

Roche

# Dia:gram

EDITION 2018 Vol 4

**Rising to the threat  
of antimicrobial  
resistance**

**When every  
minute counts**

*Making the one-hour diagnosis  
of heart attacks possible*

**Thailand  
in focus**

*Managing thalassemia*

IN CONVERSATION WITH PROF CAROLYN LAM

# *Trailblazers*

WOMEN IN DIAGNOSTICS







*People are different and so are diseases.*

That's why we are committed to discovering and developing personalised medicines and targeted diagnostic tests to help people live better, longer lives.



## Note from the editor



Welcome to the fourth edition of **Dia:gram** – our bi-annual publication from Roche Diagnostics Asia Pacific. In the past three issues, we have explored the impact of diagnostics on healthcare in Asia Pacific - looking at the future of healthcare, and shining the spotlight on healthcare professionals and laboratory experts who are transforming the industry.

In this issue we continue to unpack how the power of diagnostics shapes our reality in healthcare. We speak to leading healthcare experts on pressing public health topics like antimicrobial resistance, and haemoglobinopathies in Asia Pacific. A special feature in this issue is the 'Women in Diagnostics' centre spread that celebrates women who have made their mark in the industry. We speak to a leading Cardiologist from Singapore, the Founder of a private laboratory in Pakistan, the Head of the National Pathology Services in Malaysia and the Laboratory Director at one of South Korea's largest reference laboratories.

This is my first edition of **Dia:gram**, and also my first time exploring the world of diagnostics. It has been an exciting journey thus far, as I learn more about a side of healthcare that is often in the background. Coming from the pharmaceutical industry, we have many dialogues on the impact we have on patients, but we hardly mention, or think about, what goes on behind the scenes.

I am excited to be a part of a publication that brings diagnostics to the forefront of this conversation. As we uncover the patient stories behind each test tube and slide, we share the Power of Knowing.

Michelle Medeiros  
Editor

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*Editorial*  
Editor: Michelle Medeiros  
Assistant Editor: Shruti Bose  
Editorial coordinator:  
Patricia Anne Carthigasu

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8, Kallang Avenue, #10-01/09  
Aperia Tower 1,  
Singapore 339509  
Tel: +65 6272 7500  
www.roche.com

If you have any suggestions or story ideas, write in to us at [diagram.apac@roche.com](mailto:diagram.apac@roche.com)

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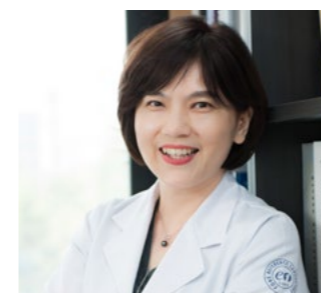


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# THE PREVALENCE OF THALASSEMIA

Thailand's emergence as a role model for thalassemia screening and diagnosis

## DR VIP VIPRAKASIT

Over the past decade, knowledge relating to the clinical diagnosis and management of thalassemia has progressed extensively. In Thailand's case, the country has made significant strides in just two decades. **Dr Vip Viprakasit**, Professor of Paediatrics at the Department of Paediatrics and Thalassemia Center at Siriraj Hospital, Mahidol University, Bangkok, has played a pivotal role in firmly placing thalassemia on the national agenda. In this interview with **Dia:gram**, Dr Viprakasit shares how Thailand has become a model for countries in Asia and the Middle East.

**T**halassemia is an inherited disorder of haemoglobin (Hb) synthesis that results in reduced or absent globin chain production. In Southeast Asia,  $\alpha$ -thalassemia,  $\beta$ -thalassemia, Hb E and Hb Constant Spring (CS) are most commonly prevalent. The abnormal genes in different combinations lead to more than 60 different thalassemia syndromes, making Southeast Asia the sub-region with the most complex thalassemia genotypes<sup>1</sup>.

Local estimates state the incidence of  $\alpha$ -thalassemia is at about 20–30%, at 3–9% for  $\beta$ -thalassemia, up to 54% for Hb E and nearly 8% for Hb CS<sup>2</sup>. In all, about 30–40% of the Thai population is a carrier of at least one of these abnormal genes<sup>3</sup>. This figure places

Thailand among the highest percentile of thalassemia carriers in the region.

Carriers of thalassemia usually have no clinical symptoms, and can be detected only through a screening program. "In countries where thalassemia and haemoglobinopathies are common, preventive measures are needed. Thailand was among the first countries in Southeast Asia to introduce a program in 1990 to screen pregnant women for the carrier gene. Apart from this, the National Health Corporation has helped make thalassemia treatment accessible through its national healthcare coverage scheme," said Dr Viprakasit.





*“We need better prevention to prohibit new patients from coming into the pool. Otherwise, the 20,000 patients today could go up to 50,000 or 60,000 patients in the future if we don’t prevent new cases.”*

“When I first started, the prevalence of thalassemia in the country was about 30–35%, today it stands at 40–50%. This is because of the increase in screenings but also the poor awareness that remains among those with the carrier gene, that thalassemia will pass down to their children. There’s still a lot to do,” added Dr Viprakasit.

To mitigate late screenings in pregnant mothers, Dr Viprakasit has advocated for, and implemented, a National Newborn Screening Program. At the moment, the program is still in the pilot phase, screening 1–2% of the approximately 650,000 newborns in Thailand every year but Dr Viprakasit has ambitious plans and wants to increase the screening to at least 10%.

**Overcoming hurdles**

However, getting to this stage has not been without its challenges.

Dr Viprakasit explains that under the national screening program for the carrier gene, once the mother has been identified as being a carrier, the father is also encouraged to undergo screening for the carrier gene. But, he notes, that it is sometimes a challenge to convince men to undergo screening. “At present, I would say the number of male partners who come for the check-up ranges from about 20% to 80%. Now, if we could get this number consistently up to 80%, that would be ideal. But it’s often not the case.”

Because thalassemia is a lifelong genetic condition, it can often throw up other challenges such as requiring to take leave from work for regular blood transfusions, a weakened immune system and the ongoing cost of treatment.

In Dr Viprakasit’s view, with around 20,000 patients who are transfusion-dependent, the economic cost of thalassemia in Thailand is about 400,000 Thai baht per patient, per year. “This comes up to nearly four to five billion baht a year. This is an annual recurring expenditure for the rest of the patients’ lives.”

This is why he is a staunch advocate of screening. “We need better prevention to prohibit new patients from coming into the pool. Otherwise, the 20,000 patients today could go up to 50,000 or 60,000 patients in the future if we don’t prevent new cases.”

**Establishing Thailand as a centre of excellence**

Thailand has been one of the world leaders in advancing haemoglobinopathies research and Dr Viprakasit and his team at Siriraj Hospital have been at the helm of many innovations in the field of thalassemia. As a result, Thailand is often called on to collaborate with other countries around the world to share best practices and clinical know-how.

One such example is his research pertaining to iron overload. “Excessive iron overload can lead to organ damage and cause mortality and morbidity in patients. So the evaluation of iron overload is one of my recent interests, because I need to help my patients through early detection, recommend the proper treatment and follow up with the proper tools”.

For this, Dr Viprakasit and his team developed a set of algorithms and software (for MRI) to calculate the level of iron in patients. This tool has proven effective in the early detection of iron overload, leading to treatment and follow-ups initiated in a timely manner. The software has been so successful that the results have been published in numerous international scientific journals, and is now being patented. Thailand is also collaborating with the Philippines and Brunei to ensure that the software is made accessible in these countries.

“We have a high prevalence of thalassemia in our country and that means we need to be the ones to find a solution. This is our commitment to the patients,” said Dr Viprakasit.

Dr Viprakasit sees diagnostics playing a crucial role at every step. “You cannot deny the value diagnostics adds throughout the patient’s journey. From screening for the carrier gene, conducting haemoglobin analysis, detecting genetic mutation to

predicting clinical severity, monitoring and following up on treatment efficacy, diagnostics can help manage financial costs, and enhance the quality of life of patients,” he added.

**Raising the bar**

Dr Viprakasit is a man on a mission. “When we first started, there was no specific national budget for thalassemia. As education and awareness grew, so did the budget – it started at 10 million baht a year, grew to 50 million baht and now it’s at 300 million baht,” Dr Viprakasit explains. “We hope the fund will grow to 600 million baht this year.”

He cites a number of initiatives that are underway to further increase awareness and education on thalassemia. On the educational front, more and more haematologists and paediatricians are being trained to identify the symptoms of thalassemia to be able to make quicker diagnosis – Thailand now has around 600 trained haematologists and paediatricians.

Thalassemia has also been incorporated into the main curriculum for medical education in Thailand.

Furthermore, a thalassemia network has been established to provide relevant resources for general practitioners, as well as raise awareness of the inter-hospital referral system that exists in Thailand.

