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Original Article

The 2017 Seventh World Congress of Pediatric Cardiology & Cardiac Surgery: Week in review: electrophysiology*

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The electrophysiology subsection at the 7th World Congress of Pediatric Cardiology & Cardiothoracic Surgery Meeting conducted in Barcelona, Spain, in July, 2017 consisted of 15 electrophysiology plenary sessions, symposiums, debates, and bridging sessions with other disciplines in the field. More than 66 international speakers represented 19 countries with additional moderators from seven additional countries. This was the largest gathering of paediatric electrophysiologists at a World Congress to date. In addition, this was the first time that a joint electrophysiology symposium was held between the Pediatric & Congenital Electrophysiology Society and the Association of European Pediatric Cardiologists on topics pertinent to the general ambulatory cardiologist.

The spectrum of paediatric electrophysiology ranges from the care of the fetus and neonate with arrhythmias and channelopathies to the adult with CHD and includes complex atrial and ventricular arrhythmias. In addition, paediatric electrophysiologists are responsible for the management of all patients with implantable cardiac electrical devices and the identification through non-invasive and invasive testing of patients at risk for sudden cardiac death. The theme of this particular World Congress was bridging. Electrophysiology is truly one of the unique subspecialities within paediatric cardiology that bridges ambulatory general paediatric cardiology, adult congenital cardiology, intensive care, and interventional catheterization, and with the advent of devices that help in the management of heart failure the bridge has extended to include imaging and heart failure. Throughout the meeting, there were more than 100 well-prepared and excellently presented talks relating to arrhythmias. Unfortunately, given the constraints of this review, not all talks can be summarised, but rather we have chosen a few main subheadings with key points that we hope you will find of relative interest.

Neonatal arrhythmias

Congenital complete atrioventricular block is a relatively rare condition (1–11,000–1–22,000) associated with certain immunologic conditions, as well as CHD substrates such as heterotaxy/polysplenia or atrioventricular discordant heart. Despite increasingly encouraging clinical results, many of these patients have significant morbidity and mortality. Hisaaki Aoki (Japan) stressed the importance of electrophysiologists to partner with imagers in not only looking at traditional signs of left ventricular dysfunction, but also paying careful attention to the presence of endocardial fibroelastosis, right ventricular dysfunction, and endocardial thickness, which may also reflect patients at high risk. Mortality rates vary from 10 to 29% for the serologic positive newborn with congenital complete AV block, and hydrops has been shown to identify the fetus at

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highest risk. Although a number of treatment strategies have been used, including intravenous gammaglobulin IVIG, plasmapheresis, and hydrochlorquine, all have had limited success. Similarly, electrophysiologists have struggled over the past four decades to build and implant an effective fetal pacemaker. In the late-breaking clinic sessions, Yaniv Bar-Cohen (United States of America) presented an encouraging novel fetal percutaneously implantable micro-pacemaker (VOO at 100 bpm) (Fig 1) that has exhibited promising early animal studies using a fetal sheep model. Current clinical trials are underway in high-risk fetuses with immunologic AV block and hydrops. It is anticipated by the 8th World Congress of Pediatric Cardiology and Cardiothoracic Surgery (September, 2021, Washington, DC) early result will be available.

In infants and children with congenital AV block who meet heart rate criteria for pacemaker implantation, increasing evidence as presented by Jan Janousek, (Czech Republic) supports left ventricular epicardial pacing to prevent or delay late-onset electro-mechanical dyssynchrony. As a follow-up to the neonatal session, echocardiographer Mark Friedberg (Canada) gave an excellent presentation to the electrophysiologists on understanding the pattern of dyssynchrony, septal activation, late free-wall activation, and speckle tracking. Jan Janousek and Anne Dubin (United States of America) explored patients with a failing right ventricle and left ventricle, respectively, who may benefit from cardiac resynchronisation.

