

TAN TOCK SENG HOSPITAL

# MEDICAL DIGEST

JANUARY - MARCH 2019



Tan Tock Seng  
HOSPITAL

11 Jalan Tan Tock Seng  
Singapore 308433

Tel: 6256 6011  
Fax: 6252 7282

[www.ttsh.com.sg](http://www.ttsh.com.sg)

*Medical Digest is a quarterly publication of Tan Tock Seng Hospital written by healthcare providers for healthcare providers, as a service to the medical community.*

TTSH Research News

Interviews with  
Associate Professor  
Teoh Lam Chuan &  
Associate Professor  
Chiu Ming Terk

Pancreatic Cancer – Public  
Knowledge and Awareness

Running: Boon Or Bane

Perioperative Management  
of Patients Receiving DOACs:  
A Balancing Act

Deprescribing: Doing It Better,  
Not More

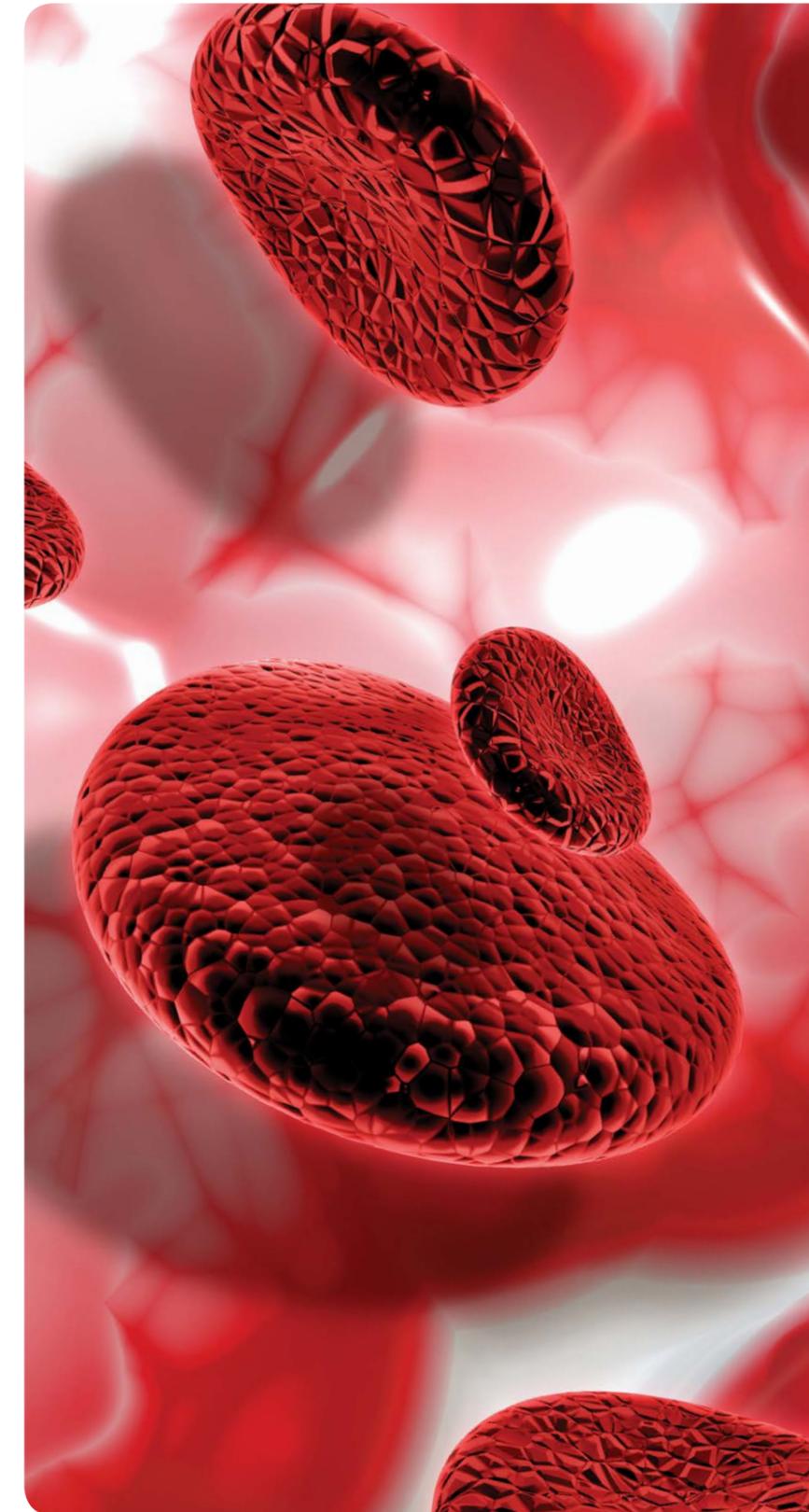
Radiology Quiz

ECG Quiz



Tan Tock Seng  
HOSPITAL

MCI (P) 126/09/2018



# FROM THE EDITOR

In the 2 January 2019 episode of the BBC World Service programme *Witness*, author Joe McAleer was interviewed regarding his meeting with Barbara Cartland, the romance novelist, in the mid-1980s. An interesting point was that Barbara Cartland said that her books were so historically accurate that they were used in America to teach history. McAleer said, “Untrue ... absolutely untrue. She perhaps convinced herself that it was true.”

I'd like to bring up the painful topic of doctors deceiving themselves. Doctors, enjoying great intelligence (debatable at times), weighty responsibility and elevated social stature, involved in high-stakes work with oftentimes unpredictable outcome, have ample opportunities for self-deception. In fact, I think it's a daily occurrence.

Here are some of the plaintive laments I have heard: “I perform coronary angiograms to screen for ischaemia in retiring schoolteachers because the government pays for them”, “We may be weaker in research and education but we have superior clinical skills”, “My colleagues do not like me because they are jealous of my abilities”, “I ruptured the patient's uterus but she is wrong to seek an abortion anyway”, and “If they are really serious about X, they should fund us properly, give us protected time and sufficient headcount”.

One writer argued that nurses sometimes justify the poor care they have delivered by resorting to Sartre's determinism, that is, by believing that the environment they work in compelled them to do so, against which they have little or no control (Roberts M. *Nurse Educ Today* 2016; 46:1-3). They apparently forgot that, as individuals, they could exercise freedom and choice and insist on the right thing in spite of the circumstances.

Besides soothing our internal anguish, it is suggested that self-deception has evolved because it facilitates deceiving others (Von Hippel W, Trivers R. *Behavioral and Brain Sciences* 2011; 34:1-16). It is written in the Ekdhamma Suttas: ‘I don't envision a single thing that, when untamed, leads to such great harm as the mind. The mind, when untamed leads to great harm.’

What I am suggesting that we do is very hard. We must be totally objective and courageous. We must see things for what they are, uncoloured by our biases and prejudice, and we must speak up if we think things are not right. If we did wrong, we own up and move on. We don't need to be right, or be seen as being right, all the time.

We from the TTSH Medical Digest wish all readers a wonderful 2019. May the New Year bring you clarity, joy and contentment.

**Dr Leong Khai Pang**  
EDITOR  
*Medical Digest*

## MEDICAL DIGEST

### EDITOR

Leong Khai Pang

### ASSOCIATE EDITORS:

Charmaine Manauis  
Raymond Ng  
Melissa Tien  
Mohd Fadil Muhammad Farhan

### MEMBERS:

Tang Yee Lin  
Rafael Saclolo  
Ivan Huang Kuang Hsin  
Noorhazlina bte Ali  
Deshan Kumar  
Tan Choon Chieh  
Shirley Bang  
Chong Yaw Khian  
Kalaiyarasi Kaliyaperumal  
Adeline Teh  
Yew Min Sen  
Shirlene Ho Shu Min  
Gavin Lim Hock Tai  
Binedell Trevor Brian

### COPY EDITOR

Safiyya Mohamed Ali

### DESIGNER

Clinton Low

We value your feedback. Please email your questions, comments or suggestions to: [ttsh\\_ccs@ttsh.com.sg](mailto:ttsh_ccs@ttsh.com.sg)  
Please also contact us for notification of change of postal address or requests of additional copies.

While every endeavour is made to ensure that information herein is accurate at the time of publication, Tan Tock Seng Hospital shall not be held liable for any inaccuracies. The opinions expressed in this publication do not necessarily reflect those of Tan Tock Seng Hospital. The contents of this publication may not be reproduced without written permission from the publisher.

RESEARCH

## TTSH RESEARCH NEWS

Every year, TTSH clinicians publish about 300 scientific papers. In this section, we selected a few reports and asked one of the authors of each to summarise and discuss the clinical relevance of their research. The theme this issue are the medical disciplines.

## RESEARCH EXCERPT 1

# A comparison of undergraduate clinical ophthalmology learning methods: Smart phone television display versus slit lamp teaching tube

Wenting SZ, Samin MM, Sanjay S, Neelam K, Shibli K, Chang S, Cheng J. Can J Ophthalmol. 2017;52(4):385-391.

**T**his is a prospective, randomised cross-over comparative study that compared medical students' preference of smart phone television display (SPTD) to a slit lamp teaching tube (SLTT) in undergraduate clinical ophthalmology education. The medical students in groups of two were randomly assigned to two teaching sessions using either the SPTD followed by SLTT or vice versa. After both the teaching sessions, students were asked to feedback on the two teaching methods by scoring six questions in a survey. All participating students were sent the results of the study 1 month after the completion of the study and asked to reflect upon the outcome by answering three further questions.

In total, 38 students were recruited. The overall satisfaction scores were significantly higher in students tutored using the SPTD than the SLTT (mean  $8.6 \pm 1.5$  vs  $7.5 \pm 1.0$ , respectively,  $p < 0.01$ ). The students preferred the SPTD compared to the SLTT in terms of "visualising exactly what was described" ( $8.5 \pm 1.4$  vs  $7.0 \pm 1.3$ ,  $p < 0.01$ ), "seeing the signs described all the time" ( $8.4 \pm 1.3$  vs  $7.2 \pm 1.2$ ,  $p < 0.01$ ), "understanding ocular anatomy" ( $8.3 \pm 1.2$  vs  $7.6 \pm 1.2$ ,  $p < 0.01$ ), and "confidence in identifying clinical signs" ( $8.4 \pm 1.2$  vs  $7.5 \pm 1.2$ ,  $p < 0.01$ ). All the 14 students who responded to our follow up survey agreed with our interpretation of the data and would support the use of the SPTD in undergraduate clinical ophthalmology teaching.

Our study has demonstrated that the utility of SPTD as a teaching aid can significantly increase the satisfaction of undergraduate medical students during their ophthalmology attachment.



*This excerpt was written by Dr Zhou Wenting, senior resident in the Department of Ophthalmology, Tan Tock Seng Hospital.*

### IMPORTANCE IN CLINICAL PRACTICE

*In this paper, we compared medical students' preference of smart phone television display to a slit lamp teaching tube in undergraduate clinical ophthalmology education. The smart phone display showed a great advantage over the traditional slit lamp teaching tube. This is important because the introduction of the new teaching method may significantly increase the satisfaction of undergraduate medical students during their ophthalmology attachment. The portability affordability and connectivity of a smartphone ophthalmoscope make it a promising technique to overcome the shortage of current ophthalmology teaching for undergraduate medical students.*

## RESEARCH EXCERPT 2

# Hearing impairment and hearing aid usage in Singapore

Ho EC, Zhang H, Ong WMW, Li K, Bei YTE, Medapati SVR, Seneviratna A. Int J Audiol. 2018;57(4):291-301.

## Factors influencing hearing loss at presentation, hearing aid choice, and usage in first time hearing aid users in Singapore

Ho EC, Ong WMW, Li K, Zhang H, Bei YTE, Medapati SVR, Seneviratna A. 2018. Int J Audiology. [Epub ahead of publication] DOI: 10.1080/14992027.2018.1476781

**T**he first paper examines the epidemiological and audiological profile, patterns of hearing aid (HA) fitting and usage among first time HA users in Singapore. The second paper examines the factors associated with late presentation at first time HA fitting, and factors affecting HA choice and usage. Both studies are retrospective cross-sectional in design and include 1,068 first time HA users from Tan Tock Seng Hospital between 2001 and 2013.

*This excerpt was written by Dr Ho Eu Chin, senior consultant in the Department of Otorhinolaryngology, Tan Tock Seng Hospital.*

### IMPORTANCE IN CLINICAL PRACTICE

*The World Health Organization estimates that over 5% of the world's population, or 466 million people, suffer from disabling hearing loss (HL), defined as having HL worse than 40 dB (moderate HL) in the better hearing ear in adults. The prevalence of disabling HL rises sharply to 30% among older adults.*

*The 2016 Global Burden of Disease study has identified HL as the third leading cause of years lived with disability (YLDs) globally. This translates to 36.3 million YLDs shared among 1.27 billion people with varying degrees of HL worldwide and represents 4.5% of all YLDs.*

*Despite being a high-income economy, the 2010 Singapore National Health Survey found that among adults with disabling HL, only 3.3% wore a HA, which is very low compared to other developed countries. We found that by the time patients seek help for their HL for the first time, they were elderly with a mean age of 70 years and more than half had already developed moderate-severe HL (>55 dB).*

*The multi-ethnic nature of the population of Singapore provided us the unique opportunity to examine the impact ethnicity has on HL. Nearly a third of subjects of Malay ethnicity already had severe HL (>70 dB) at first presentation. In fact, Malay subjects were twice as likely as Chinese and thrice as likely as Indian subjects to present with severe HL of their better ear.*

*Although 99% of patients had bilateral HL, only 18% were fitted with bilateral HAs. Patients who were younger were more likely to opt for bilateral HAs. More than 85% used their HAs more than 4 days a week but only a third used them for more than 7 hours per day. Older patients and those with better hearing were less likely to use their HAs regularly.*

*There is a clear need for further research, education and advocacy from health care professionals to improve the hearing health of the Singapore population.*

### RESEARCH EXCERPT 3

## Non-prosthetic peri-implant fractures: classification, management and outcomes

Chan LWM, Gardner AW, Wong MK, Chua K, Kwek EBK; Singapore Orthopaedic Research Collaborative (SORCE). Singapore Orthopaedic Research Collaborative (SORCE). Arch Orthop Trauma Surg. 2018;138(6):791-802.

**N**on-prosthetic peri-implant fractures (NPPIFs) are an under-reported entity. Management is challenging because of alterations in anatomy, the presence of orthopaedic implants and phenomena such as stress shielding, disuse osteopenia and fracture remodelling. The aims of this paper were to review patterns of injury, management and outcomes, and to propose a classification system to aid further research.

This study is a multi-centred retrospective case series. Sixty NPPIFs in 53 patients were analysed. Of these, 38 fractures involved the femur, 12 the radius/ulna, five humeri, three tibia/fibula and one clavicle. Thirty-nine patients had fractures around plates and screws, 12 around nails and three around screws. Fractures were managed with a variety of surgical techniques. Six patients had surgical complications, with refracture in four cases and non-union in two. Two patients had multiple refractures (total 12 additional fractures). All surgical complications required further surgery. Three patients had deep vein thrombosis and one patient died of post-operative pneumonia. Fractures were classified according to the initial implant (plate or nail), the position of the new fracture relative to the original implant (at the tip or distant) and the status of the original fracture (healed, not healed or failing). Surgical strategies for common subtypes were reviewed.