Under this system, tests can be referred to main or regional hospitals, while haematologists in these hospitals can refer patients back to hospitals in their province to receive treatment, once patients have been diagnosed.

“In order to do more, we need to have collaborations to widen our network,” Dr Viprakasit says.

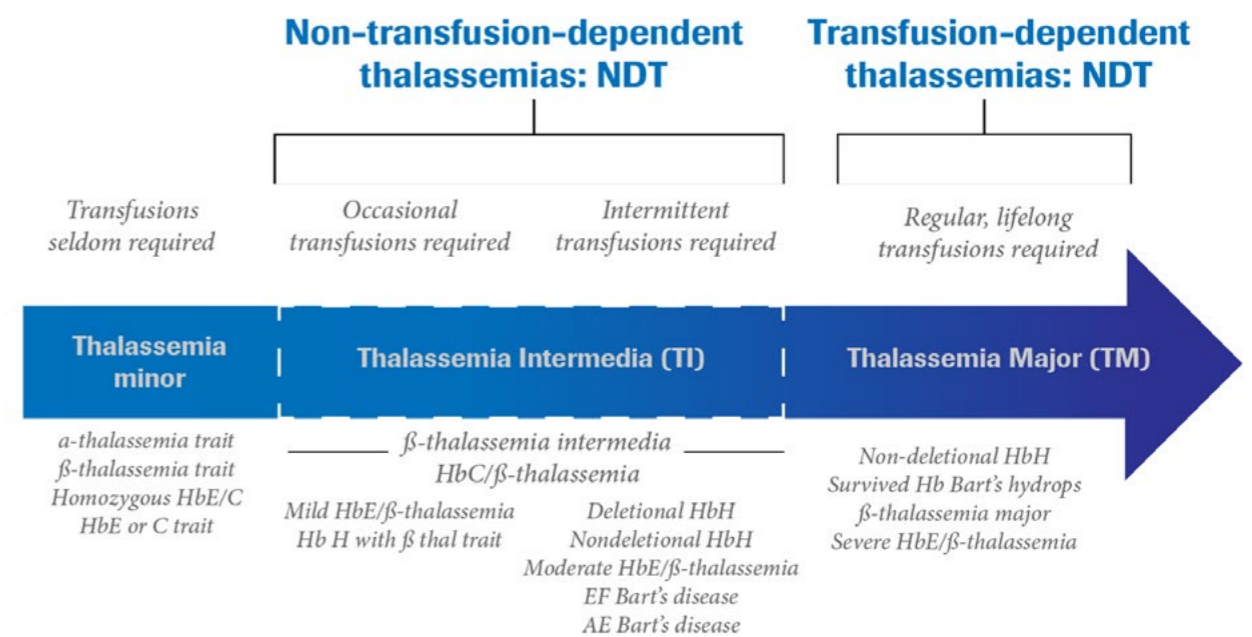
Another avenue is to have certified labs in different parts of Thailand that can process samples. Beyond that, Dr Viprakasit also envisions integration with information technology and data analytics.

In the end, Dr Viprakasit feels empowering patients is the key to beating thalassemia. “In this regard, I am very proud of what we have achieved as a country. Our campaigns target people across all sections of society and by doing this, we have managed to destigmatise thalassemia.”

“When they see someone like them come forward and say ‘I’m a carrier or patient with thalassemia, but there’s nothing wrong with that’, they find hope. They know there is life beyond the disease.”

<sup>1</sup>Ekwatanakit, Siritanaratkul, Viprakasit. (2018). *American Journal of Hematology*.  
<sup>2</sup>Viprakasit, Ekwatanakit. (2018). *NCBI*.  
<sup>3</sup>Viprakasit et al. (2018). *American Journal of Hematology*.

**Clinical spectrum for thalassemia syndromes**



Reference: Ekwatanakit, Siritanaratkul, Viprakasit. (2018). *American Journal of Hematology*



# “This is the only life I’ve known”

*Living with thalassemia*

ARINTHORN PATCHIMPIHONG

**Arinthorn Patchimpihong**, or Fai as she likes to be called, says these words without a hint of despair. An inherited disease, thalassemia is passed on from parents, who carry the mutated thalassemia gene, to their children. In Fai’s case, she’s had the disease all her life and was diagnosed with thalassemia major when she was only four months old. In her first-ever interview, she talks to **Dia:gram** about why she doesn’t see herself as a patient and her mission to live a full life despite the odds.

Fai considers Siriraj Hospital in Bangkok, Thailand her second home. She has been going to the hospital every three weeks for blood transfusions for the last 33 years. As an administrative assistant, this is also where she works. You could call it sheer coincidence or a chosen path.

“What are some of your childhood memories?” she asks when we meet her at work. “For me, it was going to Siriraj hospital for blood transfusions. My earliest memories are the smiling faces of the nurses and the kind words of the doctors. That’s why I never dreaded these visits. In fact, they lifted my spirit.”

It was a constant reminder that her disease didn’t define who she was. Fai does not have any physical symptoms of thalassemia, such as yellow or pale skin, bone deformities especially in the face, or a short stature<sup>1</sup>.

“When I graduated, I applied for a job at a fashion design studio. I did not manage to get this job – perhaps due to the perception that thalassemia patients need time off every few weeks for blood transfusions,” she said matter-of-factly.

Not one to be bogged down by rejection she continues, “I was determined to make it on my own and managed to get a job selling clothes for two years. But it was tiring and, on a deeper level, I didn’t feel fulfilled. Was I making a difference?”

Thankfully, her doctor offered her a job at the Siriraj Hospital Thalassemia Center where she would be able to work and get her blood transfusions. “Working here gives my life real meaning. The team here is great to work with and I find joy helping people like me at the center.”

According to a 2008 World Health Organization (WHO) bulletin, about 45.5% of the population in Southeast Asia is affected with different types of haemoglobinopathies<sup>2</sup>. With more than 60 different thalassemia syndromes, Southeast Asia has the most complex thalassemia genotypes in the world<sup>3</sup>.

*“When I was growing up, people did not know what thalassemia was. My mother received antenatal care but wasn’t told about any screenings for thalassemia. They had no way of knowing if they were carriers.”*

“When I was growing up, people did not know what thalassemia was. My mother received antenatal care but wasn’t told about any screenings for thalassemia. They had no way of knowing if they were carriers. Today, there is a lot more information on the disease and people have greater understanding, which makes family planning easier.”

According to the WHO, a policy of detecting carriers of thalassemia and informing them of their risk, and possibilities for reducing it, usually leads to a fall in births and deaths of affected children<sup>2</sup>.


Fai knows first-hand what a difference the right level of care makes. The doctors encouraged her parents to let her live as normally as possible so Fai had a typical childhood, without restrictions on her activities in school. Despite having to take sick leave every three weeks to visit the hospital for her blood transfusion, Fai managed to keep up with her schoolwork.





## WHAT IS THALASSEMIA?

Thalassemia is an inherited blood disorder caused when the body doesn't make enough of a protein called haemoglobin, an important part of red blood cells.



### Symptoms

- **Fatigue**
- **Abdominal Swelling**
- **Pale or Yellowish Skin**
- **Weakness**
- **Facial Bone Deformities**
- **Dark Urine**

### Causes

*Thalassemia is caused by mutations in the DNA of cells that make haemoglobin - the substance in your red blood cells that carries oxygen throughout your body. The mutations associated with thalassemia are passed from parents to children.*

### Complications

- **Iron Overload**
- **Susceptibility to Infections**
- **Heart Problems**
- **Bone Deformities**
- **Enlarged Spleen**

*“Without the guarantee of safe blood, we are at risk each time we get a transfusion.”*

As part of her job, Fai regularly meets patients from all parts of Thailand and provides insight into the struggles they face. “Many patients who come here travel from provincial areas to the city to get treatment. This often means they have to stay in a hotel for the night after their transfusion.”

“That’s time away from work plus cost of travel and accommodation in the city. So proper treatment for thalassemia can be impossible for some to manage and as a result, severely affects their quality of life.” Fai is thankful that she gets her treatment at the Siriraj Hospital where she trusts the doctors and the care that she receives.

Despite the challenges they may face, Fai advocates for thalassemia patients to live as normal a life as possible, and not to let their illness hold them back. “Our disease should not determine our self-worth. We can still have a positive outlook on life and not think of ourselves as disadvantaged. Like everyone else, we should just give priority to our health first and then concentrate on other responsibilities - our education, job or lifestyle.”

<sup>1</sup>Rachmilewitz, Giardina. (2011). *Blood Journal First Edition Paper. How I treat Thalassemia.*

<sup>2</sup>Modell, Darlison. (2008). *WHO International Bulletin, Global epidemiology of haemoglobin disorders and derived service indicators.*

<sup>3</sup>Fucharoen, Winichagoon. (2011). *Indian Journal of Medical Research. Haemoglobinopathies in Southeast Asia.*

<sup>4</sup>Eleftheriou. (2017). *International Alliance of Patients’ Organisations (IAPPO) Blood, blood safety and blood availability - A global challenge.*

<sup>5</sup>Hans, Marwaha. (2014). *Asian Journal of Transfusion Science. Nucleic acid testing - benefits and constraints.*

“I wasn’t treated like a patient so I never felt like one.”

