

# JOHNS HOPKINS ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA/CARDIOMYOPATHY PROGRAM

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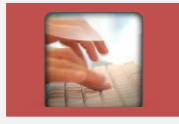
\* \*\* \*\*\*!!!HAPPY HOLIDAYS!!!\*\*\* \*\* \*

We hope you and your families have had a wonderful Holiday Season and are looking forward to the New Year! This year has been no different. The ARVD/C Program has been hard at work with collaborators around the world. Thank you again for your dedication to the work of our program. Our work would not be possible without your continued enthusiasm and willingness to participate in our many research endeavors. As always, we are available for consultations and evaluations in order to determine the best management strategies for you. Please do not hesitate to contact our program with any questions or concerns. We look forward to seeing many of you at our upcoming Patient & Family Seminar in May 2013. Details are enclosed. Best wishes to each of you for a Healthy 2013!

~ The ARVD/C Program



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## Remembering Tink

Flashing fingers, flaming keyboard and...way past midnight. Tink is at her command station and doing just fine. She is helping one faceless person after another who is in front of a monitor and/or on a phone somewhere. The help needed is usually bright red critical and...she is way up to the task.

- “Tink, I need your help with...”
- “Tink, I need some information...”
- “Tink, I hurt real bad right now and might not make it...”
- “Tink, I think I need some prayer...”



- “Tink, I need...”
- “Tink, I hurt...”
- “Tink, I am so glad you are here right now--way past midnight, I know. God Bless you.”

And she always was up way, way past midnight, helping our heart friends find information or answers or prayer or just warmth. She did this for many years - many nights until almost dawn. Everyone knew that if they could just get Tink on line they would make it, things would get easier.

And I am Tink's husband. Just a salesman for a company. As salesmen we are taught that we must be busy to be successful, but that activity is not the same as results. Tink got results. You know. I miss her continually. Forever. In my opinion the world could use more like our Tink. Don't you think so?...

It is with great sadness, that the ARVD community has lost someone who has helped so many and contributed so much - Micheline Long aka "Tink" passed away on July 5<sup>th</sup>, 2012. She was the calming voice on the other end of the phone and the helpful advice behind emails. She will surely be missed by her many friends and family, including the entire ARVD Community of patients and physicians world-wide.

# 14<sup>th</sup> Annual ARVD/C Patient and Family Seminar

Presented by  
The Johns Hopkins ARVD/C Program

Please join us for our annual ARVD/C Seminar! This is a great opportunity to meet others affected by ARVD/C and to learn the latest advances. We are thrilled to have both Dr. Peter van Tintelen from the Netherlands and Dr. Samuel Sears, Cardiac Psychologist from East Carolina University joining us this year. Topics and presenters include: "Overview of ARVD/C and the Role of Exercise" (Hugh Calkins, MD), "Genes, Mutations and ARVC; One Big Family?" (Peter Van Tintelen, MD, PhD), "Confident Living 2013" (Samuel Sears, PhD), and "Catheter Ablation" (Hari Tandri, MD). After lunch, there will be an opportunity to ask questions in a "Question and Answer Session with the Experts", as well as an "Under 30" Discussion Group and opportunities to participate in research. Make plans to come into Baltimore early so you can attend a reception at the Hilton Garden Inn on Friday evening. Once again, we have an exciting and packed agenda so we look forward to seeing many of you in May! Specific details are enclosed. Tentative Agenda can be found on our website under News and Events. Please register early!

**WHEN:** Saturday, May 4<sup>th</sup>, 2013 8:00am-5:00pm

**WHO:** Patients and Families affected by ARVD/C, Healthcare Professionals

**WHERE:** Chevy Chase Conference Center Auditorium, main level of Sheikh Zayed Tower at 1800 Orleans Street, Baltimore, Maryland 21287

**COST:** FREE

**REGISTRATION:** All participants must register! Please indicate on your registration form the names of other family members that are planning to attend. Register online by April 15<sup>th</sup>.

