Johns Hopkins Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy Program

Volume 5, Issue 2 **Summer 2015**

2015 ARVD/C Family Seminar

Keep Calm and Carry On! That was the theme for seminar weekend!

Despite the unrest in Baltimore in May, the 16th Annual ARVD/C Patient and Family Seminar was well-attended and another success. Those that arrived into Baltimore early Friday evening attended a Meet 'n Greet at the Hilton Garden Inn and enjoyed some hors d'oeuvres and company of old and new friends.

The ABC's of ARVD/C was beyond capacity and offered a mini-course on what one needs to know about ARVD/C. This has been a must-attend session for the past 2 years it has been offered. After breakfast, we heard from a number of speakers addressing topics including diagnosis, management, genetics, disease mechanism, iPS cells, drug discovery, catheter ablation, exercise, and pregnancy.

We were thrilled to have a number of featured speakers this year. Dr. Richard Hauer, MD, PhD from Utrecht, The Netherlands shared results of the Hopkins/Netherlands Transatlantic Collaboration. Dr. Vincent Chen, MD, PhD, from Sanford-Burnham Medical Research Institute in California shared the work he is doing in "Modeling ARVC with Patient-Specific Stem Cells". And back by popular demand was Dr. Samuel Sears, PhD from East Carolina University who spoke about how to "Keep Calm and Carry On." As an added bonus, Dr. Angeliki Asimaki, PhD from the Saffitz Lab also joined us to share her work on protein signaling.

After lunch, a Question & Answer Session with Dr. Hauer, Dr. Chen, Dr. Sears, and Dr. Calkins was held. We also offered Discussion Group Workshops for the Youth Group (under 30ish), the over 30 affected group, as well as for family members and support persons. In addition, research opportunities were held throughout the afternoon, including blood draws, ICD interrogations, ECGs and Holters, and cheek swab studies. Thank you to everyone who was able to stay and participate in the various research studies. You are a vital part of our research success.

In this Issue… **page**

Contact Us

Johns Hopkins Hospital
600 North Wolfe Street
Blalock 545
Baltimore, Maryland 21287

P: 410-502-7161
F: 410-502-9148

www.ARVD.com

JOHNS HOPKINS MEDICINE

More Seminar…

Photo courtesy of Kiele Binsted

Save the Date!!!

Next Seminar tentatively planned for April 30th, 2016

Read what people are saying about the ARVD/C Seminar…

I was impressed by the breadth of information offered during the workshops. I found it all fascinating and hopeful for future treatment and management.

The presenters were effective, informative, and succinct with their presentations.

Excellent seminar this year!

They [afternoon workshop offerings] were extremely informative and very helpful for the newly diagnosed.

Enjoyed the session with Sam Sears immensely. Having a session focusing on the Psychological effects of ARVC is very important.

We enjoyed meeting other people/families dealing with ARVC and learning from the professionals.

On so many levels it was incredible. The perfect alignment of science, technology, and the human experience. Everyone there took what they needed from the Seminar. From the "Meet 'n Greet" that Friday…to the Hospitality of your colleagues…from the Brilliance of the Doctors, Researchers and Presenters, to the survivors and caretakers themselves…it was a life-changing, healing event.

Save the date for next year…

Did you miss the ARVD/C Seminar this year? Do you still want to learn the latest about ARVD/C? Then click the link below to view the 2015 ARVD/C Seminar Presentations. While definitely not a substitute to the overall Family Seminar experience, you still have the opportunity to view some of the presentations online. Unfortunately, we can't recreate the special opportunity to interact with the leaders in the field or share personal experiences with other families, a critical aspect to learning how to live with ARVD/C, so start planning now for next year's seminar!

