Dia:gram

EDITION 2018 Vol 3

Breaking the cycle

Asia's invisible malaria problem

Predicting preeclampsia

A new era in cancer care

How a pathologist's sketches revolutionised tissue diagnostics

Embracing the future of Laboratory Medicine

Professor Tan Puay Hoon

Note from the editor

Dear Readers,

Welcome to the third edition of Dia:gram, where we continue to explore the impact of diagnostics on healthcare in Asia Pacific. While it is clear that diagnostics has transformed healthcare, quantum changes are yet to come. With the ubiquity of genomics, artificial intelligence and embedded sensors, diagnostics itself is changing to provide vital prognostic and theragnostic information. These innovations will be crucial in meeting the needs of ageing populations and the growing middle class, which has greater expectations around digitisation and shared decision-making.

Given the forces at play, this issue looks to the future with Steve Monaghan who suggests healthcare should learn from other industries such as technology and retail to stay relevant and sustainable. We talk to Dr. Thomas Grogan, who pioneered the automation and standardisation of tissue biopsy testing, opening the door for more personalised treatment of patients. We also feature stunning photographs from Pearl Gan, a Singapore-based photographer, who has been travelling around the region, documenting the lives of people living in malaria-affected communities. Her photos, some of which have featured in *The Lancet*, are a clear reminder of the struggles of ordinary people living in the developing parts of our region.

This will be my last issue editing Dia:gram as I take up a new role in our pharma division. In my time here, I have encountered healthcare leaders who are passionate about making a difference, clinicians who are pushing the boundaries of innovation and patients willing to share their experiences. Through all of this, the common thread has been to document how diagnostics transforms lives.

That is the power of diagnostics, that is the power of knowing.

Rachael Bylykbashi
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Improving cancer diagnostics for patients everywhere

How one pathologist on a mission transformed millions of lives

DR. THOMAS GROGAN

Dr. Thomas Grogan is an American pathologist and the founder of Ventana Medical Systems, which was acquired by Roche in 2008. He pioneered the automation and standardisation of tissue biopsy testing, which has radically changed cancer detection and treatment. But his mission didn't end there. He and his team expanded their research to the chemistry of cancer biopsies, which has enabled physicians to personalise diagnosis and treatment options for individual cancer patients. In this interview with **Dia:gram**, Dr. Grogan, now Founder Emeritus, gives us a glimpse into what he calls the joy of discovery and the advancements in tissue diagnostics since then.

What shocked Dr. Thomas Grogan the most when he was a medical student was that death from cancer was seen as inevitable. "I was always bothered by that. To me, if something is particularly threatening, you need to rise to the threat and use everything you have against it," he said.

This attitude of pushing boundaries, never settling or taking 'no' for an answer, led to extraordinary achievements that continue to benefit millions of cancer patients across the world. On a personal front, it helped Dr. Grogan drive his own diagnosis and recovery from metastatic melanoma two years ago. This provided inspiration for yet another invention to simplify decision-making for cancer treatment in the information age. "One of the things I hear from oncologists today is that they get more information than is actionable. They are inundated by reports from multiple laboratories. The molecular, immunologic and radiologic reports are not integrated. As a physician, you don't treat a lab result, you don't treat a number, you treat a person," he said.

This patient-centred thinking set Dr. Grogan off on the path of discovery and invention. In the early 1980s, Dr. Grogan joined the University of Arizona's faculty of health sciences after completing a post-doctoral fellowship at Stanford University.

The path to earning this degree was remarkable in itself as he was the first member of his family to go to college. Since he was about 12 years old, Dr. Grogan said he knew he wanted to be a medical doctor.

"I had a brother who was mentally disabled. I remember even as a small boy feeling that it was very awkward and painful that we didn't understand what the doctors were telling us, and it left me with a yearning. I wanted to know more."

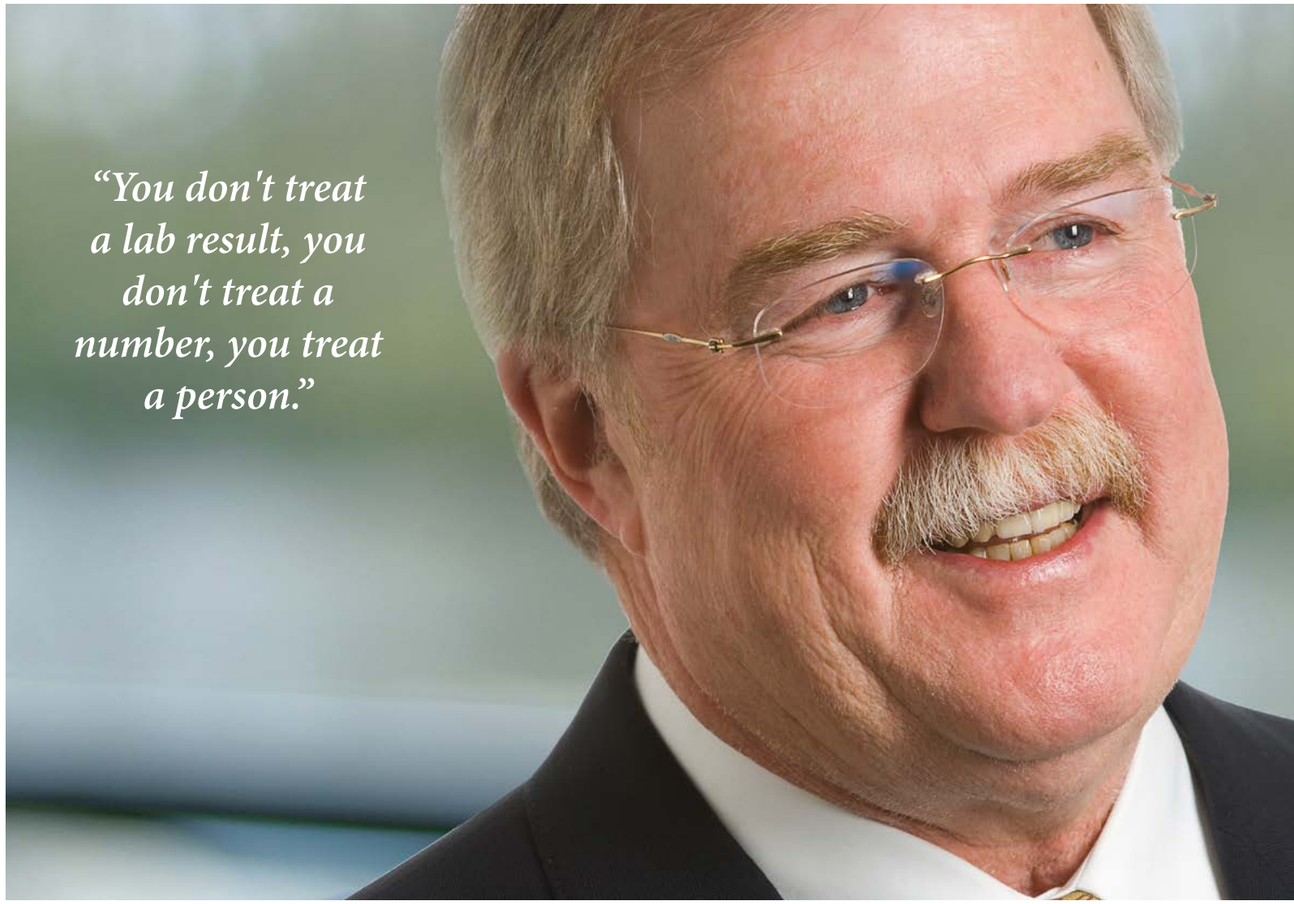
He went into pathology because he wanted to be the one who knew what the diagnosis was. "A radiologist can tell you where it is, a surgeon can take it out, but do they know what it is, and how much they should take out?"

From name-callers to navigators

Dr. Grogan credits his professor at Stanford for the idea of using monoclonal antibodies on human biopsies to discover additional information about the tissues. "With this approach, we could begin to see the 'vocabulary' of more than a 100,000 proteins," he said. At the time, the idea that you could look at a biopsy and decode its chemistry was absolutely new to medicine. "It opened a new door where we could say it's not just breast cancer, but it is estrogen receptor positive or HER2 positive. We went from being name-callers to getting at the biology of the tumour cell."

Dr. Grogan describes the University of Arizona as a perfect cauldron of clinicians, engineers and scientists who shared an unbounded enthusiasm for discovery. The head of the oncology department was a graduate of Stanford and already familiar with Dr. Grogan's work. "He was over-the-moon enthusiastic for me to tell him about the chemistry of his patients' biopsies. We would have weekly conferences and I would show him my findings. Before I knew it, I had younger people coming up to me in the lab wanting to make an antibody, test a theory or write the next paper," he said.

Almost every single problem the team worked on proved worthy of a paper. "I published a paper every six weeks for 30 years. More than 260 papers and a number of them in top journals. So it was really a discovery tool, and it turns out all those discoveries were relevant to understanding the nature of a person's cancer and choosing the right therapy," he said.



This took place while half of Dr. Grogan's time was still spent covering the hospital. With each case, he and his team turned to the practical matter of whether they could refine their diagnoses. "People in training would see us pull a rabbit out of our hats, figure something out and come to a diagnosis that surprised them. They then understood the power of doing all this chemistry."