But Fai is aware of the realities of living with the disease. She recalls the time she contracted a hepatitis infection because of a blood transfusion. “Blood safety is important for all patients but for thalassemia patients, transfusions are our primary treatment. Without the guarantee of safe blood, we are at risk each time we get a transfusion.”

The Thalassemia International Federation (TIF) estimates that 70-80% of thalassemia patients are born and live in countries where blood safety, blood-related and other policies related to the indicated clinical management of thalassemia are

abysmal (or even non-existent)<sup>4</sup>. Nucleic acid testing (NAT) – a molecular testing technique for blood screening – is used to reduce the risk of transfusion transmitted infections (TTIs) like HIV and hepatitis.

With greater sensitivity and specificity, the NAT technique therefore provides another layer of security for thalassemia patients, by ensuring a safe blood supply<sup>5</sup>. Thankfully, NAT is mandated in Thailand and the blood supply in Thailand is NAT tested.

“Having the confidence that the blood is tested before transfusions gives us patients’ peace of mind – we know we won’t have another illness on our hands,” Fai added.

# Women in DIAGNOSTICS

The case for amplifying women’s voices in the world of science and diagnostics grows stronger as diversity drives discovery and advancement. Many female scientists, researchers, and academics have brought pioneering approaches to complex disease areas such as preeclampsia, breast and cervical cancer, and cardiovascular disease, with a sense of urgency as well as a depth of personal understanding. Often their approach contributes a point of view on the nuanced needs and unique biological differences of the female population - an area that is often overlooked.

This edition of **Dia:gram** looks at female leaders in diagnostics who are spearheading many of our industry’s breakthrough innovations, research and education initiatives. We take a closer look at the women who are changing the face of diagnostics in bold and exciting ways.





# DR ZEENAT HUSSAIN

## Pakistan's trailblazer

*Spearheading the country's first private laboratory*

86-year old **Dr Zeenat Hussain** is the founder of The Medical Laboratories in Pakistan. She is still as actively involved in the day-to-day running of its operations as she was when she opened her first laboratory back in 1963. Known for introducing the latest innovations and technologies in her laboratory, Dr Hussain is a true pioneer in the diagnostics industry in Pakistan. In this exclusive interview with **Dia:gram**, Dr Hussain talks about how she built her laboratory from the ground up as well as her community initiatives with the Zeenat Foundation.

**D**r Zeenat Hussain is not someone who swims with the tide. She started her laboratory nearly 55 years ago, making it the first and only private laboratory in Lahore, Pakistan at the time. But it didn't start out this way.

At a time when women didn't have as much freedom as they do today, Dr Hussain left Pakistan in 1954 in her mid-20's for a one-year internship at the University of Iowa Hospital in the United States. "There were just so many ways you could immerse yourself in this specialty. It wasn't just lectures. There were other learning opportunities such as attending conferences and workshops – it was so interesting," says Dr Hussain, explaining how her career in pathology began.

She returned to Pakistan and took up a job in King Edward Medical College's pathology department. "In those days, women weren't allowed to become assistant professors and I felt this would restrict my career. So I left King Edward Medical College and joined Fatima Jinnah Medical College (now called Fatima Jinnah Medical University)."

From there, she took off once again, this time to the United Kingdom. She lived in England for eight years and earned a Masters in Microbiology. While there, she purchased some laboratory equipment and then some more. "And before you know it, I had photometers and other equipment which I brought back with me to Pakistan and decided to start my own small laboratory," she says.

### A tough beginning

During the laboratory's early days, Dr Hussain's work day would start at 10 in the morning and go well past midnight.

Today things are different. "Back then, it was difficult to get qualified staff. In the early days, there weren't institutions in Pakistan which taught medical technology courses. But now there are many courses which technologists can attend. As a result, there's a growing talent pool. So now I come in later at around 2pm and leave at about 11pm."

From learning how to operate every instrument to conducting quality checks, Dr Hussain was involved in all the aspects of her laboratory. To this day, even as her laboratory processes more than 1,200 samples per day, Dr Hussain signs off on every single report herself.

"I didn't know whether the laboratory would be successful, so I kept my job with Fatima Jinnah Medical College to have a steady income source, while running my laboratory in parallel," Dr Hussain recalls.

The support of her family, especially her husband, kept her going. "We've been married for over 60 years and I don't think I could have achieved all that I set out to, without his support."



### Changing laboratory environment

"It was definitely tough in the beginning. Each week I did my work – microscopy and cultures and certain basic chemistry because in those days you must remember there were no kits, like there are now. So one had to make one's own solutions to carry out chemical tests."

As her laboratory built up its reputation and presence, more and more samples started coming in. It was at this point that Dr Hussain realised that she would need assistance in processing these samples. She learned of Boehringer Mannheim's auto analysers, and it was a turning point for her laboratory. The automated analysers enhanced the laboratory's quality control, quality assurance and proficiency testing.

In the business of laboratory medicine, Dr Hussain believes that at the end of the

day, people only want to know that their results are accurate. To that end, she is an advocate of advancements and innovation that will enhance the quality and accuracy of the laboratory's results.

Today, nearly half a century later, Dr Hussain's ISO certified The Medical Laboratories has more than 100 collection points and employs around 100 staff members. In fact, some of the employees are long-timers who have been with her since the establishment of the laboratory. "One employee has been with me for 50 years and he is still working with me," she told Dia:gram.

Her biggest achievement? "Without a doubt, it's my laboratory. Since the beginning I knew

I wanted to be independent and that was the path I chose. But looking back, maybe the path chose me."

### Desire to give back

Her boundless energy intact, Dr Hussain can easily put people half her age to shame. "My days go by swiftly and there's still so much to do."

One such passion project is the Zeenat Foundation which she set up over 30 years ago. It comprises a group of doctors

who go into villages to provide healthcare to those in need.

The team has been involved in examining and diagnosing diabetics as well as patients with hepatitis B and hepatitis C. In some instances, the Foundation has also provided free treatment and medication. Beyond healthcare, the Zeenat Foundation has also supported students facing financial difficulties with scholarships.

When asked about her retirement, Dr Hussain simply said, "There's no time to think about that."

It's hard to imagine having the same passion and commitment after all these years. But then Dr Hussain is just the person to prove everyone wrong. ■



# Ten questions with Dr Arni Talib

**Dr Arni Talib** is the Head of the National Pathology Services in Malaysia and the Head of the Department of Pathology at Kuala Lumpur Hospital. Her laboratory serves as the National Referral Centre for the Ministry of Health which provides diagnostics services to the whole country. In this interview with **Dia:gram**, Dr Talib talks about her vision for the pathology industry in Malaysia.



## 1 How did you get into the field of pathology?

When I started my housemanship, I was not quite sure which specialty to focus on. I was fortunate to have good mentors, and one of them suggested that I consider pathology. I knew very little about pathology back then, so I decided to find out more. What I discovered really piqued my interest.

I am someone who likes to constantly learn and be exposed to new information and knowledge. I find pathology naturally fits with this interest because it gives you the satisfaction of understanding the basis of certain diseases. It unravels many mysteries by putting the pieces of a puzzle together.

Pathology also gives you the opportunity to interact with different people because it requires collaboration among different teams. My plan originally was to specialise in paediatrics, which did not work out, but now I am lucky to find myself at a juncture where I can put both my interests together. A few years after qualifying as an Anatomical Pathologist, I pursued a fellowship training in Paediatric Pathology in the United Kingdom. Since then, I have further developed my interest in Paediatric Pathology.

## 2 What has surprised you the most about the industry?

I found that many people, including those in the clinical field, are unaware of the role of pathology. The perception is that pathology is just a place where you send patients' specimen for testing to get the results. They don't see what is happening behind the scenes, how vital it is for the specimen to be sampled well and the number of critical processing steps that occur in order to get a good test result.

Laboratories are seen as a 'support' service, when in reality we are so much more than that. Pathologists are on par with clinicians and in many ways, we are the doctors' doctor.

## 3 Who should advocate the role of pathology?

The responsibility lies with us, the pathologists. There's a famous saying "If you want something done, do it yourself", and I firmly believe in this. We play a big part in elevating the role of pathology.

I always tell my team that they need to interact with the clinicians and communicate with them. If their specimens are not up to standard, tell them. Meaningful results can only be obtained from an acceptable sample. The onus is on the pathologists to interact with our clinical colleagues, especially the younger doctors, on the right pre-analytical sampling of the specimen.

The key word is communication. When we communicate and interact well with each other, it is easier to get better cooperation. There is a lot more to do and we have to keep on this path and continue to champion the significance of pathology.