<https://www.surveymonkey.com/s/2013ARVCSeminar>

## **HOTEL ACCOMODATIONS**

Hotel rooms are available (limited) at the Hilton Garden Inn, Baltimore Inner Harbor (625 South President Street, Baltimore, Maryland 21202) at a special rate of \$135/night plus tax (single/double) until March 19<sup>th</sup>, 2013. Call 1-877-STAY-HGI or 1-877-782-9444 and mention the "ARVD Group" to receive the special rate. Check-in 3pm / Check-out 12pm. Hotel front desk phone is 410-234-0065. Self-Parking is available at a rate of \$23 and valet \$32 per day. [www.baltimoreinnerharbor.hgi.com](http://www.baltimoreinnerharbor.hgi.com)

## **TRAVEL TIPS**

The Baltimore/Washington International (BWI) Thurgood Marshall Airport is the closet international airport to Johns Hopkins ([www.bwiairport.com](http://www.bwiairport.com)). It is approximately 30 minutes from the seminar location.

A bus will be available to transport seminar participants to the seminar on Saturday, departing only from the Hilton Garden Inn at 7:45am. The bus will leave the seminar to return to the Holiday Inn at 5:00pm.

Taxi Services – For Taxi services call Sun Cab at 410-235-0300 or Yellow Cab at 410-752-1096.

## **SPECIAL EVENT**

Join us for a Meet 'n Greet Reception, 6:30-8:30pm, on Friday, May 3<sup>rd</sup>, 2013 in the Great American Grill at the Hilton Garden Inn. Heavy h'ors deuvres will be served. Please register for this event when you register for the seminar or contact Crystal.

## **CLINIC CONSULTATIONS**

Dr. Hugh Calkins and the genetic counselors will be available both Friday, May 3<sup>rd</sup> and Monday, May 6<sup>th</sup> for consultations. Diagnostic tests can also be arranged if necessary. These appointments will be billed to your insurance. Please contact Crystal ASAP to schedule an appointment.



### Clinical and Genetic Investigations of Right Ventricular Dysplasia (Registry)

**Who:** Children and Adults with ARVD

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

**How to Join:** Contact Crystal at 410.502.7161 or [ctichnell@jhmi.edu](mailto: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! Contact Crystal at 410-502-7161 or [ctichnell@jhmi.edu](mailto:ctichnell@jhmi.edu)

## Abstracts and Presentations

The American Heart Association's Scientific Sessions is the leading annual convention for scientists and healthcare professionals devoted to the science of cardiovascular diseases and stroke, and the caring of patients suffering from these diseases. Its mission is to build healthier lives, free of cardiovascular diseases and stroke. The American Heart Association Scientific Sessions were held in Los Angeles, CA in November 2012. Five abstracts were presented at this year's conference with three of them highlighted below including one that resulted in a manuscript.

#### **IMPACT OF GENOTYPE ON CLINICAL COURSE IN ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA/CARDIOMYOPATHY ASSOCIATED MUTATION CARRIERS**

*Aditya Bhonsale, Judith A. Groeneweg, Cynthia A. James, Dennis Dooijes, Crystal Tichnell, Jan D.H. Jongbloed, Brittney Murray, Jeroen F. van der Heijden, Harikrishna Tandri, Arthur A. Wilde, Daniel P. Judge, J Peter van Tintelen, Hugh Calkins and Richard Hauer*

The goal of this study was to compare the clinical course of those ARVD patients identified with a desmosomal mutation (*PKP2* and *DSP*) vs nondesmosomal mutation (*PLN* and *TMEM43*). 571 patients (239 families) from US and Dutch ARVD/C cohorts were included in these analyses. Clinical presentation with sudden cardiac death and/or ventricular fibrillation occurs at a significantly younger age as compared to VT occurrence. Among the 430 patients with a *PKP2* mutation, 2% died, 35% had sustained VT or VF, 9% developed left ventricular dysfunction, 3% experienced heart failure and 1.4% required cardiac transplant. *DSP* mutation carriers had a 3 fold higher occurrence of LV dysfunction (27%) and heart failure (18%). Non-desmosomal gene mutation carriers and multiple pathogenic mutations are associated with worse long term arrhythmic and heart failure outcomes.