Beyond congenital AV block, neonatal bradycardia is a relatively common observation, although it is usually transient and has a benign outcome. However, neonatologists and cardiologists should be cognisant that bradycardia, especially if occurring *in utero* (Bettina Cuneo, United States of America), may be a marker for long QT syndrome. Hitoshi Horigome (Japan) reviewed neonatal channelopathies and the association of long QT type II (KCNH2) and type III (SCN5A) as associated with bradycardia. Horigome discussed that even in high-risk LQT neonates (2:1 AV block, QTc >550 ms, and brief runs of torsades de pointes) many can be managed with β-blockers, pacing, mexilitine, and occasionally a left-cardiac sympathetic denervation before immediately placing an ICD. The decision to implant an

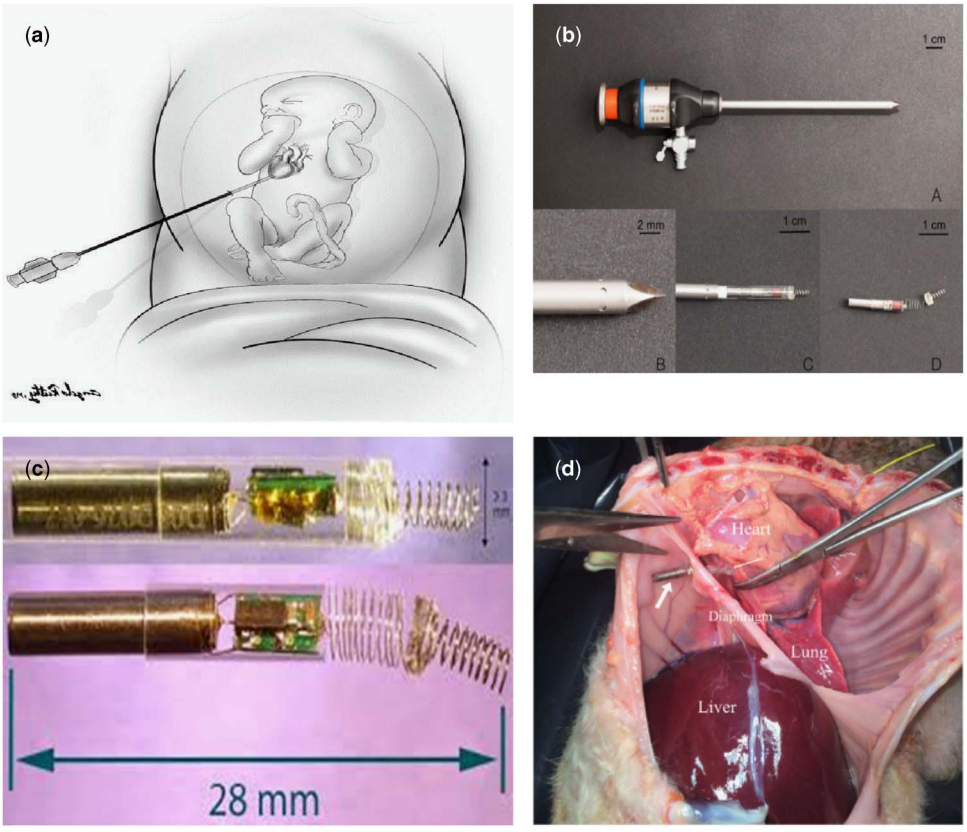

Figure 1.
*(**a,b**) Cartoon depicting the trochar and cannula (4.5 mm external diameter, 3.5 mm internal diameter) entering the fetus with deployment of the micro-pacemaker. (**c**) Pacing lead. (**d**) Necropsy specimen of the fetal sheep with the pacing lead through the diaphragm and penetrating the left ventricular epicardium (Courtesy Yaniv Bar-Cohen MD USC, Children's Hospital Los Angeles).*

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ICD in a neonate must be individualised with the risk–benefit balance measured on an individual basis given the challenges and complexity associated with placing an epicardial system.

