CRY's Research Fellows are an integral part of the work we do at CRY. CRY funds doctors for 2 years who choose to specialise in the field of inherited cardiac diseases, sudden cardiac death, screening and sports cardiology. The research that they produce advances our understanding of conditions that can lead to sudden cardiac death.

In April, CRY's Research Fellows attended EuroPRevent 2011. Organised by the European Society of Cardiology (ESC), it is the biggest meeting in Europe on Cardiovascular prevention and rehabilitation. Held over 3 days, it includes meetings, presentations and courses with the aim of advancing knowledge. Both existing and previous CRY Research Fellows presented their research to attendees from all over the world.

Update Editor Mair Shepherd spoke to some of CRY's Research Fellows to find out more.

CRY Research Fellow Dr Hari Raju presented his work during a 'Meet the Experts' session on sports cardiology.

What was the Meet the Experts session about?

The Meet the Experts session was about difficulties in sports cardiology. It was centred around descriptions of cases and scenarios in sports cardiology that pose problems for specialists, in terms of differentiating between people who have definite pathology (that is a heart condition) and the normal physiological changes that happen in the heart as a result of exercise and chronic exercise.

What was your presentation about?

I was specifically talking about the difficulties between the changes that occur in the heart during exercise versus the appearance of hypertrophic cardiomyopathy (HCM) on testing. HCM is a heart condition characterised by thickening of the heart muscle and we diagnose this with an ECG (electrical recordings of the heart) and an echocardiogram (ultrasound of the heart) with additional tests such as treadmill tests, cardiac MRI tests and occasionally with holter monitors. We add up all the information from those tests to try and differentiate between these conditions.

I was illustrating this with a particularly difficult case where it appeared that a 35 year old was suffering from a traditional heart attack, although the blood supply to the heart was completely normal on investigation with an angiogram. Having essentially ruled that out, or as we felt at the time, the ECG reading was most consistent with HCM. However, the changes on the ECHO (ultrasound) were very subtle and certainly within the parameters of what we would see in athlete's heart – that is changes that can be related to chronic exercise training. So it certainly wasn't with absolute certainty that we made the diagnosis of HCM but it was the most likely thing. This was complicated by an MRI scan which suggested again that actually this might have represented a traditional heart attack, which is a temporary blockage in flow in the blood vessels that supply the heart muscle. Through this case study I was illustrating how exercise, training and detraining in somebody who ultimately appears to have HCM can change the appearance of their tests. Not only can it be difficult to differentiate between athlete's heart and HCM, but you can sometimes have other conditions like traditional heart attacks added to the mix and also tests can change with time depending on whether people are training or not. The important thing being that if there is any uncertainty it's important to repeat tests in the context of training and detraining.

Are you saying that the athlete's heart often has a thicker wall than a normal heart and this can look similar to HCM?

Yes, chronic exercise training as in the same way as if you go to the gym and bulk out your arms and your legs your heart does exactly the same thing. Your heart is a muscle and hence it gets bigger when it's worked with any kind of chronic training.

And when you say detrain what exactly do you mean?

By detraining I mean stopping exercise for a period of about 6 to 8 weeks.

In this particular case he had been training as a cyclist and hence his ECG looked abnormal. When giving the diagnosis of HCM, while we don't necessarily tell people that they have to completely stop doing all exercise, we say that people shouldn't be doing endurance sports or competitive sports. In this case, he essentially chose to stop doing everything and his investigations almost completely normalised at that stage.

How is this relevant in day-to-day practice?

As a cardiologist it's important to keep an open mind for any patient where all of the tests don't neatly fit into a single category. It's also important to be able to allow people to train and detrain

and then repeat tests in those scenarios to see whether that moves your diagnosis towards definite heart condition versus physiological change within the heart.

How does this relate to CRY's screening programme?
Obviously CRY's screening programme uses ECG and occasionally with the addition of echocardiography to pick up conditions like HCM, which is the most common inherited condition that we would see in the general population and amongst athletes. So in those people who have these changes it's important to differentiate between normal exercise training and pathology. What we don't want to prevent athletes unnecessarily from continuing with their chosen career.

CRY Research Fellow Dr Nabeel Sheikh was nominated for the Young Investigator of the Year Award

What is the Young Investigator Award?
The Young Investigator Award (YIA) is open to those under 35 years of age who have produced original research that has the potential to change or have a significant impact on clinical practice. When abstracts are submitted to EuroPRevent, they are marked by experts in the field and the ones deemed to be of the most outstanding quality go forward to the YIA.