View presentations now at: http://tinyurl.com/2015ARVDSeminar

JOHNS HOPKINS MEDICINE

Featured Manuscript

CLINICAL PRESENTATION, LONG-TERM FOLLOW-UP, AND OUTCOMES OF 1001 ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA/CARDIOMYOPATHY PATIENTS AND FAMILY MEMBERS

Groeneweg JA, Bhonsale A, James CA, Te Riele AS, Dooijes D, Tichnell C, Murray B, Wiesfeld AC, Sawant AC, Kassamali B, Atsma DE, Volders PG, de Groot NM, de Boer K, Zimmerman SL, Kamel IR, van der Heijden JF, Russell SD, Jan Cramer M, Tedford RJ, Doevendans PA, van Veen TA, Tandri H, Wilde AA, Judge DP, van Tintelen JP, Hauer RN, Calkins H. Circ Cardiovasc Genet. 2015 Jun;8(3):437-46.

Judith Groeneweg, MD, PhD

The goal of this study was to define the long-term outcomes of 1001 patients (n=439) and family members (n=562) in a transatlantic cohort between the Johns Hopkins ARVD/C team and the Netherlands. Mutations were identified in 276 index patients. During follow-up, 72% of the index patients experienced sustained ventricular arrhythmias. Sudden cardiac death during follow-up occurred more frequently among the index-patients who did not have an ICD. Overall, cardiac mortality and need for cardiac transplantation were low.

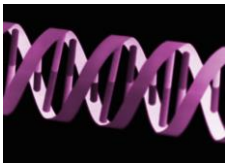
Family members with mutations were more likely to meet Task Force Criteria for ARVD/C (40% vs 18%), experience sustained ventricular arrhythmias (11% vs 1%) and die from a cardiac cause (2% vs 0%) than family members without mutations. In conclusion, long-term outcome was favorable in diagnosed and treated ARVD/C index-patients and family members. Outcome in family members was determined by symptoms at first evaluation and mutations.

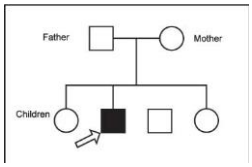
Clinical Services at Johns Hopkins

The Johns Hopkins ARVD/C Program also provides a variety of clinical services. We see patients for second opinion consultations to discuss diagnosis and management, genetic counseling and testing, as well as routine ICD management and family member screening. We can also arrange concurrent cardiac testing.

Patients are seen in consultation with Dr. Hugh Calkins or Dr. Hari Tandri and one of the genetic counselors to discuss test results, family history, and to provide guidance regarding further management. We see all of our patients for genetic counseling to discuss the diagnosis, the psychosocial impact of living with ARVD/C and with an ICD, as well as to discuss the benefits and limitations of appropriate genetic testing. In selected cases we also offer catheter ablation as a treatment for difficult to manage ventricular tachycardia. Appointments with our heart failure specialists, Drs. Stuart Russell, Daniel Judge, and Ryan Tedford can also be arranged. These appointments are billed to your health insurance. To schedule an appointment, contact Crystal at 410-502-7161 or ctichnell@jhmi.edu.

Coming this fall!! Starting this fall we will offer the world's only specialized Pediatric ARVD/C Clinic. This will be a twice monthly clinic staffed by a genetic counselor, Brittney Murray, and our specialized pediatric ARVD/C specialist, Dr. Jane Crosson, pediatric electrophysiologist. We will offer second opinions/consults for both patients possibly affected and also screening for family history of ARVD/C. This will be a coordinated day of completing whatever testing may be necessary along with consults with Brittney and Dr. Crosson. Contact Crystal for information regarding upcoming dates for this new special service.





Mycvmd.com

JOHNS HOPKINS MEDICINE

Heart Rhythm Society Abstract Presentations

The 36th Annual Heart Rhythm's Scientific Sessions were held in Boston in May 2015. The research and collaborative efforts of the Johns Hopkins ARVD/C Program were once again well-represented by several presentations and posters, some of which have been listed/summarized below.

