Dear APHRS members,

Now that the New Year begins, I would like to extend my deepest gratitude to Dr. Shih-Ann Chen for his passionate and dedicated leadership as president of the APHRS for the past two years. Over the course of the last two years, the APHRS have positioned itself as an international organization like the HRS and the EHRA by gaining a wide-ranging foothold after its inception in 2008. Dr. Chen will be permanently remembered in APHRS history as a president to solidifying its footing by riding out difficulties. APHRS2013 in Hong Kong provided a productive annual scientific session, where APHRS members released their academic achievements and were encouraged to do more researches through the exchange of ideas and insights. The session also served as a significant venue to bring together world-renowned experts and professionals in the field of arrhythmia to discuss the future of this sphere. I would like to take this opportunity to express my sincere thanks to Dr. CP Lau, Dr. HF Tse, Dr. J Kalman, and other members of the APHRS2013 Organizing Committee for making every effort to ensure the successful hosting of APHRS2013.

The APHRS is not just a body to prepare for the hosting of an annual scientific session but it is also designed to establish infrastructure for basic and clinical researches in the arrhythmia field of Asia-Pacific countries, provide systematic educational opportunities for young researchers and clinicians wanting to specialize in this field, and to promote multinational researches.

The APHRS still has a long way to go before reducing the current divide and heterogeneity inside Asia-Pacific countries and taking basic and clinical arrhythmia in this region to a higher level.

In an attempt to successfully develop and maintain the APHRS, we need to boost the reputation of the Journal of Arrhythmia, the official journal of the APHRS, by including various, high-quality research papers. As part of efforts to obtain this goal, our leader Dr. Shih-Ann Chen will act as editor-in-chief from 2014; furthermore, your keen interest and active cooperation are highly required.

The APHRS will pursue multinational, multi-organizational clinical researches on a variety of topics including atrial fibrillation and sudden cardiac death through which we will be able to gain valuable data specifically for Asia-Pacific patients.

The APHRS will not just depend on the host countries of annual scientific sessions but also on society-based organizations led by scientific program committee members. This will help organize and maintain higher...
quality of sessions efficiently.

The APHRS will do everything within its capacity and through mutual cooperation with the HRS and the EHRA to successfully organize an annual scientific session and frequently produce guidelines and consensus documents on various topics related to arrhythmia. To that end, more data and research results should be accumulated; I will spare no effort/support to encourage all subcommittees to play their own role.

The APHRS exists for you and your patients because our mission is to end heart rhythm disorders and to help arrhythmia patients receive better treatment to restore health. I wish you continued success both personally and professionally, and a New Year filled with blessings and happiness. The APHRS can promise a better tomorrow thanks to unseen heroes like you making contributions and dedication toward our future.

Thank you.