Discovering the nature of the beast

The abiding question that remained was why one person could be cured while another with the same diagnosis could not. "It had to do with the nature of the beast. Not everything with four legs and hooves was a horse, sometimes it was a zebra," he said. Dr. Grogan knew that the answer lay in interrogating the biopsy for the vocabulary of gene expression. This revealed what the cancer cells were dependent on, what their growth factors were and therefore, the answer as to what might be a good target for therapy.

Dr. Grogan credits many aspects of the birth of his company to the team of people he worked with and the patients he helped. He was on faculty at one of the top ten cancer centres in the country. Every time he analysed the tumour chemistry for a patient, he would get a call from the oncologist who said: 'I want you to do this with every one of my patients.' He recalls the pivotal role his head technician, Catherine Rangel, played.

"I had put up a sign in the clinic in the operating room which said: 'Before you remove the tissue, call the Grogan lab,' and my head technician along with one of the residents, would always go and talk to the patient before the surgeon or the oncologist. The next thing I knew, she was promising that the results would be out by the next day," he said.

Dr. Grogan said she connected him with the people in those rooms. "In the lab, we were living in splendid isolation. And she would say she had told the patient we would deliver results by tomorrow afternoon. It brought home the fact that what I was doing in academia for my professorial colleagues should actually be done on every biopsy, and every patient in every hospital, in every city and in every country in the world," he said.

"Not everything with four legs and hooves was a horse, sometimes it was a zebra."

A tale of rejection and triumph

It was at this point that Dr. Grogan had the idea to build a platform to allow everyone to do what he was doing. He remembers discussions with engineers and graduate students on automation and the rough sketch of the idea that would become the first automated slide-staining instrument.

Dr. Grogan realised then that this was more than an academic project and that it needed professional financing. He got on a plane and flew to Chicago, Dallas and Silicon Valley to secure funding which would only come after 18 months and 35 rejections.

"My wife, Cande, always said that my fundamental ability is to talk people into something that they wouldn't do otherwise." Dr. Grogan remained tenacious because he believed in the idea and the implications.

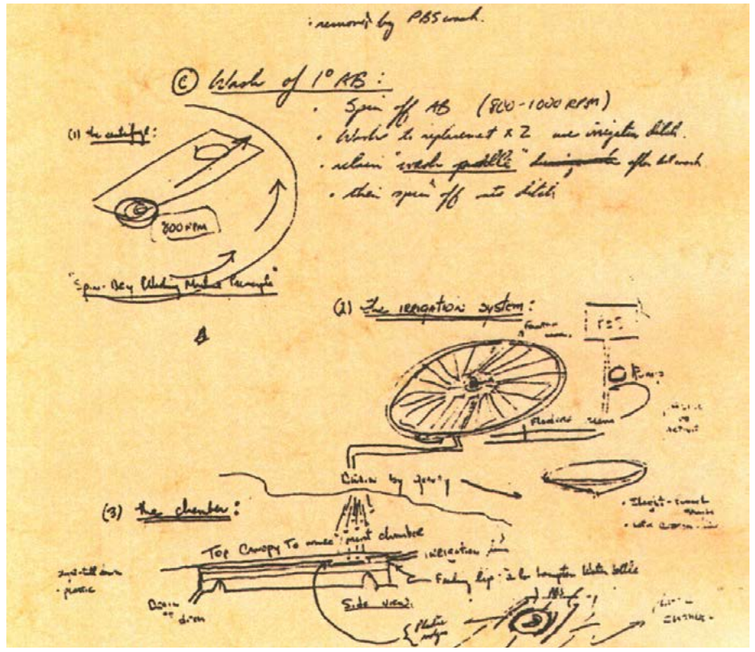
After the 25th rejection, he had an epiphany. He realised he was presenting to investors to prove that he had a viable business idea that would make money. Instead, he started to show cases where his method actually worked. "I began presenting four patients, whose diagnoses and treatment I had changed in the hospital because of doing this chemistry. These were dramatic cases. I started to go with the fact that if you had the new immunohistochemistry, you could provide this improved diagnosis to people everywhere."

From all the rejections, Dr. Grogan learned a valuable lesson that he applied carefully when he went on to build his company. He recalls going to Silicon Valley where the groups he was talking to were nowhere near a hospital.

"A few times, groups that I presented to said, 'we talked to physician consultants and they said they don't need this.' I knew that these groups simply did not have proximity to the problem, and I said to myself 'when somebody gives me a definitive dismissal because of a technological reason, or a better way to do this, then I'll surrender. But so long as they're dealing with this superficially, I'm not going to give in.' I would say a righteous twig snapped in me."

Leading with the concept of proximity to the patient

This spirit kept him going until he finally found Venture Capitalist No. 36 – a man who wanted to see the idea in action.



Legal pad sketches led to the automation and standardisation of tissue biopsy testing.

When he came to the lab for the first time, the case they were working on was of a 30-year-old mother of three who had breast cancer that had been misdiagnosed. "He sat there with the microscope and he saw how we corrected the diagnosis. The next day there was another case, and he realised what the need was. He was the first one to actually come into the hospital and experience this himself," Dr. Grogan said.

Another core driver was Dr. Grogan's belief in the power of teams. He does not subscribe to the notion of a singular genius entrepreneur. "My advice to someone starting out is to find the other people who want to climb the mountain with you and really build those alliances. You're not going to make it to the top of Mount Everest alone. It needs to be a team."

Today, Dr. Grogan looks back at his own persistence and laughs: "Can you imagine proposing marriage 35 times? I should have gone to the monastery." But he looks back with immense pride that his discoveries eventually reached 100 countries and continue to help millions of patients each year.

Dr. Grogan believed in weaving this proximity to the patient into the fabric of the company he built. He felt that the business side did not often have visibility to the consequences of their work. So he started to interview cancer patients during quarterly employee meetings.

Over time, his employees got to know these patients and what happened to them. They began to see the impact of their work and the ways it affected the lives of patients. "The culture is not strong if it's one person. It is strong if it's transmissible, and therefore sustainable. I am proud to have transmitted this culture to 1,200 people in a sustainable way," he said.

Driving a higher level of information to power personalisation

At 72, Dr. Grogan is just old enough to remember a time when patients were not told they had cancer because not much could be done about it. Today, he sees it as a highly informed equation in which the patient gets some combination of surgery and radiotherapy or chemotherapy or immunotherapy. He experienced this first-hand with his own diagnosis of a malignant melanoma with an 80 per cent chance of recurrence. When the neck dissection showed that the lymph nodes were negative, the initial advice was to just wait and use targeted therapy if there was a recurrence.

But Dr. Grogan did not want to wait given the aggressive nature of his cancer. This was a threat and he wanted to fight it with everything he had.

He approached the company's team of pathologists and scientists who were working on a multiplexed test that could detect several immune biomarkers simultaneously, and together they figured out his tumor had an immune blockade. Dr. Grogan also had his team pull together the many streams of information, which amounted to some six feet of filing cabinet space, on to his iPad. Dr. Grogan was familiar with the groundbreaking work of a professor of oncology at the University of California, Los Angeles, and took this information to him.

"We got into the treatment room, and I whipped out the iPad that the team had organised to show all of my results. By this means, six feet of paper was reduced to my pushing of buttons to show him what my tumour looked like, what the immune blockade looked like and what my immune response to this looked like. This professor looked at me and he said 'how did you do this?' I joked, well, it's complicated. You have to create a company; you have to have 1,200 employees and you have to get them to do this," Dr. Grogan said. The professor found the results actionable and put Dr. Grogan on immunotherapy, which sent his cancer into remission.

"So I've lived because of a higher level of information, thanks to our latest automated instrument and latest multiplexed tests. But it's not just about me, it's about everyone. Every patient should have that and not just a professor and founder, so globalising our technology remains a high priority," he said. For much of history, cancer treatments have lagged behind diagnostics. Dr. Grogan sees that changing now with the advent of immunotherapy. "For the first time, the therapies have gotten ahead of the diagnostics and in some cases we are rushing to get the diagnostics done to match the therapy," he said.

This means the role of the pathologist is more vital than ever. Dr. Grogan is a very strong proponent of the pathologist becoming an integral part of the multi-disciplinary care team. "There is a notion that pathologists are just in the basement doing autopsies," but Dr. Grogan really sees the pathologist as the chief navigator.

"I think pathologists by nature of vocation are intellectual, and not loud or overbearing. I'm not advocating that they change their personality but I am advocating that they be more assertive about their contribution to the practice of medicine," he said.

"I said to myself when somebody gives me a definitive dismissal because of a technological reason, or a better way to do this, then I'll surrender."

Dr. Grogan and Catherine Rangel with one of the first automated tissue biopsy stainers.

Time to move diagnostics and medicine onto the technology curve

Insights from other industries to make healthcare more sustainable

STEVE MONAGHAN

From commercial pilot to senior roles in consulting and banking for world-leading brands, ***Steve Monaghan*** is a well-known voice on innovation. He shares a fresh perspective with **Dia:gram** on how healthcare companies can build a more inclusive future.

Steve Monaghan believes we are at a unique point in history, where healthcare has an enormous social and economic opportunity to help people avoid getting sick. This requires a strategic shift in what he calls the "healthcare industry mindset", which is still too focused on market share over market growth.