Beth Stephenson (Canada) reviewed neonatal supraventicular arrhythmias to determine whether certain key *in utero* historical features of tachycardia could predict neonatal recurrences. Features that appeared to be predictive of postnatal arrhythmias included female sex, *in utero* hydrops, later gestational age at fetal supraventricular tachycardia (SVT) diagnosis, and lack of conversion to sinus rhythm *in utero*. However, conversion *in utero* does not reliably assure the absence of neonatal SVT. To comfortably exclude the likelihood of a postnatal reoccurrence of SVT, excluding atrial flutter that rarely occurs after neonatal conversion, Stephenson suggested that a window of 48 hours of postnatal observation allows for the assessment of any postnatal recurrence. In the absence of such a recurrence, transoesophageal pacing may be used to assess for SVT inducibility. If tachycardia (reentrant SVT) can be started, 6–12 months of anti-arrhythmic therapy should be considered.

Ambulatory cardiology and electrophysiology

Syncope remains one of the most frequent complaints presenting to paediatric cardiologists and elicits anxiety among children, parents, friends, and teachers, and results in physical activity and sports restrictions, irregular school attendance, and frequent physician visits. Although the vast majority of patients will be diagnosed with vasovagal syncope or neurally mediated syncope, clinicians should be aware of red flags that warrant additional investigation. Mitchell Cohen (United States of America) presented red flags that general cardiologists should pay attention to, and these include exertional syncope, syncope secondary to auditory stimuli, family history of sudden unexplained death, syncope with a fever, abnormal physician examination, abnormal electrocardiogram, syncope without a prodrome, and syncope preceded by chest pain or palpitations. Although both the Heart Rhythm Society and American College of Cardiology have recently published guidelines on the evaluation and treatment of syncope, all cases need to be individualised. Maria Cecilia Gonzalez (Belgium) discussed the increased use of implantable loop recorders in children with unexplained syncope. In patients with concerning syncope where routine ambulatory monitors and 30-day event recorders do not provide adequate information, implantable loop recorders may have a role and should be monitored with routine home monitoring similar to outpatient pacemaker follow-up. Fabrizio Drago (Italy) presented the Italian experience regarding paediatric syncope units designed to improve the diagnosis and evaluation of childhood syncope and eliminate costly and even unnecessary hospitalisations and procedures. Admission to the syncope unit could be through the emergency department or via ambulatory clinics. Over a 13-year period, 1867 patients were evaluated at the Bambino Gesu Pediatric Syncope Unit, with 48% being evaluated in the outpatient ambulatory setting, 49% requiring a daytime evaluation, and only 3% requiring a hospital admission. This proactive approach based on the Italian Syncope Guidelines and an adequately staffed paediatric syncope unit successfully reduced the number of hospital admissions, costs, duration of hospital stay, and number of unnecessary tests. In an era where cost–value and quality are increasingly being assessed, this model deserves further attention and may be beneficial in other countries worldwide. Andreas Pflaumer (Australia) ended the session on the importance of syncope in patients previously diagnosed with a channelopathy and tailored the presentation to treating patients based on the type of syncope and the specific gene mutation.

Chest pain is a relatively common complaint among children and teenagers and often invokes a fair bit of anxiety among parents, yet is rarely a sign of cardiac disease. Juha Mati-Happonen (Finland) presented an excellent review of paediatric chest pain presenting to a variety of large tertiary children's hospitals where 0–4% were identified as having a cardiac aetiology. Pericarditis was the most common cardiac diagnosis in the emergency room followed by myocarditis, anomalous right coronary, hypertrophic cardiomyopathy, and dilated cardiomyopathy. Other forms of supraventricular tachyarrhythmias often had associated palpitations in addition to the chest pain. Interestingly, of patients diagnosed with an anomalous coronary artery right from the left-facing sinus or left from the right-facing sinus, chest pain was the presenting symptom in nearly one in four patients. Historical elements that should raise suspicion include the occurrence of chest pain with exertion and chest pain that occurred with palpitations. A thorough and detailed family history should be obtained. Any concerning physical examination findings or an abnormal electrocardiogram should prompt a cardiology consultation. This talk was followed by an excellent lecture by Konrad Brockmeier (Germany) on finding clues in the presentation of children with palpitations that should warrant a more thorough evaluation by a paediatric electrophysiologist.

