



Impact Report for Cure JM Foundation

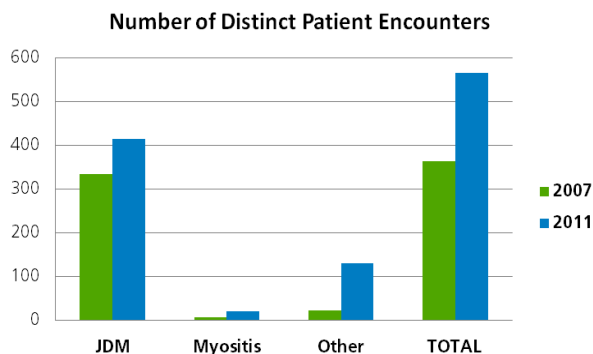
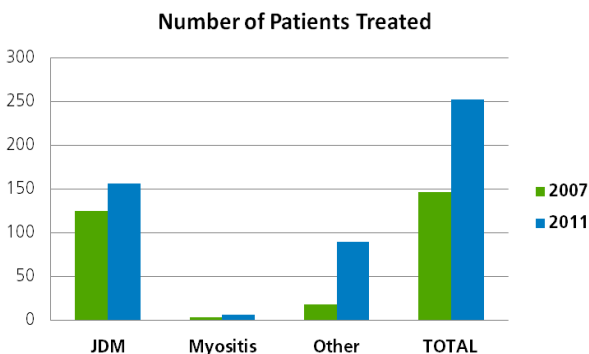
September 2011

Thank you for your partnership!

The JM Clinic and the Program of Excellence in JM Research at Children's Memorial Research Center, under the expert leadership of Lauren Pachman, MD, provides the highest quality care to children with juvenile inflammatory myopathies, including juvenile dermatomyositis (JDM) and juvenile polymyositis (JPM). This year the team's research has led to several seminal contributions documenting the critical importance of both rapid, accurate diagnosis and implementation of effective medical care as well as providing evidence for new therapies to treat the child's symptoms. Over the past seven years, Cure JM Foundation has played an essential role in the success of our program by providing generous, ongoing grant support. The following report highlights our accomplishments over this past year, many of which would not have been possible without your help. We are truly grateful for your involvement in the well-being of children with JM and our work on their behalf.

Improving Care and Outcomes for Children with JM

As you know, Dr. Pachman and her team are deeply committed to each patient who walks through our doors and are dedicated to providing each child with an individualized treatment protocol. Over the past four years, the number of patients with JM we treat has increased by 72 percent and the number of distinct patient encounters has increased by 25 percent, requiring a 30 percent increase in the number of Juvenile Myositis clinics to provide appropriate medical care in a timely way.



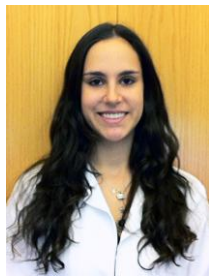
This marked increase in patients who visit from all over the United States as well as South America, has provided a wealth of data which will be subject to a 360 degree assessment, once both the clinical symptoms and the experimental data have been fully entered into a comprehensive Xenobase program for analysis. This demanding work is executed by our data base manager, Gabrielle Morgan, MS, aided by our newly recruited Research Nurse, Lori Ferguson, RN and project manager, Maria Amoroso, MPH. This database allows us to incorporate molecular data with clinical

data to provide a comprehensive picture of JM. This is important because problems with the immune system can possibly be identified before clinical symptoms appear. Research conducted with the help of Xenobase can help scientists develop earlier and more specific treatments for JM. Early diagnosis and treatment can reduce the number of flare-ups, which can be more difficult to suppress as time goes on. There are now over 21,000 samples in the Inflammatory Myopathy Repository.