Monaghan points to the extraordinary gains made by technology companies in the last decade. "Take a look at Google. It drops advertising prices by about 11 per cent per annum because it drives massive growth on the back of that inclusion. You really need to have a different mindset about how you grow markets. Otherwise, you will always be restricted to very low penetration or people behaving in ways that do not drive the right outcomes," he said.

Monaghan believes the move towards predictive and preventive healthcare requires profound ecosystem shifts. Current incentives in this space are misaligned, starting with the way insurance is structured. "Health insurance is so complex that people don't understand it as a product to begin with. Very few people can articulate what they're actually insured for and what's excluded." Monaghan explains that even when they have the product, people have a genuine fear of making a claim. "We know that people delay or don't do medical tests for fear of ruining their insurance, which is a stupid concept," he said.

In an ideal scenario, people would test at the right time and catch chronic disease early, which would in turn, save on downstream treatment costs. For this to happen, the industry needs to become more inclusive. If you look at smart phones, almost everybody has one – the economic barriers to access technology are not that high, he said.

"Once you move diagnostics and treatment to those technology curves, it could be very interesting. It really comes down to two things: how you manage and mitigate risk, and how you remove transaction costs," he said.

These two lessons come from Monaghan's diverse work experience, which includes leadership positions at

corporations and financial institutions including Dell, Compaq, Citigroup, OCBC, Shinsei, DBS Bank and AIA. He has experience introducing new business models and products in the region and is a private investor in artificial intelligence (AI), life sciences, healthtech and fintech.

But before all this, Monaghan was a commercial pilot and he saw quite early on what automation was doing to his job. "I thought I could spend the rest of my life on autopilot in these great aircraft or I could do something very interesting in business."

Monaghan cites the three laws of technology, which continue to drive disruption of industries from banking and retail, to music and medicine.

The first is Moore's law, which shows that processing power doubles every 18 months for the same cost. The second is Metcalfe's law, which is the law of networks. It stipulates that the value of the network grows at the square of its participants. Lastly, there is Kryder's law, which postulates that capacity for data storage doubles every 18 months. "Look at the impact on genome sequencing. It cost one hundred million dollars to sequence one genome in 2001. Today, it costs about $500 and by mid-2020, it will fall to less than 3 cents," he said.

However, even as the laws of technology drive affordability in some areas, medical care continues to become more and more exclusive. "The implications of an ageing population combined with rising healthcare costs with flat to negative incomes plus a diminishing tax base, are huge. So we need to rethink our approach and how we can drive medical inclusion," he said.

Revisiting his two principles of managing and mitigating risk, Monaghan says that genomics combined with AI is already moving the needle from the concept of generic risk to specific and individualised risk. "Risk is as dynamic as you are," he said.

According to Monaghan, the concept of dynamic risk is well accepted especially in aviation technology. "GE used to sell airplane engines and react to failure. Now they're proactively monitoring those engines in real-time. Why wouldn't you want to monitor yourself?"

Monaghan believes that the ubiquity of genomics will transform the importance of diagnostics. "Being continuously connected to diagnostics is definitely one of the mega trends. If you have a heart attack, do you really want to wait 30 minutes to get treatment? If you catch it really early, which we can do today and in fact predict it, your chances of survival skyrocket," he said.

But how do we maintain the privacy and integrity of all this sensitive patient data? “I think individuals should own their own data 100 per cent. This is why I’m a huge fan of blockchain. I think being able to put individuals in control of their own data to take it where they want to, to be able to give it over, and also withdraw that information if you don’t prove trustworthy with it, is the right way to go,” he said.

Monaghan provides an illustrative example of ways that people could use their health data. Take a person with cancer. From an insurance perspective, what reinsurance does is redistribute financial risk around this eventuality.

“Why shouldn’t I be able to, for instance, sell cancer risks to a diagnostic or device company who could manage that cost down as a business? Shouldn’t the customer have the right over whether that happens? I think they should,” he said. Ultimately, healthcare needs to learn from customer and end-user focus of technology companies.

It also needs to overcome the resistance from the more traditional sections of the industry and find ways to collaborate with regulatory bodies. There is a tendency, he said, to be passive and treat regulators as prohibitionists. “You really need to engage and point out those deficiencies in a much more open dialogue with regulators. This is also why many regulators are building sandboxes – essentially closed testing environments to safely test new technology and business models. This is a powerful approach,” he said.

Monaghan finds it interesting that technology can replace a restricted view with a much more granular view. However, this view requires a different lens. He gives the example of pharmacogenomics: “Some of the FDA-approved assessments will tell you today that 40 per cent of the drugs that you ingest are either inappropriate or ineffective, or perhaps harmful for your genotype. If you look at this through the old lens, there will be resistance. If you assess it through the new lens, you’ll actually look at how you can better utilise this sort of technology to drive better outcomes.”

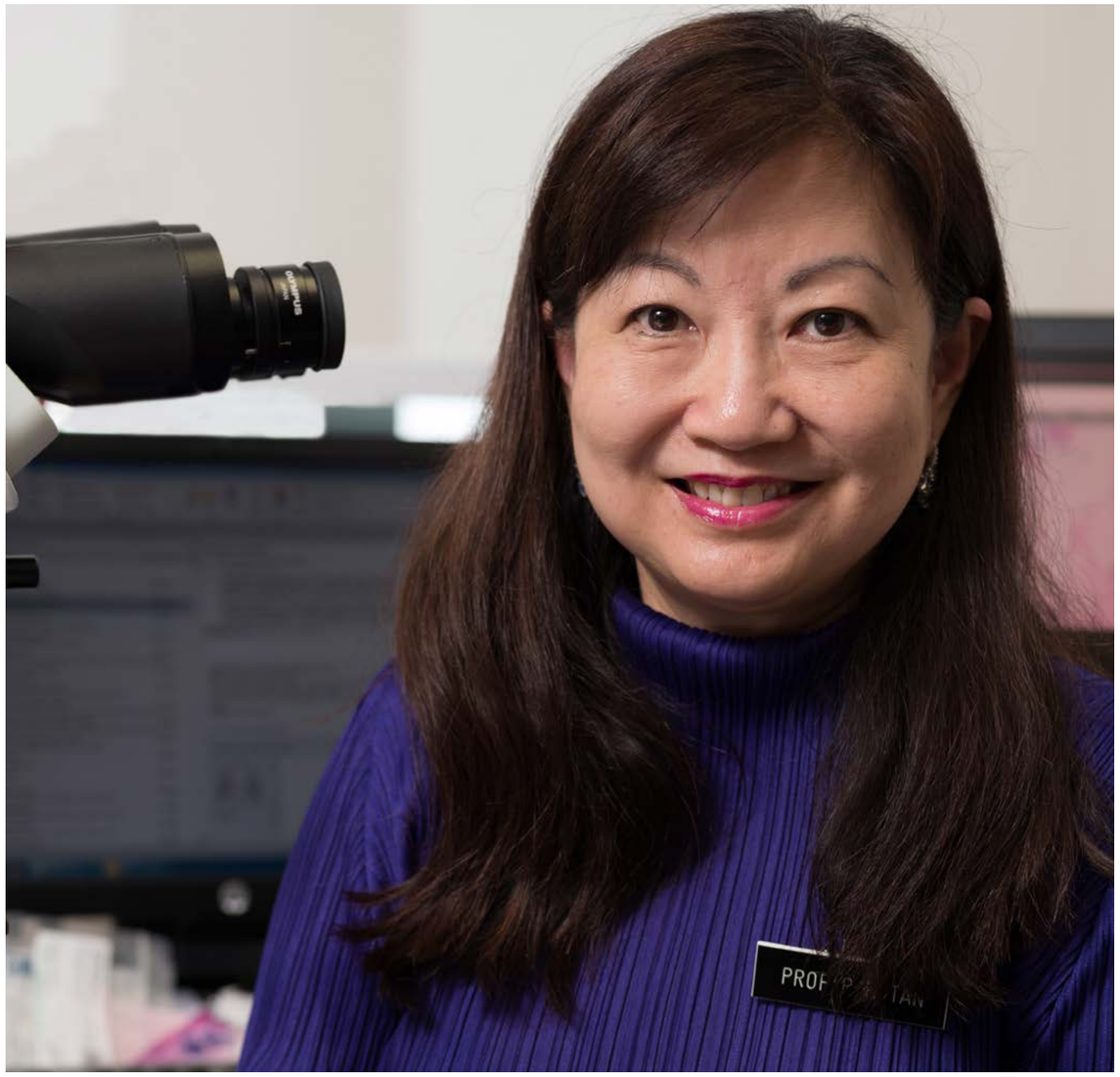
The interdisciplinary sharing of systems-level best practice will be essential to driving better healthcare outcomes, according to Monaghan. As our region faces significant growth opportunities coupled with challenges in diagnosis, delivery and access, continuing to look outside of the healthcare silo will become an important exercise for decision makers.

The new wave in laboratory medicine

A pathologist's perspective

PROF. TAN PUAY HOON

Prof. Tan Puay Hoon, Chairman, Division of Pathology and Senior Consultant, Department of Anatomical Pathology at Singapore General Hospital (SGH) enjoys the rare distinction of being the first woman from Singapore to be a volume editor of the World Health Organisation’s Classification of Tumours of the Breast. A key figure in Singapore’s anatomical pathology scene, Prof. Tan shares her views with **Dia:gram** on what makes pathology the foundation of medicine and the forces shaping its future.