Cardiomyopathies and electrophysiology

With increasing surveillance programmes throughout the world, hypertrophic cardiomyopathy has been

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increasingly diagnosed in adolescents and young adults. However, given the variable expressivity of this autosomal dominant condition, identifying which hypertrophic cardiomyopathy patient warrants an ICD remains a challenge. Data were presented by Emanuel Kaltenecker (Germany) regarding the clinical benefit of specialised care centres for patients with cardiomyoapthies, akin to adult CHD speciality clinics. Aside from traditional hypertrophic cardiomyopathy risk factors such as syncope, family history of sudden cardiac death, non-sustained ventricular tachycardia, and septal thickness >30 mm, Juan Pablo Kaski (United Kingdom) discussed emerging risk factors in hypertrophic cardiomyopathy patients such as the presence of late gadolinium enhancement on MRI. Although 60% of hypertrophic cardiomyopathy patients harbour mutations in sarcomeric genes, there is early evidence that patients with troponin T mutations may have a greater arrhythmic risk. Although the European Society of Cardiology has published a risk score for hypertrophic cardiomyopathy, Dr Kaski cautioned the attendees to be careful with this score, as it is not applicable to patients <16 years of age. Two current registries are available for patients with hypertrophic cardiomyopathy. Gabrielle Norrish (United Kingdom, Great Ormond Street) is chairing an international registry for patients with hypertrophic cardiomyopathy, and Michael Ackerman and Rachel Lampert (United States of America) are actively enrolling patients with hypertrophic cardiomyopathy to determine the effects of lifestyle and exercise on clinical outcomes. It is anticipated that more effective screening, better risk assessment, and recommendations regarding activity allowances will provide future benefit to patients with hypertrophic cardiomyopathy over the next few years. Robert Hamilton (Canada) also presented information on novel biomarkers that will be available soon for patients potentially diagnosed with arrhythmogenic right ventricular dysplasia. Although arrhythmogenic right ventricular dysplasia is mostly a disease of adulthood, new data have emerged that ~10% of children have life-threatening arrhythmias related to arrhythmogenic right ventricular dysplasia.

Devices

One question that is frequently posed to paediatric electrophysiologists is whether or not a patient with a cardiac implantable electrical device can undergo an MRI. MRIs are frequently used in the assessment of patients before surgery, especially those undergoing complex intracardiac baffles, as well as to assess ventricular function and volumes in adult congenital heart disease patients. Salim Idriss (United States of America) presented recently published guidelines by the Heart Rhythm Society and the importance of understanding that MRI-compatible systems relate to both the device and the leads. It is critical as patients' transition to adult CHD physicians that there is a clear delineation and understanding of which active and old retained leads are present. Most importantly, a team approach should be undertaken at each hospital regarding the management of patients with pacemakers and ICDs that require MRI testing. This plan should involve cardiology, radiology, anaesthesiology, nursing, and local industry support if needed.

Alpay Celiker (Turkey) presented novel pacing therapies such as leadless pacing and ultrasound pacing, which have a limited application in children but may become applicable with certain device modifications to young adults with CHD over the next decade.

Adult CHD and arrhythmia

The session on bridging electrophysiology and adult CHD featured a number of excellent international talks. Hiroko Asakai (Japan) gave an excellent review on transitional care for adults living with pacemakers and ICDs. John Triedman (United States of America) discussed arrhythmias in adults with complex CHD who have either baffle leaks or fenestrations and stressed the importance of communication between the adult cardiologist and the electrophysiologist. Such intended shunting pathways (fenestrated Fontan) or unintended baffle leaks (Mustard/Senning) may provide an effective avenue for successful manipulation of an ablation catheter. Closure of such fenestrations and baffle leaks could be considered after an effective ablation procedure if the haemodynamics warrant such an approach.