A NOVEL AND SIMPLIFIED APPROACH TO RISK STRATIFICATION OF ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA/CARDIOMYOPATHY FAMILY MEMBERS

Anneline te Riele, MD; Cynthia A. James, PhD; Judith A. Groeneweg, MD, PhD; Abhishek Sawant, MD, MPH; Kai Dammers, PhD; Brittney Murray, MS; Crystal Tichnell, MS; Jeroen F. van der Heijden, MD, PhD; Dennis Dooijes, PhD; Daniel P. Judge, MD; Peter van Tintelen, MD, PhD; Richard N.W. Hauer, MD, PhD; Hugh Calkins, MD, FHRS and Harikrishna Tandri, MD.

The purpose of this study was to evaluate a novel approach to assess risk of arrhythmias in ARVD/C family members. Since the revised criteria now include family history as a major criterion, many ARVD/C relatives are being diagnosed at an early disease stage with an unknown sudden death risk. We examined the outcomes of relatives based on whether they met diagnostic criteria when family history was either included or excluded. All subjects who experienced ventricular arrhythmias had moderate or severe disease and therefore met criteria without the inclusion of family history. Prognostic value is increased by applying modified risk stratification criteria that exclude family history.

PREGNANCY IN ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA/CARDIOMYOPATHY IS ASSOCIATED WITH A LARGELY UNEVENTFUL COURSE AND DELIVERY

Anke R. Hodes, BSc; Crystal Tichnell, MGC; Anneline S.J.M. te Riele, MD; Brittney Murray, MS; Judith A. Groeneweg, MD; Abhishek C. Sawant, MD; Stuart Russell, MD; Maarten P. van den Berg, MD, PhD; Arthur A. Wilde, MD, PhD; Harikrishna Tandri, MD; Daniel Judge, MD; Richard N.W. Hauer, MD, PhD; Hugh Calkins, MD; J. Peter van Tintelen, MD, PhD; Cynthia A. James, ScM, PhD.

In a combined Johns Hopkins/Dutch ARVD/C registry, the cardiac and obstetric outcomes of 26 women (39 pregnancies) meeting task force criteria for ARVD/C were ascertained. ARVD/C was diagnosed prior to most pregnancies. Treatment during pregnancies included beta blockers, other cardiac medications and ICDs. Most pregnancies were uneventful. A single sustained VT or appropriate ICD therapy occurred in 5 pregnancies. Two women with significant structural disease developed heart failure. All pregnancies resulted in live-born children without major obstetric complications. Of 11 C-sections, only 1 was exclusively ARVD/C-related. At last follow-up all children were healthy and mothers had no cardiac mortality or transplant.

PARTICIPATION IN AHA-RECOMMENDED EXERCISE IS SAFE FOR FAMILY MEMBERS WITH ARVD/C ASSOCIATED DESMOSOMAL MUTATIONS

Abhishek C. Sawant, MD, MPH; Cynthia A. James, PhD; Anneline S. te Riele, MD; Aditya Bhonsale, MD; Crystal Tichnell, MS; Brittney Murray, MS; Stuart Russell, MD; Harikrishna Tandri, MD; Ryan J. Tedford, MD; Daniel P. Judge, MD and Hugh Calkins, MD

Among carriers of ARVD/C associated desmosomal mutations, we have shown that athletes have an increased risk of developing disease, ventricular arrhythmias, and heart failure. We also recognize that some exercise is important in promoting and maintaining good health. We aimed to test whether participation in the AHA-Recommended guidelines of weekly participation in 450-750 MET-Minutes per week (MM/wk) of exercise was considered "safe". Family members who limited their exercise to <750 MM/wk were less likely to meet diagnostic criteria and less likely to experience a sustained arrhythmia. Those who did in fact meet diagnostic criteria had mild disease. None of the family members who limited their exercise had evidence of structural heart disease.