This study represents the largest series in the literature. NPPIFs are a challenging clinical problem with a high rate of post-operative complications. They are distinct from peri-prosthetic fractures and should be understood as a separate entity.

### IMPORTANCE IN CLINICAL PRACTICE

*This research paper is the first publication of the Singapore Orthopaedic Research Collaborative Group, a multi-centered group of orthopaedic surgeons with an interest in trauma with representatives from all of the public general hospitals in Singapore. Non-prosthetic peri-implant fractures are an increasingly common clinical problem where a fracture occurs around a previously inserted orthopaedic implant. Such fractures are challenging for the managing surgeon with the lack of evidence-based guidelines. The incidence of such fractures is increasing because of ageing population demographics, combined with increased utilisation of surgery for primary fracture fixation. This paper analysed observed patterns of injury and their outcomes, and the proposed classification provides a rational foundation for further research.*

*This excerpt was written by Dr Lester Chan, consultant in the Department of Orthopaedics, Tan Tock Seng Hospital.*



TTSH Research News is curated and edited by DR MELISSA TIEN, a consultant in the Department of Ophthalmology, Tan Tock Seng Hospital.



## INTERVIEW WITH ASSOCIATE PROFESSOR TEOH LAM CHUAN

*Associate Professor Teoh Lam Chuan is a senior consultant in the Department of Orthopaedic Surgery. He is one of the pioneers of hand surgery in Singapore and the region, and helped to establish the Hand & Reconstructive Microsurgery Section in TTSH. We speak with Prof Teoh, recipient of the Lee Foundation-NHG Lifetime Achievement Award, to find out more about his role in developing hand surgery as a subspecialty.*

## Please tell us about your career pathway and involvement in hand surgery.

I graduated with my MBBS from the National University of Singapore in 1976 and went on to pursue general surgery training in 1981. I saw myself as someone who liked 'carpentry work' so I focused on orthopaedic surgery, and through the HMDP around 1986 I received training in hand surgery in the US. After completing my fellowship in 1987, I returned to Singapore as a consultant in Orthopaedic and Hand Surgery. I was appointed to continue the development of the Hand Surgery Department, the first to be established locally, at Singapore General Hospital. After serving as the chief of the department for 15 years, I came over to TTSH in 2009 to assist Dr Winston Chew to further develop the hand surgery service here.

Today, TTSH has seven consultants in the Hand Surgery Service and manages the whole range of Hand Surgery conditions from traumatic injuries and amputations to infections, nerve conditions, degenerative conditions, autoimmune diseases, and conditions of the upper limb that affects the hand function. The service provides replantation microsurgery and reconstructive microsurgery.

## What entails a comprehensive hand surgery service?

Using the American definition, a comprehensive hand surgery service should comprise medical, surgical and rehabilitative treatment of conditions and diseases of the upper extremities that affect function and form of the hand and wrist. By this definition, hand surgery does not just focus on conditions of the hand per se, but also in hand diseases caused by brain injuries such as stroke, nerve injuries or infections. We treat hand and wrist injuries which affect task performance (e.g. writing, manual assembly). Form refers to the cosmetic component, which is highly relevant because if someone's hands were deformed, they would not want to show it to the world. Hand function and form can be affected due to congenital reasons or trauma such as when the hand is completely amputated or extensively crushed. We also see cases of infected hands due to flesh-eating bacteria, as well as hands affected by autoimmune diseases such as rheumatoid arthritis and degenerative conditions like osteoarthritis.

Hand surgery encompasses reconstructive surgery – where parts of the hand may need to be reassembled or replaced. A unique and key component of hand



Figure 1. Anastomosis of tiny blood vessels under a microscope.

reconstructive surgery is microsurgery, where hand surgeons reattach blood vessels and nerves so that the hand can regain its function.

## What kind of hand injuries have you seen and are there any that are striking?

We see amputations very often and some cases where the hands are completely irreversibly mangled. These injuries are usually a result of occupational hazards (e.g. sugar cane machines) and less commonly road accidents.

One of the obvious things to realise is that the hand has a compact anatomy. In about a 2-cm diameter, there are five tissue structures involved in maintaining dexterity. Hand microsurgery is akin to repairing a watch rather than fixing a bicycle. The most challenging part of hand microsurgery is repairing tiny blood vessels or nerves, which are about 1.0 to 0.5 mm in diameter. To fix them, we need a size 10-0 microsuture to sew about 6–8 stitches. This suture is even thinner than a strand of hair; it has a diameter of 28 microns, and if it is not obvious, 1 micron is a thousandth of a millimetre! Since this is on a micron scale, the surgery has to be done under a microscope (figure 1). This attention to finer details is what I feel sets hand surgery apart from other orthopaedic subspecialties.

Some of the more interesting cases involve replacement of the whole gross tissue, be it the bone, tendon or skin. In Case 1, we used the patient's toes to replace his damaged fingers.

## What are the traits required in a good hand surgeon?

The traits a good hand surgeon must have are related to what I mentioned previously about the hand being a tiny anatomy.

Firstly, the surgeon should have the patience and tenacity to last the entire surgery without thinking of giving up. A typical procedure including microsurgery takes about 6–12 hours and requires a collective team effort.

Secondly, the surgeon should be happy to 'wonder around the world of Lilliput' given the size of the hand. They should enjoy assembling a ship in a bottle. As I mentioned above, you'll be tinkling with tiny structures in a small diameter of 2 cm most of the time, so if you prefer gross anatomy, it is not for you. Many surgeons cannot appreciate the intricacy of small anatomy, hence this group of surgeons is unique.

Finally, the hand surgeon must be able to be fast but not hurried. For example, there may be eight tiny stitches that need to be done under a microscope but there could be hundreds of steps in between that take time. However, hurrying through these steps may not result in optimal outcome so each step should still be done carefully. Rushing through the surgery will affect recovery of the limb and cause

surgeon fatigue. Hence, pacing oneself is very important.

## Finally, what should general practitioners know about hand injuries?

Any condition of the hand affects work and livelihood. GPs should not assume that just because a hand injury looks small, e.g., a cut, or that because the hand is only a small part of the whole body therefore any injury can be ignored. However small the injury may be, GPs should not assume it is minor because the disability may be prolonged. For example, infections from a small wound can lead to loss of an anatomical part or function of the hand. A crush injury may look minor but if not treated early may lead to complete loss of function.

GPs should be aware about the urgency for treatment and focus on recovery of function rather than wound healing. This is because return to work is the main aim for hand injuries, and delayed treatment may lead to poorer rehabilitation to normal function.

## CASE 1

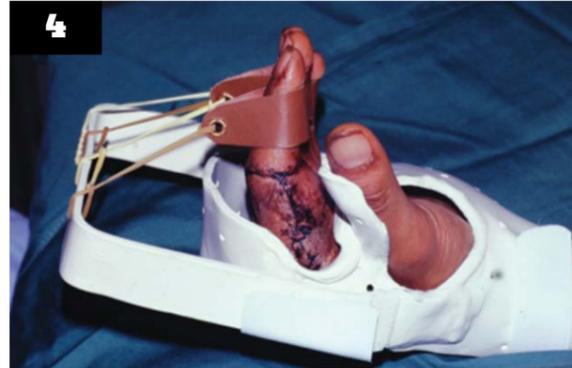
This was our first case in TTSH in 1987 in which a lorry driver sustained proximal amputation of his right arm when the vehicle overturned in an accident. We successfully reattached his arm in a ten-hour surgery. After 6 months of rehabilitation he was able to return to lorry-driving. In a 25-year long term review, he continued to be able to drive in his own transportation company.



## CASE 2

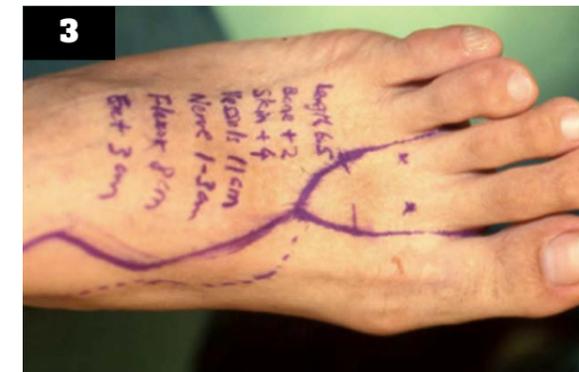
This patient's left hand was crushed during the construction of the mass rapid transit system in Singapore. We rejoined and reconstructed the hand and although it appears shorter than the right hand, it has regained close to normal function following 6 months of rehabilitation. He even plays golf now and cherishes the quality time he spends with his wife and children.

This patient taught me the economic value of the hand – how he was able to resume working and get married once his hand recovered. Our years of experience have taught us that we need to work as a team and develop new things along the way to help the patient. For example, we devised the splint contraction (below) by ourselves, and we learnt that we did not need to wait for the wound to completely heal before we started physiotherapy. This speeds up the recovery process.



## CASE 3

This man sustained a severe crush injury when his left hand was caught in a roller at work when he was 39 years old. He lost all his four fingers and was not able to function with his left hand. We transplanted two toes from his left foot to replace two of the fingers. After several months of rehabilitation he regained adequate function and returned back to work. In the 22-year review period, his left hand continued to function well, and he is still working in the same company as a foreman.





## INTERVIEW WITH ASSOCIATE PROFESSOR CHIU MING TERK

*We also had the opportunity to interview Associate Professor Chiu Ming Terk, Head and senior consultant in the Department of General Surgery, Tan Tock Seng Hospital. Prof Chiu is a pioneer of Trauma Surgery in Singapore and had a pivotal role in setting up what is now the largest trauma centre in Singapore. He recently received the NHG Distinguished Achievement Award for his extensive contributions in elevating trauma education and services locally and in the region.*

### Please share with us your journey so far in Trauma Surgery.

I went to the US in 1998 for fellowship training in Trauma Surgery. In Singapore, Trauma Surgery as a subspecialty was first set up in Singapore General Hospital and Alexandra Hospital when two trauma surgeons returned to Singapore in 1997/1998 after being trained overseas. I was in Alexandra Hospital when I returned, and came to TTSH in 2000 where I helped to set up our Trauma Surgery service. Trauma Surgery was then a very new concept but almost two decades later, we have the heaviest trauma load in Singapore because of our central location and dense population.

I used to be very active in humanitarian efforts around the region: teaching locally and overseas, conducting hands-on training, setting up registries, and sharing protocols in places like Sri Lanka, Indonesia and Cambodia. Since my stroke in 2017, I have been focusing on administrative work but I hope to return to clinical work slowly, soon. In the meantime I do some teaching locally and managed one trip abroad.

### What was it like setting up and developing what is today the largest trauma centre in Singapore?

Trauma Surgery was very new when it was first set up in 2000 in TTSH. Comparatively, in the US, Trauma Surgery started in the 1960s. I was lucky, setting up the trauma centre here was quite

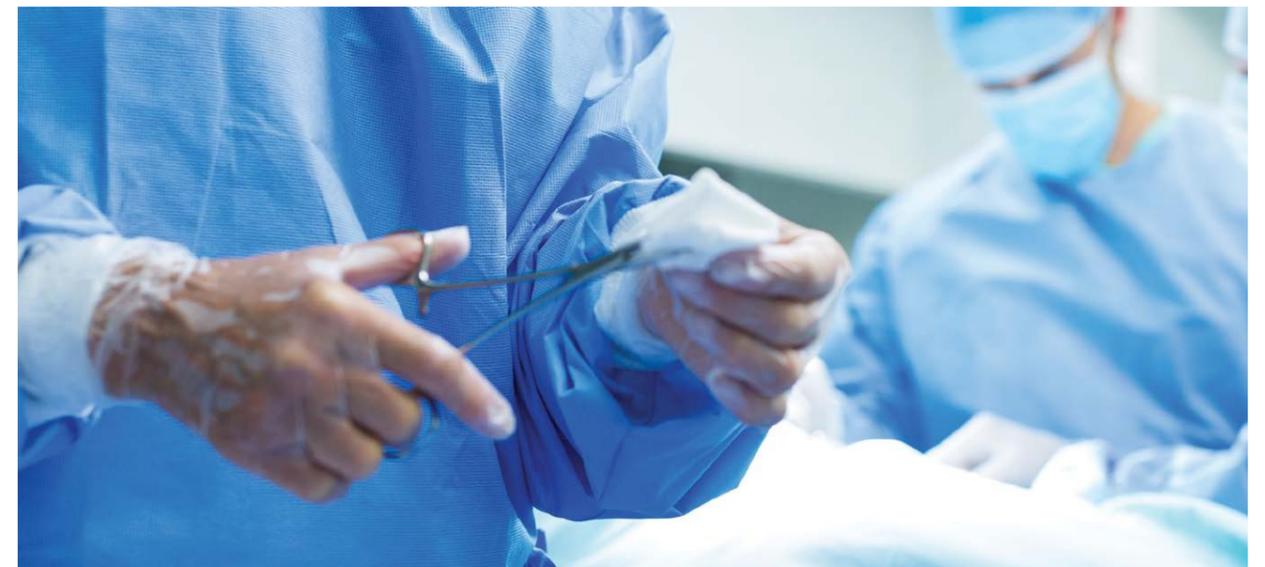
When a physician decides to go into Trauma Surgery, he or she must not be focused on the monetary rewards as the field is not as lucrative as it may appear to be. It also causes disruption in your lifestyle because cases tend to occur in the middle of the night when people are disinhibited.

easy because the hospital administration was very supportive since we already had a huge trauma load. Moving forward 18 years, Trauma Surgery is now an established, albeit a resource-heavy discipline in Singapore. Each cluster has at least two trauma surgeons; in TTSH, we have five presently.

We also have a Trauma Training Centre which has many courses helping different levels of medical personnel in trauma: from paramedics, nurses, and doctors of different specialties.

### What important lessons have you learnt throughout your career in trauma?

When a physician decides to go into Trauma Surgery, he or she must not be focused on the monetary rewards as the field is not as lucrative as it may appear to be. It also causes disruption in your lifestyle because cases tend to occur in the middle of the night when people are disinhibited. This is when





people get drunk and fights and accidents occur, and you have to be prepared to return to the hospital any time of the night. The night shift usually only has one consultant so expect a busy night while on duty.

Trauma surgeons must be ready to improvise. For instance, certain equipment and the full team of medical experts may not be available at certain hours of the night. Or when you are involved in clinical work overseas, the infrastructure available may be different or inadequate and you have to improvise. For example, the trauma surgeon must be ready to stitch up wounds if stapling equipment is unavailable or fails.

Trauma Surgery has received more attention in the past few years, becoming a bit more glamorous.

I still believe though that at the end of the day, trauma surgeons must not focus on the glamour and prestige of Trauma Surgery, but rather achieve contentment by knowing that saving a person's life is a huge reward in itself.