## 4 Are you happy with the pace of change in the industry?

Slowly but surely, the perception towards pathology has been changing. In comparison to two to three decades ago, pathology is held in much higher regard now. I do think we need to pick up the pace further because there are still many things to accomplish. This includes ensuring that our pathologists are equipped with the right skills and training to be able to keep up with the technological evolution taking place in the industry. And in today's value-based environment, we have to do a good job of demonstrating the value of pathology at every level of care.

The main factor that will help spur these changes is cultivating advocates within the industry. This will ensure that we have strong support and buy-in to develop the industry further.

## 5 The Department of Pathology has developed over the years into a modern multidisciplinary centre providing state-of-the-art healthcare diagnostics, consulting and laboratory services in Malaysia. Can you talk about its evolution?

We have come a long way since being established in the 1960s. Before this, pathology was only available at the Institute for Medical Research (IMR). The gradual transfer of services to the hospital commenced from clinical and biochemistry laboratories which back then were manually equipped and run by a rather lean team.

Slowly, the range of services and the skills within the department expanded to other fields of pathology such as microbiology and histopathology followed by cytology and finally haematology and genetics.

Now, we are a 400-strong, almost fully-automated laboratory that provides the full range and scope of services. Our staff consist of pathologists in the various disciplines of pathology, medical officers, scientific officers, medical laboratory technologists, as well as operational and clerical personnel. Our services continue to expand from routine clinical tests to specialised molecular tests such as thalassemia screening, haemato-oncology, solid tumours and infectious disease. Testament to the expansion of our services and skills is that our pathology laboratory currently receives around 14 million tests a year, and some specialised tests are referred from all over the country.



### What are some of the projects you are working on?

We are working on some very exciting projects. Most notably, we are in the midst of reviewing the scope of pathology services that are offered across the whole country. We are also working on a system to standardise data collection nationwide. Going hand-in-hand with this is the development of a network among the testing centres through a shared Laboratory Information System (LIS).

Our pathologists and laboratory professionals are extensively involved in developing this LIS as we are going to be the ones to use it, and we want to ensure that it is useful and usable. The long-term sustainability of our industry requires a cost-efficient and quality-focused approach, so what we are also doing is taking a holistic view and reviewing different aspects of the pathology service such as resources, procurement and capital building among others. Finally, I am also focusing on quality management. It is my hope that by the time I retire, all the main laboratories in Malaysia will have received well-recognised laboratory accreditation.

### What is your vision for the Department of Pathology and the pathology industry in Malaysia?

Malaysia, similar to other nations in Asia Pacific and globally, is facing a rise in the ageing population and chronic non-communicable diseases such as diabetes and cancer, as well as rapid and increased healthcare spending. By integrating pathology services at every point of the care spectrum, we can enable proactive and early intervention, as opposed to reactive intervention.

When this becomes a reality, pathology will prove to be a significant service for the Ministry of Health, not only in strengthening healthcare delivery, but also in helping to keep healthcare costs under control. Other than that, it is also my vision for the pathology specialty to become more seamless as well as comprehensive in its service delivery.

In terms of the industry, I strongly believe that the industry has a bright future, and is set to become the main function of the healthcare system. After all, pathology is already a key driver at every level of care – prevention, diagnostics, monitoring. We are now evolving towards personalised treatment.

### Do you think the industry is well-equipped to train the future generation of pathologists?

Rapid change has become a defining feature of our industry, and it is no different for pathology. As a result, we need to continue to build up our skills and knowledge in the face of new developments. Training certainly forms a crucial part of this industry.

When the industry was still in its infancy, senior pathologists who received training abroad, would come back and hold in-house trainings for other junior trainees at their respective institutions. Then, local postgraduate programs started flourishing and the various disciplines offered training. This directly correlated with the increase of specialists in our laboratory. Since then, our education and training program has not only strengthened and expanded exponentially, but a uniform conjoint body was also formed to standardise the curriculum and examinations conducted by the local postgraduate trainings in pathology. The training not only includes the universities but has progressed to involve the Departments of Pathology in the Ministry of Health (MOH) hospitals. Hence, many MOH laboratories in the larger hospitals provide both structured and informal training for their “open system” candidates who enjoy the benefits of training from both universities and public hospitals.

All in all, as diagnostic tools and technologies evolve so must the role of the pathologist. Take for instance digital pathology. It is gaining a lot more prominence today though it was practically non-existent 20-30 years ago. Such advancements mean that pathologists need to keep up in terms of both training and skills. By developing such capabilities, they can optimise their role in the healthcare delivery model today, and lead the transformation of pathology services well into the future.

### What is the most exciting thing about your job?

That I can help people – help patients get the right diagnosis and help clinicians manage their patients effectively. I am happy that we are able to play an important role and are being recognised as a member and part of a multi-disciplinary team involved in the decision-making related to patients. I think recognition is important – having colleagues tell you that you have been helpful really gives you a boost and makes your day.

### What's next for you personally?

I want to ensure that I have put things into the right perspective so that when I retire, I hope that I have helped set the right path for young pathologists. When I retire, I hope to still keep in touch with the field of pathology by being a go-to resource and playing an advisory or educational role. Other than that, I want to read all the books that I have accumulated over the years. I love to read because reading allows you to learn, think and see things differently. I don't have much time now to read more diverse and varied books though, except journals and articles related to my field of work. All the same, every time I walk into a bookshop, I always buy a book and pray that I still have good eyesight and good concentration power to indulge in reading when I retire!

# The evolution of South Korea's laboratory medicine industry

DR GWI-YOUNG OH

**Dr Gwi-young Oh** is the Laboratory Director of EONE Laboratories, a large reference laboratory in Song Do, Incheon and the first commercial laboratory to introduce radio-immunoassay testing in South Korea. In this interview with **Dia:gram**, Dr Oh looks at the evolution of laboratory medicine in South Korea and the exciting developments ahead.

**D**r Gwi-young Oh's love for all things science and mathematics, coupled with a desire to understand the principle behind how things work, led her to medical school. Still, she felt something was incomplete. When she attended a class on laboratory medicine in her second year of medical school, she realised that this was the path that she was meant to take. She has never looked back since. “It is one of the best decisions, career-wise, that I have ever made,” she says. “The field of laboratory medicine is the right fit for my interests and personality. No two days are alike. You learn something new, gain a fresh perspective and are constantly challenged to keep up with the pace of change.”

She has seen how the field has grown throughout her career, and shares her views on the key changes that have impacted the industry.

### Universal healthcare: paving the way for efficient healthcare delivery

South Korea established universal health coverage in 1989, 12 years after the introduction of mandatory health insurance for employees in large corporations. With this, timely diagnosis and quality care became the cornerstones of the Korean healthcare system.

Diagnostics outcomes today are advancing beyond measuring technical performance (accuracy, sensitivity, specificity), and shifting to providing hard evidence of benefits to patients and savings that are quantifiable by country and by region.

This is why, says Dr Oh, that unlike many countries where cost is considered a major key performance indicator (KPI) for a



laboratory, in South Korea which has an advanced healthcare system, efficiency and turnaround time (TAT) are of paramount importance.

“Laboratories in South Korea work with high volumes so our focus has consistently been on automation and consolidation. The industry is growing tremendously and while this presents a number of challenges it also puts pressure on the laboratory staff. Ultimately, if the laboratory cannot handle all the samples within the expected timeframe it results in a delayed TAT,” said Dr Oh.

“So growth at the cost of efficiency is not a sound approach,” continued Dr Oh. “Laboratories need to consider solutions that would help them increase capacity to meet the growing demands, whilst improving efficiency by reducing TAT.”

“With an ageing population and rising incidence of chronic diseases, the volumes in the lab will continue to increase. Moreover, for smaller clinics and hospitals it doesn't make business sense to invest in analysers so they rely on reference laboratories like ours,” she stated.





# THEN & NOW

In an American Journal of Clinical Pathology Special Report<sup>1</sup>, Dr Desmond Burke stated: The enormous advances in science and technology that have characterised the 20<sup>th</sup> century have transformed the practice of clinical medicine dominated by the use of medical technology - in particular, laboratory testing. There is every reason to believe that this trend will continue into the 21<sup>st</sup> century.

Moreover, it will continue against a background of ongoing advances in information technology and computer-based electronic communications - advances that could revolutionise the provision of medical care. These changes are likely to have profound effects on the practice of laboratory medicine; effects that will be determined by the competing demands of cost containment, assurance of quality, and financial support of education and research.

After almost a century of enormously successful growth and development, laboratory medicine faces serious challenges.

Less clear is how the two traditions - academic laboratory medicine, with its emphasis on teaching and research, and clinical pathology, with strengths in test strategy and interpretation of results - will fare in an environment dominated by cost containment and a public increasingly concerned with avoidance of error and the assurance of quality.