SMALL MOLECULE RESCUES DISEASE PHENOTYPES IN ARRHYTHMOGENIC CARDIOMYOPATHY

Stephen P. Chelko, Angeliki Asimaki, Djahida Bedja, Rohan Wagle, Nuria Amat, Deeptankar Demazumder, Calum A. MacRae, Andre G. Kleber, Jeffrey E. Saffitz, Daniel P. Judge

The ARVD/C program was honored to have post-doctoral fellow Stephen Chelko and his work chosen as a finalist for the HRS Young Investigator Award. ARVD/C, is characterized by redistribution of intercalated disc (IDs) proteins, arrhythmias and progressive myocardial disease. It was previously reported that SB2, a chemical that inhibits the enzyme GSK3B, reverses the disease phenotype in a zebrafish model. This study shows that SB2 prevents myocyte injury, cardiac dysfunction and arrhythmias in 2 new mouse models of ACM. The results suggest that a common disease mechanism involving abnormal activation of an important enzyme, GSK3B, is responsible for the complex clinical picture of ACM.

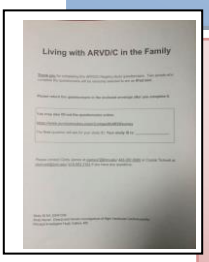
What's New in ARVD/C Research at Johns Hopkins?

GENETICS, MECHANISMS AND CLINICAL PHENOTYPES OF ARRHYTHMOGENIC CARDIOMYOPATHY

The Johns Hopkins ARVD/C Program is participating in a newly funded, multicenter, NIH-sponsored grant as an enrolling center. We are looking for subjects diagnosed with ARVD/C who participated in the previous NIH-sponsored ARVD/C study to re-enroll, as well as their family members. We are also looking for new patients diagnosed with ARVD/C to enroll, along with their family members.

In this study we are trying to find the gene(s) that are responsible for ARVD/C, and to see how the gene(s) affect the onset, the course and the severity of the disease in one individual and/or in a family. Participation will involve sending us your records, yearly follow-up, ECGs, 24 hour Holter monitoring, Signal averaged ECG, 6-minute walk test, and blood donation. In-person visits are required.

If you are interested and want to learn more about your participation and eligibility, please contact Crystal Tichnell, MGC at 410-502-7161 or ctichnell@jhmi.edu.



How Does Family History Influence Psychosocial Adaptation to Inherited Cardiomyopathies?

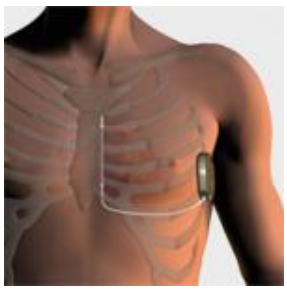
The goal of this project, sponsored by the National Society of Genetic Counselors 2015 Jane Engelberg Memorial Fellowship, is to determine how family history influences the overall well-being of individuals diagnosed with an inherited cardiomyopathy and their at-risk family members. Participation involves enrollment in our ARVD/C Registry and completion of one questionnaire. Many of you have already completed the online questionnaire or the blue book questionnaire. There is still time to complete your questionnaires. The next phase of this study will be to conduct telephone interviews with a subset of questionnaire respondents. Thank you for your participation!

The S-ICD – Is it for me?

We are launching a sub-study of our current ICD Registry to assess the efficacy of the new sub-cutaneous device or S-ICD in patients with a diagnosis of ARVD/C. If you have been diagnosed with ARVD/C and had your ICD (transvenous or subcutaneous) implanted after January 2013, you are eligible to participate. Participation involves:

1) Enrollment in our ARVD/C Registry
2) Sending us medical records
3) Sending us interrogations from your device
4) Contact us if you have an ICD therapy, ICD shock, ICD replacement, or other procedure related to your device.
5) Completion of questionnaires.

Email Crystal at ctichnell@jhmi.edu to discuss your eligibility and enrollment.



Bostonscientific.com

JOHNS HOPKINS MEDICINE

Ongoing Research Opportunities at Johns Hopkins

Clinical and Genetic Investigations of Right Ventricular Dysplasia (ARVD/C Registry)

Who: Children and adults with ARVD/C

What: Collection of pertinent past medical records and continued collection for 5 years. A blood sample for DNA for genetic mapping of ARVD/C genes

How to Join: Contact Crystal at 410-502-7161 or ctichnell@jhmi.edu. She will need to send you a consent form, then review the submitted records and make arrangements for obtaining and shipping the blood sample.