### What are the major changes in Trauma Surgery over the past two decades?

These days surgery has evolved to minimally invasive approaches such as laparoscopic procedures or robotic surgery. Although minimally invasive surgery has its advantages, general surgeons must be trained for emergency surgeries where time and adverse conditions become crucial factors in saving a life.

“It is crucial that young doctors do not forget the basics of surgery, especially in the face of rapidly developing technology. No matter how sophisticated technology is, the basics will enable them to get out of precarious situations, something as simple as being familiar with stitching versus stapling.”

If handling severe trauma, GPs should remember the basic principles of advanced trauma life support (ATLS), which is to regulate airway, breathing and circulation. Trauma Surgery is resource-intensive, hence bring the victim to the nearest hospital capable of supporting such a case immediately.

We have also set up a national trauma registry, which took a long time. It started out as a simple spreadsheet and has now been converted into a rather sophisticated cloud registry. Having a good database enables us to study trends and outcomes in trauma cases in Singapore and compare them with patterns overseas. One obvious example is the types of cases we see, which is largely made up of industrial accidents, e.g. falls from heights due to our plentiful high-rise buildings, and falls in the elderly due to our large ageing population. The trend in industrial accidents is similar to cities like Hong Kong and Tokyo where skyscrapers are also common, and is in contrast with less urbanised places like Cambodia or Vietnam, where road accidents are common. Again, due to different infrastructure, time taken to arrive to the appropriate hospital in the city from a rural place in Cambodia will be an important factor, and the condition of the patient upon arrival to the hospital and resources available will be fairly different from what we get here.

### What advice do you have for young doctors considering a career in trauma?

It is crucial that young doctors do not forget the basics of surgery, especially in the face of

rapidly developing technology. No matter how sophisticated technology is, the basics will enable them to get out of precarious situations, something as simple as being familiar with stitching versus stapling.

### What should general practitioners keep in mind if they see a trauma patient?

If handling severe trauma, GPs should remember the basic principles of advanced trauma life support (ATLS), which is to regulate airway, breathing and circulation. Trauma Surgery is resource-intensive, hence bring the victim to the nearest hospital capable of supporting such a case immediately.

We are currently trying to organise the trauma system in Singapore whereby each healthcare region has one big trauma centre with good resources. As it is important to treat the victim in a well-equipped centre which is experienced from high patient load, this system will be important in ensuring that severe trauma cases are sent to the nearest appropriate hospital as soon as possible rather than just the nearest hospital.



# PANCREATIC CANCER – PUBLIC KNOWLEDGE AND AWARENESS

Pancreatic cancer (PC) is a lethal disease with grim prognosis and high case fatality rate. PC incidence is projected to increase globally to become the second most common cause of cancer death by 2030.<sup>1</sup> The Singapore Cancer Registry Interim Annual Report 2010–2014 ranked PC 10th in prevalence among local residents, and it is the fifth and sixth most common cause of cancer-related deaths among men and women respectively.<sup>2</sup> Despite advances in cancer therapy, the outlook for patients diagnosed with PC remains dismal and this has not improved over the past four decades.

**A**etiology of PC is multifactorial, in which a minority is due to genetic and hereditary disorders. Smoking doubles the risk compared to non-smokers. The rising epidemic of diabetes (diabetes mellitus [DM] and obesity) is likely going to increase its incidence. This was demonstrated in a previous local study where asymptomatic presentation and early-stage PC typically occur in DM patients.<sup>3</sup>

Symptoms are usually vague or absent. Common presenting symptoms include jaundice, dark-coloured urine, and abdomen or back pain. By the time such symptoms appear, the tumour would have usually spread to other organs. Surgery is the only cure and paradoxically majority of patients present with advanced disease which precludes surgery.

Early detection of PC is challenging as there is no screening test. The pancreas sits deep in the torso and no external lumps can be palpated during a routine physical exam, as is the case for breast cancer screening. It is also not as easily accessible by digital examination as compared to the rectum, cervix or prostate. Neither is it amenable to routine diagnostic endoscopy as with colorectal cancer screening. This is further augmented by the lack of public awareness. Combining all these features results in delay in seeking medical attention and contributes to the nihilistic outlook.

**Early detection of PC is challenging as there is no screening test. The pancreas sits deep in the torso and no external lumps can be palpated during a routine physical exam, as is the case for breast cancer screening. It is also not as easily accessible by digital examination as compared to the rectum, cervix or prostate.**

Current imaging methods used to detect PC include computerised tomography (CT), magnetic resonance imaging (MRI) and endoscopic ultrasound (EUS) scans. Each of these modalities have their strengths and limitations. CT and MRI scans are non-invasive but may fail to detect a small tumour. EUS is an invasive procedure which

Q15. How much do you know about the following cancers?

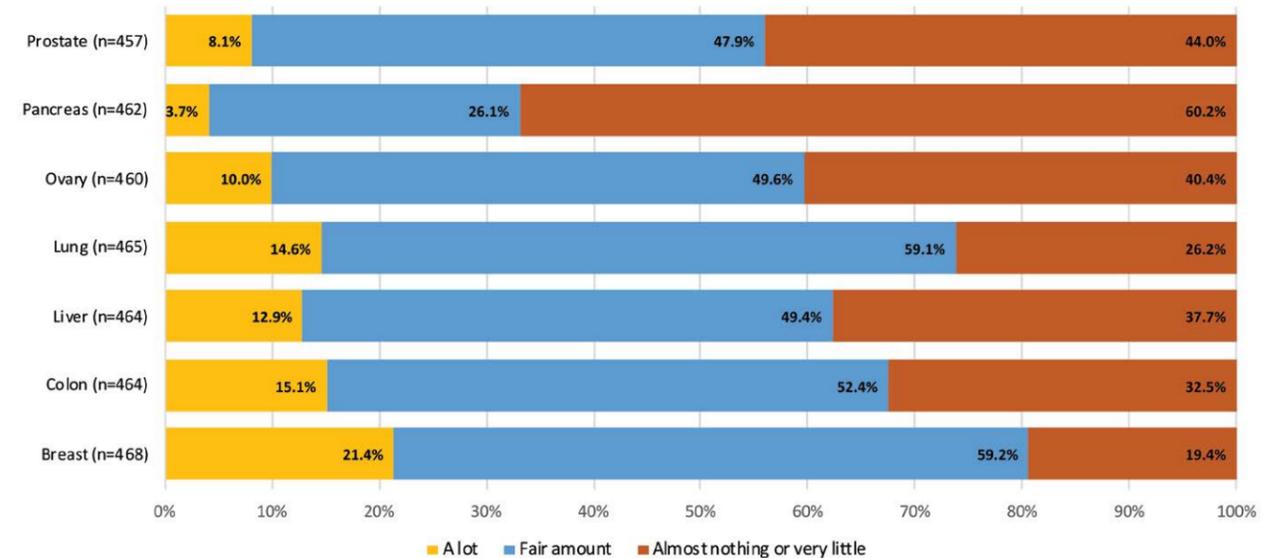
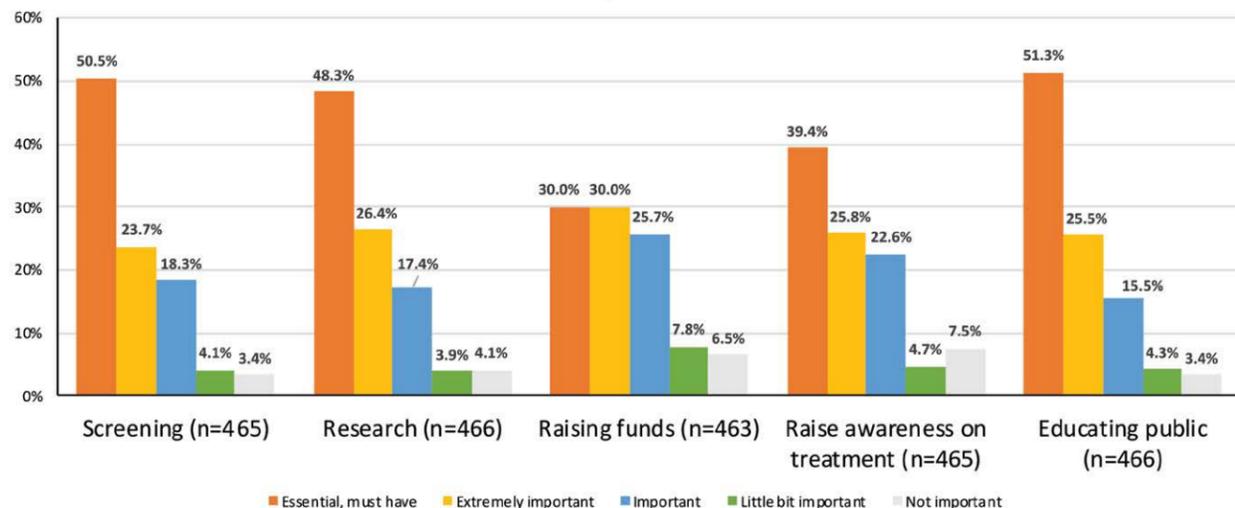


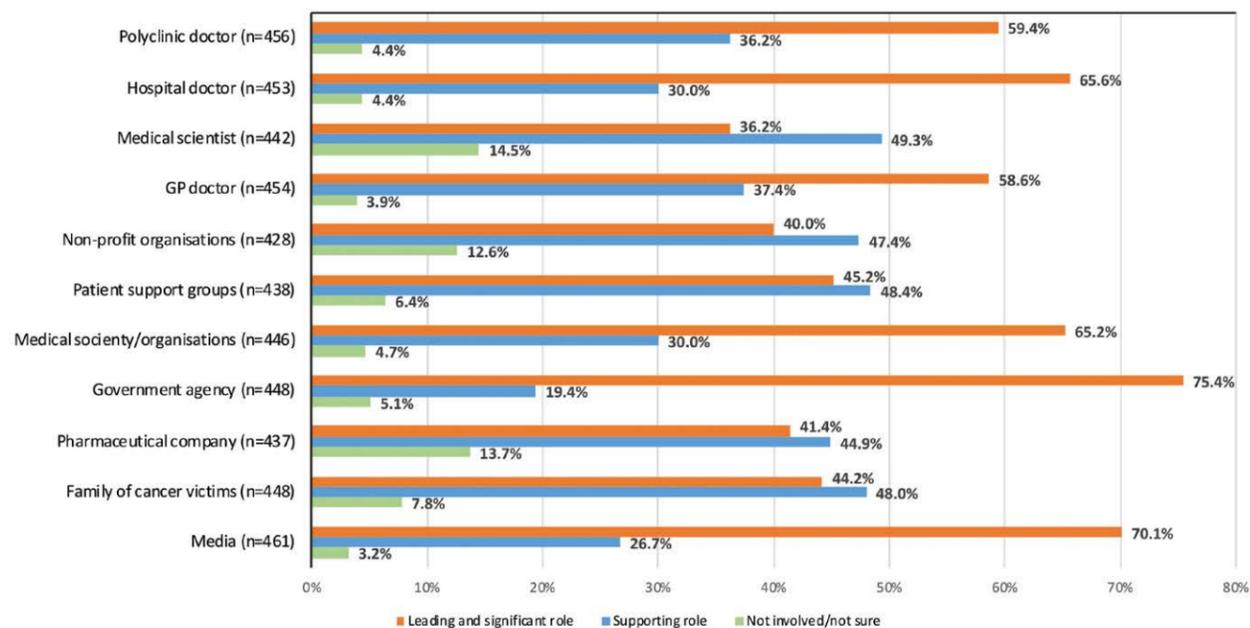
Figure 1. Level of knowledge for each cancer type.

**Q19. When raising public awareness about pancreas cancer, which of the following is the most important? Rank priority from '1-5 scale'.**



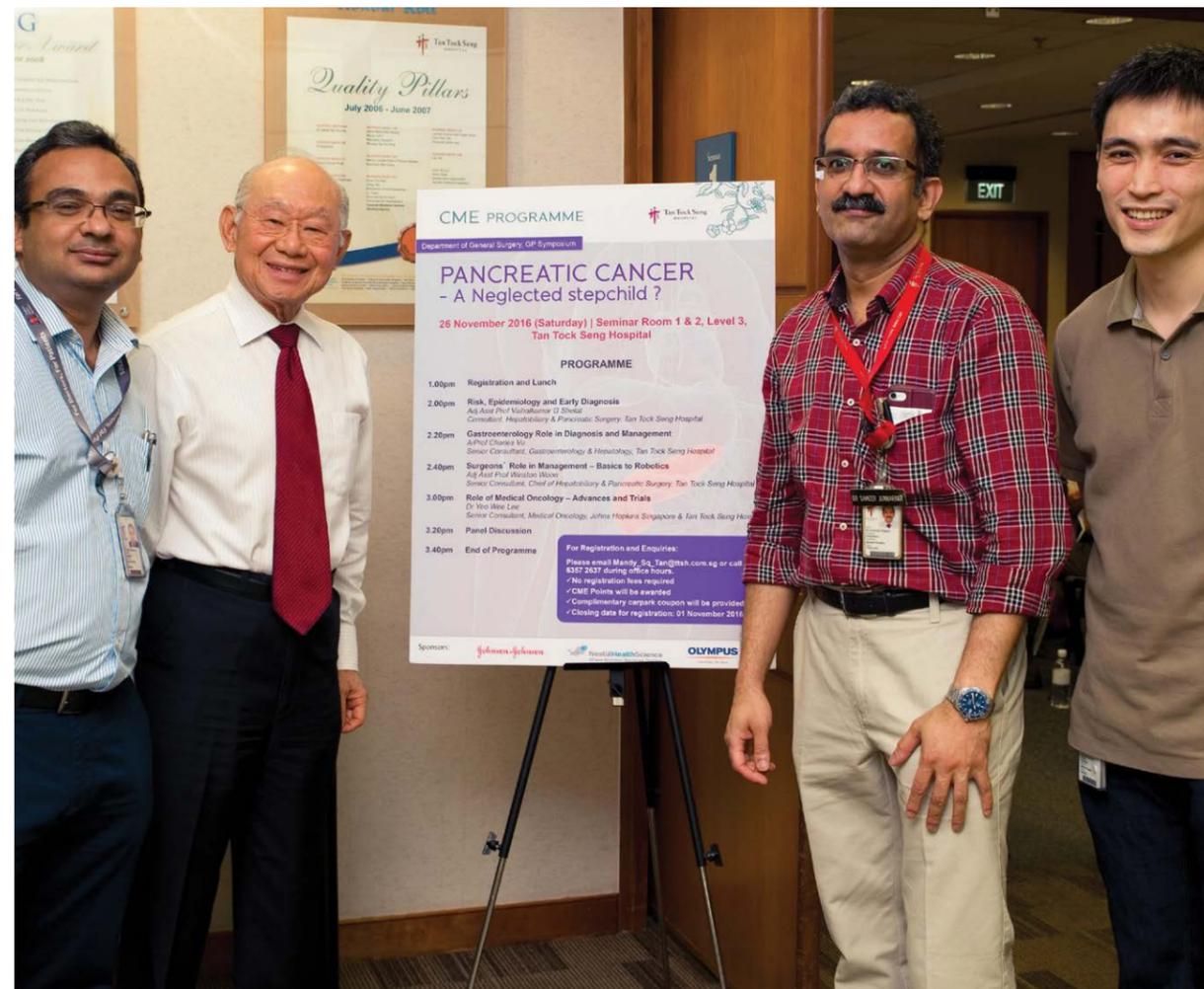
**Figure 2. Ranking of the different aspects of raising public awareness about pancreatic cancer. 'Educating the public about pancreatic cancer' (51.3%) and 'Screening of pancreatic cancer' (50.5%) emerged as the top two themes.**

**Q17. Who do you think should be working to raise awareness of cancer in Singapore?**



**Figure 3. Bar chart showing the opinions on who should play a 'leading and significant role' in raising public awareness of pancreatic cancer.**

One drawback is that a validated measure of cancer awareness was not utilised. Despite the lack of awareness, overall there is enthusiasm to know more about this disease.



