

# Dia:gram

EDITION 2017 Vol 1

## Power to prevent cervical cancer

*The story of the HPV DNA test*

## Surviving preeclampsia

*Why women need to be their own advocate*

## Reinventing blood testing for the digital age

*Unlocking the*  
**Value Of Diagnostics**

*Lance Little*





What's causing it  
**will it get worse**  
*is my diagnosis correct*  
**am I sick**  
which woman is  
at highest risk of  
cervical cancer  
how can i reduce  
my post-operative  
hospitalisation costs  
**Is something  
wrong with me**  
do i have cancer  
Am i at risk

how can we prevent strokes  
**and save millions**  
what diseases do I have  
who should manage  
her heart disease  
*who is the best candidate  
for treatment*  
**did my pap  
miss something**  
is he suffering  
a heart attack  
is he HIV+  
will this patient  
**recover quickly**  
after surgery  
**Is my baby  
in danger**  
is my treatment  
**working**  
**can I  
still get  
pregnant**

*I know I  
am not at risk  
we caught it early  
I know I am ok  
I know the treatment  
will work*  
I am in control  
*my baby is  
fine*

# I KNOW MY RISK

Roche Diagnostics gives you the Power of Knowing that you're using accurate information to make the right decisions today, so your patients can experience a healthier tomorrow.

## THE POWER OF KNOWING

# Note from the editor



Welcome to the inaugural issue of Dia:gram - a bi-annual publication from Roche Diagnostics Asia Pacific that will explore the forces transforming health care across the region.

Our mission is to document the many ways in which diagnostics impacts health care, from detection and risk stratification to monitoring and disease management. We also want to tell the stories of today's innovators and change-makers who are dreaming of a better tomorrow and fighting to make it happen. From the patients who face difficult questions to laboratories that provide simple answers, we aim to share stories of growth, change and innovation.

In this issue of Dia:gram, we speak with Dr. Tom Wright who has spent many years actively studying better ways to prevent cervical cancer. We also speak with Prof. Fang, President of the Chinese Association for Clinical Biochemistry (CACB), chairperson of the November 2016 APFCB Congress and professor at Taiwan's NTU about the future for today's biochemistry students.

Diagnostics is the bedrock of healthcare and there are many stories to be told.

Rachael Bylykbashi  
Editor  
**Dia:gram**

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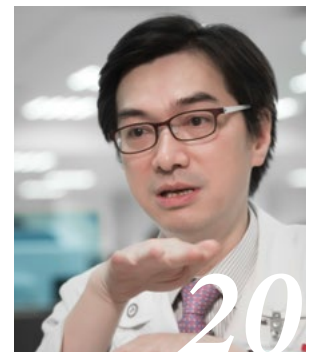


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# Power to prevent cervical cancer

The story of the HPV DNA test and what 47,000 women can tell us about the future of cervical cancer screening.

DR. TOM WRIGHT

*Dr. Thomas C. Wright Jr*, Professor Emeritus of Pathology and Cell Biology at Columbia University is actively involved in the study of the pathogenesis of cervical cancer and novel approaches to cervical cancer prevention. He has been on expert panels for the World Health Organization, National Institutes of Health, American Cancer Society and the Centers for Disease Control and Prevention. In this exclusive interview with **Dia:gram**, Dr. Wright discusses the potential of vaccination and new screening technologies to ultimately eradicate cervical cancer.

When it comes to cervical cancer, there is today an unprecedented opportunity to detect cancer even before it develops and save lives. Yet, cervical cancer remains one of the most common and deadliest cancers affecting women across the world. In less developed regions, cervical cancer is the second most common cancer in women – accounting for 84 per cent of the total cases worldwide in 2012.<sup>1</sup> In the same year, more than 85 per cent of the approximately 270,000 cervical cancer deaths occurred in low- and middle-income countries in Asia<sup>1</sup>. This is especially tragic as the disease tends to strike women in their prime – when their families are still young and when many of them are trying to establish themselves in their careers. So it also has a huge social and economic impact on the community at large.