2014-15 Cabinet

President
Young-Hoon Kim

Immediate Past President
Shih-Ann Chen

President Elect
Wee Siong Teo

Vice President
Shu Zhang

Secretary General
Chu-Pak Lau

Secretary General
Jonathan Kalman

Treasure Chair
Yoshinori Kobayashi

Scientific Program Chair
Jonathan Kalman

Chief Editor of the Official Journal
Shih-Ann Chen

Representative of Australia
Jonathan Kalman

Representative of Hong Kong
Hung-Fat Tse

Representative of India
Mohan Nair

Representative of Japan
Ken Okumura

Representative of Thailand
Tachapong Ngarmukos

Representative of Malaysia
Imran Zainal Abidin

Representative of New Zealand
Martin Stiles

Representative of China
Congxin Huang

Representative of Indonesia
Muhammad Munawar

Representative of Korea
Doung-Gu Shin

Representative of the Philippines
Maria Belen Carisma

Representative of Singapore
Wee Siong Teo

Representative of Taiwan
Tsu-Juey Wu

Advisory
Masayasu Hiraoka

Allied Professionals
Yong Seon Oh/Korea

Basic Research
Wataru Shimizu/Japan

Cardiac Implantable Devices
Juin-Chueh Wang/Taiwan

Clinical Research
Hung Fat Tse/Hong Kong

Document Writing
Prashanthan Sanders/Australia

Education and Scientific Programs
Jonathan Kalman/Australia

Fellowship
Martin Stiles/New Zealand

Fund Raising
Shu Zhang/China

Global Relations
Chu-Pak Lau/Hong Kong

Membership
Chi-Keong Ching/Singapore

Practice Guideline
Satoshi Ogawa/Japan

Public Affairs
Chang-Sheng Ma/China

Scientific Publication and Journal
Shih-Ann Chen/Taiwan

Surgery
Takashi Nitta/Japan

Web and Arrhythmia News
Kazuo Matsumoto/Japan
Congenital long QT syndrome (LQTS) is well known hereditary disorder characterized by prolongation of QT interval in the standard 12-lead electrocardiogram (ECG) and a polymorphic ventricular tachycardia known as Torsade de Pointes (TdP).

**Clinical Diagnosis**

The clinical diagnosis of congenital LQTS is mainly based on the rate corrected QT (QTc) interval at rest, cardiac events such as syncope, aborted cardiac arrest and sudden cardiac death, and a family history of apparent LQTS. When we measure QTc to diagnose congenital LQTS, it is important to exclude secondary causes of QTc prolongation, which can occur with QT prolonging drugs and/or cardiac conditions, such as electrolyte imbalance and bradycardia. The Schwartz score has long been used to diagnose congenital LQTS. Very recently, expert consensus statement on the diagnosis and management of patients with inherited arrhythmia syndromes including congenital LQTS has been proposed. This statement is the collaborative effort of three medical societies representing electrophysiology in North America, Europe and Asian-Pacific area: the Heart Rhythm Society (HRS), the European Heart Rhythm Association (EHRA) and the Asia Pacific Heart Rhythm Society (APHRS). Congenital LQTS can be diagnosed, when the patient has a Schwartz LQTS risk score of > 3.5 in the absence of a secondary cause for QT prolongation, and/or an unequivocally pathogenic mutation in one of the LQT genes, or a QTc of > 500 ms in repeated 12-lead ECG in the absence of a secondary cause for QT prolongation. Congenital LQTS can be also diagnosed in the presence of a QTc between 480-499 ms in repeated 12-lead ECGs in a patient with unexplained syncope in the absence of a secondary cause for QT prolongation and in the absence of a pathogenic mutation.

**Electrocardiographic Diagnosis and Low Penetrance**

The electrocardiographic diagnosis at baseline, however, misses some patients affected by congenital LQTS (so called “concealed” LQTS) as evidenced by syncopal events occurring among family members with a “normal” QT interval. It is estimated that 30 - 40% of genetically affected subjects are concealed LQTS with a normal or borderline QTc interval at rest in congenital LQTS, especially in LQT1, suggesting “low penetrance” of LQTS. Low penetrance in congenital LQTS has been genetically proved for the first time by Vincent et al. They reported that 5 (6 percent) of 82 mutation carriers from 3 LQT1 families had a normal QT interval. Among the 3 major genotypes, Priori et al. reported that the percentage of genetically affected patients with a normal QTc was significantly higher in the LQT1 (36%) than in the LQT2 (19%) or the LQT3 (10%) syndromes. We also found that the sensitivity (penetrance) by the ECG diagnostic criteria was lower in LQT1 (68%) than in either LQT2 (83%) or LQT3 (83%). The identification of patients with concealed LQTS is important in that it may afford the opportunity to initiate potentially life-saving pharmacotherapies and health style modifications. Therefore, novel tools to unveil concealed mutation carriers of LQTS, especially those with LQT1, has long been expected.

**Catecholamine Provocative Testing**

The majority of congenital LQTS patients experience cardiac events such as syncope and/or sudden cardiac death during physical exercise or mental stress. Therefore, provocative testing using catecholamine infusion or exercise has long been used to unmask concealed forms of congenital LQTS, before genetic testing became available. Intravenous infusion of epinephrine, an α + β adrenergic agonist, or isoproterenol, a β-adrenergic agonist, was reported as a useful provocative test in LQTS more than 2 decades ago. Since the heart rate is usually increased to more than 120 beats/min by isoproterenol infusion, especially by the use of bolus injection, it is often difficult to measure the QT interval precisely due to an overlap of the next P wave on the terminal
portion of T wave.\textsuperscript{9} Accordingly, epinephrine infusion has become a standard test.