The late effects of repaired and palliated CHD bridge the interventional cardiologist and the electrophysiologist. Although transcatheter pulmonary valves have been used with increasing frequency in adolescents and adults with pulmonary valve regurgitation and right ventricular dilation following tetralogy of Fallot, patients remain at risk for ventricular tachycardia even after the insufficiency has been resolved. In addition, the nature of the stented valve implant may limit effective catheter ablation delivery as that region may be encased in the valve conduit and not easily reached. A joint team discussion with the interventionalist and the electrophysiologist should take place before the transcatheter pulmonary valve procedure is scheduled. Although ICDs remain the mainstay of therapy for patients with resuscitated life-threatening arrhythmias, Maully Shah (United States of America) presented concerning evidence that 25% of patients have device complications and 25% sustain inappropriate

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ICD shocks. In fact, while guidelines for primary prevention ICD implantation in adults with CHD have been published, only 35–40% of patients receive appropriate therapies following these recommendations. Electrophysiologists need to continue to work with industry to create better leads and diagnostic and therapeutic software specifically designed for patients with congenital disease. Electrophysiologists need to continue working with adult CHD specialists to identify at-risk patients early who may benefit from catheter ablation and to identify which patients are truly at risk for a life-threatening arrhythmia and warrant an ICD. The last talk of the adult congenital heart disease/EP session by Natasja DeGroot (the Netherlands) discussed the growing epidemic of atrial fibrillation in our adult congenital heart disease population. The pathophysiologic and teleological development of atrial fibrillation in the adult congenital heart disease population is likely to be different from the adult with a structurally normal heart. Ongoing research and innovative catheter strategies will need to be advanced over the next decade to address this challenging arrhythmia.

Anti-arrhythmic medications

Anti-arrhythmic medications remain the first line of therapy for most arrhythmias. Numerous talks throughout the meeting emphasised the importance of caution when giving intravenous anti-arrhythmic agents. For example, amiodarone is often used in the paediatric intensive care setting; however, information was presented that 11% of patients receiving amiodarone may have a cardiovascular collapse and will require extracorporeal membrane oxygenation support. Younger patients appear to be at the highest risk, and slowing the infusion rate over 45–60 minutes appears to be safer than infusions given over a shorter time frame.

Debates

There were three excellent debates during the EP section. The first debate (Andrew Papez, United States of America, and Fabrizio Drago, Italy) centred on non-invasive versus invasive risk assessment in asymptomatic patients with Wolff–Parkinson–White syndrome. Increasing evidence shows that while non-invasive testing can be helpful in select patients it cannot predict the risk of a life-threatening event with 100% certainty. Similarly, catheter ablation continues to have excellent success (>90%), yet the risk of AV block and coronary artery injury is not 0%. As always, there remains a risk–benefit balance that should be discussed with patients and parents. What has emerged and was well represented at the World Congress was that intermittent pre-excitation may not be as benign as initially suspected, and additional non-invasive or invasive testing may be warranted.

The second debate (Shubhayan Sanatani, Canada, and Arthur Wilde, the Netherlands) addressed the issue of ICDs as first-line therapy for patients with catecholaminergic polymorphic ventricular tachycardia resuscitated from ventricular fibrillation events. Similar to many debates, both presenters shared similar views, including the central role of β-blockers at optimal dosing and compliance. Both presenters agreed that the adjunctive therapies, flecainide and cardiac denervation, have not been fully used or evaluated. ICDs in inherited arrhythmia conditions, especially catecholaminergic polymorphic ventricular tachycardia, are associated with a high incidence of complications and should always be considered carefully. The two debaters are collaborating on an international catecholaminergic polymorphic ventricular tachycardia registry that hopes to improve our understanding of the condition.

The third debate addressed the clinically relevant questions as to how to approach patients with a ventricular arrhythmia burden >20% and a structurally normal heart. George Van Hare (United States of America) proposed that such patients are at risk of developing a cardiomyopathy and should be considered for catheter ablation. Thomas Kriebel (Germany) posited that the natural history of the condition favours eventual spontaneous disappearance of the ectopy and a wait-and-see approach may be reasonable as long as frequent assessment of the ventricular function is performed. A prospective registry should be considered to help address this question.