Prof. Tan Puay Hoon has many firsts to her credit. Among them, is being appointed the first Chairman of the Division of Pathology at one of Singapore's leading hospitals. The role was created following the formation of this Division in 2016 to oversee four departments – Anatomical Pathology, Clinical Pathology, Molecular Pathology and Microbiology.

"Prior to this, Pathology was one large department with many laboratories that functioned separately even though there were synergies among them. We realised we could tap on the collective experience and expertise that rest within our teams by consolidating laboratories with complementary services into Departments, to ultimately strengthen pathology subspecialty support for patient care. The Division of Pathology interfaces with existing and new Divisions in SGH, allowing seamless interaction with medical and surgical disciplines as well as the SingHealth Duke-NUS Disease Centres," said Prof. Tan.

The Division has over 500 employees comprising laboratory professionals, technical staff and clinicians, making it the largest of its kind in Singapore.

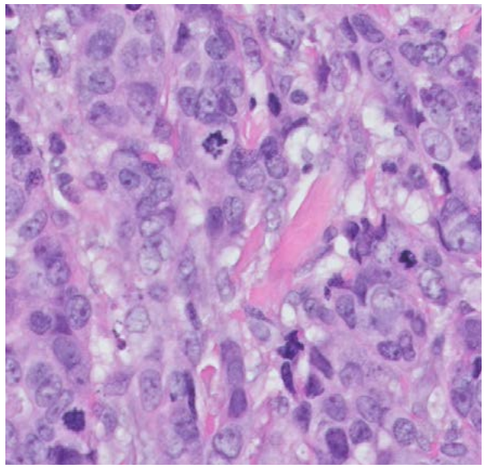
"Our endeavour now is to build a forward-looking and innovative pathology service that keeps pace with the latest developments, and better still, leads the way in formulating novel pathology tools and technologies," she added.

This, Prof. Tan said, is largely because the field has evolved tremendously. Gone are the days when pathologists were occupied primarily with the diagnosis, classification, and subclassification of disease. Today, pathologists play a crucial role by providing prognostic and predictive information that helps the physician in rendering appropriate treatment.

The evolving role of the pathologist

"I have always been fascinated by pathology. I liked the systemic manner of identifying disease patterns and coming to a pathological diagnosis. Looking down at the slides through a microscope made me appreciate the beauty of this discipline even more. It was, and still remains, such a knowledge-rich subject that has both breadth and depth, spanning causation of disease to clinical manifestations that lead to appropriate diagnosis and therapy. It truly is the foundation of medicine, underpinning all medical practice," Prof. Tan said.

As healthcare evolves so does the role of pathologists. "Cancer diagnosis, for instance, cannot be made without pathological confirmation. Pathologists prognosticate disease which determines how long patients will survive, and predict the response of patients to various therapies based on assessment of the tumour and its biological features. This makes them an integral part of the cancer management team," she added.



High magnification view down the microscope, of an invasive breast cancer that shows crowded malignant cells with enlarged nuclei and many mitoses.

"But more needs to be done to raise the profile of pathology as a specialty, giving it the recognition it deserves," cautioned Prof. Tan. "In the absence of direct patient contact, it tends to play a supporting rather than starring role in medicine." On this point, Prof. Tan also said pathologists need to step up and take charge rather than continue the status quo.

Prof. Tan believes there needs to be a greater appreciation for the role of pathology in medicine, in order to sustain the future talent pipeline. Sometimes perspective from the next generation helps. A mother-of-four, Prof. Tan remembers a conversation with her daughter who was a medical student then, and is now an internal medicine resident. She said to me: "Many of us think all you (pathologists) do is research.' It made me realise that it is up to those of us in senior positions to showcase its value so that we can encourage our best and brightest to join."

Keeping pace with changes in healthcare

Advancements since the 1970s, as seen with automation, computerisation, and immunoassay and molecular techniques, have transformed the practice of laboratory medicine. Which is why Prof. Tan advocates keeping up with developments in medicine, "Otherwise one gets readily left behind by the rapid advances in disease classification, prognostic and therapeutic developments."

"We need to continuously upskill ourselves and embrace technologies that can help us to make a positive impact. Automation in pathology continues to be at the fore, with improved technologies reducing the requirement for labour intensive processes, promoting standardisation and consistency in laboratory testing, and alleviating manpower constraints," she added.

When asked whether the pathologist's role could become irrelevant in the time to come, she said: "Molecular tools are revolutionising how we diagnose and treat diseases. With new therapies emerging and the growing shift towards individualised treatment, we are now facing a molecular information explosion which requires a pathologist to carefully curate and interpret the data."

Speaking about the exciting developments in diagnostics, Prof. Tan said, "Point of care testing, which may in the future provide an extensive laboratory menu for patients within the community itself, could very well be the norm moving forward – bringing pathology services

"Digital pathology, artificial intelligence and deep learning will equip pathologists with tools that will redefine healthcare."

right to the patient's doorstep. Digital pathology, artificial intelligence and deep learning are other areas that will equip pathologists with tools that will redefine healthcare." Prof. Tan was the first to introduce digital pathology at Singapore General Hospital. Her department at the hospital was also one of the first in the world to look at digital pathology in a routine laboratory setting.

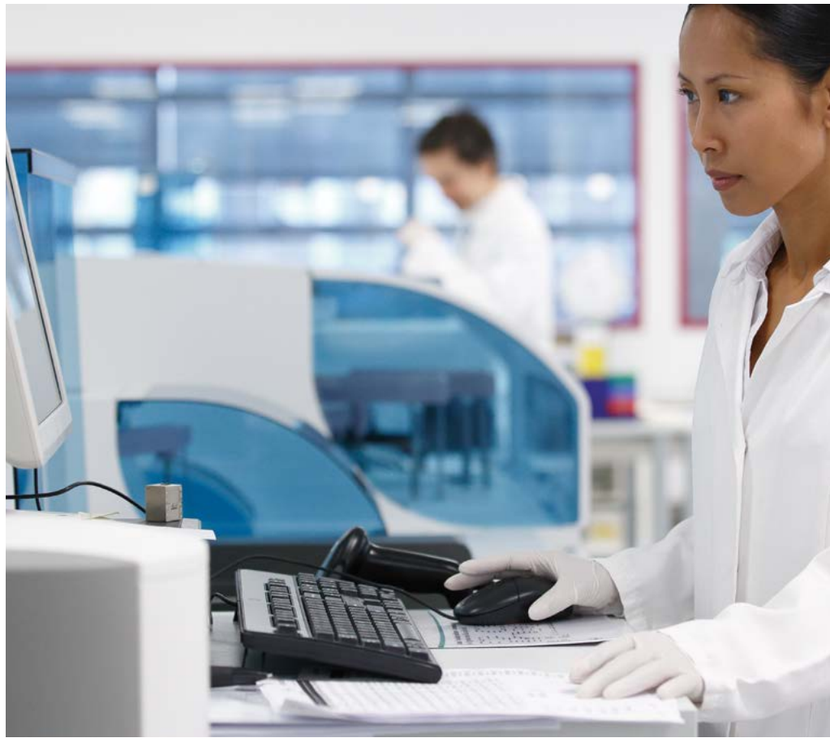
From research to best practice

She is equally passionate about her work in breast cancer. "My interest in breast pathology began as a trainee and then Senior Registrar during the Singapore Breast Screening Pilot Project. It was wonderful to see a program being piloted for early detection of breast cancer among women in Singapore. The results of this pilot program led to the launch of the National Breast Screening Program, BreastScreen Singapore in 2002." Prof. Tan has continued to be a part of this initiative since inception.

Through that experience she recalls, "I began to study early breast cancer diagnosed through screening and gather local data on the disease. When I embarked on a Doctor of Medicine thesis I focused on breast ductal carcinoma in situ (DCIS). Our research group continues to work on breast DCIS to this day." Prof. Tan has authored more than 400 publications. Her latest book titled *Atlas of Differential Diagnosis in Breast Pathology*, which was five years in the making, was recently published.

Prof. Tan was also part of a multi-disciplinary team of scientists that discovered MED12, a gene that is responsible for the formation of fibroadenomas, the most common benign breast tumour in women. It is estimated that millions of women around the world are diagnosed with fibroadenoma annually. The group's breakthrough research went on to be published in the seminal scientific journal, *Nature Genetics*.

Not one to rest on her laurels, Prof. Tan continues to pursue breast pathology



research. She is currently studying triple negative breast cancer, a type of breast cancer that does not express estrogen, progesterone or HER2 receptors. This means therapeutic options for such patients are often limited as there are no targets for treatment. She is also currently looking at breast fibroepithelial lesions and the translational application of the team's research discoveries to diagnostics. In conjunction with this research, Prof. Tan hopes to seek approval for establishing a data registry that tracks consented patients with fibroepithelial lesions, so that more information can be gleaned to help improve clinical management.

She is also active as a member of several renowned associations, often collaborating with pathologists to share best practices and exchange ideas. One area that Prof. Tan keenly supports is capacity building efforts in the Association of Southeast Asian Nations (ASEAN) region where pathologists often have limited access to technology or tools. Prof. Tan, together with her colleague Dr. Angela Chong, helms the annual SGH Breast Pathology Course which, now in its 9th year, brings together experts from the region and around the world.

Preparing for the future

The changing economics of healthcare provision calls for new ways of working. Yet, the opportunities in pathology have perhaps never been greater – with more focus on care collaboration, the adoption of newer advances in testing technologies, and the shift towards personalised medicine.