Two major protocols developed for epinephrine provocative testing include the escalating-dose protocol by Ackerman’s group (Ackerman/Mayo Clinic protocol),\textsuperscript{10} and the bolus injection followed by brief continuous infusion by Shimizu’s group (Shimizu protocol).\textsuperscript{11} Both protocols are useful, safe, and well tolerated, but should be viewed as diagnostic only, not prognostic. Induction of TdP or ventricular fibrillation is extremely uncommon in both protocols. The key determinant is epinephrine-mediated changes in the QT interval for the Ackerman protocol and epinephrine-mediated changes in the QTc interval for the Shimizu protocol.

**Ackerman Protocol (Incremental, Escalating Epinephrine Infusion)**

Ackerman and co-workers examined the usefulness of a 25-minute incremental, escalating infusion protocol (0.025 to 0.2 µg/kg/min) in the LQT1, LQT2, LQT3 patients and genotype-negative patients.\textsuperscript{10,12,13} With this protocol, paradoxical QT prolongation, defined as a 30-ms increase in the QT interval during low-dose epinephrine infusion, is specific in the LQT1 patients (92%), but not in the LQT2 (13%), the LQT3 (0%), and the genotype-negative patients (18%). The paradoxical QT prolongation had a sensitivity of 92.5%, specificity of 86%, positive predictive value of 76%, and negative predictive value of 96% for LQT1 vs. non-LQT1 subjects, and provides a presumptive, pre-genetic clinical diagnosis of patients with LQT1 syndrome.

Lower incidence of false-positive responses and better tolerance of patient are major advantages of the escalating infusion protocol. However, this protocol seems less effective in exposing patients with LQT2 compared to the bolus protocol by Shimizu et al. described below. With this regard, Khositseth et al. reported that epinephrine-induced notched T wave was more indicative of LQT2 status.\textsuperscript{13}

**Shimizu Protocol (Bolus Injection Followed by Brief Continuous Infusion)**

Shimizu and co-workers used bolus protocol and suggested that sympathetic stimulation with epinephrine produces genotype-specific responses of the QTc interval in patients with LQT1, LQT2 and LQT3 (Figure 1).\textsuperscript{16} Epinephrine markedly prolonged the QTc interval at peak effect of epinephrine when the heart rate is maximally increased (1 – 2 minutes after the bolus injection), and the QTc remained prolonged during steady-state epinephrine effect (3 – 5 minutes) in patients with LQT1 (Figure 1A).\textsuperscript{17,18} This steady-state effect likely corresponds with the paradoxical QT prolongation seen with the Ackerman protocol (Figure 1A). The QTc was also prolonged at peak epinephrine effect in patients with LQT2, but returned to close to the baseline levels at steady state epinephrine effect (Figure 1B).\textsuperscript{19} In contrast to LQT1 and LQT2 patients, the QTc was less prolonged at peak epinephrine effect in the LQT3 patients, and was shortened below the baseline levels at steady state epinephrine effect (Figure 1C).\textsuperscript{7} The steady state epinephrine effect improved the clinical electrocardiographic diagnosis (sensitivity) from 68% to 87% in the 31 patients with LQT1 and from 83% to 91% in the 23 patients with LQT2, but not in the 6 patients with LQT3 (from 83% to 83%).\textsuperscript{7} This bolus protocol effectively predicts the underlying genotype of the LQT1, LQT2 and LQT3 (Figure 2).\textsuperscript{7} The prolongation of QTc ≥ 35 ms at steady state epinephrine effect could differentiate LQT1 from LQT2, LQT3 or control patients with a predictive accuracy ≥ 90%. The prolongation of QTc ≥ 80 ms at peak epinephrine effect could differentiate LQT2 from LQT3 or control patients with predictive accuracy of 100%.

