damage score. Additionally, there is a correlation between levels of CXCL10, a protein controlled by IFNs, and both creatine phosphokinase levels and muscular function assessed by CMAS. Lastly, an important result was the confirmation of a higher type I IFN score in patients with active disease.

Dr. Nicolai's study has established correlations and data that will guide future research, advance understanding of JDM, and provide direction for more targeted interventions and treatments.

Rebecca Nicolai, M.D., Rheumatology Clinician and Researcher, Bambino Gesù Hospital, Rome, Italy

MYOSITIS AND AUTOIMMUNE DISEASE STUDIES AT THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)

Lisa G. Rider, M.D., Adam Schifffenbauer, M.D., and Frederick W. Miller, M.D., Ph.D., are conducting several clinical research studies on myositis and autoimmune diseases for the National Institute of Environmental Health Sciences (NIEHS), one of twenty-seven institutes of the National Institutes of Health (NIH). Clinical research studies are exciting because the patient plays an active role in their health care and helps identify potential treatment options.

Several studies at the NIEHS are underway and currently enrolling patients, including:

- The Twin Sibling Study, which seeks to identify the genetic and environmental factors that may result in autoimmune disease in one sibling but not the other. Researchers will look at individuals with juvenile or adult Myositis (diagnosed in the past five years), or other autoimmune conditions, and their close-in-age, same sex, healthy sibling or twin.
- The MYORISK (Environmental Risk Factors for the Anti-Synthetase Syndrome) Study will explore whether certain factors are associated with Myositis, particularly in people with Jo1 or anti-synthetase autoantibodies, who typically have lung disease and/or arthritis.
- The Myositis Natural History Study involves a comprehensive evaluation of each patient's Myositis and then NIEHS physicians can make treatment recommendations.
- The Sodium Thiosulfate for Calcinosis Dermatomyositis Study will evaluate intravenous sodium thiosulfate as a treatment medication for calcinosis in adult or juvenile dermatomyositis patients.

These studies can significantly further research by establishing new knowledge, testing a possible new treatment, and getting closer to a cure.

Lisa G. Rider, M.D., Deputy Chief and Senior Research Physician, Environmental Autoimmunity Group, National Institute of Environmental Health Sciences

TREATMENT TRIAL FOR CALCINOSIS IN JUVENILE AND ADULT DERMATOMYOSITIS

Adam Schiffenbauer, M.D., is leading a treatment trial for the National Institute of Environmental Health Sciences (NIEHS) to test whether a drug called sodium thiosulfate is a good treatment for calcinosis in juvenile and adult DM patients.

The study will invite patients with juvenile and adult DM with calcinosis on the arms, legs, trunk, or torso to the NIH Clinical Center for testing. If they are eligible, pre-treatment tests will establish a baseline level of disease activity. These assessments will include physical exams, blood and urine testing, imaging studies including MRI, CT, bone density (DEXA) scans, visits with medical specialists like physical therapists, and at-home questionnaires. These assessments will occur throughout the entire study so that Dr. Schiffenbauer can make accurate measurements about disease activity and measure the effects of the sodium thiosulfate.

Once a pre-treatment period is complete, patients will start treatment at the NIH Clinical Center. Once more assessments are done, the patient will start intravenous (IV) sodium thiosulfate (STS) treatment, three times weekly for ten weeks.

After treatment, follow-up calls between doctor and patient will update disease status. At fourteen and fifty-two weeks after ending treatment, participants will return to the NIH for assessments and a re-evaluation of disease activity. The entire study will last seventy-two weeks and reimbursement for participation is offered throughout the study.

This clinical trial will help doctors and researchers better understand calcinosis and DM in terms of detection, control, care and treatment. In addition, clinical research is a way that patients can get involved in their health care.

Adam Schiffenbauer, M.D., Staff Clinician, Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health

QUALITY MEASUREMENT IN JUVENILE DERMATOMYOSITIS

Heather Tory, M.D., M.P.H., and the Childhood Arthritis and Rheumatology Research Alliance (CARRA) JDM Quality Measures Workgroup have been working to create a set of quality measures to evaluate the impact of JDM on children with this disease. In the past, a survey was sent to Cure JM patients and families asking them to rank the importance of different quality items from a list created by the CARRA group. The results of the survey were beneficial, but there were likely additional items of importance that were not included on the list.

To gather a list of quality items that truly represent the goals and outcomes of JDM patients and their families, the CARRA JDM Workgroup would like to engage a small group of Cure JM members in a broader discussion of quality metrics. In preparation for that aim, this poster has been created to outline the results of prior work and provide a background and context for the discussion of quality measures. Through partnership in this process, we can help establish the most relevant quality measurements for patients with JDM and their families.