The survival of both in such an environment depends on the ability to add value. That ability depends in turn on how effectively academic laboratory medicine and clinical pathology exploit advances in science and technology - particularly advances in computer-based electronic communications and information technology - to add value to the care of patients.

<sup>1</sup> Am J Clin Pathol 2000;114:841-846

To meet the rising demand, in 2013, EONE installed a track system that enables the connection of pre-analytical systems with analysers. This helps to automate sample transportation and guarantee a predictable TAT, while still retaining the advantages of a stand-alone automation system such as high throughput and flexibility.

Currently, EONE processes more than 600,000 blood samples and over four million tests per month with a comprehensive test menu of more than 3,000 tests. Test results are provided quickly and precisely by dedicated teams who focus on clinical chemistry, immunochemistry, urine chemistry, cytogenetic and cytopathology.

### Investing in people and technology

Another evolution that the industry is going through is related to the adoption of new technologies. Dr Oh said it's important to have an open mind. "There needs to be an understanding that a higher cost will be involved, staff will need to be trained to operate new technologies along with the understanding that it will take some time for these new technologies to break even." However, new tests and technologies

are to be contextualised so that they do not cause confusion. This requires the laboratory professionals to take on the role of a navigator and get more involved with clinicians on the interpretation of a result. Increased levels of automation provide an opportunity for laboratories to evolve from their role of 'service provider' to that of central player who drives maximum patient care value through the efficient, accurate and timely deployment of testing.

So, a lab technician needs to have a versatile set of skills. These range from administration and cost management to areas such as data analytics, as well as sales and marketing. "A good understanding of industry trends and developments in reimbursement and technology are a definite plus," said Dr Oh.

In the past, Dr Oh explains, the laboratory professionals had limited scope. "The laboratory was not seen as an integral part of healthcare delivery. The job entailed doing routine tests and dispatching results."

But, it's an entirely different ball game today. "Laboratory science involves diagnostic laboratory testing from A to Z. Laboratory

*“The question now is how can we enrich individual lab results with algorithms that combine various test results with real world data to provide more actionable information for clinicians.”*

professionals do everything from providing cancer test results, to advising on the correct drug to prescribe, to determining treatment options as part of a multi-disciplinary care team."

Dr Oh credits the Academic Association for Lab Medicine in making significant strides

to diversify the path in laboratory medicine for talents who are looking to explore this field. "We need to see more role models in the field of laboratory medicine, who can deliver the message to the younger generation that there is a career in laboratory medicine," Dr Oh said.

EONE invests in the learning and development of its employees. Every month, the lab holds an internal conference to provide education and training for all staff. Additionally, staff who have clocked in a number of years of service, and who display great potential, are sent for overseas conferences to further enhance their knowledge.

### Harnessing the power of the future

Predicting the next big changes in the field of laboratory medicine, Dr Oh cites genomics and artificial intelligence (AI) as game-changers. As genetic testing becomes more sophisticated, Dr Oh sees this leading to the development of preventative medicine, while AI will be able to lead to cases being sorted into a more accurate database.

Betting big on a promising future, Dr Oh said, "Traditionally in laboratory medicine, we have been risk-averse preferring to stick to the tried-and-tested. But as the world around us changes, we need to upskill and upgrade to keep up and stay ahead of the curve. Take for instance, the amount of clinical data that is currently being generated in a laboratory each month. The question now is how can we enrich individual lab results with algorithms that combine various test results with real world data to provide more actionable information for clinicians."

"These changes cannot happen overnight. In order to conduct tests in a more accurate way, we need to continue to make investments - in science, in diagnostics, and in people," Dr Oh concludes. ■



## PROF CAROLYN LAM

*Pioneering research on cardiovascular disease in women*

# Straight from the heart

**Prof Carolyn Lam** is a Senior Consultant and the Director of the Women's Heart Clinic at the National Heart Centre Singapore. In this interview with **Dia:gram**, Prof Lam shares her passion for biomarkers and what she calls 'truly personalised medicine'.

Prof Carolyn Lam's interest in decoding the mysteries of the biomarkers B-type natriuretic peptide (BNP) and N-terminal (NT)-pro hormone BNP (NT-proBNP), started while she was a research student in a Mayo Clinic laboratory. She recalls being intrigued by their paradoxical nature: "They are the heart's protective hormones. So why is it that high levels are bad?"

This curiosity continued unabated while she was training at the Framingham Heart Study in Massachusetts. Prof Lam's research showed that there was cross talk between sex hormones and the heart. Her research delved into the fact that estrogens boost natriuretic peptides while testosterone suppresses them<sup>1</sup>.

Prof Lam hypothesised that this could be why men have earlier cardiac events when compared to women. Exploration of this hypothesis continues to be at the core of Prof Lam's pioneering work in understanding the ways in which sex and gender differences affect heart disease in women. Her work is increasing awareness on the need to personalise treatment for women and men.

Professor at the Duke-NUS Cardiovascular Academic Clinical Program.

Basic cardiology specialty training from Singapore, heart failure and advanced cardiology specialty training from the Mayo Clinic and clinical epidemiology training from the Framingham Heart Study in Massachusetts, USA.

PhD from University Medical Centre Groningen, Netherlands focused on heart failure with preserved ejection fraction (HFpEF) and sex differences, as well as executive management training from Stanford University Business School.

Recognised globally for her expertise in heart failure clinical trials and her focus on women's cardiovascular disease.

Women  
&  
Heart  
Disease



### A passionate advocate for women's heart health

Research on heart disease in women is only just catching up to the knowledge and understanding of how it manifests in women, according to Prof Lam. She points out the interplay between sex-based differences and gender. "Sex" refers to the biological construct such as sex chromosomes and sex hormones. When referring to 'gender' think about the social construct – for example, many young girls are discouraged from rough and tumble activities whereas boys are encouraged to be physically active, and these factors can impact heart health," she said.

For all these reasons, Prof Lam felt that a heart clinic focused on women made a lot of sense. She was instrumental in launching the first such women's heart clinic in Singapore. "It's really not the case that women are a smaller version of men, as is often assumed. There are factors such as pregnancy, menstruation and menopause that we just do not have to consider in men," she said.

Prof Lam cites heart failure (HF) as a condition that starkly illustrates gender difference. Heart failure is primarily defined on the basis of ejection fraction, a measurement that assesses the pump function of the heart. A heart attack can damage the heart muscle and thereby reduce ejection fraction. However, in heart failure with preserved ejection fraction (HFpEF), the heart pumps normally but is too stiff to fill up properly with blood. This condition represents almost 50% of heart failure cases worldwide and is a leading cause of death and disability. Studies show that HFpEF is particularly prevalent among women and the elderly who have comorbid conditions like obesity, hypertension and diabetes<sup>2</sup>. Elevated NT-proBNP levels can be used to confirm whether a patient has HFpEF.

Prof Lam is particularly interested in utilising NT-proBNP as a prognostic indicator in Asian patients with established heart failure, as well as Asian individuals at risk of heart failure. Prof Lam's research team, is currently studying the interplay between gender, ethnicity and the development of HFpEF<sup>3</sup>. She is involved in several research projects that will help refine our understanding of how heart failure differs by ethnicity, gender, sex and other local and regional determinants. She is the Program Lead of the Asian Network for Translational Research and Cardiovascular Trials (ATTRACT). She is also the principal investigator of an ongoing nation-wide heart failure study in Singapore (the Singapore Heart Failure Outcomes and Phenotypes [SHOP] study).

As part of the International Federation of Clinical Chemistry (IFCC) committee, Prof Lam is currently contributing to the development of an educational paper on natriuretic peptides for laboratory specialists and clinicians. Furthermore, as part of the European Society of Cardiology Heart Failure Association writing group, she is contributing to new international recommendations for the diagnosis of HFpEF, which are expected to be published this year. Prof Lam hopes the guidelines will help accelerate accurate diagnoses, especially for elderly women who may go undiagnosed due to the perception that breathlessness is a natural byproduct of ageing.

"It goes a lot like this in the female patient's head: I'm unfit, I ate too much, it's my own fault, I didn't exercise... the list goes on! The first step is for patients to recognise that something is actually wrong and not just blame themselves. Then, the General Practitioner (GP) should know what to look for. When we look at the echocardiogram and see that the pump function is normal, we can't just immediately say that the patient is unfit or anxious. We need to look at diastolic function, not just the systolic function. Is the heart muscle thick? Is it stiff? We all need to be aware that it's not just about ejection fraction," she said.

### A connector, educator and mentor

Apart from her many achievements, Prof Lam is also a prolific author and broadcaster. She is an Associate Editor for *Circulation* and the *European Journal of Heart Failure* and even does a podcast for *Circulation*. To educate the public, she is seen regularly on television as the Resident Doctor of the health program "Body and Soul" by Mediacorp Singapore.