#### **PREDICTION OF PATHOGENICITY OF MISSENSE VARIANTS IN ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY**

*Judith A. Groeneweg, Aditya Bhonsale, Cynthia A James, Jeroen F van der Heijden, Brittney Murray, Arthur AM Wilde, Crystal Tichnell, Jan DH Jongbloed, Harikrishna Tandri, J Peter van Tintelen, Daniel P Judge, Richard N Hauer, Hugh Calkins, Dennis Dooijes.*

This is another study performed in collaboration with our Dutch colleagues. The goal of this study was to evaluate the pathogenicity (causing disease) of missense variants which is often controversial. Missense variants were considered pathogenic when 1) both algorithms SIFT and PolyPhen-2 predicted pathogenicity and 2) minor allele frequency in 1000 genomes was  $<0.014$ . Survival and arrhythmic outcome was compared between missense and pathogenic non-missense mutation carriers. A pathogenic missense mutation was identified in 86/571 patients (15%). ARVC related missense mutations have a similar pathogenic character as non-missense mutations, regarding survival and substantial arrhythmic burden (VT/VF or appropriate ICD therapy).



## Featured Manuscript

*Anneline S.J.M. te Riele first came to our program in April 2012 to work on some collaborative ARVD projects between the Johns Hopkins ARVD/C Group and the Dutch for 5 months. She recently completed the requirements for her MD degree from the University Medical Center Utrecht in Utrecht, The Netherlands. She is now pursuing her PhD in Cardiology and will be returning to our program in March 2013 to continue various research projects in ARVD/C. One of her research projects is featured below and has been accepted for publication in Journal of the American College of Cardiology and also presented at the American Heart Association Scientific Sessions in November 2012.*

### **INCREMENTAL VALUE OF CARDIAC MAGNETIC RESONANCE IMAGING IN ARRHYTHMOGENIC RISK STRATIFICATION OF ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA/CARDIOMYOPATHY ASSOCIATED DESMOSOMAL MUTATION CARRIERS**

*Anneline S.J.M. te Riele, Aditya Bhonsale, Cynthia A. James, Neda Rastegar, Brittney Murray, Crystal Tichnell, Srinivasa Madhavan, Daniel P. Judge, David A. Bluemke, Jeremy R. Burt, Stefan L. Zimmerman, Ihab R. Kamel, Hugh Calkins, Harikrishna Tandri*

More and more patients with ARVD/C are undergoing genetic testing with pathogenic ARVD/C associated mutations being identified in over half of these patients. As a result, asymptomatic family members are now being identified as mutation carriers and cardiologists are questioning how they should be managed. The purpose of the study was to determine the role of MRI in patients identified to carry an associated desmosomal mutation without a prior history of sustained ventricular arrhythmias. Sixty-nine patients carrying a pathogenic mutation were included in the study. ECGs and Holter monitors were analyzed for electrical abnormalities. Cardiac MRIs were also done to assess abnormal cardiac structure and/or function. Overall, 42 (61%) patients presented with electrical abnormalities on ECG/Holter. Twenty (48%) of these patients also had an abnormal MRI. Of the 27 patients who had normal ECG/Holter, only 1 (4%) had an abnormal MRI. During followup, 11 (16%) patients with both electrical abnormalities (ECG/Holter) and abnormal MRI experienced a sustained ventricular arrhythmia. These results suggest that electrical abnormalities on ECG and Holter precede detectable structural abnormalities in ARVD/C mutation carriers. Therefore, an evaluation of cardiac structure and function using cardiac MRI is probably not necessary in the absence of baseline electrical abnormalities. Among, ARVD/C mutation carriers, the presence of both electrical and MRI abnormalities identifies patients at high risk of events and thus patients who might benefit from prophylactic implantable cardioverter-defibrillator implantation.

## Other Important News

Planning to come to the seminar in May?? Would you like to schedule a consultation with a genetic counselor and electrophysiologist to discuss your diagnosis, management, genetic testing?? Then schedule your appointment now! We will be available for consultations on Friday, May 3<sup>rd</sup> and Monday, May 6<sup>th</sup>. These appointments go quickly. Your insurance company will be billed for these services. Contact Crystal @ 410-502-7161 or [ctichnell@jhmi.edu](mailto:ctichnell@jhmi.edu) to schedule an appointment.