For those considering pathology as a career option, Prof. Tan has this advice, "Pathology is a great career option for individuals who love the challenge of being immersed in a discipline where the investigative mind unravels myriad information points to reach precise diagnoses and beyond."

PATIENT PERSPECTIVE

Heart failure in women: Taking control

A resilient woman shares her story of hope

SAPARIAH AHMAT

Dia:gram catches up with ***Mrs. Sapariah Ahmat*** from Singapore about her experience of living with heart failure. Her particular type of heart failure – with preserved ejection fraction (HFpEF) – is increasingly the predominant form of heart failure (HF) in the developed world, and remains a challenging clinical condition to diagnose and treat[1].

Two days after her 51st birthday, Mrs. Sapariah Ahmat felt unwell. It was around six in the evening and she was waiting for her husband to get home from work. At first, she had trouble breathing. Then, she started sweating. "It wasn't normal. I was soaked from head to toe," she said. When her husband got home, he was concerned. The couple, who speak Malay, rang her brother, who speaks English. They felt he would be able to communicate more effectively if they needed to see a doctor. While they waited for her brother to arrive, Mrs. Sapariah paced in and out of her bedroom. "I couldn't lie down or get comfortable, I was only able to breathe very slowly," she said.

"Even when my friends make small jokes, I love to laugh," she said. Well known for her cooking, she ran a small catering business for large gatherings, especially during the festive seasons. Before her illness, she ate whatever she liked and never exercised. "But in the hospital, when I was fighting for my life, I decided I would change my lifestyle, starting with food and exercise," she said.

So she diligently went to the hospital-mandated cardiac rehabilitation for three months and learned the exercises that she could do at home. She and her husband bought an exercise bike which sits in the living room where she can use it while watching her favourite television shows.

> *"They told my brother that if he had not called the ambulance then, I would not have made it."*

When her brother arrived, he immediately called for the ambulance. "I don't think we can wait," he said. Mrs. Sapariah recalled the ambulance ride and the paramedics asking her to strap on the oxygen mask. "They kept saying to me, 'try not to sleep, just keep talking to us' and so I did." Mrs. Sapariah managed to stay awake until they got to the Accident & Emergency department. She did not think her condition was serious. "There was really no pain at all. I thought maybe I was just very tired," she said.

Doctors discovered that Mrs. Sapariah was suffering from myocardial ischaemia, which is the lack of blood supply to her heart muscle due to blockage of her heart arteries, and heart failure caused by a build-up of fluid in her lungs because her heart was not functioning properly. Luckily, she received treatment at the hospital just in time. "They told my brother that if he had not called the ambulance then, I would not have made it," she said.

Mrs. Sapariah remembers going home with various medications. "I had to take about 10 pills a day. Like kacang puteh (crispy Malay snack)," she said with a laugh. She has a naturally sunny personality.

But, changing her diet proved a little more challenging. "The first time I tried eating oats, I couldn't bring myself to swallow it. I had to pray to God to help me to eat healthy," she said before breaking into another laugh. She also substituted steaming for deep-frying and upped her intake of fruit and vegetables.

That was in 2007. Five years later, in 2012, her symptoms started. Once again, she experienced breathlessness and sweating, though it was far less intense than the first time. This time around, however, she knew she had to go to the hospital immediately and her son drove her there.

Doctors diagnosed Mrs. Sapariah with heart failure with preserved ejection fraction (HFpEF). Ejection fraction is 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 HFpEF, the heart pumps normally but is too stiff to fill up properly with blood. This condition represents almost 50 per cent of heart failure cases worldwide and is a leading cause of death and disability[2].

Studies show that HFpEF is particularly prevalent among women and the elderly who have comorbid conditions like obesity, hypertension and coronary artery disease[3]. Effective treatments are yet to be established and experts are still building consensus on how best to diagnose the condition. Symptoms can be non-specific such as feeling breathless and tired with little to no exertion. This is why accurate diagnosis of the condition in the primary care setting can be difficult.

Current diagnostic algorithms rely on echocardiography and biomarkers called natriuretic peptides. The B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) are hormones mainly secreted by the left ventricle of the heart in distress. NT-proBNP can enable the selection of patients who need to undergo a confirmatory echocardiography and predict future risk of adverse events[4]. Mrs. Sapariah's doctor, Prof. Carolyn Lam, is a senior consultant with the department of cardiology at the National Heart Centre Singapore and oversees a research unit looking at heart disease in women. With a focus on HFpEF, the unit is studying the interplay between gender, ethnicity and development of HFpEF[5]. Prof. Lam is particularly interested in utilising NT-proBNP as a prognostic indicator in Asian patients with HF.

In Mrs. Sapariah's case, her diagnosis of HFpEF was confirmed by elevated NT-proBNP, and she was stabilised with medication and asked to maintain her lifestyle changes. Despite the challenges she faced, Mrs. Sapariah remains highly motivated. "I even encouraged my husband to eat salad. For him, that really was the limit. He told me this was food fit for a goat," she said with a big smile.

Mrs. Sapariah also credits a close bond with her cardiologist, Prof. Lam. "She always takes the time to explain everything to me. I can feel her genuine interest and concern. Each time she explained my blood test results, I noticed she always said my kidneys were good. So I asked her why this was important for my heart. This way I learned more about my condition," she said.

Prof. Lam even invited Mrs. Sapariah to a Singapore Heart Foundation event to share her experience and introduced her as the "patient who manages to stay out of the hospital."

Mrs. Sapariah said people asked her what her secret was and she said it was to follow her doctor's advice and change her lifestyle. She keeps busy with her granddaughter's care and upbringing. "Playing with her makes me happy," she said.

Mrs. Sapariah is now often a source of inspiration for friends who are facing diagnoses of chronic health issues. "I advise them to take it one step at a time. You can't change your sickness overnight, so I tell them to take baby steps."

[1] Sharma, K., Kass, D. A. (2014). Circulation Research. 2014; 115:79-96. Heart Failure with Preserved Ejection Fraction.
[2] Andersson C., Vasan R.S. (2014). Heart failure clinics. 2014: 10 (3): 377-388. Epidemiology of heart failure with preserved ejection fraction.
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[4] Tromp, J., Lam, C., et al. (2018). ESC Heart Fail. N-terminal pro-B-type natriuretic peptide and prognosis in Caucasian vs Asian patients with heart failure.
[5]Lam,C., Anand, I., Zhang, S., et al. (2013). Eur J Heart Fail. Asian Sudden Cardiac Death in Heart Failure (ASIAN-HF) registry.

Ten questions with Sunil Sethi

Associate Professor Sunil Sethi took up the role of President of the Asia-Pacific Federation of Clinical Biochemistry (APFCB) in 2017. He is Senior Consultant Chemical Pathologist at the National University Hospital, Singapore; Associate Professor of Pathology at the National University of Singapore; and Group Director of the Applied Sciences Group with Singapore's Health Sciences Authority. In this interview with **Dia:gram**, A/Prof. Sethi talks about his vision for the APFCB and some of his own personal passions.

> *"We need to be operating at the highest end of our capabilities. When we do that, we will attract good people to the profession."*

1 How did you get involved in laboratory medicine?

I started out as an internist. When I finished my specialist medicine degree, I realised that biochemistry was a very dynamic area and that diagnostics was at the cutting edge. So I opted to focus on laboratory medicine instead. That was 30 years ago.

Back then, it was a very manual process, with lots of paperwork and doctors who were far less demanding. Today, there is a complete change. The process is now faster and much more robust in terms of quality and accuracy. Everything is digitised and automated. There is also a much greater expectation from doctors to deliver results that help them manage their patients better.

2 What is your key area of interest in laboratory medicine?

I really enjoy the operational areas of the laboratory – workflow, automation, process improvement and informatics. I'm most interested in how we can link these to improvements in patient outcomes.

I'm also particularly interested in test utilisation. If we don't test correctly, the patient suffers. I don't think we really know the extent to which tests are under or over-used. Both are a problem. If we over-order, we see incidental findings; if we under-order, we don't optimise a patient's management. We need good scientific evidence of what is the proper order set for a given disease, particularly chronic conditions. That's led me to my latest project.

3 What is the latest project you're working on?

I'm working on a dashboard to help doctors with the management of their diabetes patients. Most doctors spend only a minimal amount of time with a given patient. In diabetes, there are at least 20 biomarkers that need to be under control. How can a doctor know all of this quickly? At any given visit, he may only be able to focus on one or two of those biomarkers, which is not the best scenario for the patient. So, my vision for a dashboard is one that quickly shows all biomarkers for the specific patient. I hope to finalise this in 2018.

4 As the current president of the APFCB, what is your vision for the organisation?

The APFCB is the largest of the regional federations within the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC). We cover a population of around 4.5 billion or around

> *"My plan is to use the expertise of the advanced countries to help the others, so that we get to a point where, at a minimum, laboratory results are not questioned."*

60 per cent of the world's population. However, this is not a homogenous region and has the most diverse practice of laboratory medicine. There are of course, peaks of excellence. On the one hand, we have countries like Australia with high-level intellectual capacity and others like Japan and Korea with very good mechanical expertise (automation, robotics, keeping processes simple and streamlined). But then there are the developing countries, where laboratories face credibility issues with stakeholders not trusting the quality of results. Patients travel to other countries for screening and doctors reach out to others for confirmation of results. My plan is to use the expertise of the advanced countries to help the others, so that we get to a point where, at a minimum, laboratory results are not questioned.