Channelopathies

The world congress hosted sessions on genetics and channelopathies. There was a bridging session between Ambulatory and Genetics that provided a bench-to-bedside approach to genetics, appropriate for the broad audience. This session started with the basics of genetics with Martjin Bos (United States of America) and Genetics 101 – How do you spell D-N-A? This talk focussed on recognising and understanding the most common inheritance patterns (autosomal dominant, autosomal recessive, X-linked dominant, X-linked recessive, and germline mosaicism) illustrated by pedigree examples. Basics of the four-letter DNA alphabet and understanding the background and effects on the protein of the most common genetic mutations, such as missense, non-sense, in-frame deletions and insertions, frame-shift mutations, and splice site mutations, were reviewed. Jeff Towbin (United States of America) expanded on this with a talk on the power of genetic testing in Paediatric

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Cardiology. Pharmacogenetics is a new field, and a talk by Martin Tristani (United States of America) enlightened the audience about the state-of-the-art aspects of the field and where we are today with pharmacogenetics in the clinical realm. Pharmacogenomics is the most practical application of Precision Medicine and offers the potential to predict therapeutic outcomes, such as efficacy and adverse drug reactions. Cytochrome P450 enzymes are crucial for drug metabolism and bioactivation. Single-nucleotide variants that localise to key functional regions in Cytochromes P450 affect an individual's response to specific medications and serve as the basis for FDA-recommended genotype-based dosing. The majority of single-nucleotide variant effects have been studied in individuals of European ancestry, leaving other races and ethnicities without sufficient data to make genotype-based dosing recommendations. Of the cardiovascular medications, warfarin is the most studied medication from a pharmacogenomics standpoint, with strong evidence for genotype-based dosing.

Mutation calling and what makes a mutation "Disease-Causing" was outlined for the audience by Sabine Klaasen (Germany), who provided strategies for understanding the differences between important genetic data and for understanding for variants of unknown significance. The session ended with Michael Ackerman (United States of America) illustrating the five reasons NOT to order genetic testing. Dr Ackerman further explored this in an EP session on Genetically Inherited Sudden Death Syndromes in Children: Challenges and Dilemmas in Channelopathies. In this session, Dr Ackerman further outlined the gaps in the knowledge of the genetics and channelopathic disease. Research in the genetics of channelopathies has advanced our understanding of the importance of genetics in diseases that affect the heart. We have come to understand that these conditions, similar to many cardiac diseases of genetic origin, are characterised by incomplete penetrance and variable expressivity, and although genetic information can guide and empower therapy misuse of this powerful tool can result in misunderstanding and even harm. There were talks in this session outlining the up-to-date recognition, diagnosis, and management of Brugada Syndrome (Georgia Brugada, Spain), Long QT Syndrome (Jan Till, United Kingdom), and Short QT Syndrome (Juan Villafane, United States of America). We were provided insight into a potential biomarker that may allow us to better diagnose children with arrhythmogenic right ventricular dysplasia by Robert Hamilton (Canada), who has developed and is studying this biomarker. Finally, Joel Kirsh (Canada) outlined the importance of collaboration and cooperation with coroners and medical examiners. He outlined the shortcomings of both the death investigation systems and clinical cardiology practice in identifying, and preventing death from, inherited heart rhythm disorders when working in isolation, and presenting the collaborative approach that was developed in Ontario, Canada. Dr Kirsh was the perfect person to deliver this message as the new Regional Supervising Coroner – Central East Region, Office of the Chief Coroner for Ontario. This is an important collaboration that will allow for a more comprehensive approach to, and a better understanding of, sudden death in the young. In this way, we hope to move towards the identification of the causes of sudden death, find a strategy for prevention, and protect the family from recurrent events.

International bridging

As mentioned, this World Congress had the largest electrophysiology content to date. This reflects several processes. As patients with CHD survive longer, we are increasingly recognising arrhythmias as common, late health issues. The rapid growth in cardiogenetics and the field of inherited arrhythmia has also increased the relevance of this field to the paediatric cardiology community. In addition to the significant advances in EP in the past decade, as highlighted above, the Pediatric & Congenital Electrophysiology Society has made a concerted effort to engage electrophysiologists and general cardiologists with an interest in EP from all over the world. A meeting was held, which included representatives from more than 20 countries and a discussion was held with the purpose of bringing EP support to more countries. Concrete action plans were formulated, including establishing a network of international paediatric electrophysiologists who would share challenging cases. In addition to the formal programme, this year's congress offered many opportunities for networking and research collaborations.

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