**Figure 4. Annual Liver Symposium 2016 entitled 'Pancreatic Cancer - The Neglected Stepchild?'**

needs technical expertise. Another alternative is CA 19-9, a pancreatic cancer marker that is easily measured by a blood test. However, it is not sensitive or specific and marker levels are falsely elevated in smokers. Hence there is no value of doing a blood test for the CA 19-9 marker in healthy people. Increased levels lead to unnecessary anxiety with the possibility of exclusion of pancreatic disorders from healthcare insurance.

### Knowledge and awareness survey

We conducted a prospective survey in 2017 to evaluate the level of awareness, knowledge and perception that Singaporeans have about PC. Data were collected through a self-administered questionnaire-based survey from. Four hundred and eighty healthy individuals, 21 years old and above, were invited from outpatient clinics at Tan Tock Seng Hospital (TTSH) to participate.

Majority of respondents were in the 21-40 years age group (52.5%) and female (59.4%). Majority resided in HDB flats (68.9%) and about half were employed (55.0%). About 20.4% had completed secondary school or lower education and 9.2% were current smokers. Some 13.6% of respondents (65 individuals) were not even aware that an organ named 'pancreas' existed in the human body!

Respondents were most familiar with breast, lung and colon cancers. Knowledge levels of PC were the lowest, with 60.2% of respondents revealing that they know almost nothing or very little about PC (figure 1).

After reading a statement on the lethality of PC in Singapore, respondents were largely very supportive of education and awareness campaigns. There were 77.8% of respondents who were very supportive of education efforts and public awareness campaigns. Those who were very supportive also:

- Believe that it is very important for Singaporeans to be aware of cancer (92.7%),
- View cancer as a very serious public health problem (90.3%), and
- Consider Singapore to be making progress in terms of dealing with cancer (66.5%).

'Educating the public' and 'Screening' were highlighted as most important aspects to raise awareness about PC. On the other hand, raising funds for PC research was lowest in priority (30%) (figure 2).

A large proportion of respondents (75.4%) believe that government agencies should take charge of campaigns which raise public awareness, followed by the media (70.1%) and hospital doctors (65.6%) (figure 3).

### Conclusion

This is the first such study in Singapore and it showed that awareness on PC remains startlingly low as compared to other body organ cancers like breast, lung, colon, and liver. This could be due to

**Majority of respondents were in the 21-40 years age group (52.5%) and female (59.4%). Majority resided in HDB flats (68.9%) and about half were employed (55.0%). About 20.4% had completed secondary school or lower education and 9.2% were current smokers. Some 13.6% of respondents (65 individuals) were not even aware that an organ named 'pancreas' existed in the human body!**



Figure 5. Huge turnout at a public symposium on pancreatic cancer.

the fact that these cancers are common and various awareness campaigns have been organised by health authorities and non-profit organisations. The Hepato-Pancreato-Biliary Association (HPBA) of Singapore has also been organising the Liver Disease Awareness Week since 2013 to raise awareness on liver cancer. However, there is no organised effort to raise awareness on PC in Singapore. Each year, the month of November is designated as PC awareness month and is commemorated with the colour purple. Since 2013, TTSH has been organising an annual public symposium to raise awareness and provide education about hepatobiliary and pancreatic cancers (figures 4 and 5). The event has attracted a turnout of more than 250 participants yearly with positive participant feedback. Since 2016, TTSH has also been organising a General Practitioner CME event on PC which is attended by over 110 registered doctors across Singapore.

Our study has shown that respondents are generally supportive of education and awareness campaigns on PC. The study was sufficient in highlighting the severe lack of public awareness on PC, particularly in individuals with lower education levels. One drawback is that a validated measure of cancer awareness was not utilised. Despite the lack of awareness, overall there is enthusiasm to know more about this disease. It was interesting to note that people voted for government agencies and the media to lead public awareness programmes in preference to doctors. The widespread support for a public awareness campaign on PC even surpassed that of US respondents as reported by Celgene Corporation.<sup>4</sup> It is therefore imperative that health authorities, the media and healthcare professionals step up efforts to meet the demand for raising awareness and education about this neglected stepchild of modern oncology.

#### REFERENCES

1. Rahib L, Smith BD, Aizenberg R, Rosenzweig AB, Fleshman JM, Matrisian LM. Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreatic cancers in the United States. *Cancer Res* 2014;74(11):2913-21.
2. Teo MCC, Soo KC. Cancer trends and incidences in Singapore. *Jpn J Clin Oncol* 2013;43(3):219-24.
3. Chia CLK, Lee AYS, Shelat VG, Ahmed S, Junmarkar SP, Woon WWL, Low JK. Does diabetes mellitus affect presentation, stage and survival in operable PC? *Hepatobiliary Surg Nutr* 2016;5(1):38-42.
4. Celgene Corporation/Ipsos Public Affairs. Pancreatic cancer awareness survey. November 2014. Available at <https://media.celgene.com/content/uploads/2014/11/pancreatic-cancer-awareness-survey.pdf>.



**DR VISHALKUMAR G SHELAT**  
is a consultant in the Department of General Surgery, Tan Tock Seng Hospital. This project was part of a final year project conducted by **MS RUTH LEE** from the School of Biological Sciences, Nanyang Technological University.

“ Our study has shown that respondents are generally supportive of education and awareness campaigns on PC. The study was sufficient in highlighting the severe lack of public awareness on PC, particularly in individuals with lower education levels. ”

# RUNNING: BOON OR BANE

One of the common questions I receive in my practice from my patients is whether running is a good exercise for them, whether it is suitable for them or if it is the best exercise (or some other similar permutations). I am often flummoxed by these questions and this is due in part to the inherent subjectivity of what constitutes “good” to the patient and that the pros and cons of embarking on running is also dependent on the patient’s health profile. It did set me thinking on the pros and cons of running in general, in particular if the literature bears out the perception of running as a good/bad form of exercise.

**I**t is certainly a question we will probably encounter more often as running has increased in popularity over the decades with a burgeoning number of events and the increasing participant rates in marathons. Conversely, our ageing population of runners will encounter musculoskeletal problems and become concerned about their joint health.

## Benefits of running?

The benefits of running (as a form of vigorous exercise) in reducing all-cause mortality and cardiovascular morbidity is well known. The beneficial effects of running is due to the positive effects on risk factors for cardiovascular diseases such as obesity, hypertension and dyslipidaemia. It is also due to its effect on improving endothelial health of the cardiovascular system, and the effect of aerobic exercise in increasing cardiovascular reserve and on energy expenditure which is important for maintaining weight in the healthy range. For instance, the population attributable fraction of not running is 16% for all-cause mortality and 25% for cardiac mortality. The effect size is comparable and in some instances exceeds some of the well-known risk factors associated with cardiovascular disease such as hypertension, smoking and dyslipidaemia.

It is interesting that running per se confers additional health benefits compared to vigorous exercise in general.

Lee D et al. found that the hazard ratio for all-cause mortality in individuals who exercise vigorously was 0.88 compared with the sedentary population but the risk declines further to 0.70 when they look specifically at running. The study, being cross-sectional in nature, does not eliminate confounding factors to bias the results in favour of running, but it raises the possibility that running has additional qualities that reduce mortality.

However, it is not a case of some is good and more is better. When the data are stratified according to weekly training load, an inverted ‘U’ relationship can be seen for the risk of coronary heart disease and all-cause mortality. This suggests that there is an optimal running load for health benefits. The point of

diminishing return lies in the vicinity of 4.5 hours/week, 30 miles per week and 6 times a week, which probably represents the upper limit of the training load of all but the most ardent recreational marathoners. There are circumstantial data suggesting that prolonged and chronic aerobic training at the elite level leads to cardiac adaptation which may not be entirely reversible despite detraining. These cardiac changes include conduction abnormalities, left ventricular hypertrophy as well as subtle interstitial fibrosis. Physiological studies of ultra-marathoners highlight the phenomenon of cardiac drift in which cardiac output decreases over time beyond that which can be accounted for by non-cardiac factors such as dehydration. The jury is still out regarding the significance of this transient decreased cardiac function but there does not appear to be deleterious effects.

Opponents of running argue that while one might live longer because of running, all the extra time gained is spent in the pursuit of more miles (avid runners might disagree). Fortunately, studies suggest that, on average, lifespan is extended by seven hours for every one spent running.

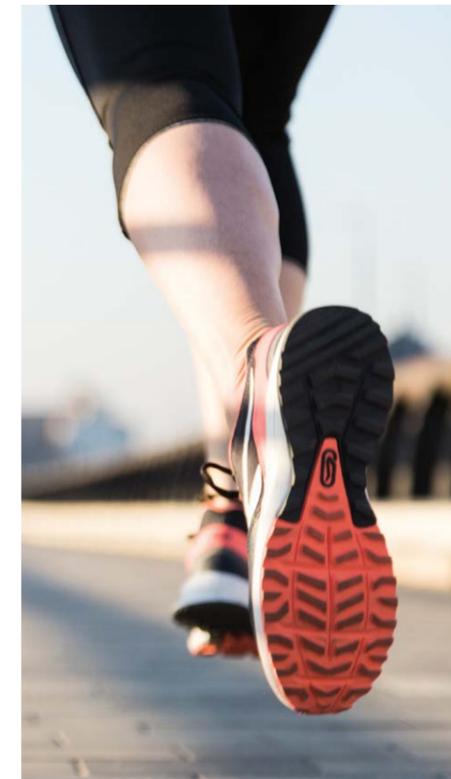
## Should we all be running?

Despite the many health benefits, it is not apparent that running should be the default form of exercise for everyone.

The distinctive characteristic of running (as opposed to walking) is the float phase where neither feet is in contact with the ground. In effect running is essentially a series of single leg jumps.

Runners are often concerned about the risk of sustaining injuries from the high impact nature of the sport. The injury rates differ between studies but have been estimated to be as high as 20%. While the types of injuries differ between running events of different distances, the predominance of injuries in the lower limbs is consistent with the impact inherent in running.

Sprinters have a higher incidence of hamstring injuries while distance runners are commonly afflicted by Achilles enthesopathy. One of consistent risk factors for injuries is inexperience; novice runners are at higher risk of injury compared to seasoned ones. One reason is that novices have poor biomechanics for managing impact.



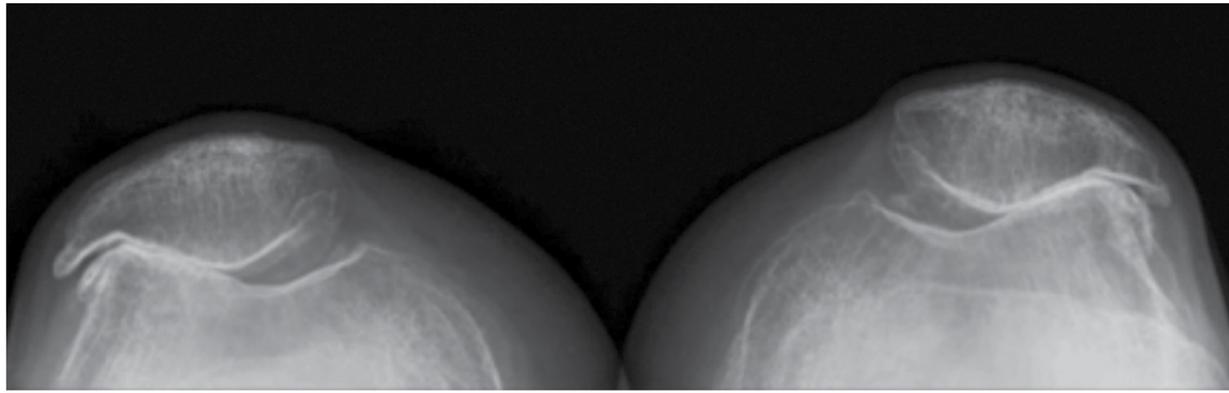


Figure 1. X-Ray showing severe patellofemoral osteoarthritis.

Despite the role of impact in running injuries, the data suggest that this is not the entire story. For instance, running injury rates over the last 40 years has not shown any secular trend. Despite the evolution of running shoes to include materials with shock absorption properties, there is no sustained decline in running injury rates. However, the profile of the runners might have changed with the increased participation of older individuals who have a lower threshold for injuries. The higher participation rates in longer running events might have offset any reduction in injuries due to technological advances in footwear.

Furthermore, research into the effect of midsole hardness and its impact on running produced unexpected results. While it is intuitive that cushioning in the shoes reduces ground reaction force, research indicates quite the opposite, with greatest ground reaction associated with the softest midsole. The ankle and knee of runners wearing softer insoles show the greatest stiffness in landing. This highlights the difficulty

Despite the evolution of running shoes to include materials with shock absorption properties, there is no sustained decline in running injury rates. However, the profile of the runners might have changed with the increased participation of older individuals who have a lower threshold for injuries.

of instituting mechanical solutions in biological systems that have feedback loops which adapt and adjust to the sensory input as opposed to inanimate mechanical systems like a car.

In view of this, what are the other interventions that might reduce impact on the joints?

One potential area is to improve running biomechanics. Novice runners have poorer control of the hip stabilisers resulting in increased dynamic genu valgum and sub-optimal patello-femoral joint loading, which can be improved with core and hip strengthening. Biomechanical studies show that relatively small changes to running cadence and trunk tilt can reduce patello-femoral loading. Some studies show that simple exercises to strengthen hip muscles can alter running biomechanics. It is possible to retrain the running gait over a few months to improve biomechanics and these changes persist after the training has ceased. More drastic changes to forefoot running have been shown to decrease anterior compartment pressure in runners afflicted with chronic exertional compartment pressure syndrome of the leg.

There is some evidence that running on a treadmill does not reduce the impact on the joint compared to over-ground running. Running on the treadmill however allows runners to maintain level ground running as small changes in elevation and declination and elevation of the running surface can increase patella-femoral stress.