5 What are your thoughts around the future of the profession?

The next few years will be challenging for laboratory professionals. To move our profession forward, there are three key areas that we need to focus on.

Firstly, resilience. The advancements in diagnostic equipment mean that we essentially have a number of black boxes in our laboratories, and while they work 99.5 per cent of the time, when they do break down, the manufacturer is called. I believe our laboratory technology specialists really need to be more innovative in the way they deal with problems so they can react quicker. Their patients rely on them to do so.

The second area is Information Technology (IT). This is the backbone of our laboratories and our technologists need this skill to optimise operations and result delivery, particularly critical result reporting.

And finally, patient interaction. My dream is that one day it will be the norm to see laboratory technologists doing ward rounds with the rest of the medical team and providing advice at the point of patient care.

Of course, all this means that university courses need to be revised. What was relevant five years ago is no longer relevant today. Ours needs to be a profession which is empowered to take responsibility for the laboratory result.

We need to be operating at the highest end of our capabilities. When we do that, we will attract good people to the profession.

6 Is the laboratory profession ready for the changes ahead of them?

No, as a profession, we are not really ready right now. For one, we are far more comfortable talking to machines than to doctors and patients. However, younger people are much more adaptable. They like a challenge and a purpose. I'm sure they will be up to the task.

7 What are you reading now or recently that has left an impression on you?

I'm currently reading *The Happiness Of Pursuit.* It's by a young American writer called Chris Guillebeau. I also read his previous book, *The Art Of Non-Conformity. The Happiness of Pursuit* is essentially telling people to reexamine their lives and have some purpose. Pursue something with passion.

8 If you weren't in the field of laboratory medicine, what would you be?

I always wanted to work in medicine, so I'm very fortunate. My back up plan was to join the army and become a pilot.

9 What inspires you and keeps you going?

The people I work with every day both in the laboratory and at the Health Sciences Authority. Both these teams encourage me to do more.

10 What do you do outside your work life?

Every year I participate in around three health missions across the region. I have been part of clinics in places like Indonesia, Thailand and Nepal. Last April, I spent four days in a remote village five hours away from Kathmandu, Nepal. We saw 600 patients in just three days – the whole village came to see us. We did blood pressure screening and saw many common ailments that were easily treatable. I'm also part of a longer-term program in Indonesia where we go back every three months to monitor a group of patients who are being treated for diabetes and hypertension. These missions are my way of spreading some goodwill. I find them very rewarding because the impact is enormous.

My two children, who are also doctors, now in their twenties, joined me on these trips from a very early age and now participate in their own medical missions.

COUNTRY FOCUS

Making malaria visible

A vector-borne disease that puts nearly half the world's population at risk

PROF. KEVIN BAIRD

Prof. Kevin Baird, heads the Eijkman-Oxford Clinical Research Unit (EOCRU) at the Eijkman Institute of Molecular Biology in Jakarta, Indonesia on behalf of the Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, United Kingdom, where he is Professor of Malariology. In this interview with **Dia:gram**, he talks about how more needs to be done to mitigate the threat of malaria in Asia Pacific.

A former Microbiologist with the US Navy Medical Service Corps, Prof. Baird has spent the last four decades focusing on malaria. Yet, he is equally at ease talking about the history that surrounds the majestic Eijkman Institute building and the colonial occupation of Indonesia, his home for the last 30 years, as he is highlighting the vital role research plays in combatting malaria.

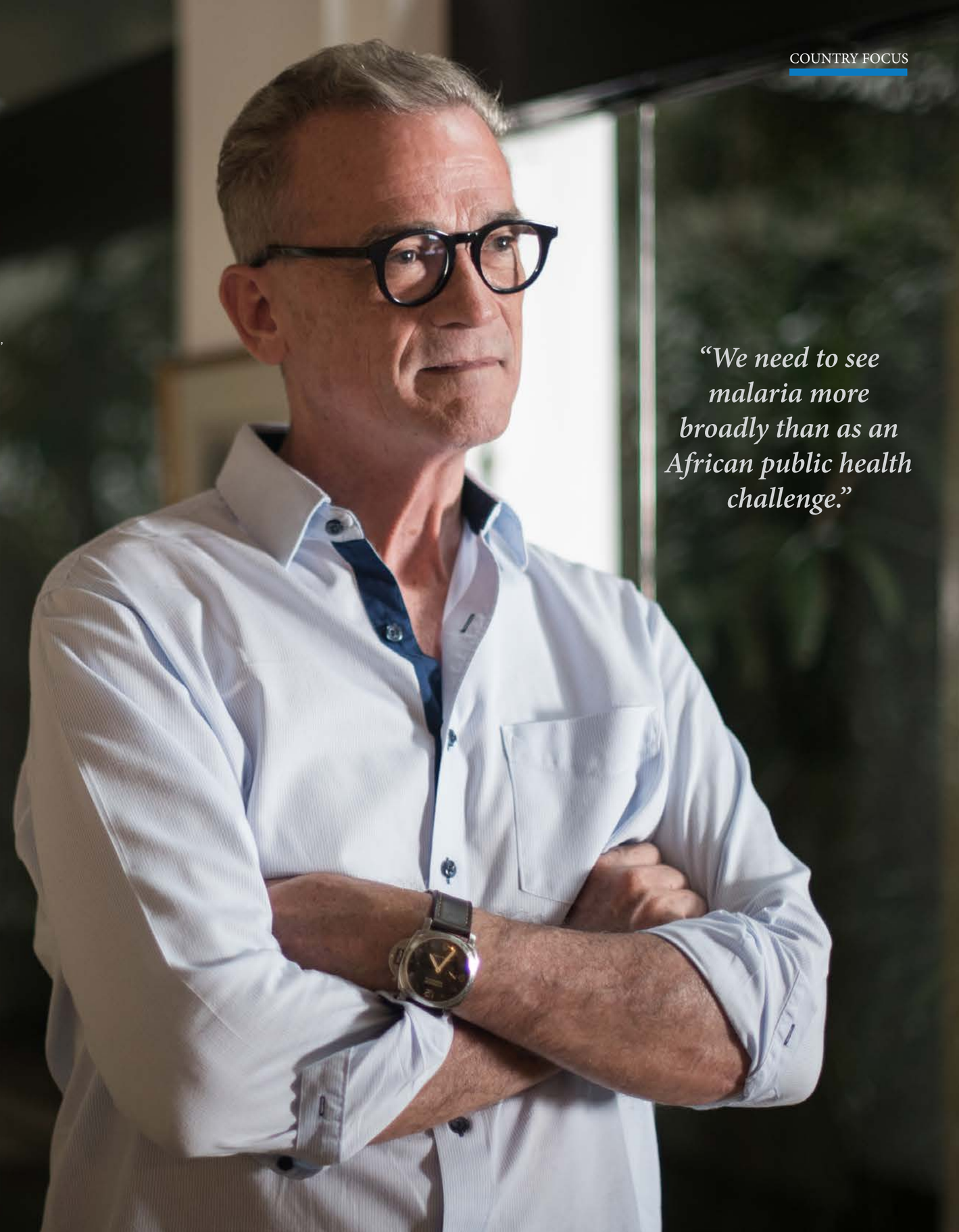
While he fell into malaria research by accident, his beliefs as a self-confessed naturalist made him stay on. "Malaria is a naturalist's disease with its complex lifecycle intimately tied to ecology by anopheline mosquitoes."

The World Health Organisation (WHO) World Malaria Report 2017 estimated there are about 216 million cases of malaria in 91 endemic countries[1].

According to Prof. Baird, there tends to be greater focus on Africa and not enough on Asia Pacific when it comes to malaria. Consequently, research efforts and investments seem to reflect this. For instance, in 2016, an estimated US $2.7 billion was invested in malaria control and elimination efforts globally, with 74 per cent of it going to Africa and 7 per cent towards efforts in South East Asia[1].

Which is why Prof. Baird laments the global generalisation of malaria. "We need to see malaria more broadly than as an African public health challenge. There is no denying that malaria is a serious issue wherever it occurs in the world. But it is also important to understand that malaria in Asia Pacific is different."

"In sub-Saharan Africa, Plasmodium falciparum transmitted by the Anopheles gambiae group of mosquitoes overwhelmingly dominate. However, in Asia, Plasmodium falciparum (P. falciparum) and Plasmodium vivax (P. vivax) occur in nearly equal measures at lower levels of transmission and are transmitted by several dozen important anopheline vector mosquito species," he said. "Vivax malaria is a fundamentally different problem," he explained.



"We need to see malaria more broadly than as an African public health challenge."

"Asian malaria needs its own implementation of malaria control measures because the adoption of solutions that are suited for malaria in Africa are inadequate to address the situation here," he further added.

Prof. Baird said his immediate concern is a resurgence of malaria in Asia, which could unravel the years of progress that has been made since the resurgence that occurred here during the 1980s and 1990s.

Drug resistance threatens most people living with malaria. However, the greatest problem with malaria in Asia is the inadequate access to diagnosis and treatment along with derelict vector control capacities.