**Dr. Daniel Judge's lab, here at Johns Hopkins, has created a mouse model of ARVD/C with a mutation in the desmoglein-2 gene. These mice have the same features of ARVD/C that are present in people. We are investigating gene expression pathways that may contribute to development of ARVD/C in people, and we also hope to use the mice to test new medications that might help people with this condition.**



*The "Feel the Beat" section of the newsletter is dedicated to patient stories. If you would like to share your story in a future newsletter, contact Crystal at [ctichnell@jhmi.edu](mailto:ctichnell@jhmi.edu)*

It's hard to believe it has only been slightly over a year since my son's diagnosis. He had just graduated high school and decided that a prep school year would benefit him. He was a good student in high school, but didn't really have the study discipline that he would need in college. My son also enjoyed athletics, starting on his high school's football and baseball teams. He enjoyed being active since he could walk. He played organized soccer, basketball, football, and baseball. When he wasn't playing an organized sport, he would be outside or inside running around; he was perpetual motion.

He was looking forward to his year at Bridgton Academy. He never really enjoyed the practice part of any sport, but was determined that he was going to work hard so that he could play college baseball. He already had some interest from college coaches, but decided a prep school year would give him an edge. Everything seemed to be falling into place for him. We were busy that summer getting him ready for his prep school year.

About two weeks before he was supposed to report to school, he had his wisdom teeth out. The oral surgeon told me after the procedure that it went well however, he noticed some irregular heart rhythms when my son was under anesthesia. He emphasized several times that it may be nothing, however, we should really follow up with his primary care doctor.

We were able to get an appointment a few days later. An EKG was ordered. The primary care doctor noted that the heart rate was very low, but also noted that this may be normal since my son was so athletic. He left it up to us if we wanted to pursue things further. I reminded him about the time when my son was about nine years old and was complaining about chest pain. An Echo and EKG were performed at that time, and everything appeared to be okay. I remember the doctor's words to me at that time, "at least you know that your son has a healthy heart". However, being a mom I felt we needed to test further.

The doctor who performed this recent EKG couldn't see my son for another two months. I was not comfortable sending him off to school and waiting that long. I asked a friend at work if her husband, who worked in hospital administration in Massachusetts, could suggest a couple of doctors for me to call to see if I could get an appointment sooner. Within five minutes her husband called me back and my son had an appointment with a cardiologist who agreed to see my son the next business day on his lunch hour.

During that appointment, the cardiologist was ready to approve my son for full physical activity. He noticed a "blip" in his EKG. My husband remarked that he had a similar incident in his previous EKG. The doctor said he wanted to give my son a full work up to ensure everything was okay. He had an echocardiogram performed that day.

We were in Olympia Sports buying my son baseball gear when I got the call. The cardiologist wanted further testing and for us to see an electrophysiologist that he was consulting with at Mass. General. For now, baseball was off the table. My son was devastated. We explained to my son that it was important for all the testing to be done. As weeks dragged into months, the opportunity for him to play fall ball slipped away. The doctor said he would try to shoot for spring. However, when all testing was in, the diagnosis by the electrophysiologist was suspected ARVD. I knew what this meant. I had done the internet searching and had found out all I could about the condition, which wasn't a lot. My son had been put on a beta blocker, and soon after an ICD was recommended. My son would not agree to the ICD. The electrophysiologist encouraged a second opinion. I had already made up my mind that we would travel to Johns Hopkins to see Dr. Calkins. The electrophysiologist shared with me that it was Dr. Calkins that he had also consulted with.

We met Brittany and Dr. Calkins. They confirmed the diagnosis, and noted that presently, the condition was mild. He was given the okay to play baseball, provided that he had an ICD and did not participate in any strenuous workouts. They did note that if the condition progressed, his activity would have to be reevaluated.