Another concern of runners is the effect of accumulative impact on articular cartilage health and the subsequent progression to osteoarthritis (figure 1). This is a valid concern as the mechanism of osteoarthritis has not been fully elucidated. Animal studies show that articular cartilage in animals can adapt when there is articular loading, where the cartilage size increases after prolonged running (on a treadmill) and even after load

bearing, without increased incidence of osteoarthritis. The situation is very different when the joint is abnormal. Surgical transection of the anterior cruciate ligament in animals results in joint laxity and loss of proprioception which accelerates the degeneration of the joint.

In humans, epidemiologic studies have shown that lifelong manual labour involving heavy lifting and climbing is associated with accelerated joint degeneration; the data on running is surprisingly sanguine. Running, in most studies, does not significantly increase the risk of osteoarthritis of the knee, despite the impact of 1–2 times the body weight borne by the joint. Perhaps the detrimental impact of running over a long period of time is offset by its health benefits such as maintenance of a healthy body weight.

In the studies that show some correlation between running and radiological signs of osteoarthritis, runners did not experience greater pain or functional impairment compared to the general population. In a

subset of runners, there may be correlation between risk of osteoarthritis and the pace (rather than volume) of running. Interestingly, the association between osteoarthritis and team sports at an elite level is stronger, perhaps due to the higher training intensity and higher pressure to perform despite injury. The risk factor for osteoarthritis is significant knee injury which destabilises the joint or compromises the impact absorption capacity, such as meniscal tear.

In summary, running, like most forms of exercise, when performed regularly, has health benefits. There is some data to suggest that running per se may have added benefits compared to other forms of exercise but the effect of confounding factors cannot be discounted. Most of these benefits can be achieved with modest levels of running. While there is a point of diminishing returns, this occurs at very high levels of running. Participation in sports at elite levels may accelerate joint degeneration but this may result from continued activity despite an injured knee rather than the accumulative effect of running.

In the studies that show some correlation between running and radiological signs of osteoarthritis, runners did not experience greater pain or functional impairment compared to the general population.



#### REFERENCES

1. Lee DC, Brellenthin AG, Thompson PD, Sui X, Lee IM, Lavie CJ. Running as a key lifestyle medicine for longevity. *Prog Cardiovasc Dis.* 2017;60(1):45-55.
2. Hood S, Northcote RJ. Cardiac assessment of veteran endurance athletes: a 12 year follow up study. *Br J Sports Med.* 1999;33(4):239-43.
3. Pelliccia A, Maron BJ, De Luca R, Di Paolo FM, Spataro A, Culasso F. Remodeling of left ventricular hypertrophy in elite athletes after long-term deconditioning. *Circulation.* 2002;26:105(8):944-9.
4. Lindsay MM, Dunn FG. Biochemical evidence of myocardial fibrosis in veteran endurance athletes. *Br J Sports Med.* 2007;41(7):447-52.
5. Lopes AD, Hespagnol Júnior LC, Yeung SS, Costa LO. What are the main running-related musculoskeletal injuries? A Systematic Review. *Sports Med.* 2012;42(10):891-905.
6. Schmitz A, Russo K, Edwards L, Noehren B. Do novice runners have weak hips and bad running form? *Gait Posture.* 2014;40(1):82-6.
7. Theisen D, Malisoux L, Genin J, Delattre N, Seil R, Urhausen A. Influence of midsole hardness of standard cushioned shoes on running-related injury risk. *Br J Sports Med.* 2014;48(5):371-6.
8. Gerrard JM, Bonanno DR. Increasing preferred step rate during running reduces plantar pressures. *Scand J Med Sci Sports.* 2018;28(1):144-51.
9. Teng HL, Powers CM. Sagittal plane trunk posture influences patellofemoral joint stress during running. *J Orthop Sports Phys Ther.* 2014;44(10):785-92.
10. Conaghan PG. Update on osteoarthritis part 1: current concepts and the relation to exercise. *Br J Sports Med.* 2002;36(5):330-3.
11. Lefèvre-Colau MM, Nguyen C, Haddad R, Delamarche P, Paris G, Palazzo C, Poinraudeau S, Rannou F, Roren A. Is physical activity, practiced as recommended for health benefit, a risk factor for osteoarthritis? *Ann Phys Rehabil Med.* 2016;59(3):196-206.

DR JASON CHIA is a senior consultant in the Department of Orthopaedic Surgery, Tan Tock Seng Hospital.

# PERIOPERATIVE MANAGEMENT OF PATIENTS RECEIVING DOACS: A BALANCING ACT

In the perioperative management for patients on oral anticoagulants, clinicians often struggle to strike a balance between the risk of thromboembolism and of periprocedural bleeding. In this article, we share our practice of the management of direct oral anticoagulant (DOAC) therapy in the perioperative setting.

## Overview of DOACs

Oral anticoagulants are indicated for prophylaxis and treatment of thromboembolism and stroke prevention in patients with nonvalvular atrial fibrillation. Vitamin K antagonists like warfarin were the mainstay for conditions requiring oral anticoagulation.<sup>1</sup> However, warfarin use is complicated by the need for frequent monitoring and numerous interactions with foods, herbs and drugs.<sup>2</sup>

DOACs were developed to overcome the shortcomings of warfarin. Since their regulatory approval in 2010, they have been popular with physicians and patients largely due to the simplified monitoring requirement and minimal drug-food and drug-herb interactions.

DOACs are classified according to their mechanism of action. Direct thrombin inhibitors (such as dabigatran) target the enzymatic activity of thrombin while factor Xa inhibitors (e.g. rivaroxaban, apixaban, edoxaban and betrixaban) block the activity of activated clotting factor Xa. Currently, only dabigatran (Pradaxa®, Boehringer Ingelheim Singapore Pte Ltd), rivaroxaban [Xarelto®, Bayer (South East Asia) Pte Ltd] and apixaban (Eliquis®, Pfizer Pte Ltd) are available in Singapore.



## Factors to consider in perioperative management of elective procedures

Factors to consider in the perioperative management of patients treated with DOACs are thromboembolic risk of the individual, bleeding risk of the procedure and duration of DOAC interruption required before the procedure.

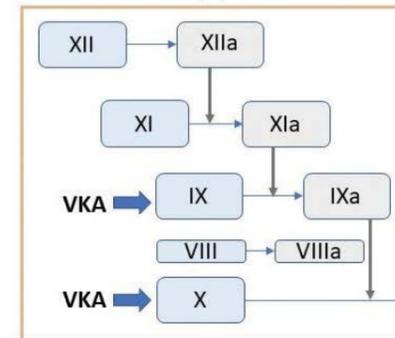
### Thromboembolic risk

For patients with a high risk of repeat thrombotic events (e.g. stroke or deep vein thrombosis within the recent month), postponement of the surgery should be considered.<sup>4</sup>

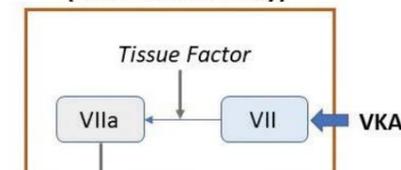
### Bleeding risk of the procedure

Based on Tan Tock Seng Hospital (TTSH)'s Pre-Admission Counselling and Evaluation (PACE)

### Contact Pathway (Intrinsic Pathway)



### Tissue Factor Pathway (Extrinsic Pathway)



### Common Pathway

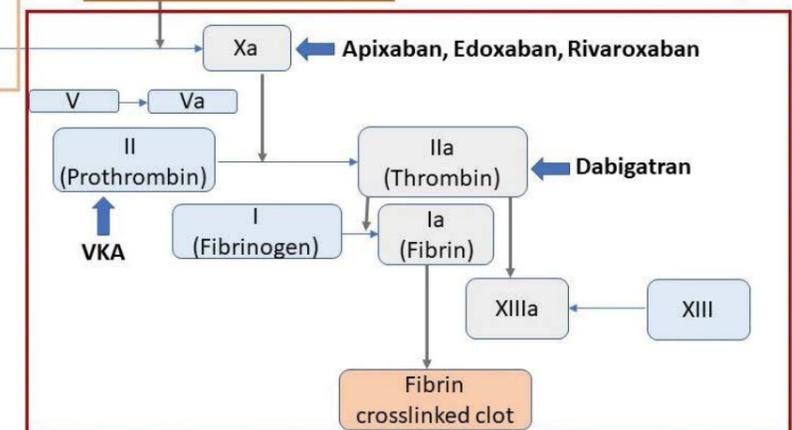


Figure 1. Mechanism of action of DOACs on the clotting cascade. Diagram modified from Raval AN, et al.<sup>3</sup>

MINOR BLEEDING RISK	MODERATE BLEEDING RISK	HIGH BLEEDING RISK
<ul style="list-style-type: none"> <li>Cataract or glaucoma intervention</li> <li>Appendectomy</li> <li>Superficial surgery (e.g. abscess incision, lump excision)</li> <li>Hand/finger procedures</li> <li>Foot/toe procedures</li> <li>Excision of bursas/ganglions</li> <li>Tendon repairs</li> <li>Rigid cystoscopy or double J-stent insertion</li> <li>Mastoidectomy</li> <li>External ventricular drain / ventriculoperitoneal shunt</li> </ul>	<ul style="list-style-type: none"> <li>Total knee arthroplasty</li> <li>Above/below knee amputation</li> <li>Hemiarthroplasty</li> <li>Carotid endarterectomy</li> <li>Cervical spine surgery</li> <li>Pituitary surgery</li> <li>Laminectomy 1–2 levels</li> <li>Fenestration and discectomy</li> <li>Temporal bone resection</li> <li>Thyroidectomy</li> <li>Urethroplasty</li> <li>Orchidectomy</li> <li>Arteriovenous fistula – creation, revision</li> </ul>	<ul style="list-style-type: none"> <li>Craniotomy</li> <li>Open reduction internal fixation of pelvic bones</li> <li>Revision of spinal instrumentation</li> <li>Spinal decompression &gt;2 levels</li> <li>Revision hip/knee arthroplasty</li> <li>Total hip arthroplasty</li> <li>Nasopharyngectomy</li> <li>Major head and neck surgery</li> <li>Prostatectomy</li> <li>Total gastrectomy</li> <li>Biliary bypass, Whipple's</li> <li>Aortic procedures</li> </ul>

Table 1. Bleeding risk of elective surgical procedures<sup>4</sup>

Guidelines,<sup>4</sup> bleeding risk of surgical procedures can be stratified into minor, moderate or high. Examples of procedures and the corresponding bleeding risk are shown in table 1.

#### When to stop administering DOAC prior to procedure

The time period to withhold DOAC therapy prior to a procedure depends on the patient's renal function (represented by the creatinine clearance), the half-life of the DOAC and the bleeding risk of the procedure.

In general, patients with poorer renal function (e.g. CrCl 15–30 ml/min) require a longer period of pre-procedure DOAC interruption compared to patients

DOAC	t <sub>1/2</sub>
Dabigatran	12–17 hours
Rivaroxaban	5–9 hours (young) 11–13 hours (elderly)
Apixaban	12 hours

Table 2. Elimination half-life (t<sub>1/2</sub>) of DOACs

with good renal function (e.g. CrCl >50 ml/min) to allow most of the drug to be eliminated prior to the procedure (table 2).

TTSH's PACE guidelines provide a clear guide on the recommended duration of DOAC interruption prior to surgery or invasive procedures (table 3).<sup>4</sup>



Creatinine Clearance (CrCl)	Procedures with Low Bleeding Risk		Procedures with Moderate/High Bleeding Risk*	
	Dabigatran	Apixaban/Rivaroxaban	Dabigatran	Apixaban/Rivaroxaban
CrCl >50 ml/min	1 day	1 day	2 days	2 days
CrCl 30–50 ml/min	2 days	1 day	4 days	2 days
CrCl <30 ml/min	4 days**	2 days	6 days**	4 days

DOAC, direct oral anticoagulant; PACE, Pre-Admission Counselling and Evaluation

\*Patients are required to undergo a pre-operative prothrombin time and activate partial thromboplastin time check at the Day Surgery Centre 1 hour prior to the procedure

\*\*Dabigatran is not indicated for patients with CrCl <30 ml/min

Table 3. Recommendations for DOAC interruption prior to surgical procedures according to TTSH PACE Guidelines

For procedures with very high bleeding risk (e.g. spinal anaesthesia, epidural anaesthesia or lumbar puncture), some guidelines suggest a longer interruption period of 5 days for dabigatran and 3 days for rivaroxaban and apixaban.<sup>5</sup>

#### Bridging therapy with parenteral anticoagulants

Given the predictable response of DOACs and their short half-lives, preoperative bridging with parenteral anticoagulants like low molecular weight heparin or heparin is generally not recommended as they increase the risk of bleeding without providing much clinical benefit.<sup>5,6</sup>

#### Post-operative resumption of DOACs

After the procedure, DOACs should be recommenced when haemostasis is secured to reduce the risk of thromboembolism. The recommended time period for post-operative resumption of DOACs is 24 hours for procedures with low bleeding risk. For procedures with high bleeding risk, DOACs can be resumed 48 to 72 hours post-procedure.<sup>4</sup> DOACs should be resumed at their usual dose as there is limited evidence on the safety and efficacy of using reduced dose for post-operative patients.<sup>5</sup>

#### Management of DOACs in emergencies

When emergency surgery is required, the DOAC should be discontinued immediately. Urgent blood investigations should be ordered to guide subsequent management: full blood count, renal panel, liver panel, prothrombin time (PT), activate partial thromboplastin

time (aPTT), fibrinogen level, thrombin time (TT, for patients receiving dabigatran), and anti-Factor Xa levels (for patients receiving rivaroxaban or apixaban).<sup>7</sup>

Reversal strategies include administration of antidotes, reduction of intestinal absorption, increasing DOAC clearance and administration of coagulation factors (table 4).<sup>5</sup>

DOACs were developed to overcome the shortcomings of warfarin. Since their regulatory approval in 2010, they have been popular with physicians and patients largely due to the simplified monitoring requirement and minimal drug-food and drug-herb interactions.

MILD BLEEDING	MODERATE-SEVERE BLEEDING	LIFE-THREATENING BLEEDING
<ul style="list-style-type: none"> <li>Local measures (e.g. anti-fibrinolytics for gum bleeds)</li> <li>Delay next dose or withhold one dose of DOAC</li> </ul>	<ul style="list-style-type: none"> <li>Symptomatic treatment</li> <li>Mechanical compression of bleeding site</li> <li>Surgical or radiological intervention</li> <li>Fluid replacement and haemodynamic support</li> <li>Blood product transfusion (for blood loss or thrombocytopenia or coagulopathy)</li> <li>Consider IV tranexamic acid</li> <li>Oral activated charcoal (if last ingestion was within 3 hours)</li> <li>Dialysis for dabigatran in cases of severe renal failure</li> </ul>	<ul style="list-style-type: none"> <li>Use of reversal agents (e.g. idarucizumab, andexanet alfa)</li> <li>Blood product transfusion</li> <li>Coagulation factors products [e.g. prothrombin complex concentrate (PCC), activated PCC (aPCC, FEIBA), rFVIIa]</li> </ul>

Table 4. Management of bleed in patients receiving DOACs

## Antidotes for DOACs

### Idarucizumab

Idarucizumab (Praxbind®) is a fully humanised monoclonal antibody fragment that specifically binds to dabigatran and its metabolites with a 350-time higher affinity than that of thrombin to dabigatran.<sup>8</sup> It was approved by the United States Food and Drug Administration (FDA) in October 2015 for reversal of dabigatran's anticoagulant effect in emergency surgery, urgent procedures, or in cases of life-threatening or uncontrolled bleeding. It received approval by the Health Sciences Authority in Singapore in 2016.