She enjoys motivating her patients and mentoring women interested in cardiology. "I am so happy to see women pursuing cardiology and if I could play even a small part in that choice, it makes my life worthwhile," she said.

Inspiringly, her dynamism is fuelled by a desire to bring out the best in others – whether it is family, patients or the people she mentors. "The singular focus I hope to have is to be a loving and positive force. If I bring out the best in my patients, they will naturally do well and have better health." ■

<sup>1</sup>Lam C., Cheng S., et al. (2011). *Journal of the American College of Cardiology* 58 (6) 618-626. *Influence of Sex and Hormone Status on Circulating Natriuretic Peptides.*

<sup>2</sup>Oktay, A. A., Shah, S.J. (2015). *Curr Cardiol Rev*; 11(1): 42-52. *Diagnosis and management of heart failure with preserved ejection fraction.*

<sup>3</sup>Lam, C., Anand, I., Zhang, S., et al. (2013). *Eur J Heart Fail. Asian Sudden Cardiac Death in Heart Failure (ASIAN-HF) registry.*



# Two doctors. One idea.

Can the diagnosis of heart attacks in one hour be made a reality in Asia?

DR KENJI INOUE &  
DR LEE CHIEN-CHANG





Dr Kenji Inoue

levels in the blood and ascertain whether a patient has suffered a heart attack.

**Life and death decisions**

But there is a challenge.

Earlier generations of these blood tests, which are still used in several hospitals in Asia, require considerable time to detect the troponin release, sometimes requiring up to six hours with less sensitive troponin tests. This means patients may end up waiting for several hours in the emergency department.

However, newer generation troponin tests such as the high sensitivity troponin T tests are starting to change that. Prompt treatment is essential as every 30 minutes of delay increases the relative risk of mortality by 7.5% in patients with AMI<sup>1</sup>.

A high sensitivity test can detect subtle increases in troponin levels which allows earlier detection of heart attacks; shortening the time required for diagnosis by almost three hours. In addition, it also improves risk stratification of patients with elevated cardiac troponin levels with and without acute cardiac events.

**Quick diagnosis to save lives**

On that fateful day in Beijing, sitting next to Dr Lee was Dr Inoue, a well-regarded cardiologist, who had been grappling with a peculiar challenge. “There is no doubt that cardiac biomarkers such as the high sensitivity troponin T tests are reliable indicators

It was by sheer coincidence that Dr Kenji Inoue, Associate Professor, Department of Cardiology, Juntendo University Nerima Hospital in Tokyo, Japan and Dr Lee Chien-Chang, Associate Professor of Emergency Medicine at the National Taiwan University Hospital in Taipei, met.

They were attending a cardiac biomarkers seminar in Beijing, China in 2016. Dr Inoue was there because this was pertinent to his area of practice while Dr Lee decided to attend as the topic was of interest. As an emergency department (ED) physician, Dr Lee had first-hand experience dealing with patients brought in with sudden and acute illness or severe trauma. “The whole process from the moment a patient arrives in the emergency department until they leave is very carefully managed and monitored by senior medical staff. Our aim is to ensure patients that need critical, life-saving treatment get it right away”.

“And, it’s no different in cardiac cases. In Taiwan, patients with chest pain and other heart attack symptoms account for 6 to 8% of all emergency department consultations. In most cases, we found the time from the heart attack to diagnosis and then treatment could be a couple of hours. So I was keen to hear what experience other doctors had using cardiac biomarkers and how it helped to speed up diagnosis,” he said.

Used in conjunction with clinical information, the rapid and accurate testing of cardiac markers is crucial especially in acute events like heart attacks where every minute counts.

A heart attack, or acute myocardial infarction (AMI), is a cardiac event in which the blood supply to an area of the heart muscle is interrupted, causing the muscle cells to die. When a heart attack occurs, the heart releases a protein called troponin into the blood stream. Doctors use cardiac troponin tests to detect the troponin



Dr Lee Chien-Chang

of heart attacks and help to speed up the diagnosis of heart attacks. But new tests are only effective if doctors use them. What happens in the absence of protocols?”

“The real game-changer for me was the research led by Prof Christian Mueller which provided concrete evidence that confirmed observation time needed to rule-in or rule-out a heart attack could be reduced from three to six hours to just one hour.”

TRAPID-AMI, a prospective observational study, investigated more than 1,200 patients with acute chest pain during 2011-2014<sup>2</sup>. The study was conducted in 12 institutions from nine countries and three continents, led by Professors Christian Mueller from the University of Basel (Switzerland), and Bertil Lindahl of the University of Uppsala (Sweden). It is the first clinical trial validating a short diagnostic procedure constructed from two blood tests taken from the patient one hour apart in early chest pain patients. Following this, the European Society of Cardiology (ESC) recommended the use of high sensitivity troponin T testing with the accelerated algorithm in its 2015 guidelines<sup>3</sup>.

**On a quest for answers**

“I must admit I was relentless in my pursuit. I wanted to know whether this could work in Asia where we have such diverse healthcare settings. But I needed more data and I needed a like-minded collaborator,” remembers Dr Inoue.

“Since Dr Lee and I were sitting next to each other, we began talking and soon discovered a lot in common,” said Dr Inoue. One of which was their passion for research.

“The Severe Acute Respiratory Syndrome (SARS) outbreak in Taiwan in 2003 really changed my perspective. While we were dealing with this crisis, I began to wonder how the families of SARS patients did not get infected in spite of living in such close proximity. Since all emergency doctors had to be in quarantine for a month after the outbreak subsided, I used this time to dig deeper. We collected serum from people in close contact with the SARS patients to understand whether they were immune to the virus or not infected at all and found that none of them had been infected. We had only 20 samples on the basis of which

I did my research. To my surprise, the findings were published in several medical journals and thus began my journey into clinical research,” said Dr Lee.

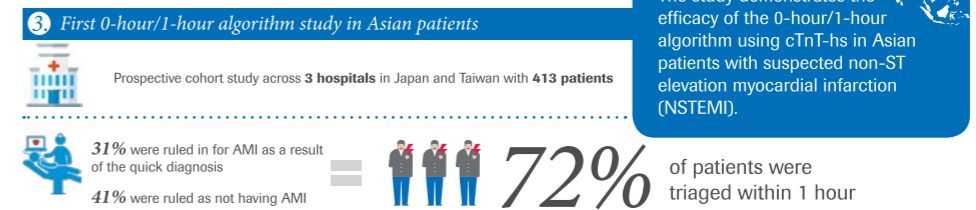
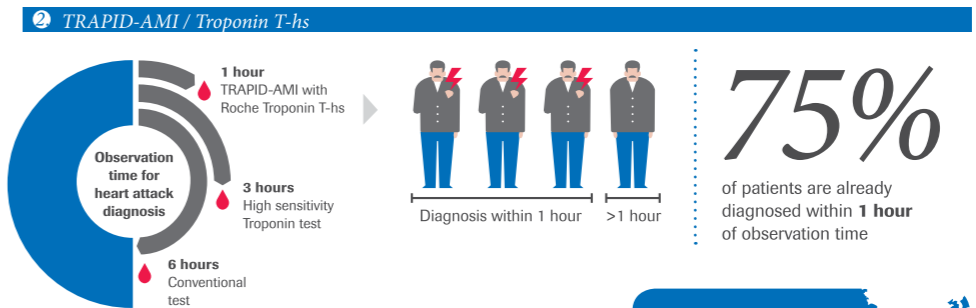
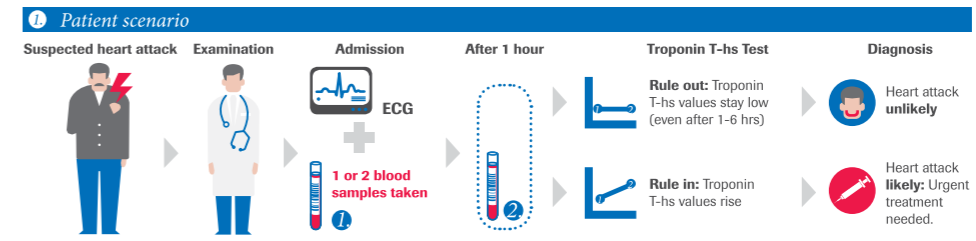
“Emergency medicine physicians are so busy that I didn’t think they have time for clinical research. So I casually mentioned the idea to Dr Lee and told him I wanted to study whether the 0-hour/1-hour algorithm could work in Asian patients. Before you know it, we were discussing the practicalities involved in the research,” added Dr Inoue.

**Strained healthcare resources: the on-ground reality**

With increasing incidence and the high cost of care for cardiovascular and metabolic diseases, early diagnosis and improved treatment options are vitally important to clinicians, healthcare systems and, above all, to patients. With the rising burden of chronic diseases and fast-ageing populations in Asia, emergency departments are getting busier.