* * * * *

Have you had an epicardial ablation?

We are looking for people with ARVD who have had an epicardial ablation to join our Registry. Help us discover how this new technique affects the course of ARVD/C! Contact Crystal at 410-502-7161 or ctichnell@jhmi.edu.

* * * * *

THANK YOU FOR YOUR PARTICIPATION IN ALL OF THESE IMPORTANT STUDIES!!!

Meet Our New Staff Members

Bryana Rivers

Ms. Bryana Rivers is a recent graduate from the University of Maryland, College Park. She graduated with a bachelor's degree in Cell Biology and Molecular Genetics and she plans to continue on to earn her master's degree in Genetic Counseling. Bryana recently joined the ARVD/C in July as a Genetic Counseling Assistant and we are happy to have her!

Gabriela Orgeron

Dr. Gabriela Orgeron is from Cuenca, Ecuador, a city named as UNESCO world heritage site because of its rich South American history and beauty. She graduate medical school from the University of Azuay and came to the United States to pursue her dreams of becoming a clinical cardiologist. She completed her Internal Medicine residency at Union Memorial Hospital in Baltimore, where she received an award for her research work while there. She has recently joined the ARVD/C team as a post-doctoral research fellow and will be focusing her work on studies related to ICDs.

How You Can Help

None of the research by the ARVD/C Program would be possible without the active participation of families affected by ARVD/C. To join our research, the first step is to enroll in the ARVD/C Registry and send us copies of your cardiac tests. We will then invite you to be a part of other research efforts that are appropriate for you.

While we continue to apply for funding to support our various research projects, we rely heavily on the generosity of families to financially support this program.

If you are interested in making a financial contribution to the ARVD/C Program, please contact Shannon Wollman, Director of Development for the Johns Hopkins Heart Institute at swollma3@jhmi.edu or 443-287-7383. You can also make an Online Gift through our encrypted, secure server at http://www.arvd.com/donations.html

If you are hosting an ARVD/C Fundraiser and would like to include information regarding your event in our newsletter, please email Crystal at ctichnell@jhmi.edu.

THANK YOU FOR YOUR CONTINUED SUPPORT!!!

ARVD/C Program Info

ARVD Program Staff

Hugh Calkins, MD—Director
Harikrishna Tandri, MD—Faculty
Daniel Judge, MD—Faculty
Stuart Russell, MD—Faculty
Theodore Abraham, MD—Faculty
Gabriela Orgeron, MD—Post Doctoral Research Fellow
Anneline te Riele, MD—Post Doctoral Research Fellow
Cynthia James, ScM, PhD—Genetic Counselor
Brittney Murray, MS—Genetic Counselor
Crystal Tichnell, MGC—Genetic Counselor
Bryana Rivers—Genetic Counselor Assistant

Don't forget to keep us informed of your most up-to-date contact info! Please send any changes and updated medical records to Crystal at ctichnell@jhmi.edu Thank you!

Looking for a support group?

ARVD support group on Google:
Search for "ARVD ARVC Support Group" on google groups. Any issues joining this group, email Bob at ralla52@yahoo.com

FACEBOOK Groups:

- **ARVD/C Youth Society** – private group on Facebook (request invite from group admin)
- **Hope for ARVD** – private – request access
- **The Broken Heart Club – ARVD Edition** – private – request access

ARVD/C Mentor Program:
Get matched with an ARVD/C mentor! Connect with a mentor who has navigated the challenges of life with ARVD/C and receive: Support, Connection, Understanding, and Strategies for Thriving with ARVD/C. Contact Nancy Bogle at nbstjohn@gmail.com for more information.

JOHNS HOPKINS MEDICINE