The drug is available in 2.5 g/50 ml vials and the recommended dose is 5 g (two vials) administered intravenously, either as continuous infusions or as a single bolus dose. Its effect can be observed within minutes; in the RE-VERSE AD trial, the median time to bleeding cessation was approximately 9.8 hours.<sup>8</sup>

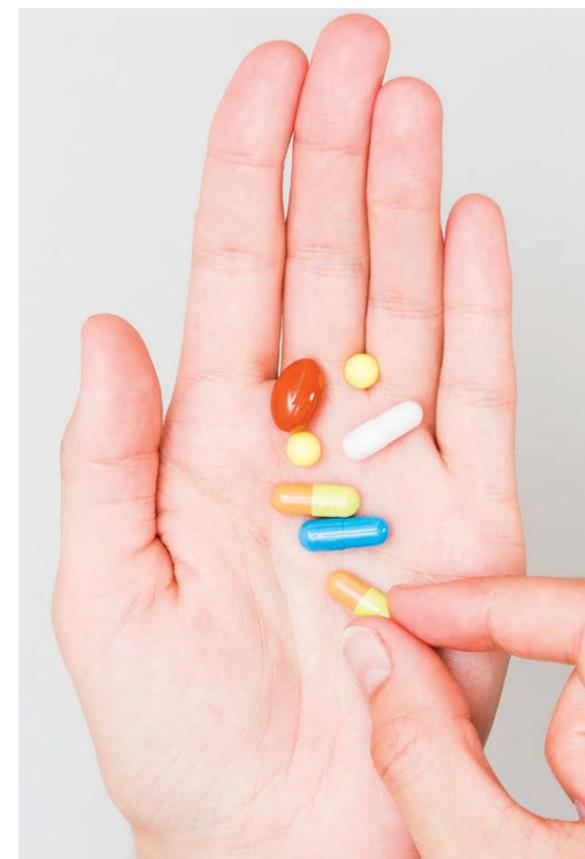
### Andexanet alfa

More recently, in May 2018, Andexanet alfa (Andexxa®) received FDA approval for reversal of life-threatening or uncontrolled bleeding in patients receiving rivaroxaban and apixaban. This is a recombinant modified human factor Xa protein that acts as a decoy and binds to rivaroxaban and apixaban to inhibit their action. It has a rapid action onset of 2 to 5 minutes, and has been shown to successfully reverse factor Xa inhibition in healthy volunteers.<sup>9</sup>

The drug is given as a bolus followed by an infusion, with its dose determined by the type of factor Xa inhibitor used and timing of last ingestion (for rivaroxaban). Unfortunately, the antidote is not available in Singapore currently.

### Ciraparantag (PER 977)

Ciraparantag is a small synthetic molecule that is designed as a broad spectrum antidote for oral



In general, routine tests are not specific to DOACs. While clotting times may detect the presence of clinically significant levels of DOACs, they cannot accurately reflect drug levels and their corresponding anticoagulant effect. It should be noted that the tests can also be prolonged in many other situations (e.g. bleeding states or disseminated intravascular coagulation) apart from DOAC ingestion.

factor Xa inhibitors, thrombin inhibitors and low molecular weight heparin.<sup>10</sup> Unlike other antidotes, it binds to anticoagulants through ionic charge interaction. The drug is currently still in its developmental phase.

## Limitations of laboratory tests

Although routine coagulation monitoring is not required for DOACs, there are some scenarios whereby laboratory monitoring may be useful. For example, routine coagulation tests can be used to exclude clinically significant levels of DOACs in bleeding patients or those who require urgent surgical interventions. When interpreting the coagulation test results, it is important to note the difference between the time of the last DOAC intake and time of blood sampling.

### Prothrombin time

Dabigatran has negligible effect on PT, while factor Xa inhibitors like rivaroxaban and apixaban can prolong PT. However, the result is dependent on the type of reagents used. In addition, certain PT reagents are less sensitive to apixaban compared to rivaroxaban. As such, a normal PT result does not exclude residual anticoagulant effect of any DOAC.

### Activated partial thromboplastin time

In contrast to PT, aPTT is prolonged in the presence of dabigatran, and may be used to detect clinically significant plasma levels of the drug. However, the result is dependent on the sensitivity of the assay reagent, and a normal aPTT result does not exclude the presence of low drug concentrations. The test is also unable to exclude the activity of rivaroxaban and apixaban.

### Thrombin time

The presence of dabigatran in serum plasma can be detected by TT, which is highly sensitive to the drug; a normal TT indicates the absence of the drug in patients. Rivaroxaban and apixaban, however, have no effect on TT.

### Anti-factor Xa (Anti-Xa)

Since rivaroxaban and apixaban directly inhibit factor Xa, their levels can be quantitatively measured using anti-Xa chromogenic assays. Anti-Xa activity correlates with the various factor Xa inhibitors in a linear fashion, and a normal anti-Xa level excludes clinically significant levels of the drugs.

Ideally, the assays should be calibrated to the respective factor Xa inhibitors. However, such

assays may not be readily available. In the absence of these drug-specific assays, anti-Xa assays that are calibrated to low molecular weight heparins may be used but the measured drug concentrations may vary among different assays and results can be affected by the presence of heparin. It should also be noted that dabigatran has no effect on anti-Xa activity.

In general, routine tests are not specific to DOACs. While clotting times may detect the presence of clinically significant levels of DOACs, they cannot accurately reflect drug levels and their corresponding anticoagulant effect. It should be noted that the tests can also be prolonged in many other situations (e.g. bleeding states or disseminated intravascular coagulation) apart from DOAC ingestion. Hence, the results should be interpreted with caution and routine monitoring of anticoagulant activity in stable patients is not recommended.<sup>4</sup>

### Conclusion

In summary, with the increasing use of DOACs, it is important for clinicians to know the perioperative management of patients who have

been taking these drugs. The period of DOAC interruption prior to surgery requires careful consideration of patients' thrombosis risk, his renal function, procedural bleed risk, as well as the pharmacokinetics of the specific DOAC he has received.

Although the routine laboratory tests have limitations in monitoring DOAC activity, they can be used as part of perioperative management to exclude clinically significant drug levels, especially for patients scheduled for urgent procedures.

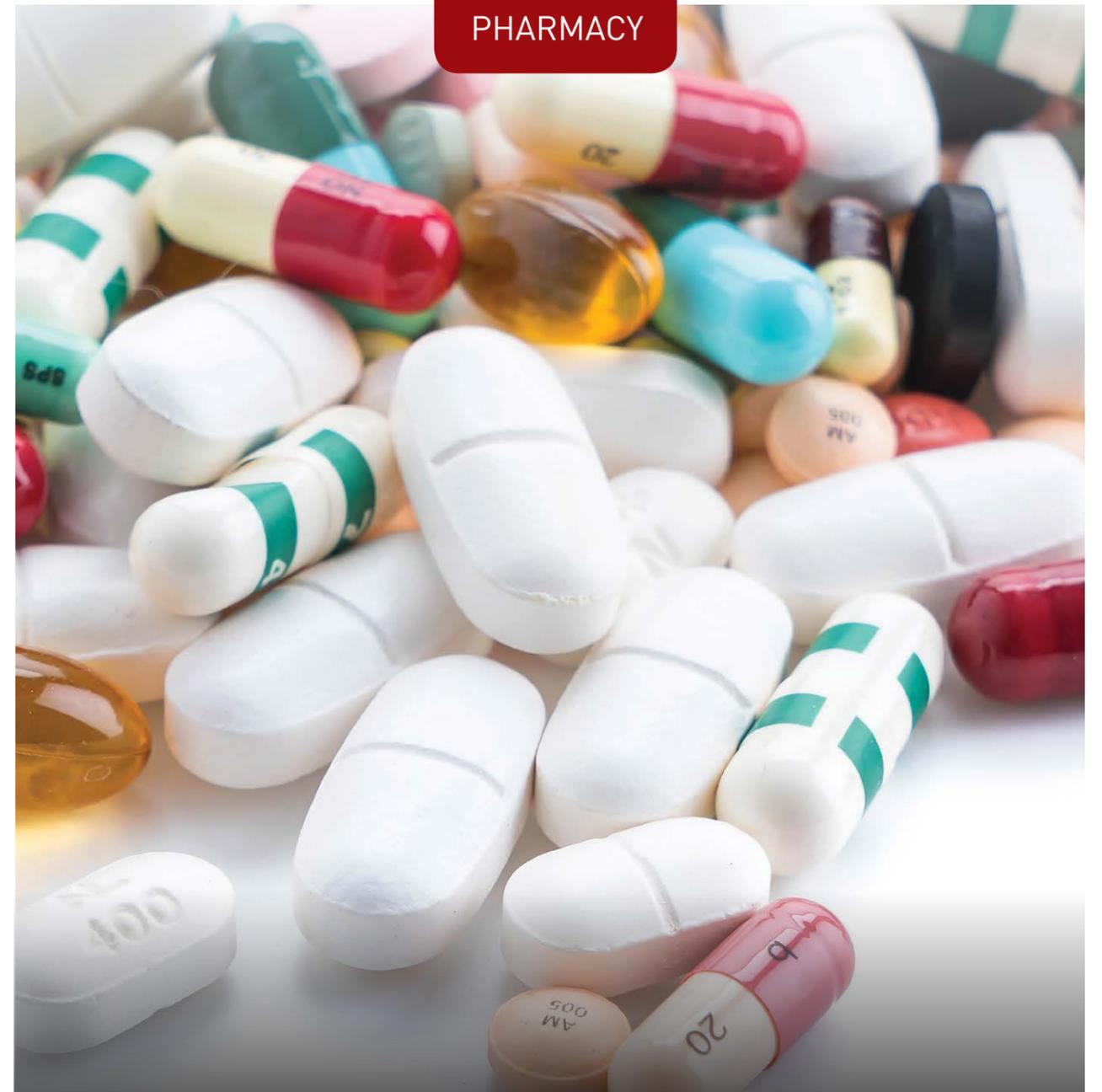
**Factors to consider in the perioperative management of patients treated with DOACs are thromboembolic risk of the individual, bleeding risk of the procedure and duration of DOAC interruption required before the procedure.**

#### References

1. Ahrens I, Lip GY, Peter K. New oral anticoagulant drugs in cardiovascular disease. *Thromb Haemost.* 2010; 104:49-60.
2. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol.* 2014; 64:e1-76.
3. Raval AN, Cigarroa JE, Chung MK, Diaz-Sandoval LJ, Diercks D, et al. Management of patients on non-vitamin k antagonist oral anticoagulants in the acute care and periprocedural setting: A scientific statement from the American Heart Association. *Circulation.* 2017;135(10):e604-33.
4. Tan Tock Seng Hospital Pre-Admission Counselling and Evaluation (PACE) Guidelines (updated Jan 2017).
5. Steffel J, Verhamme P, Potpara TS, Albaladejo P, Antz M, Desteghe L, et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. *Eur Heart J.* 2018; 39(16):1330-93.
6. Beyer-Westendorf J, Gelbricht V, Forster K, Ebertz E, Kohler C, Werth S, et al. Peri-interventional management of novel oral anticoagulants in daily care: Results from the prospective Dresden NOAC registry. *Eur Heart J.* 2014;35:1888-96.
7. Ng HJ, Chee YL, Ponnudurai K, Lim LC, Tan D, Tay JC, et al. Consensus recommendations for preventing and managing bleeding complications associated with novel oral anticoagulants in Singapore. *Ann Acad Med Singapore.* 2013;42(11):593-602.
8. Pollack CV Jr, Reilly PA, Eikelboom J, Glund S, Verhamme P, Bernstein RA, et al. Idarucizumab for dabigatran reversal. *New Engl Med.* 2015;373(6):511-20.
9. Connolly SJ, Milling TJ Jr, Eikelboom JW, Gibson CM, Curnutte JT, Gold A, et al. Andexanet alfa for acute major bleeding associated with factor Xa inhibitors. *New Engl J Med.* 2016;375(12):1131-41.
10. Ansell JE, Bakhru SH, Lalic BE, Steiner SS, Grosso M, Brown K, et al. Use of PER977 to reverse the anticoagulant effect of edoxaban. *New Engl J Med* 2014;371:2141-42.



MS CHAN LI XIN is a senior pharmacist from the Department of Pharmacy, Tan Tock Seng Hospital.



## DEPRESCRIBING: DOING IT BETTER, NOT MORE

Singapore's population is ageing. In just 16 years, the number of residents aged 65 and above has more than doubled from 200,000 in the year 2000 to 487,000 in 2016. And clearly this is not slowing down as this number is expected to double again in the next 12 years.<sup>1,2</sup>

**I**mprovements in healthcare over the years have allowed people to live longer. Yet, longevity comes with a price. As patients age and fall sick, new medications are layered upon existing ones every time a new medical condition is diagnosed. Consequently, many elderly patients are prescribed a long list of medications,<sup>3</sup> a phenomenon known as polypharmacy. To make matters worse, because the global burden of disease has shifted from infectious diseases to chronic diseases only in the past few decades, we are the “pioneer generation” of clinicians who have to deal with this change.



Polypharmacy is broadly defined as the concurrent use of five or more chronic medications.<sup>4</sup> While we initiate drug therapy with good intentions, patients who receive multiple medications concurrently have reduced compliance, increased risk of adverse drug events, unnecessary hospital admissions,<sup>5</sup> disability,<sup>6</sup> and even death.<sup>7</sup> This is a special concern in elderly patients due to the pharmacokinetic and pharmacodynamic changes associated with ageing; certain medications suitable for middle-aged adults may not be so for the elderly.<sup>8</sup> It is estimated that approximately 30% of patients in developed countries aged 65 or above are on five or more medications,<sup>3</sup> and my day-to-day experience in Tan Tock Seng Hospital (TTSH) confirms this. This is worrying because one in five medications used in the elderly may be inappropriate.<sup>9</sup>

Deprescribing has been proposed as one of the solutions of the growing problem of polypharmacy.<sup>10-12</sup> This is the systematic process of identifying and discontinuing drugs that are unnecessary or more likely to cause harm than benefit.<sup>4</sup> While this concept is centuries old, it did not have much traction until recently when it became increasingly relevant in a world plagued by multimorbidity and polypharmacy. For one, much credit must be given to my colleagues at the Pharmaceutical Society of Singapore for putting it in the spotlight at the annual Pharmacy Week outreach and coming up with a deprescribing toolkit to help clinicians get started with the process. This has shaped our own TTSH guidelines on deprescribing proton-pump inhibitors (PPIs) which has supported more conscientious prescribing of PPIs over the past few years.