A presumptive, pre-genetic diagnosis of either LQT1, LQT2, or LQT3 based upon the response to epinephrine can facilitate the molecular diagnosis by targeting the first gene for screening and the use of β-blockers and the avoidance of QT-prolonging drugs. Clur and co-workers recently evaluated the role of epinephrine test (using Shimizu protocol) in the diagnosis and management of children suspected of having congenital LQTS, who showed a borderline baseline QTc interval (441±28 ms) and non-diagnostic Schwartz score. They reported that the epinephrine test cannot be used to diagnose genotype-positive LQTS, but suggested that it can be a tool to guide clinical decision making in a pediatric cohort with a suspicious LQTS phenotype.\textsuperscript{15}

**Exercise Stress Testing**

Exercise stress testing, e.g. treadmill exercise testing is more often conducted for a long time.\textsuperscript{9,16,17} Takenaka et al. used treadmill exercise testing with a modified Bruce protocol and reported marked prolongation of QTc interval during exercise in LQT1 patients, but much less prolongation in LQT2 patients. On the other hand, they combined a qualitative assessment of T-wave morphology, i.e. broad-based T waves in LQT1 patients and notched (bifid) T waves in LQT2 patients, and facilitated genotyping of LQT1 and LQT2 subjects.\textsuperscript{16} Wong and co-workers focused on the QTc changes with changes of posture (stand-
They speculated that the QTc prolongation with standing was due to a complex physiological response involving sympathetic and parasympathetic mediated pathways. Viskin et al. also reported the usefulness of bedside stand-up test for easily diagnosing LQTS.

Conclusions

The clinical and electrocardiographic diagnosis is still and will be definitely important in patients with congenital LQTS, although the molecular diagnosis has already been a golden standard. Provocative testing using catecholamine infusion or exercise has some clue to facilitate the electrocardiographic diagnosis in some patients with “concealed” LQTS.

Acknowledgements

Dr. W Shimizu was supported in part by the Research Grant for the Cardiovascular Diseases (H24-033) from the Ministry of Health, Labour and Welfare, Japan.
References

ECG Quiz

The model commentary will be provided in the next issue No. 12

Yenn-Jiang Lin, MD / Shih-Ann Chen, MD
Taipei Veterans General Hospital, Taipei, Taiwan

ECG case: A 67 y/o female of previous history of pulmonary vein isolation with suspicion of recurrence

Patient is a 67 y/o female who had previous history of pulmonary vein ablation for atrial fibrillation (AF) two years ago. AF recurrence was suspected due to symptoms of palpitation and irregular heart beat clinically. What is the rhythm and where is the origin of arrhythmia?
The History of Electrophysiology in Malaysia

Dr Imran Zainal Abidin
University Malaya Medical Centre

Cardiology and Cardiothoracic services in Malaysia began on the 8th of August 1955 when a missionary hospital called the Lady Templar Hospital was officially opened. The first university in Malaysia, Universiti Malaya was established on 1st January 1962. Following that, the first Faculty of Medicine in Malaysia was subsequently formalised in 1963. Instruction started in 1964 with the first batch of students. On August 5th, 1968, the spanking new university hospital was officially opened. Rumah Sakit Universiti Malaya, as it was called, became the national cardiology referral centre, after the services at Lady Templar started to diminish. The first cardiac and coronary catheterization was performed in this hospital. It was also at this centre, that the first single chamber pacemaker was implanted, using an Australian made Teletronic pacemaker.

Dr Nik Zainal Abidin remarkable leadership was responsible for the initiation of cardiac electrophysiology services in Malaysia. With careful planning and delegation of his work force, the first electrophysiology unit in the country was formed in 1989, headed by Malaysia’s first Electrophysiologist, Dr Ahmad Murtazam. He received training in electrophysiology at the Freeman Hospital, University of Newcastle on Tyne by the legendary Prof Ronald W.F Campbell. The late Professor ‘Ronnie’ and his colleagues in Newcastle branched out and were fundamentally responsible for providing training and setting up arrhythmia services outside UK. He visited Malaysia numerous times to help Dr Ahmad set up the first cardiac electrophysiology lab in Malaysia. Diagnostic EP was started but in the early years most patients with accessory pathways and ventricular tachycardia were surgically treated. The first ever attempt to ablate was around 1991. DC energy using a modified external defibrillator was used on a patient with incessant VT and poor left ventricular systolic dysfunction. Unfortunately this attempt failed.
In order to expand the cardiology services further without depending too much on government financial support, Dr Mahathir Muhammad, Malaysia’s former prime minister, made the crucial decision to corporatize the cardiology services in the Kuala Lumpur General Hospital. A separate building was constructed complete with state-of-the-art equipments for cardiology and cardiothoracic surgery. On the 1st August 1992, Institut Jantung Negara Sdn Bhd was officially opened.