"If we believe and act as though drug resistance is the primary problem, we may be missing the chance to address a far more widespread and lethal problem – delayed or absent diagnostic services, poor access to treatment and unchecked vector mosquito populations." To increase the understanding of malaria in Asia, Prof. Baird's research group and partners have spent many years studying the neglected malaria parasite P. vivax.

"Most vivax malaria occurs in Asia and the historic neglect of that species is directly linked to the broader neglect of Asian malaria. I focused my research on vivax malaria, very simply, because I live and work in Asia where this malaria – relatively difficult to diagnose and properly treat – mostly affects the isolated rural poor. Treatment against repeated attacks of vivax malaria requires a drug called primaquine, and that drug is very dangerous to patients with an inherited abnormality called Glucose-6-Phosphate Dehydrogenase deficiency. About eight per cent of Asians in South and Southeast Asia have this abnormality. Giving primaquine blindly and without monitoring is dangerous. Research that gives these patients safe access to the right treatment and prevents unnecessary repeated malaria attacks, will yield immediate and substantial health dividends for the entire region. Access to diagnosis of G6PD deficiency may be the most important technical problem to solve with regard to the Asian malaria problem."

"Our communities would benefit enormously by more vigorous efforts aimed specifically at the Asian malaria problem."

Hopeful that diagnostic tools, advances in treatment and continued research will deliver tremendous value, Prof. Baird said: "With the right approach we can very well change malaria from the major problem it is in Asia today to a relatively minor one. That probably means reducing the burden from hundreds of millions of cases by seven species of parasites to merely hundreds or thousands of cases by just two or three relatively rare species[2]. We don't necessarily require elimination or eradication of all malarias as a benchmark for great success. Our communities would benefit enormously by more vigorous efforts aimed specifically at the singular and diverse Asian malaria problem. We need research and better tools to get us there."

[1]World Health Organisation. (2017). World Malaria Report.
[2]Phuong MS, Lau R, Ralevski F, Boggild AK. (2016). Malar J. 2016 Nov 10;15(1):550. Parasitological correlates of Plasmodium ovale curtisi and Plasmodium ovale wallikeri infection."

Malaria in Asia

Malaria in Asia is a photo-series which documents the many faces of malaria in the Asia Pacific region. The project, in partnership with the Oxford University Clinical Research Unit, Vietnam; the Eijkman-Oxford Clinical Research Unit (EOCRU), Jakarta; and the Wellcome Trust, aims to raise awareness about the impact of malaria in remote communities.

Singapore-based photographer, ***Pearl Gan*** travelled through the Asia Pacific region, including Cambodia, Indonesia, Thailand and Pakistan, to capture the photographs and stories of people and communities impacted by malaria. Her photos have appeared in *The Lancet* and one of her photos from the series won third prize in the Care Together category at the Swiss Malaria Photography Contest in April 2017 and was exhibited in Geneva, Switzerland.

Photo credits: Pearl Gan in association with Oxford University Clinical Research Unit, Vietnam; EOCRU, Jakarta and The Wellcome Trust.

Jama Bee accompanies her mother during a visit to the maternity ward of the Mawker Antenatal Clinic near the Thai-Myanmar border.

She is wearing Tanaka, a herbal paste made from tree bark and known for its cooling and sun protection properties.

COUNTRY FOCUS

In Cambodia, malaria transmission is endemic in 21 out of 25 provinces[1].

A Cambodian forest worker, Mr Vong Phou recovers at home from yet another attack of malaria, this time by both Plasmodium Falciparum and Plasmodium vivax.

[1] *World Health Organisation Western Pacific Region. Factsheet on Malaria in Cambodia.*

A man in Nowshera, Pakistan is going about his daily errands in one of the most ancient methods of transportation - a donkey cart.

A family of migrant workers is resting on a hot afternoon after a morning spent hard at work in the field, on the outskirts of Mae Sot, near the Thai-Myanmar border.

Venerable Ong Kim Leang is a Buddhist monk who lives in a secluded monastery in a malaria endemic area called Samlot in Cambodia. A volunteer malaria worker at a mobile clinic is doing a blood test using the Rapid Diagnostic Test (RDT).

67-year-old Daw Ngwe Tein is babysitting her grandchild, Blu Nay L'Paw. Blu's mother works as a Medic in one of the field clinics of the Shoklo Malaria Research Unit (SMRU) in Mae Sot, Thailand.

A young Cambodian boy is sitting in front of a traditional family house in the rural countryside. The families living here depend on forest and agricultural work as an income source.

Predicting preeclampsia

An innovative approach to accurately detect a woman's risk of preeclampsia

DR. YI-NING SU

Dr. Yi-Ning Su is the Chairman and CEO of Sofiva Genomics Ltd and CEO of Dianthus MFM Clinic, based in Taiwan. He is a leading obstetrician and a clinical geneticist specialising in prenatal diagnosis and genetic testing. A pioneer in the field of maternal-fetal medicine, Dr. Su was the first in Taiwan to publish a paper on the correlation between preeclampsia and a protein called Placental Growth Factor, or PlGF[1]. This led to a new era in preeclampsia screening in Taiwan, safeguarding millions of women by accurately diagnosing their risk. In this interview with **Dia:gram**, Dr. Su discusses an innovative new approach for the triage of women suspected of developing this pregnancy-related complication.

Dr. Yi-Ning Su's interest in maternal health dates back to his days as a PhD student at the National Taiwan University. One of his projects was on preeclampsia, and it left a lasting impression on the young student.

Back then preeclampsia was seen as a condition that, in Dr. Su's words,"remained unsolved". Not much was understood about its causes or screening methods. While the medical community was aware of PlGF, not many knew about the soluble fms-like tyrosine kinase-1 (sFlt-1), which meant doctors weren't on the lookout for altered sFlt-1 levels.

In the absence of any clinical evidence, there was no national program to screen pregnant women for preeclampsia. But Dr. Su's clinical paper showed that the use of PAPP-A, PlGF and Uterine Artery Resistance, could detect preeclampsia in the early trimester.

This became a career defining moment for Dr. Su. "Before this, there was a lot of guesswork. We had no sure shot way of identifying whether or not an expectant mother was showing signs of preeclampsia."

Putting millions of women at risk

A serious pregnancy complication, preeclampsia is characterised by the onset of hypertension and proteinuria (protein in the urine). But detecting it is not easy. Nicknamed "the great imitator", preeclampsia often mimics symptoms of many typical pregnancies, such as nausea, lower back pain, weight gain and swelling of the limbs.

When left undetected or untreated, the condition can lead to serious complications for both mother and baby. Women may suffer from stroke, seizures, organ failure, and in some cases it can lead to death. For babies, complications include slower growth inside the uterus and low birth weight.

Preeclampsia is responsible for around 15 per cent of all premature births[2] and 42 per cent of maternal deaths[3] worldwide. Women with a history of preeclampsia also have an increased risk of dyslipidaemia, hypertension, and cardiovascular and renal disease.

In the context of Taiwan, he says, "There is definitely a rising trend of preeclampsia among women. The risk for preeclampsia increases with age and we're seeing more women having children later in life. So I would say overall about 5 per cent have a high risk of developing preeclampsia and for 2 per cent it will be very severe."

Although the precise pathophysiology of preeclampsia remains unknown, the sFlt-1 and PlGF biomarkers have the potential to offer major advances in the diagnosis and management of this common and potentially life-threatening condition, according to Dr. Su.

Currently, the worldwide medical gold standard for diagnosing preeclampsia is the combination of high blood pressure and proteinuria. Both are considered poor predictors for which women will develop preeclampsia and how the disease will progress[4]. Furthermore, many women with preeclampsia experience no symptoms at all. As a result, healthcare providers spend an estimated US $120 billion every year treating preeclampsia[5].

The value of predictive diagnosis

Discussing the challenges in diagnosing preeclampsia, Dr. Su said, "The clinical presentation of preeclampsia and subsequent clinical course of the disease can vary tremendously, making diagnosis

The role of angiogenic biomarkers to predict preelampsia

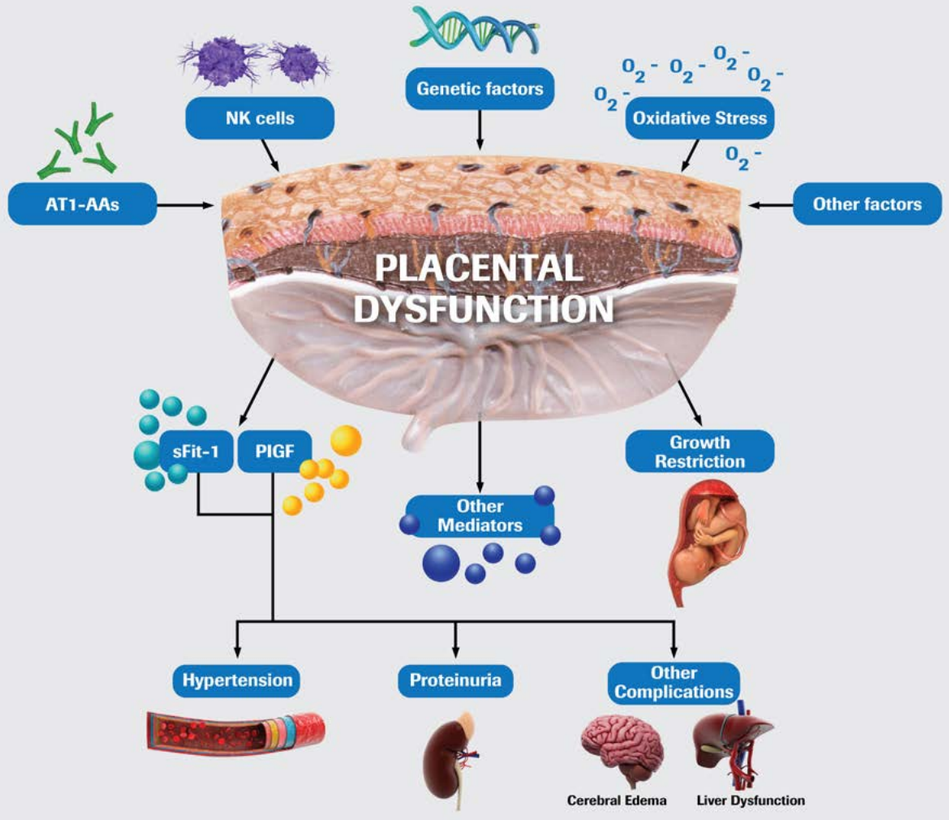


Figure 1: Several factors may cause placental dysfunction, which in turn lead to imbalance of angiogenic factors: SFlt-1 and PlGF.
Reference:
[1]Levine et al. (2004). N Engl J Med.
[2]Wang et al. 2009. Physiology.