### **The deprescribing triad**

Deprescribing, however, does not succeed solely based on a physician's willingness to stop a patient's medication. Successful deprescribing depends on three factors that make up what I term the “Deprescribing Triad”. The three factors are availability of evidence-based guidance, physicians' willingness to discontinue medications, and the patients' (or their caregiver's) willingness to do the same. Akin to how air, food and water is required for an organism's survival, no one of these factors can do without the other two. Recognising this, and the fact that there is a dearth of information on how our patients and physicians in TTSH feel about the concept of deprescribing, my colleagues and I embarked on a study last year to understand our patients' and physicians' attitudes towards deprescribing.

What we found did not surprise us. From our patient survey, we found that the average number of chronic medications a patient aged 65 or above in TTSH was on was 6.2, meaning that the average elderly patient we encounter daily is already experiencing polypharmacy. Approximately nine out of 10 of these patients or their caregivers indicated that they were willing to stop one or more of the medications if their doctor said it was possible to do so, concurring with what one local study found previously.<sup>13</sup> Moreover, about 50% of patients also felt that their medications were a burden to them.

Deprescribing is an essential part of continuing care. Contrary to what some think, deprescribing is not denying effective treatment to patients who are eligible to receive them. It is in fact quite the opposite – it is intended to optimise effective

treatment for patients. Often, it is easy to start a patient on a particular drug, but the fact that it becomes inappropriate after some time is frequently overlooked. As part of continual care for a patient, it is important and necessary for prescribers to critically re-examine a patient's existing medications and prune any weeds that detract from the treatment goals. This a fundamental responsibility that prescribers bear in fulfilling their commitment in a physician-patient relationship.

### **Barriers and enablers to deprescribing**

While most physicians understood the problem of polypharmacy and its harms, close to 60% indicated that they did not feel sufficiently skilled to deprescribe medications in their practice. Some physicians acknowledged that it is easier to prescribe medications than to deprescribe them because it was intuitive to do so, rather than the converse. This problem is compounded by the many disease management guidelines that provide recommendations on drug initiation but little help in when and how therapy should be discontinued if the treatment risks outweigh the benefits.

Dr Tan Yan Ru, an associate consultant in our General Medicine Department, acknowledges this, and shares with us how she approaches this uncertainty. We had the privilege of speaking to her as part of Pharmacy Week 2018 to gain some insights into her deprescribing experiences.

“Doctors and patients may sometimes overestimate the benefits and underestimate the risk of drugs. As clinicians, we should carefully consider the risk/benefits of the drug therapy and engage in shared decision-making with patients. By educating patients on potential symptoms that may arise after deprescribing, patients may have more confidence to discontinue drugs while monitoring for any symptoms that necessitate resumption,” she said. More than 60% of physicians pointed out that having a pharmacist involved in the process of deprescribing increases their comfort and could boost take-up rates. As advocates of medication safety with good drug knowledge in the areas we practice in, feel free to approach us – we are most happy to offer friendly deprescribing advice.

Like many other physicians, Dr Tan also told us that lack of time at each patient encounter is one of the major factors holding back deprescribing in

**While most physicians understood the problem of polypharmacy and its harms, close to 60% indicated that they did not feel sufficiently skilled to deprescribe medications in their practice. Some physicians acknowledged that it is easier to prescribe medications than to deprescribe them because it was intuitive to do so, rather than the converse.**

practice. Because of a high workload, more than 50% of physicians indicated that there are other issues of higher priority than deprescribing.

While some physicians desire having protected time to think about deprescribing, this may be difficult to achieve in a busy environment. Perhaps investing a marginal increase in time and effort at several key touch points may be a more viable answer. These touch points include history-taking on hospital admission or at discharge counselling, or when prescribing medications using the electronic prescribing platform in an outpatient setting. These situations present good opportunity for deprescribing because it is inevitable that prescribers review medication lists before deciding on the next step of a patient's care. General practitioners (GPs) can also take advantage of integrated medical and medication records like the National Electronic Health Record (NEHR) to holistically manage their patients and find opportunity to optimise their medications. The existence of many pharmacist-led medication review services that are offered in the community are possibly another resource GPs can consider exploiting.

Over 80% of physicians surveyed indicated that they were reluctant to deprescribe medications initiated by other physicians, even if they were no longer

appropriate, to avoid conflict with their colleagues. This was more so if the other physicians were specialists in different disciplines. Fragmented care lacking a primary physician makes things even more complicated. While we acknowledge it may be easier said than done, better communication and collaboration between prescribers would mitigate this problem.

Junior physicians also cited reasons such as “consultant’s decision” or “consultants don’t have such a culture” as to why they may not practice deprescribing. However, Dr Tan believes that “junior doctors of the team play a pivotal role in the deprescribing process.” She advises her junior colleagues: “Do go through patients’ medication charts on admission and on a regular basis and review the indications for drugs which patients may not require. When writing discharge summaries or discharge prescriptions, highlight to senior doctors should there be medications which risks may outweigh benefits and may be considered for deprescribing.”

That being said, our hopes are as much as the junior doctors in that deprescribing becomes a culture within the medical profession.

A small group of physicians also believed that patients were the ones who were unwilling to discontinue inappropriate medications, although our results from the patients’ survey suggested otherwise.

To this, Dr Tan adds that in her experience, “patients are often appreciative and receptive when doctors review their medications and in turn reduce their pill burdens. The key is communication and explaining the rationale of deprescribing to the patient.”

Nonetheless, because medication use is highly personal and different patients feel differently about their medications, physicians are encouraged to discuss deprescribing with patients even if they were not successful in previous attempts.

### THE 5-STEP DEPRESCRIBING PROCESS



Figure 1. Pocket card from “Introducing Deprescribing to Singapore” Kit, Pharmacy Week 2015 (with courtesy of the Pharmaceutical Society of Singapore)

QUESTIONS	SCORE (IF ‘NO’ IS ANSWERED)
1. Is there an indication for the drug?	3
2. Is the medication effective for the condition?	3
3. Is the dosage correct?	2
4. Are the directions correct?	2
5. Are the directions practical?	2
6. Are there clinically significant drug-drug interactions?	2
7. Are there clinically significant drug-disease/condition interactions?	1
8. Is there unnecessary duplication with other drugs?	1
9. Is the duration of therapy acceptable?	1
10. Is this drug the least expensive alternative available compared with others of equal utility?	1
<b>MAXIMUM SCORE OF INAPPROPRIATENESS</b>	<b>18</b>

Table 1. Medication Appropriateness Index.<sup>15</sup>

## The 5 steps of deprescribing

More than 60% of physicians indicated that additional training to equip them with skills would help push them towards deprescribing. Today we help fill some of those gaps by doing a quick recap on the deprescribing process.

The Pharmaceutical Society of Singapore first promoted the use of “The 5-step deprescribing process” (figure 1) as part of their deprescribing toolkit<sup>14</sup> for clinicians in 2015. This is a particularly useful tool for physicians to get started on deprescribing.

While these 5 steps are rather easy to understand, we find that someone new to the practice of deprescribing often finds difficulty in assessing medications if they could be discontinued. One of my favourite tools is the Medication Appropriateness

Index.<sup>15</sup> While it is not the only tool to assess medication appropriateness, it is intuitive and simple to use regardless of the level of training or experience of the user.

The Medication Appropriateness Index (table 1) consists of 10 ‘yes / no’ questions which are scored if a ‘no’ is answered. This gives a combined score of 0 to 18, with 0 meaning appropriate medication use and 18 meaning maximal inappropriateness. A score of more than 0 signals inappropriate medication use and warrants review.

While this list is not exhaustive, it provides a quick and easy way to detect common medication related problems. Having an inappropriateness score for each medication may also help the user prioritise medications for discontinuation.

Figure 2. 5 questions to ask about your medications poster (with courtesy of the Institute for Safe Medication Practices Canada)

Dr Tan also shares her quick tip on how she prioritises medications for discontinuation which may be helpful if time is not on your side.

“Medications that have led to harm or potentially may result in significant harm and have minimal benefit or those that are the easiest to discontinue, such as those with clearly no indications and less likely to have withdrawal effects, are my priority,” she said.

### Engage patients in the deprescribing process

Because patients form part of the triad that determines the success of deprescribing, it is imperative to engage them to achieve shared decision making about their medication use. Empowering them to ask the right questions can help to focus your conversations with them about their therapy and serve as a good reminder for both parties to regularly review treatment goals and drug therapy. Better yet, these patients may be motivated to trigger and driver the deprescribing process.

The Institute for Safe Medication Practices Canada (ISMP) has come up with a smart way to empower the public with the introduction of the “5 questions to ask about your medications” (figure 2).<sup>16</sup> It was intended to promote safe and appropriate medication

use by making patients a proactive partner in their healthcare and improving dialogue with their healthcare providers.

The ISMP “5 Questions” has garnered much positive feedback from patients and healthcare providers overseas and we think it could do the same in our local setting. We encourage prescribers to use it so that patients can help you help them with deprescribing.

### Conclusion

Deprescribing has been promoted as a solution to the growing problem of polypharmacy. Successful deprescribing involves a “triad” of factors – availability of evidence-based guidance, physicians’ willingness to stop medications and patients’ or their caregivers’ willingness to do the same. While a majority of TTSH’s patients and their caregivers expressed willingness to stop one or more of their medications, many physicians hold back because of perceived barriers which perhaps may be overcome with some effort. Patient-centric care requires healthcare professionals to insist on meaning in the things they do for the patient, even if this leads to difficult situations. Deprescribing is perhaps one of these but it is in the hope that we have provided sufficient tools and motivation to kick-start this process.

#### References

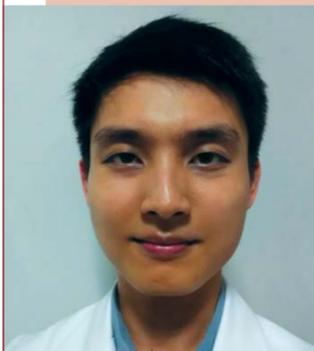
1. Ministry of Health, Singapore, Population and Vital Statistics. [https://www.moh.gov.sg/content/moh\\_web/home/statistics/Health\\_Facts\\_Singapore/Population\\_And\\_Vital\\_Statistics.html](https://www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_Singapore/Population_And_Vital_Statistics.html); Accessed 27 April 2017.
2. Singapore feeling impact of rapidly ageing population. Today Online. <http://www.todayonline.com/singapore/singapore-feeling-impact-rapidly-ageingpopulation>; Accessed 27 April 2017.
3. Pharmaceutical Society of Singapore. Polypharmacy in Singapore: The Role of Deprescribing. 2015; Pharmacy Week 2015. [https://www.pss.org.sg/sites/default/files/PW/PW15/polypharmacy-deprescribing\\_position\\_statement.pdf](https://www.pss.org.sg/sites/default/files/PW/PW15/polypharmacy-deprescribing_position_statement.pdf); Accessed 25 August 2018.
4. Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy. JAMA Intern Med. 2015;175(5):827-34.
5. Kalisch LM, Caughey GE, Barratt JD, et al. Prevalence of preventable medication-related hospitalizations in Australia: an opportunity to reduce harm. Int J Qual Health Care. 2012;24(3):239-49.
6. Opondo D, Eslami S, Vissher S, et al. Inappropriateness of medication prescriptions to elderly patients in the primary care setting: a systematic review. PLoS One. 2012;7(8):e43617.
7. Jyrkka J, Enlund H, Korhonen MJ, et al. Polypharmacy status as an indicator of mortality in an elderly population. Drugs Aging. 2009;26(12):1039-48.
8. Gnjidic D, Hilmer SN, Blyth FM, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. J Clin Epidemiol. 2012;65(9):989-95.
9. Roughead, EE, Anderson B, Gilbert AL. Potentially inappropriate prescribing among Australian veterans and war widows/widowers. Intern Med J. 2007;37(6):402-5.
10. Woodward MC. Deprescribing: Achieving better health outcomes for older people through reducing medications. J Pharm Pract Res. 2003;33(4):323-28.
11. Bain KT, Holmes HM, Beers MH, et al. Discontinuing medications: A novel approach for revising the prescribing stage of the medication-use process. J Am Geriatr Soc. 2008;56(10):1946-52.
12. Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: Addressing polypharmacy. Arch Intern Med. 2010;170(18):1648-54.
13. Ng WL, Tan MZW, Koh EYL, Tan NC. Deprescribing: What are the views and factors influencing this concept among patients with chronic diseases in a developed Asian community? Proceedings of Singapore Healthcare. 2017;2010105817699633.
14. Pharmaceutical Society of Singapore. Pharmacy Week 2015. “Introducing Deprescribing to Singapore” Kit. <http://www.pss.org.sg/pharmacyweek-2015-healthcare-professionals-only>; Accessed May 27 2017.
15. Hanlon JT, Schumacher KE, Samsa GP, et al. A method for assessing drug therapy appropriateness. J Clin Epidemiol. 1992;45(10):1045-51.
16. Institute for Safe Medication Practices Canada, 5 Questions to Ask About Your Medications. <https://www.ismp-canada.org/medrec/5questions.htm>; Accessed 22 Aug 2018.

#### Acknowledgements

I would like to express my deepest gratitude to the following people for their invaluable contributions:

1. Dr Tan Yan Ru (Associate Consultant, Department of General Medicine) for her graciousness in sharing her insights on her deprescribing experiences.
2. Ms. Lim Yi San and Ms. Lim Kai Xin (Pharmacists, Department of Pharmacy & Chairpersons, Pharmacy Week 2018) for co-ordinating the interview with Dr Tan.
3. Last but not least, the TTSH Deprescribing Workgroup for giving me an opportunity to write on this topic and providing guidance and support in my work leading up to publication of this article.

MR CHAN HAN KUAN is a pharmacist in the Department of Pharmacy, Tan Tock Seng Hospital.



# RADIOLOGY QUIZ

A 38-year-old Chinese male was referred to Tuberculosis Control Unit for follow-up. His chest radiograph had revealed a suspicious opacity in the right lower zone.

He worked as a renovator, doing tiling. He had no cough, shortness of breath, sputum production, or haemoptysis. He had some unquantified weight loss that he attributed to possible overwork and lack of sleep.

An X-Ray (figure 1) and a CT scan (figure 2) of the thorax were performed for further evaluation.