The JM Transition Program/Young Adults

We are pleased to report that another aspect of our attention to young adults, the JM Transition Program, is up and running under the leadership of Calvin Brown, MD, Professor of Medicine at Northwestern Memorial Hospital. This marks a great step forward in providing a full continuum of care to our patients. Through this program, Dr. Brown, an adult rheumatologist, was able to help young women with JM who were pregnant. With ongoing monitoring of their condition by Dr. Brown and skilled perinatologists, these women received proper care and delivered healthy babies.

Professional Training



The JM team continues to place great emphasis in training and educating other healthcare professionals about JM, its symptoms and treatment options. This year's summer students have once again proven to be talented young minds. One student, Abby Halpern, a senior from Wesleyan College, worked as a summer student in Dr. Pachman's lab, supported by a Katz Summer Scholars Award. She had been working with Simone Sredni MD, PhD, for the previous two years, to search for molecular markers of the aggressive behavior for Malignant Rhabdoid Tumors (MRT), which are among the most aggressive and unresponsive tumors in pediatric oncology. This summer, she learned about the study of the gene expression and microRNA (modulators of gene expression through post-transcriptional regulation) expression profiles of a case of MRT of the brain that initially responded to therapy and helped identify a set of genes and miRNAs differentially expressed in the responsive tumor that might represent potential new therapeutic targets, which we have applied to JM. As Dr. Sredni is a pediatric pathologist, Abby also had the opportunity to learn diagnostic procedures, including immunohistochemistry (a method of analyzing and identifying cell types based on the binding of antibodies to specific components of the cell). Using these molecular methods, she worked with Dr. Sredni on the validation of a potential diagnostic test for JDM. This test may be helpful in identifying early disease in the muscle, before there is structural damage. The successful completion of this project may lead to a new and inexpensive ancillary tool for the diagnosis of JDM.

Over the past two years, a previous summer student, Erin Kim, BA, continued her work on the role of VCAM-1 (vascular cell adhesion molecule 1) in JDM. At the Clinical Immunology Society's annual meeting, she presented her work on VCAM-1, showing that this molecule appears early in the disease and may be an important "gate-keeper" for controlling blood vessels. She is submitting an article summarizing this work. Of note, she recently received a prestigious Fulbright award.

Professional meetings and national service are another way we reach a broad audience of investigators in the field of Immunology and Rheumatology. In 2011, Dr. Pachman contributed to three myositis related conferences: the International Myositis Genetics Conference held at the University of Manchester, England (US delegate), The American College of Rheumatology, and the Cure JM Symposia on Myositis held at the University of Washington, Seattle, where, as you know,

she was one of the keynote speakers at the Cure JM Foundation meeting. In the past year, she served on a Standing Grant Review Committee of NIH as well as one for the Arthritis Foundation, and on the Abstract Review committee for the American College of Rheumatology. She is the Director of a Federation of Clinical Immunology Societies (FOCIS) Center of Excellence (COE) in Clinical Immunology (one of 44 COEs in the USA and 22 multinational) and organized two well attended workshops for the Chicago City-Wide FOCIS COE, which featured local speakers and invited distinguished lecturers, serving as a nidus for scientific exchange and collaboration.

Research

Published Articles (September 2010-August 2011)