This development provided the badly needed space for expansion of the EP services. Routine diagnostic EP and ablation began in 1992 in IJN, headed by Dr Ahmad Murtazam and Dr Ahmad Nizar. Prior to that, both of this pioneering cardiologists visited Taiwan to get help and guidance from the two renowned electrophysiologist, Prof Delon Wu of Chang Gung University College of Medicine and Prof Shih-Ann Chen of Taipei Veterans General Hospital. Both professors develop close working relationship and frequently visited IJN to do cases together. This friendship lasted till today and contributed significantly to the development of electrophysiology in Malaysia.

The number of cases started to increase and the team began implanting dual chamber pacemaker routinely. In 1995-6 both Dr Ahmad Murtazam and Dr Ahmad Nizar left the institution for private practice. The successor to the unit was and still is Dr Razali Omar. Trained in Mayo Clinic, Cleveland, it is his era that the Malaysian Electrophysiology services made leaps and bounds. His leadership brought even more EP cases and he began embarking on more complex cases. Important landmarks were made. In 1996, the first ICD was implanted. In 1998, he performed the first successful VT ablation. Subsequently in 1999, Dr Razali introduced and implanted Malaysia’s first CRT-P. Around the same year AF ablation was performed under the guidance of Prof Shih-Ann Chen. In 1999, 3D mapping using Ensite Velocity was introduced in IJN that enabled even more complex ablations to be performed successfully. The first CRTD was implanted in 2003.

Dr Razali pioneered all the latest techniques of EP in Malaysia and together with dynamic team, they organized numerous implant and EP workshops for budding cardiologists and electrophysiologists in Malaysia and in Asia. In the recent years, the growth of EP services in Malaysia has been encouraging, with more new talents expanding the services to the rest of the country. We, the Malaysian cardiologists would like to extend our eternal gratitude to those who have been instrumental to the development of electrophysiology services in Malaysia, especially to the three Professors; Prof Ronnie Campbell, Prof Delon Wu and Prof Shih-Ann Chen.
Beating heart of vibrant India
Oct 29th to Nov 1st 2014

APHRS
The 7th Asia-Pacific Heart Rhythm Scientific Session
Oct 29th to Nov 1st 2014, New Delhi, India

Important Dates

Deadline for Abstract Submission: June 15, 2014
Notification of Acceptance: July 15, 2014
Deadline for Early-bird Registration: July 31, 2014

To register log on: www.aphrsindia.com

Attractive Early Bird Registration Offer for Fellows
Registration Fee includes One year membership to APHRS

Maximum Number of Participating Nations in APHRS
This ECG seems like a regular sinus rhythm, however the peculiar P wave morphology (flat in lead I, negative in aVL) suggests the ectopic origin of atrial rhythm. He sometimes showed different cardiac rhythm with distinct P wave morphology with a longer cycle length (positive in lead I, aVL, CL: 1500ms) (Figure 2). Detailed mapping of the left atrium and pulmonary vein revealed that his baseline rhythm originated from the left superior PV, with the PV potentials preceding both the onset of the P wave and the left atrial potentials (Figure 3).

Fortunately, his AF was reproducibly initiated by ectopic firings in the left inferior PV, rather than the left superior PV. We isolated all four PVs except left superior PV, resulting in disappearance of AF without unmasking bradycardias.

In a rare case like this, it may be better to perform a minor modification of the ablation strategy, rather than a blind, all four PV isolation.

Reference
Remains Cool & Flexible Under Pressure

Just Like You

Introducing the Therapy™ Cool Flex™ Ablation Catheter – a breakthrough in ablation technology and the first fully irrigated, flexible tip catheter. Its laser cut tip electrode flexes, allowing it to conform to tissue, reduce force transmission and provide exceptional cooling throughout the surface of the tip. Now you have the perfect tool to complement your skills, one that stays cool and flexible under pressure, just like you.

SJMprofessional.com