This is a major public health concern, not only because it overburdens already

**Cardiac Troponin T-hs test**  
*Heart attack diagnosis within 1 hour*



The study demonstrates the efficacy of the 0-hour/1-hour algorithm using cTnT-hs in Asian patients with suspected non-ST elevation myocardial infarction (NSTEMI).

<sup>1</sup>Mueller, C. et al. (2015). *Ann Emerg Med*, in press. <sup>2</sup>Roffi, M. et al. (2015). *Eur Heart J*, in press. <sup>3</sup>Inoue K, Lee CC. et al. *Int J Cardiol.* (2017) 15;249:32-35 <sup>4</sup>Reichlin, T. et al. (2012). *Arch Int Med* 172, 1211-8.





strained hospital resources but because of the grave implications it has on patient outcomes.

“Over the years, the number of patients coming into the emergency department has increased, so efficiently managing resources is our number one priority. But the question always is - is there a way to determine which are the non-emergency cases and move them to the appropriate departments?” Dr Lee said.

In the case of heart attacks this was possible. The cardiac high sensitivity troponin T test had proven to work effectively in quickly ruling in or out AMI cases. “We were coming from two different sides, looking at the different challenges we face but working towards a common goal. In the emergency department, our focus is patient prioritisation and the optimal use of resources,” he added. For Dr Inoue it was determining the utility of the accelerated algorithm for Asian patients.

And so they began. Over 400 patients with suspected non-ST elevation myocardial infarction (NSTEMI) from three hospitals in Japan and Taiwan were included in the study<sup>4</sup>.

“This has been a remarkable journey. When the results were published in the International Journal of Cardiology we knew we had achieved something we could be proud of,” said Dr Inoue.

“This research is the first to demonstrate the clinical significance of the 0-hour/1-hour algorithm in Asia. We now have plans to study the cost-effectiveness of rapid diagnosis using the accelerated algorithm,” Dr Lee stated. ■

<sup>1</sup>De Luca G. et al. (2004). *Circulation*. 109(10) 1223-5

<sup>2</sup>Mueller, C. et al (2015). *Ann Emerg Med*. 10.1016

*“We now have plans to study the cost-effectiveness of rapid diagnosis using the accelerated algorithm.”*

<sup>3</sup>Roffi M. et al (2015). *Eur Heart J*. Aug 29

<sup>4</sup>Shiozaki M, Inoue K, Lee CC, et al. (2017). *Int J Cardiol*. 15;249:32-35

## Rising to the threat of antimicrobial resistance

Experts in Asia call for concerted effort to control the catastrophic increase in cases



Antimicrobial resistance (AMR) is emerging as the single biggest threat to modern day medicine, as new cases surface where patients cannot be treated with any currently available antimicrobial drugs. Today, AMR is responsible for approximately 700,000 deaths per year globally<sup>1</sup> and without adequate intervention, could kill as many as 10 million people a year by 2050<sup>1</sup>. As we fast approach a stage where infections once considered minor, thanks to effective treatment by antibiotics, could once again become fatal, we take a look at the factors responsible. In this article, we speak to experts on what can be done to stem the spread of AMR.

**C**an Asia rise to the challenge? That's a question experts in Asia are racing to answer.

Existing drug-resistant pathogens as well as emerging pathogens with the potential to become drug resistant, represent a threat to public health and national security. AMR occurs when microorganisms, including bacteria, fungi, viruses and parasites, change after exposure to antimicrobial drugs such as antibiotics, antifungals, antivirals, antimalarials and anthelmintics.

But resistance is not a new phenomenon. Scientists have known for more than half a century that patients could develop resistance to the drugs used to treat them. One of the first people to predict this was Sir Alexander Fleming, who is credited with creating the first antibiotic – penicillin – in 1928. In his Nobel prize speech in 1945 he said, “We are dealing with living mechanisms about which there are enormous gaps in our knowledge.”

Those gaps, as it turns out in the case of AMR, have been perpetuated by poor public awareness, the absence of innovation in antibiotic drug and diagnostic development, and the lack of robust surveillance and regulatory systems on the use and sale of antimicrobial medicine for humans and animals.

A major concern, according to many health experts, is that in many cases clinicians often rely on symptoms to make a diagnosis instead of diagnostic tests that can be a more accurate indicator. For instance, most upper respiratory tract infections are caused by viruses, where antibiotics have no beneficial effect. So together with assessment of signs and symptoms, testing before treatment becomes an important step in determining the appropriate course of action. Yet,

studies have demonstrated high rates of unnecessary antibiotic prescription for patients with these types of infections<sup>3</sup>.

“We have been treating minor infections and even viral infections with antimicrobials. On top of that, we have been using potent, broad spectrum antimicrobials for minor ailments, where we could have been using narrow spectrum antimicrobials,” Prof Ivan FN. Hung, Health Sciences Pedagogy at The University of Hong Kong explains. “We are all collectively responsible for creating the situation that we are now facing.”

#### **A public health crisis of epic proportions**

It should come as no surprise then that the World Health Organization (WHO) has described the current situation as a “serious threat to global public health” stating that AMR is putting the gains of the Millennium Development Goals at risk, and now endangers the achievement of the Sustainable Development Goals<sup>4</sup>.

In 2016, Jim Yong Kim, President of the World Bank Group said, “The scale and nature of this economic threat could wipe out hard-fought development gains and take us away from our goals of ending extreme poverty and boosting shared prosperity.” Estimates put the economic cost of AMR at \$100 trillion by 2050<sup>1,2</sup>.

And experts in Asia believe it is likely to get much worse without urgent action to tackle overuse of antibiotics. A government survey in Hong Kong revealed that misunderstanding on indications of antibiotics remains prevalent with over half of the respondents mistaking cold and flu as conditions treatable with antibiotics<sup>5</sup>. Similar findings related to the misperception among patients were also reported in Singapore. In a 2015

# WE ARE DEALING WITH LIVING MECHANISMS ABOUT WHICH THERE ARE ENORMOUS GAPS IN OUR KNOWLEDGE

- Sir Alexander Fleming

study conducted by the Yong Loo Lin School of Medicine at the National University of Singapore, it was found that a third of patients expected antibiotics to be prescribed by their General Practitioners (GPs) for common ailments, with half of these patients asking for the medication or going to another doctor if it was not given<sup>6</sup>.

In addition, around one-tenth of patients kept antibiotic stocks at home, and took leftover ones.

Some argue that pressure to free up hospital bed space can lead to over-prescription of antibiotics, as doctors try to keep patients in the community.

#### **Tackling the problem head on**

“We are at a critical juncture. Can we effectively mitigate the repercussions of AMR? Only time will tell,” agrees Prof Hung.

He has every right to be cautious given the extent of the problem. Data from the Department of Health's Superbug Report (2011-2016) shows the prevalence of AMR is quite high in the city<sup>10</sup>. But Hong Kong is using lessons from the past.

In response to the SARS crisis, Hong Kong established the Centre for Health Protection (CHP) in 2004, tasked with preventing and managing outbreaks.

*“The scale and nature of this economic threat could wipe out hard-fought development gains and take us away from our goals of ending extreme poverty and boosting shared prosperity.”*

According to The Centers for Disease Control and Prevention (CDC) about 30% of antibiotics, or 47 million prescriptions, are given unnecessarily in doctors' offices and emergency departments in the United States (US)<sup>7</sup>.

Exacerbating the situation further is the fact that in several countries, over-the-counter antibiotics without a prescription are easy to get. Globally, total antibiotic consumption soared 65% from 2000-2015<sup>8</sup>. At the forefront were India with a 103% increase, China with 79%, and Pakistan with 65%<sup>9</sup>.

“The ineffectiveness of drugs as a result of antimicrobial resistance is rising in both developing and developed countries. If this trend continues, we will find ourselves in a world where many infectious diseases will have no treatment or cure,” warned Peter Dedon, the Underwood Prescott and Singapore Research Professor at the Massachusetts Institute of Technology (MIT).

A three-tier alert system was created to respond to outbreaks of infectious diseases. Last year, the city launched a five-year action plan for tackling AMR, hoping to crack down on antibiotic overuse.

When a report from the Center for Disease Dynamics, Economics and Policy (CDDEP) in Delhi found India had some of the highest resistance rates in bacteria responsible for common infections<sup>9</sup>, it prompted India's government to release a National Action Plan on AMR, calling for strengthened monitoring, better education and training, improved infection control, better regulation of antibiotic use, and investment in research.

Singapore has taken this one step further by establishing the Singapore-MIT Alliance for Research and Technology (SMART). Funded by the National Research Foundation, the Antimicrobial Resistance Interdisciplinary Research Group (AMR IRG) under SMART hopes to





**Prof Peter Dedon**  
Underwood Prescott and Singapore  
Research Professor at the Massachusetts  
Institute of Technology (MIT)



**Prof Ivan F.N. Hung**  
Health Sciences Pedagogy,  
The University of Hong Kong



**Prof Peter Preiser**  
Nanyang Technological University (NTU)

*“The ineffectiveness of drugs as a result of antimicrobial resistance is rising in both developing and developed countries.”*

*“We are at a critical juncture. Can we effectively mitigate the repercussions of antimicrobial resistance? Only time will tell.”*

*There is a need for quick, well-informed decisions at the point of care. This is where rapid point of care diagnostic tests can help.”*

solve the growing threat of resistance to antimicrobial drugs.