- Shrestha S, Wershil B, Sarwark JF, Philipp T, Pachman LM. Lesional and Non Lesional Skin from Untreated Juvenile Dermatomyositis (JDM) Displays Increased Mast Cells and Mature Plasmacytoid Dendritic Cells. *Arthritis Rheum.* 2010 Sept;62(9):2813–22. PMID: 20506305
- Rouster-Stevens K, Morgan G, Wang D, Pachman LM. Mycophenolate Mofetil, a Possible Therapeutic Agent for Children with Juvenile Dermatomyositis. *Arthritis Care Res (Hoboken).* 2010;62(10), 1446-51. PMID: 20521307
- Niewold TB, Kariuki SN, Morgan, GA, Shrestha S, Pachman LM. Gene-Gene-Gender Interaction between Cytokine Gene Polymorphisms Revealed by Serum IFN- α Phenotype in Juvenile Dermatomyositis. *J Pediatr.* 2010 Oct;157(4):653-57 PMID: 20605164
- Lisa G. Rider, Lan Wu, Gulnara Mamyrova, Ira N. Targoff and Frederick W. Miller on behalf of the Childhood Myositis Heterogeneity Collaborative Study Group* Environmental factors preceding illness onset differ in phenotypes of the juvenile idiopathic inflammatory myopathies *Rheumatology* 2010;49:2381–2390; PMID:20802007
- Ruperto N, Pistorio A, Ravelli A, Pilkington C, Oliveira S, Wulffraat N, Meiorin S, Garay S, Cuttica R, Hofer M, Quartier P, Melo-Gomes J, Reed A, Wierzbowska M, Feldman B, Harjacek M, Huppertz H, Nielson S, Flato B, Lahdenne P, Michels H, Murray KJ, Punaro L, Rennebohm R, Russo R, Balogh Z, Rooney M, Pachman LM, Wallace C, Hashkes P, Lovell DJ, Giannini EH, Martini A, for the Paediatric Rheumatology International Trials Organisation (PRINTO), The Pediatric Rheumatology International Trials Organization Criteria for the Evaluation of Response to Therapy in Juvenile Dermatomyositis. Prospective Validation of the Definition of Improvement. *Arthritis Care Res (Hoboken).* 2010 Nov;62(11):1533-41. PMID: 20583105
- Ibarra MF, Klein-Gitelman M, Morgan E, Proytcheva M, Sullivan C, Morgan G, Pachman LM, O'Gorman MR. Serum Neopterin Levels as a Diagnostic Marker of Hemophagocytic Lymphohistiocytosis Syndrome. *Clin Vaccine Immunol.* 2011 Jan 26. PMID 21270283
- Vega P, Ibarra M, Prestridge A, Pachman LM. Autoantibody to PL12 (anti-alanyl-tRNA synthetase) in an African American girl with juvenile dermatomyositis and resolution of interstitial lung disease. *J Rheumatol.* 2011 Feb;38(2):394-5. PMID: 21285181
- Kim NN, Lio PA, Morgan GA, Pachman LM. Double Trouble: Therapeutic Challenges in Patients with both Juvenile Dermatomyositis and Psoriasis. *Arch Dermatol,* 2011 Mar 21. PMID:21422326
- Niewold T, Wu S, Smith M, Morgan G, Pachman LM. Familial Aggregation of Autoimmune Disease in Juvenile Dermatomyositis. *Pediatrics.* 2011 May;127(5):e1239-46. PMID:21502224

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- Eimer M, Brickman W, Seshadri R, Smulevitz B, Ramsey-Goldman R, Stone NE, McPherson DD, Pachman LM. Abnormal Cardiovascular Risk Profile in Adults with History of Juvenile Dermatomyositis J Pediatrics, 2011, July, DOI:10.1016

In addition, 8 abstracts were published in 2010-2011 by the Pachman Lab.

Highlights from 2010 – 2011

Dong Xu, MD, a vascular biologist, joined the JM team this year as the Manager of the Myositis Research Laboratory. Dr. Xu received his medical degree from Shandong Medical University in Jinan, China and completed post-graduate study in human physiology at the School of Medicine, Beijing Medical University in China. This was followed by training as a Postdoctoral Scientist, in the Department of Cardiovascular Pharmacology. He was then selected to be a Postdoctoral Associate in the Department of Molecular Genetics at the Howard Hughes Medical Institute, University of Texas Southwestern Medical Center, Dallas, Texas. Finally, as a Research Fellow, he received intensive training in endothelial cell function at the National Institute of Health's Heart and Lung Institute. Prior to coming to the Children's Memorial Research Center, he was Assistant Professor of Research at the Cardiovascular Research Institute at the University of Kansas City School of Medicine.