"What's important now is deepening scientific understanding among healthcare professionals so that the expectant mother can focus on what really matters – her health and that of her unborn child."

and assessment of disease progression difficult. But now, precise diagnostic tools can help us to predict which pregnant women with suspected preeclampsia will and will not develop the condition with greater certainty than standard diagnostics."

Dr. Su advocates the use of advanced screening tests to accurately detect a woman's risk of preeclampsia by measuring the ratio between two proteins found in the mother's blood – sFlt-1 and PlGF. "Such tests give us the ability to rule in or out the likelihood of preeclampsia. We can be confident that expectant mothers who do not show abnormal levels are unlikely to develop preeclampsia. And for the ones that do, we can take adequate steps to monitor and treat the condition."

This has enormous economic benefits too. A study in the UK showed that the use of the sFlt-1/PlGF preeclampsia test could reduce hospitalisation by 50 per cent[6], and save the National Health Service (NHS) around £28 million every year[6].

With such advancements, Dr. Su concludes, "What's important now is deepening scientific understanding among healthcare professionals so that the expectant mother can focus on what really matters – her health and that of her unborn child."

[1] Su YN, et al. (2001). Obstet Gynecol. Jun;97(6):898-904.
[2] Goldenburg, R.L., Rouse, D.J. (1998). NEJM 339:313-320.
[3] Verlohren, S., et al. (2010). Am J Obstet Gynecol 202 (161): e1-11.
[4] Verlohren, S., Stepan, H., & Dechend, R. (2012). Clin Sci 122(2): 43-52.
[5] Meads, C.A., Cnossen, J.S., Meher, S., et al. (2008). Health Technol Assess. 12(6), iii-iv. Methods of prediction and prevention of pre-eclampsia: systematic reviews of accuracy and effectiveness literature with economic modelling.
[6] Strunz-McKendry et al (2014). 20th COGI World Congress 2014.

Aggressive testing provides no benefit to patients in ER with chest pain

Researchers conclude that CT scans, cardiac stress tests do not help in ruling out heart attack[1].

A new study from researchers at Washington University School of Medicine in St. Louis, USA, suggests that patients who go to the emergency room (ER) with chest pain often receive unnecessary tests to evaluate whether they are having a heart attack - a practice that provides no clinical benefit and adds hundreds of dollars in healthcare costs.

Investigators evaluated data from 1,000 patients treated at nine medical centres across the country, that were a part of the Rule Out Myocardial Ischemia/Infarction by Computer Assisted Tomography (ROMICAT-II) clinical trial. The current study revisited data from that trial, looking for any differences in outcomes for patients who received a clinical evaluation alone (118 patients) compared with those who received a clinical evaluation plus either a CT scan or a stress test (882 patients). In the study, 88 per cent of patients received the additional non-invasive testing.

The study, published in *JAMA Internal Medicine*, showed that in the emergency room, stress testing and CT scans are unnecessary for evaluating chest pain in low-risk and intermediate-risk patients with chest pain. While providing no clear health benefit to emergency room patients, the additional tests also led to patients staying in the hospital longer than may have been necessary, and exposed them to radiation from testing that was not required to diagnose a heart attack.

Doctors diagnose heart attacks largely through clinical evaluation including medical history, blood test measuring troponin and ECG findings. The use of the high sensitivity troponin blood test was found to be more useful to doctors in making accurate diagnosis.

[1]Brown, D., et al. (2017). JAMA Intern Med. Noninvasive Cardiac Testing vs Clinical Evaluation Alone.

Co-testing not superior to HPV testing in detecting cervical cancer

Co-testing with Pap smear and HPV testing does not improve cancer detection compared to HPV testing alone[1].

A recent study, published in the *Journal of the National Cancer Institute*, has demonstrated that using human papillomavirus (HPV) testing alone as a cervical cancer screening option would perform nearly the same as HPV and cytology co-testing.

The study found that HPV testing alone identified more women who were subsequently diagnosed with cervical cancer and pre-cancer as compared with cytology.

Additionally, in cases where HPV testing produced negative results but cytology produced positive results, only 3.5 per cent of cases were found to be pre-cancerous, while 5.9 per cent were found to be cancerous.

Researchers quantified the detection of cervical pre-cancer and cancer by co-testing compared to HPV testing for 1,208,710 women aged 30 years and older who had undergone triennial cervical co-testing since 2003. Screening histories preceding cervical cancer and pre-cancers were examined to assess the relative contribution of the cytology and HPV testing components in identifying cases. Where cytology screening was added, the authors note that it resulted in earlier cancer detection of at most only five cases per million women per year. Thus, the added sensitivity of co-testing versus HPV alone for the detection of treatable cancer affected extremely few women.

Furthermore, the study concluded that there was potential harm associated with excessive screening, including the identification and overtreatment of potentially regressive CIN2 lesions and possible increased risk of negative reproductive outcomes such as preterm delivery.

[1]Schiffman, M., et al. (2017). J Natl Cancer Inst

Predicting early heart disease through genetics

Multi-gene test provides a risk score based on 182 genetic variants[1].

Recent research confirmed that some individuals with early-onset coronary artery disease (EOCAD) carry a high number of common genetic risk variants, similar to what is observed in Mendelian forms of coronary artery disease, such as familial hypercholesterolemia. EOCAD is defined as before age 40 for men and 45 for women. This research found that a risk score based on 182 genetic variants independently associated with coronary artery disease boosted prediction of EOCAD.

The polygenic test predicted an early onset risk for one in every 53 individuals in comparison to one in 256 predicted by familial hypercholesterolemia tests. An 84 per cent elevated risk of EOCAD was associated with just one standard deviation increase in the multi-variant risk score.

With the genetic risk score being mostly independent of known risk factors, this tool could be used to better identify a patient's risk and outline the best management strategy.

Therefore, determination of the polygenic risk component could be included in the diagnostic workup of patients with EOCAD. This could also allow for the genetic screening of relatives. However, further prospective studies are warranted to confirm the benefits of this approach.

[1]Theriault, S., et al. (2018). Circ Genom Precis Med.

Key Events *(January - June 2018)*

January

Arab Health
29 January – 1 February
Dubai, UAE
www.arabhealthonline.com

February

MEDLAB Congress 2018
5 – 8 February
Dubai, UAE
www.medlabme.com

Medical Japan 2018 4th International Medical Expo and Conference
21 – 23 February
Osaka, Japan
www.medical-jpn.jp/en/

13th International Conference of the Asian Clinical Oncology Society (ACOS)
23 – 25 February
Chiang Mai, Thailand
www.acos2018.com

March

2018 Highlights of American Society of Hematology (ASH) in Asia Pacific
9 – 10 March
Bali, Indonesia
www.hematology.org/Highlights/Asia.aspx

American College of Cardiology 2018
10 – 12 March
Orlando, USA
www.accscientificsession.acc.org

27th Annual Conference of the Asian Pacific Association for the Study of the Liver (APASL) 2018
14 – 18 March
New Delhi, India
www.apasl2018.in

Royal College of Obstetricians and Gynaecologists (RCOG) 2018
21 – 24 March
Singapore
www.rcog2018.com

April

MedLab Asia Pacific 2018
2 – 4 April
Singapore
www.medlabasia.com

19th Annual Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis (NATA) Symposium
12 – 13 April
Lisbon, Portugal
www.nataonline.com

8th Congress of the Asia Pacific Initiative on Reproduction (ASPIRE)
12 – 15 April
Taipei, Taiwan
www.aspire2018.com

May

International Society for Laboratory Haematology (ISLH)
10 – 12 May
Brussels, Belgium
www.islh.org

Asia Pacific Society of Cardiology Congress (APSC) 2018
15 – 17 May
Taipei, Taiwan
www.apsc2018.tw

14th Asia Pacific Congress in Maternal Foetal Medicine (APCMFM) 2018
18 – 21 May
Hong Kong
www.obg.cuhk.edu.hk/apcmfm/apcmfm-2018

June

35th International Congress of the International Society of Blood Transfusion (ISBT)
2 – 6 June
Toronto, Canada
www.isbtweb.org/toronto

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