“Our goal, first and foremost, is to understand the mechanisms of drug resistance, and then once the discoveries have been made, to take it a step further and see how we can use this to develop new drugs and move these into a clinical trial or develop approaches for a diagnostic test. So we actively try to focus on the translational and entrepreneurial science

because innovation that doesn't reach people would be pointless,” said Prof Peter Preiser from Nanyang Technological University (NTU) and the Antimicrobial Resistance Interdisciplinary Research Group at SMART.

This is timely as reports suggest 35-50% of bacterial infections in Singapore hospitals are now resistant to front-line antibiotics<sup>2</sup>. “Singapore is the ideal location for our research. We collectively have technologies

that don't exist anywhere else in the world, access to sophisticated research and healthcare facilities, and a pool of incredibly talented researchers. We can also access patient samples in infectious disease hotbeds in the region easily. When you put all that together it creates a powerful strategy,” added Prof Dedon, who is also a fellow investigator at SMART.

**Growing consensus in the fight against AMR**

Experts agree on what the best approach is to address the threat. And measures are already being taken to ‘reverse’ or slow down AMR. Prof Hung describes what is known as an antibiotics stewardship program which screens patients who have been put on antibiotics to ensure that they actually need the antibiotics or if they have been given the right antibiotics. Many hospitals in Hong Kong, for example, have been running this program, including Queen Mary Hospital where the program has been running for a decade now.

Public education is just as important as patients share equal responsibility in the use of antibiotics. As do doctors when it comes to prescribing these drugs. “We need to help alter the reliance of healthcare providers prescribing drugs based on symptoms alone. There is a need for quick, well-informed treatment decisions at the point of care. This is where rapid point of care diagnostic tests can help,” said Prof Preiser.

While on-site rapid antigen tests may be fast, they may also have a lower rate of accuracy and require confirmation of negative results. Lab cultures, on the other hand, though highly accurate, have a long turnaround time - from four hours to five days. Near-patient PCR testing can support antimicrobial stewardship efforts by allowing healthcare professionals to make a clinical diagnosis quickly and accurately.

Prof Hung believes the next generation of medical practitioners will have a critical role to play and “must be adequately

**Factors responsible**

Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.



Over-prescribing of antibiotics



Patients not finishing their treatment



Over-use of antibiotics in livestock and fish farming



Poor infection control in hospitals and clinics



Lack of hygiene and poor sanitation



Lack of new antibiotics being developed

Credit: World Health Organization infographic (World Antibiotic Awareness Week 2017)

trained.” In Hong Kong, he explains that the curriculum in medical school has been expanded to include the appropriate use of antibiotics. “After these medical students graduate, they also undergo training on the use of antibiotics in a community setting.”

Effectively combatting the growing tide of antibiotic resistance ultimately requires the healthcare community to work together to ensure that all stakeholders have access to the education and tools needed to tackle this emerging crisis.

“Antimicrobial resistance is not confined by borders. We need to have a strong interest in collaborating and supporting efforts in other countries because no one nation can address this problem alone,” concluded Prof Dedon.<sup>4</sup>

<sup>1</sup>The Review on Antimicrobial Resistance. (2016). Tackling Drug-Resistant Infections Globally: Final Report and Recommendations commissioned by the UK Prime Minister.

<sup>2</sup>Singapore-Massachusetts Institute of Technology (MIT) Alliance for Research and Technology (SMART).

<sup>3</sup>Bagger K, Nielsen AB, Siersma V, et al. (2015). Eur J Gen Pract. Inappropriate antibiotic prescribing and demand for antibiotics in patients with upper respiratory tract infections is hardly different in female versus male patients as seen in primary care.

<sup>4</sup>World Health Organization (WHO) regional office for Europe.

<sup>5</sup>Data from the Centre for Health Protection, Department of Health, The Government of the Hong Kong Special Administrative Region

<sup>6</sup>Darius Shaw TP, Mark I-Cheng Chen, et. al. (2016). BMC Fam Pract. Knowledge, attitudes and practices towards antibiotic use in upper respiratory tract infections among patients seeking primary health care in Singapore.

<sup>7</sup>The Centers for Disease Control and Prevention (CDC). (2016). Journal of the American Medical Association (JAMA).

<sup>8</sup>Klein E, Thomas P, G Sumanth, et al. (2018). PNAS. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015.

<sup>9</sup>Ramanan L, Roy Chaudhury R. (2016). PLoS Med. Antibiotic Resistance in India: Drivers and Opportunities for Action.

<sup>10</sup>Hong Kong Strategy and Action Plan on Antimicrobial Resistance (2017-2022).



## World Health Organization (WHO) publishes first-ever list of essential diagnostic tests to improve health outcomes

List provides catalogue of tests needed to diagnose common conditions and global priority diseases<sup>1</sup>.

The Essential Diagnostics List comprises 113 tests of which 58 are listed for detection and diagnosis of a wide range of common conditions. The remaining 55 tests focus on the diagnosis, screening, and monitoring of 'priority' diseases like the human immunodeficiency virus (HIV), tuberculosis, human papillomavirus (HPV), hepatitis B and C, syphilis, and malaria.

The list, which heavily focuses on in-vitro diagnostic tests, aims to provide a tool that can be useful to all countries to better diagnose and manage diseases as well as enable the efficient allocation of health funds.

Similar to the WHO Essential Medicines List, which has been in use for four decades, the Essential Diagnostics List is intended to serve as a reference for countries to update or develop their own list of essential diagnostics. The WHO plans on increasing the number of tests in the Essential Diagnostics List as it incorporates other important areas including antimicrobial resistance, emerging pathogens, neglected tropical diseases, and additional non-communicable diseases.■

<sup>1</sup>World Health Organization. (2018). *Essential Diagnostics List announcement*.

## Saliva seen as an early predictor of type 1 diabetes complications

Researchers find proteins in saliva can help identify type 1 diabetes in young patients long before clinical symptoms of complications appear<sup>1</sup>.

A study, published in *Frontiers in Physiology*, has found that proteins in saliva reflect high blood sugar and associated disease processes in young patients with type 1

diabetes, long before the appearance of clinical symptoms of complications.

This could lead to better prediction and prevention of long-term complications of the disease.

The study is the most comprehensive characterisation of the salivary proteome to date. It analysed saliva samples from young type 1 diabetics with satisfactory or poor blood sugar control, and from matched healthy subjects, using a highly sensitive technique to identify and quantify more than 2,000 different proteins.

The researchers found that young type 1 diabetics with good blood sugar control had similar saliva protein profiles to non-diabetics. In contrast, young people with poorly controlled type 1 diabetes showed a very different saliva protein profile. The differences were in proteins known to have key roles in inflammation, clotting and blood vessel function - processes that are disrupted by high blood sugar and thereby indicate the major long-term complications of diabetes.■

<sup>1</sup>Pappa E, Vastardis H, Mermelekas G, et al. (2018). *Frontiers in Physiology. Saliva Proteomics Analysis Offers Insights on type 1 Diabetes Pathology in a Pediatric Population*.

## Study shows Anti-Müllerian Hormone (AMH) can help to diagnose polycystic ovary syndrome (PCOS) in women

Research conducted in a group of 118 women showed that serum AMH had good diagnostic performance compared to the ultrasound findings to diagnose PCOS presenting with oligo/anovulation and hyperandrogenism<sup>1</sup>.

AMH has been clinically validated to help diagnose PCOS in Asian women, according to the study conducted in Siriraj Hospital, Mahidol University Thailand. The study aimed to investigate the accuracy of serum AMH and evaluate new ultrasonographic criteria, follicle number per ovary (FNPO) threshold  $\geq 25$  follicles and ovarian volume (OV)  $> 10$  mL, for the diagnosis of PCOS.

Close to 120 women participated in the study. The study showed that the mean AMH in women with PCOS was significantly higher than non-PCOS women even after adjusting for age using regression analysis. All ovarian parameters (total antral follicle count, FNPO, FNPS, OV) were also statistically more significant in the PCOS group than the control group.

PCOS affects 10% of women in their reproductive age and can lead to problems such as infertility, obesity, metabolic syndromes, insulin resistance and diabetes mellitus.

Diagnosing PCOS earlier is essential to assess women's fertility, improving quality of life for patients and allows for better planning of treatment options for clinicians.■

<sup>1</sup>Wongwananuruk et al. (2018). *Taiwanese Journal of Obstetrics and Gynaecology*.



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