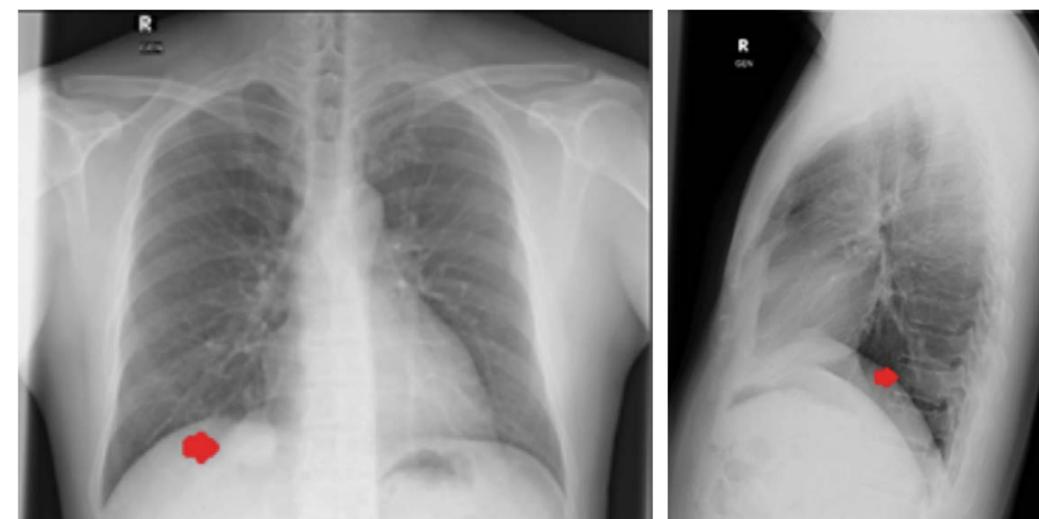


Figure 1. Anteroposterior and lateral views of the chest. Red arrows indicate the opacity in question.

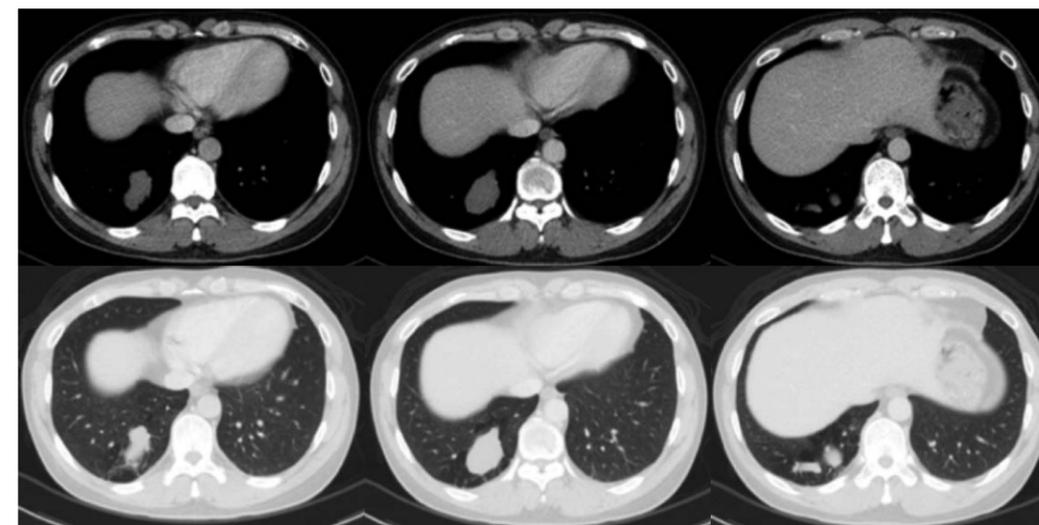


Figure 2. Selected CT sections through the bases of the lower lobes, from superior to inferior. Images on the left were viewed in the soft tissue window, with corresponding images at the same levels on the right viewed in the lung window.

### QUESTION

What is the abnormality present in the image?

## ANSWER

The opacity in the chest radiograph corresponds with a tubular, branching lesion in the posterior basal segment of the right lower lobe. It has a longitudinal axis oriented towards the ipsilateral hilum. Of important note is that the lesion is of low attenuation and does not enhance. There is an area of hyperlucent lung parenchyma surrounding this lesion. The imaging findings are in keeping with a bronchocoele, due to congenital segmental bronchial atresia.

## Discussion

Bronchocoele may also be known as mucoid impaction. It refers to airway filling by mucoid secretions. It manifests as well-defined tubular or branching opacities, which is referred to as the finger-in-glove sign (figure 3). It may also be spherical or ovoid. The longitudinal axis of the bronchocoele must be orientated toward the ipsilateral hilum.

A bronchocoele should be of low attenuation (usually between -5 to 25 Hounsfield Units), and should not enhance.

There are numerous causes for bronchocoele (table 1). A common congenital cause, as in this patient, would be segmental bronchial atresia. This is characterised by interruption of a bronchus, usually a segmental branch at or near its origin. The branches of the bronchi distal to the focus of atresia dilate and become filled with mucus, forming the bronchocoele. The hyperlucency surrounding the bronchocoele is the result of a combination of air trapping, collateral ventilation and oligoemia from hypoperfusion. Most cases are asymptomatic and detected incidentally at chest radiography or CT, and can be left alone. Some cases may be complicated by recurrent infection necessitating treatment.

A CT scan is important to evaluate for an obstructing neoplasm. It also can effectively distinguish a bronchocoele from an arteriovenous malformation (AVM). An AVM, although also a tubular branching opacity, would enhance and be of higher attenuation, similar to that of the visualised blood vessels.

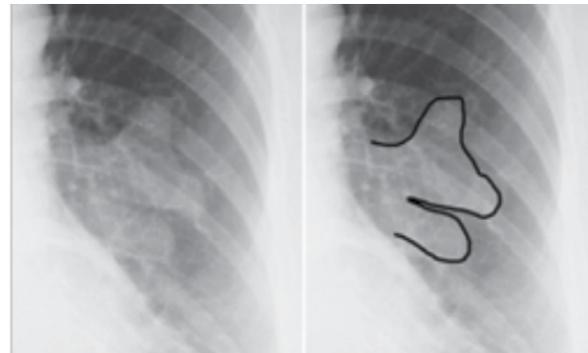


Figure 3. Radiographic appearance of a bronchocoele (outlined in black). Reproduced with permission from Martinez et al. 2008.<sup>2</sup>

<b>CONGENITAL</b>
Segmental bronchial atresia Cystic fibrosis
<b>INFLAMMATORY-INFECTIOUS</b>
ABPA in asthma or cystic fibrosis* Broncholithiasis Foreign body aspiration
<b>NEOPLASTIC</b>
Benign Bronchial hamartoma Lipoma Papillomatosis
<b>MALIGNANT</b>
Bronchogenic carcinoma Carcinoid tumour Metastasis

Note – Segmental bronchial atresia, cystic fibrosis, ABPA, foreign body aspiration, and bronchogenic carcinoma are common.  
\*ABPA = allergic bronchopulmonary aspergillosis

Table 1. Causes of obstructive and nonobstructive mucoid impactions  
Adapted with permission from Martinez et al. 2008.<sup>2</sup>



### References

- Gipson MG, Cummings KW, Hurth KM. Bronchial atresia. *Radiographics* 2009, 29(5):1531-35.
- Martinez S, Heyneman LE, McAdams HP, et al. Mucoid impactions: finger-in-glove sign and other CT and radiographic features. *Radiographics* 2008, 28(5):1369-82.
- Lee KS, Franquet T, Han J, Johkoh T. (2012). *Muller's Diseases of the Lung: Radiologic and Pathologic correlations*. Baltimore, MD: Lippincott Williams & Wilkins.

**DR PETER CHOO ZHI QING**  
is a 3rd year resident in the  
Department of Diagnostic Radiology,  
Tan Tock Seng Hospital.

# ECG QUIZ

A 50-year-old gentleman presented to the family physician for routine follow-up of his hypertension. He had no known cardiac problems. He was asymptomatic with no new complaints. On examination, an irregular heart rhythm was detected. There was a soft systolic murmur heard at the upper sternal edge. A resting 12-lead electrocardiogram (ECG) was ordered (figure 1).

## QUESTIONS

- Name two ECG abnormalities.
- What is the likely cardiac pathology given the clinical and ECG findings?

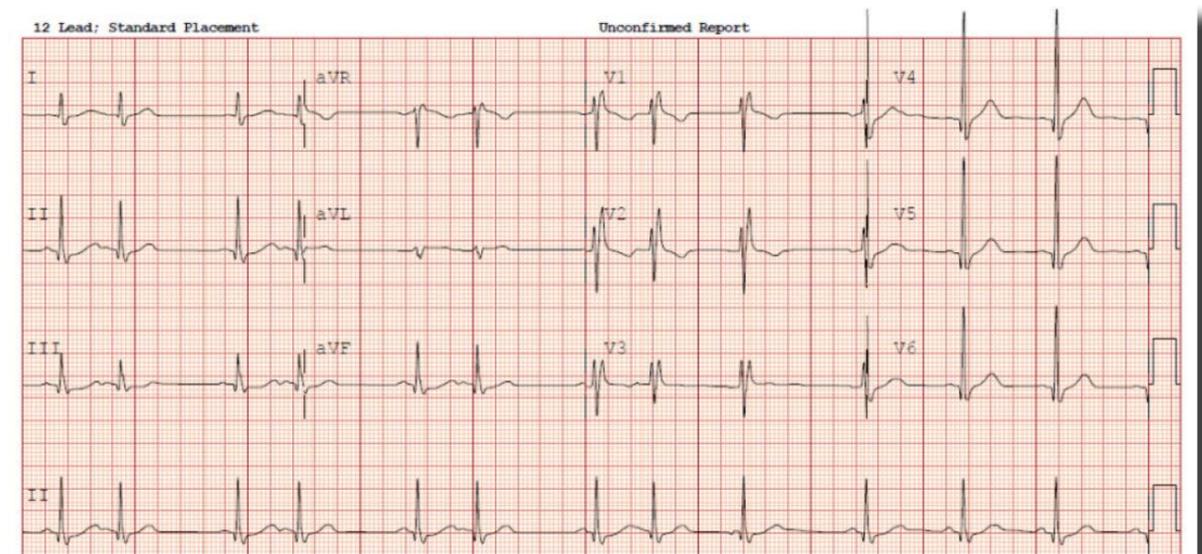


Figure 1. Resting 12-lead ECG performed in the clinic.

## ANSWERS

- Complete right bundle branch block (RBBB) and frequent premature atrial complexes (PACs).
- Atrial septal defect (ASD).

## Discussion

The family physician had initially interpreted the rhythm as atrial fibrillation (AF) and the patient was referred to a cardiologist for further management. Indeed, the ECG machine had also read this ECG as showing AF (figure 2). On closer inspection, the first eight complexes seem to occur in pairs with a normal QRS complex followed closely by another complex with a similar QRS morphology but slightly different P morphology. This is consistent with premature atrial complexes (PACs) occurring in a bigeminy pattern. The last three complexes in the strip likely represent the normal baseline sinus rhythm.

HR	82	. Atrial fibrillation
RR	732	. Right bundle branch block
QRSD	124	
QT	404	
QTcB	472	
QTcF	448	
-- AXIS --	--	
QRS	73	
T	33	
- ABNORMAL ECG -		

Figure 2. Incorrect machine interpretation for the ECG shown in figure 1.

In addition, the QRS complexes are broad (>120 ms) with a rSR' ('rabbit ear') pattern in V1-V2, fulfilling the criteria for complete RBBB.

The combination of a systolic murmur at the upper sternal edge and RBBB is suspicious for ASD. Classically, a secundum ASD manifests as a RBBB with right axis deviation on the ECG, although the axis appears normal in this patient. Indeed, a transthoracic echocardiogram performed revealed the presence of a 1.2 cm secundum ASD with left to right shunt and evidence of right ventricle dilatation (figure 3). The patient was counselled for ASD closure.

This case illustrates several learning points. First, a computerised ECG interpretation is not always accurate and should not replace a physician's assessment. Second, PACs can be differentiated from AF by the presence of an abnormal P wave preceding the QRS complex. Third, although RBBB may sometimes be seen in normal individuals, it can also represent structural heart disease such as ASD or right heart strain.

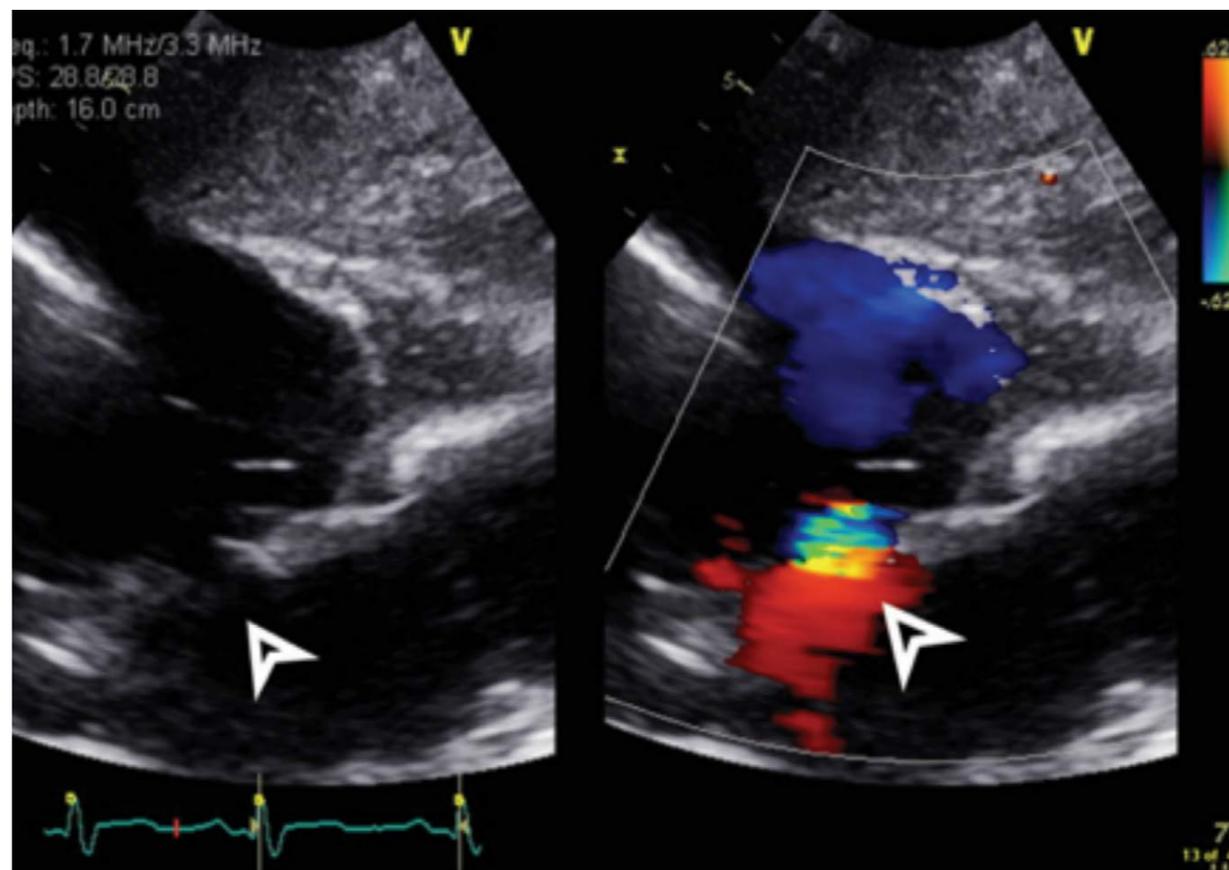


Figure 3. Secundum ASD with shunt (arrows) seen on transthoracic echocardiogram subcostal view.



**DR YEW MIN SEN**  
is an associate consultant in the  
Department of Cardiology,  
Tan Tock Seng Hospital.