What was your research about?
My work was an extension of work that our group, led by Professor Sanjay Sharma, have done previously looking at ethnicity and changes that athletes get on their ECG and echocardiogram (ultrasound scan) in response to exercise.

We know from work done in adult populations that athletes develop changes on their ECG and echocardiogram which is known as "the Athlete's Heart" and is a normal response to exercise.

We also know from adult studies that athletes of African/Afro-Caribbean (black) origin are prone to get more of a specific type of change on their ECG (known as "repolarisation anomalies") and also on their echocardiogram (larger wall thicknesses) compared to Caucasian (white) athletes.

Although these changes can be related to athleticism and race, they can also overlap with changes seen in certain cardiac conditions such as hypertrophic cardiomyopathy (HCM). So when we see these changes the question is "are these just normal ECG and echocardiogram findings for a black athlete, or is this something more?"

Now from the work we've done previously in adult athletes, we've got good evidence that some of these changes are more in keeping with ethnicity. So if we see them in a black athlete, we know from past experience that this is normal for their ethnicity, which prevents them undergoing unnecessary investigation, false and unfair disqualification, and spares them a lot of unnecessary anxiety – after all, to an athlete it's a very big deal if somebody tells them "you've got a problem with your ECG" or "you've got a problem with your echocardiogram and you've got to have more investigations" - not only are they worried about their health, it's also their whole career that is at stake.

However, all the values we use to define what represents a "normal" ECG and echocardiogram in an athlete come not only from adult populations, but adult Caucasian populations. And no-one has ever looked for these changes specifically in black adolescent athletes. So our questions were: should we be extrapolating data that we've got from adult white athletes to black athletes? And do black athletes in this particular age group even get the changes as frequently as we have observed in the adult black athletic population?

These questions are particularly important because both black athletes and adolescent athletes are two groups that have been shown in several studies to be at the highest risk of exercise-related sudden death. So by looking at black adolescent athletes, we were also looking at the group of athletes that are at highest risk of exercise-related sudden death (yet paradoxically, no studies have ever been done to look at the ECG and echocardiogram changes they develop with exercise).

What did the research actually show?
We took a group of black adolescent athletes and compared them to a group of white adolescent athletes and also compared them to a black control group – comprised of sedentary individuals who exercise for 2 hours or less a week. Our results showed that, compared to white adolescent athletes and the control group, black adolescent athletes develop more changes on their ECG and more changes on their echocardiogram, which is in keeping with the findings in adults. This suggests that some of these changes are a normal response to exercise for black athletes, which is important because it shows that we shouldn't necessarily

extrapolate results from white athletes to black athletes – given that these changes are rare in white athletes but more common in black athletes, doing so may lead to many unnecessary investigations and potential anxiety or even unfair disqualification.

When you say ECG changes, do you just mean changes from what is considered normal?

Yes. There are changes that are quite common in athletes which we know are related to athletic training and those are found across the board – in all ages, ethnicities and in both genders. However there are certain ECG changes that are uncommon and can overlap with those found in diseased states. The issue arises because these "uncommon" changes are actually more common in black athletes but we think this is due to race in combination with exercise rather than pathology.

How did you find giving your presentation? Were you quite nervous?

It was the first time I've done anything like this so I was nervous, but I was also looking forward to it because it's a great opportunity to advertise the important research that CRY supports to an international audience, and also give a flavour of the kind of research we're doing through CRY. It was also a great opportunity for me to present the research that I've done and to get experience at presenting at an international conference to a large audience which included experts in the field! Although it was nerve-wracking, and for a 15-20 minute presentation it required weeks if not months of work, it was definitely worth it because it gave me great experience of something I've never done before.

How would this relate to the CRY research programme and the CRY screening programme and how can we use this data?

It's really important actually, especially now we're doing more and more school screenings and, even though schools are technically not classed as athletic or sports screenings, you do find that a lot of young people do a lot of exercise. It gives us a basis on which to be able to correctly interpret the ECG and echocardiogram findings in different ages and ethnicities rather than just using adult values from Caucasians. We've now got evidence that we will be able to use that will enable us to better judge ECG changes and echocardiogram changes in young adolescents and particularly black athletes.

We hope to publish the research, but there is still more work to be done. We need to follow-up these people, looking particularly at those who have got ECG and echocardiogram changes, and see what happens to them. Whilst we have tested them all comprehensively and not found any problems in anyone, it's still important to follow them up long-term to see whether that remains the case. It's only then that we will have a complete picture and be in a position to say 'yes, these ECG changes mean nothing' or 'these ECG changes warrant more investigations after the initial screening'.