My son felt as if he was given a second lease on life. He agreed to the ICD, is presently playing club baseball in college and is doing great academically. I have not been referring to my son by his name because he has not shared his condition with many people. He does not want people feeling sorry for him or treating him differently. The hardest part about the diagnosis for my son is not being able to have a pickup game of hockey or basketball with his friends, both new and old. He keeps trying to push the envelope, however, takes his medication religiously, and begrudgingly curbs his physical activity.

I don't understand why this has happened to him. The genetic testing revealed that the gene thought to be responsible for his condition was inherited from me. Why him and not me? Often times I think back to before the diagnosis and what his life would be like if he wasn't affected. After attending last year's ARVD conference however, I realize how lucky my son was to be diagnosed so quickly, and what could have been had he not been diagnosed. I thank Dr. Hogan the oral surgeon who first noticed a problem. I thank Paul Quinn who put us in touch with the cardiologist Dr. Gabry, who made sure my son was seen promptly and given a full evaluation. I thank Dr. Heist, the electrophysiologist who first gave us the devastating news, but worked with us to get through it. I thank Dr. Moore who suggested the beta blocker that was the most effective for my son. I thank Brittany Murray and Dr. Calkins for their constant support and tireless dedication. I thank everyone involved in my son's care and everyone else for their continued support in helping to understand the condition and in ultimately finding a cure.

-Cheryl





## ARVD Program Staff

Hugh Calkins, MD—Director  
Harikrishna Tandri, MD—Faculty  
Daniel Judge, MD—Faculty  
Stuart Russell, MD—Faculty  
Theodore Abraham, MD—Faculty  
Aditya Bhonsale, MD—Post Doctoral Research Fellow  
Binu Philips, MD - Post Doctoral Research Fellow  
Cynthia James, ScM, PhD—Genetic Counselor  
Brittney Murray, MS—Genetic Counselor  
Crystal Tichnell, MGC—Genetic Counselor

**New address!**

**Looking for a support group?**  
ARVD support group on Yahoo:  
<http://health.groups.yahoo.com/group/mmettera/>

ARVD/C Youth Society - private group on Facebook (request invite from group admin)

### Contact Us

Johns Hopkins Hospital  
600 North Wolfe Street, Blalock 545  
Baltimore, Maryland 21287  
P: 410-502-7161, F: 410-502-9148  
Website: [www.ARVD.com](http://www.ARVD.com)

## How You Can Help

None of the research by the ARVD Program would be possible without the active participation of families affected by ARVD. To join our research, the first step is to enroll in the ARVD 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.

We also rely on the generosity of families to financially support this program. Although we have applied for many grants from the NIH and other public funding organizations, we have had only limited success. In part, this reflects the fact that ARVD is a rare disease and not considered a major health hazard. It is critical for patients or families affected by ARVD to lobby for increased funding for research on this important condition.

If you are interested in making a financial contribution to the ARVD Program, please contact Shannon Curley, Director of Development for the Johns Hopkins Heart Institute at [scurley3@jhmi.edu](mailto:scurley3@jhmi.edu) or 410-516-6607. 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 Fundraiser and would like to include information regarding your event in our newsletter, please email Crystal at [ctichnell@jhmi.edu](mailto:ctichnell@jhmi.edu).

**THANK YOU FOR YOUR SUPPORT!!!**

### Healing Hearts 8<sup>th</sup> Annual Bull & Oyster Roast

*A tribute to Bonnie Milner*

Sunday, February 17<sup>th</sup>, 2013

1:00 pm - 5:00 pm

Catonsville Lodge

2832 Frederick Road

Catonsville, MD 21228

Tickets are \$40 per person. Proceeds to benefit ARVD Research at Johns Hopkins Heart Institute. There will be raffles including a \$500 grand prize, a silent auction and more! For additional information, to reserve a table or purchase tickets, please email [HealingHeartsMD@yahoo.com](mailto:HealingHeartsMD@yahoo.com). Find "Healing Hearts" on Facebook for more info regarding this organization.

### What would you like to see in the next newsletter?

Email Crystal with your ideas  
[ctichnell@jhmi.edu](mailto:ctichnell@jhmi.edu)