Heather Tory, M.D., M.P.H., Assistant Professor of Pediatrics, University of Connecticut School of Medicine, Department of Rheumatology and Interim Executive of Quality and Safety at Connecticut Children's Medical Center

PREMATURE ATHEROSCLEROSIS IN JUVENILE DERMATOMYOSITIS

Dawn Wahezi, M.D., M.S., led a study to determine the prevalence of blood vessel (endothelial) dysfunction and artery plaque build up (atherogenic) risk factors in JDM patients, compared to healthy controls. Children with JDM may be at increased risk of a premature build up of plaque in the arteries (atherosclerosis) due to risk factors such as abnormally high cholesterol or fats in the blood (dyslipidemia), insulin resistance, obesity, systemic inflammation, high corticosteroid burden, sedentary activity, and underlying disease of the blood vessels (vasculopathy). Twenty patients with JDM and twenty healthy children matched based on age, gender, race and BMI participated in this study. Atherosclerotic risk factors were assessed including: demographic information (age, gender, race), tests that measure size and composition of the body (anthropometrics), family history, smoking history, fat (lipid) levels, tests for proteins such as lipoprotein A, apolipoprotein A1 and B, homocysteine (an amino acid), hsCRP (a measure of inflammation), and measures for the risk of diabetes (Homeostatic Model Assessment of Insulin Resistance and hemoglobin A1c). JDM assessments included muscle enzymes, Childhood Myositis Assessment Scale (CMAS), Disease Activity Score (DAS), and the Myositis Damage Index (MDI). Endothelial function was evaluated using EndoPAT (Endothelial Pulse Amplitude Testing), an FDA approved functional test that is used to detect vascular stiffness (or ability to dilate after prolonged vessel occlusion). An abnormal EndoPAT index suggests endothelial dysfunction, one of the earliest signs of atherosclerosis.

PREMATURE ATHEROSCLEROSIS IN JUVENILE DERMATOMYOSITIS, CONT.

Dr. Wahezi's results showed that atherogenic risk factors are present in the pediatric population and may be associated with endothelial dysfunction, even at very young ages. Interestingly, patients with JDM were not at higher risk for endothelial dysfunction compared to those healthy individuals of the same age, gender, race, and BMI (in fact, the seemingly "healthy" control patients had a higher proportion of endothelial dysfunction). Dr. Wahezi speculates that by matching the groups based on these BMI, a control group was inadvertently selected that may have additional risk factors for elevated BMI that were not related to corticosteroid use (ie. familial factors, poor diet, etc) and thus elevated traditional risk factors for heart disease. This was confirmed by the fact that the control group demonstrated relatively higher cholesterol levels including lipoprotein A, a classic atherogenic risk factor. This study is the first to investigate the prevalence of premature atherosclerosis in a racially diverse, pediatric population with JDM. Dr. Wahezi's results are important for understanding and identifying the risks of atherosclerosis in JDM patients. To what extent traditional versus disease specific risk factors play in the ultimate development of cardiovascular disease is yet to be determined.

Dawn Wahezi, M.D., M.S., Chief, Division of Pediatric Rheumatology, Director, Pediatric Rheumatology Fellowship Program, Associate Professor, Albert Einstein College of Medicine

DETERMINANTS OF FATIGUE IN JUVENILE DERMATOMYOSITIS

Josh Woolstenhulme, D.P.T., Ph.D., is currently conducting a study to gain insight into the causes of fatigue and fatigability in JDM. JDM disrupts the body's ability to function and often results in fatigue. Dr. Woolstenhulme's study investigates the body functions of patients with JDM in order to better understand what causes fatigue. The ultimate goal of the study is to help identify areas where treatments may help alleviate the experience of fatigue for patients with JDM.

The study will test 28 people with JDM, and 12 people without JDM (but otherwise very similar physical characteristics). Measurements include self-reported fatigue, JDM disease severity, different measures of exercise capacity, how the body responds to the stress of exercise, dietary habits, physical activity at home, and the functions of the heart, lungs, muscles and nerves.

By comparing and analyzing data from both groups, Dr. Woolstenhulme will see which body functions related to fatigue do not work properly in patients with JDM, and which are the most significant contributors to fatigue. These results will help narrow the scope of future research on fatigue and help identify the best ways to combat fatigue in JDM patients.

Josh Woolstenhulme, D.P.T., Ph.D., Assistant Professor of Health, Human Function, and Rehabilitation Sciences at the George Washington University School of Medicine and Health Sciences

UPDATE ON JUVENILE MYOSITIS CARE
AND RESEARCH

**OUR SINCERE THANKS TO THE
RESEARCHERS**

**RESEARCH SUMMARIES PREPARED
BY KEILEY GLANCY**

**DESIGNED BY CLAIRE H. JOHNSTON
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**SUMMARY OF
SCIENTIFIC RESEARCH
POSTERS**