CRY Research Fellow Dr Abbas Zaidi was also nominated for the Young Investigator of the Year Award and also presented some of his other work during a symposium 'Beyond the left ventricle'.

What was the symposium Beyond the Left Ventricle about?

Most of the work that's been done in sports cardiology has focussed on the left ventricle. Hypertrophic cardiomyopathy (HCM) is a condition that can cause sudden death in young people, particularly athletes, and in athletes the left ventricle thickens up and enlarges so you can get this difficulty in distinguishing the normal athlete's left ventricle from HCM. But there's not been much work done on what happens to the right side of the heart in athletes, which this symposium was predominantly about.

Why has the focus been on the left ventricle?

Firstly, the left ventricle is easier to study. It's a symmetrical structure which can be studied quite easily with echocardiography whilst the right ventricle is an asymmetrical structure and is much more difficult to see and to study with echocardiography. Secondly, HCM is more common and is more recognised whilst arrhythmogenic right ventricular cardiomyopathy (ARVC) has only recently been recognised as a condition that can cause sudden death in athletes. So the focus has always been on trying to pick up HCM. It's only recently that we've started looking for ARVC.

You say that most previous research has focussed on HCM and that ARVC is more recent. What do you mean by more recent?

The Italians were the ones who really started to pick up quite a lot of cases of ARVC in athletes. So it's only really become prominent within the last 10 years.

What was your talk about?

My talk was about the structural adaptations of the right ventricle in athletes. So I talked about the fact that sudden deaths occur in young people in sport, then I talked about the fact that a lot of

work has been done on the left ventricle. Then I talked about why the right ventricle hasn't been studied as much and I reviewed the literature about what happens to the right ventricle in athletes. Most of the literature suggests that there are changes in the right ventricle in athletes and that the right ventricle enlarges. However, there is conflicting evidence about what happens to the function of the right ventricle. Some evidence suggests that, although the right heart gets bigger, the function stays the same, but there is also some evidence that suggests that intense prolonged exercise over many years can actually cause some damage to the right ventricle. Then I also presented our own data from my work with Professor Sharma which is funded by CRY. We are studying a large cohort of athletes that we've screened at CRY events and we're making measurements on their right hearts. So I presented some of the data that we've got so far.

What are your preliminary findings?

Our preliminary findings confirm earlier work that the right ventricle does enlarge quite a lot in competitive athletes. Also the right heart gets so big in some athletes that they start to fulfil diagnostic criteria for ARVC although they don't actually have it.

Is that because the exercise works the heart muscle and so it enlarges?

It's basically because more blood is flowing through the right ventricle so it has to enlarge to accommodate the greater throughput. Also the pulmonary artery pressure rises in athletes, so the pressure in the right side of the heart increases. So there's greater flow and greater pressure. As they are pushing their body with intense exercise, they need their heart to work more efficiently which affects the left and right side of their heart.

How is this relevant in day-to-day practice?

We see a lot of athletes, especially in Professor Sharma's clinic because he's the head of the CRY Sports Cardiology Centre, with large right ventricles. If they have ARVC then they should be excluded from sport because they are at risk of sudden death, and they increase their risk of death by exercising. We need to know what a normal right ventricle is for an athlete, because normal for an athlete is bigger than it is for a non-athlete. Once we've established what normal is for athletes then we won't need to put them all through the tests because we'd be able to say this is normal for you because you do a lot of exercise.

How would this relate to the work that CRY does and the CRY screening programme?

All of the data has come from CRY screenings. ARVC is an inherited cardiac condition that kills a significant proportion of young athletes and young people in general. If it helps with the identification of people with this condition then it will reduce sudden deaths in young people.

Would these changes in the right ventricle also show up on the ECG or is it just on the ECHO?

That's another thing we're looking at actually: whether we can predict these changes on the ECG and whether or how we can use the ECG as another tool to differentiate healthy right ventricle enlargement from ARVC.

What do CRY Research Fellows do?

Within their role at cardiac screening events they:

- carry out consultations with every person CRY tests
- manage all the abnormal screening results

Within their role at hospitals they:

work with Professor Sharma at the CRY Inherited Cardiovascular Conditions and Sports Cardiology clinic at St George's Hospital, London and at Lewisham University Hospital. At these fast track clinics families can be seen within a few weeks of referral after the sudden death of a young family member

Within their role as an academic they:

- publish abstracts and posters of CRY's research
- publish articles in peer-reviewed journals
- present their research at international conferences