The research performed in Dr. Pachman's lab has implications for JM and other autoimmune diseases. Among the innovative ongoing and recently completed studies being done by Dr. Pachman's team are the following:

- ***Disease chronicity in juvenile dermatomyositis (JDM): Epigenetic clues***
Dr. Pachman received a prestigious R01 grant from the NIH/National Institute of Nursing Research for this project. In this study, the quality of life of children with JDM will be correlated with their epigenetic status by testing diagnostic muscle biopsies from untreated children with JDM, boys compared with girls (matched for disease duration) and age- and gender-matched healthy controls. The discovery of specific microRNA and/or methylation markers may be a key to repair the vascular damage central to JDM pathology and may lead to more effective medical interventions. The results of this research may reveal why children with JDM heal, whereas adults with the disease do not. Recently recruited research nurse, Laurie Ferguson, RN, will work on this study. We are grateful for Cure JM's support that allowed us to complete the pilot study for this project.
- ***Familial Aggregation of Autoimmune Disease in Juvenile Dermatomyositis***
Autoimmune diseases frequently run in families, and some families are predisposed to multiple types of autoimmune disease. Genetic factors and specific immune system mediators frequently are shared between autoimmune diseases and may provide insight into the familial tendency toward autoimmunity. Dr. Pachman's team found that instances of certain autoimmune conditions, including lupus and type-1 diabetes, were significantly increased in families of children with juvenile dermatomyositis. This suggests that these diseases have shared pathogenic factors. This work was completed with our frequent collaborator, Tim Niewold, MD, Assistant Professor of Rheumatology at the University of Chicago Medical Center.

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- ***Clinical Status and Cardiovascular Risk Profile of Adults with a History of JDM***
There is a paucity of long-term follow-up studies of patients diagnosed with JDM in childhood, despite their apparent predisposition to increased traditional cardiovascular risk factors. The presence of cardiovascular disease in adults who had JDM in childhood and, according to the standards of the time, were treated less aggressively at diagnosis, has not been evaluated. In this pilot study, the research team tested the oldest patients who had been diagnosed with definite JDM for whom inception data was available. We found that adults who had JDM, 29 years after disease onset, had progressive disease and increased cardiovascular risk factors. This observation was just published in the *Journal of Pediatrics*. We are now extending this project, with the help of Cure JM funds, by recruiting and studying young adults.
 - ***CellCept is useful in the treatment of children with JDM***
It has often been observed that the rash of JDM is difficult to treat, and the paper by Sheela Shrestha (September 2010) showed that mast cells (that play a central role in allergy), are increased in the skin, but not muscle of children with JDM. In the CellCept publication, Dr. Kelly Rouster-Stevens, a Pharm D, and former Pachman Fellow, studied the effect of CellCept on the clinical symptoms of 50 children with JDM. She found that both skin and muscle symptoms improved and less steroids could be used, allowing the children to obtain increased linear growth and regain their height.

The Impact of Cure JM's Funding

The generosity and long-standing commitment of the Cure JM Foundation has been instrumental to many of our achievements. Translational research requires considerable infrastructure to be successful. Staff time is required to identify, recruit and characterize patients, collect and analyze laboratory samples, write proposals and submit studies for IRB approval, develop outcome measures and other important tasks. In Dr. Pachman's words: "This is what's necessary to build a house." Infrastructure costs for one experiment can be upwards of \$8,000 and costs continue to rise. Pilot studies that lay the ground work for larger, federally-funded studies are largely dependent on philanthropic support. Indeed, contributions such as those from friends like you have been instrumental in securing government funding and achieving ground-breaking results.

In addition to funding research studies, Cure JM's support has allowed us to train young physician-scientists and researchers, who will become future leaders in the care of patients with JM and the search for the causes and new treatments for the disease. By supporting professional education, Cure JM is making a long term impact on the field.

We are very appreciative of the dedication you have demonstrated through your ongoing support of the JM Clinic and the Program of Excellence in JM Research. We thank you for your commitment, your confidence and your partnership to ensure the best medical care to children with JM – today and in the future.