Dr. Wright who is one of the world's leading experts on cervical cancer, believes that with the vaccines and screening technologies we have today, this disease does not belong on the top

10 list of cancers affecting women. “Even in countries where it is number 10, it should be number 20,” he says.

Why? Two influential discoveries have changed the course of cervical cancer and substantially reduced its burden. The Pap test discovered in 1923 by Dr. George Papanicolaou, made it possible to detect abnormal cells in the cervix. Then, in the 1970s a German scientist made the Nobel-prize winning discovery that the human papillomavirus (HPV) types 16 and 18 play a critical role in the development of many cervical cancers. Today we know HPV 16 and 18 are responsible for over 70 per cent of cervical cancer cases<sup>2</sup>. This discovery paved the way for development of the first vaccine to prevent cervical cancer.

Dr. Wright says that vaccination will be able to eradicate cervical cancer globally only in combination with screening and HPV genotyping. “Even with vaccination, it's unlikely we're going to get everybody vaccinated. So we do need to screen people two or three times during their



*“There is an unprecedented opportunity to detect cancer even before it develops and save lives.”*

lives. We therefore need the most sensitive possible screening in that situation,” he says.

That sensitive screening is now available: In 2011, the United States’ Food and Drug Administration (FDA) approved the first HPV DNA Test that allows HPV 16 and HPV 18 genotyping concurrently<sup>3</sup>. The approval was based on the **ATHENA trial**<sup>4</sup>, a multicenter, prospective study supported by Roche, which enrolled over 47,000 women above 21 years of age undergoing routine cervical cancer screening. Results from the ATHENA trial revealed that one in 10 women who tested positive for HPV 16/18 had high-grade cervical disease that was missed by the Pap test and that after 3 years of follow-up one in 4 women with HPV 16 had developed high-grade cervical disease<sup>5</sup>. The trial evaluated the performance of the HPV DNA test in multiple clinical situations including ASC-US (atypical squamous cells of undetermined significance) triage and co-testing. The trial showed that the HPV DNA test increases the detection

rate to about 93 to 95 per cent of high-grade precursors<sup>3</sup>. Cervical cancer screening guidelines in the United States now recommend HPV co-testing to women aged 30 and above<sup>6</sup>.

For many countries in the world today, the Pap test is still the primary screening tool in detection of cervical cancer and continues to be valuable in the fight against cervical cancer. But it is not without its limitations. Many studies have confirmed that the sensitivity of the Pap test is rather poor at about 52 per cent<sup>7</sup>. It is a subjective test and it can sometimes provide inconclusive results that may lead to unnecessary interventions and stress for the woman.

In contrast, HPV testing and genotyping provides a higher level of objectivity and specificity<sup>8</sup>. “HPV primary screening is now going to be the way Australia screens. The Netherlands will also be implementing HPV primary screening. The UK has recently decided based on the results of a large pilot study to implement

HPV primary screening. And there are a number of other countries which are getting ready to do it. In Italy, nine regions have adopted HPV primary screening,” Dr. Wright says.

In South East Asia, a pilot co-testing program run out of Singapore General Hospital has shown that cervical cancer can be tested for with greater accuracy by combining Pap smear (cytology) and a validated HPV DNA test<sup>9</sup>. The program aimed to improve the detection rate of high grade cervical disease (CIN3+) and reduce the number of screening tests during a woman’s lifetime.

Dr. Wright first started talking about HPV in 1995, particularly about the clarity it could bring when Pap results were inconclusive. “No one wanted to do HPV in ’95. We got it accepted through an incremental approach,” he adds. Dr. Wright’s decision to become a gynaecologic pathologist was in part fueled by the discovery of the HPV tumor virus. “HPV was becoming important at that point. The first HPV

assay was developed, the pre-hybrid capture version, and we started running clinic trials, and I've been working on HPV ever since," he says.

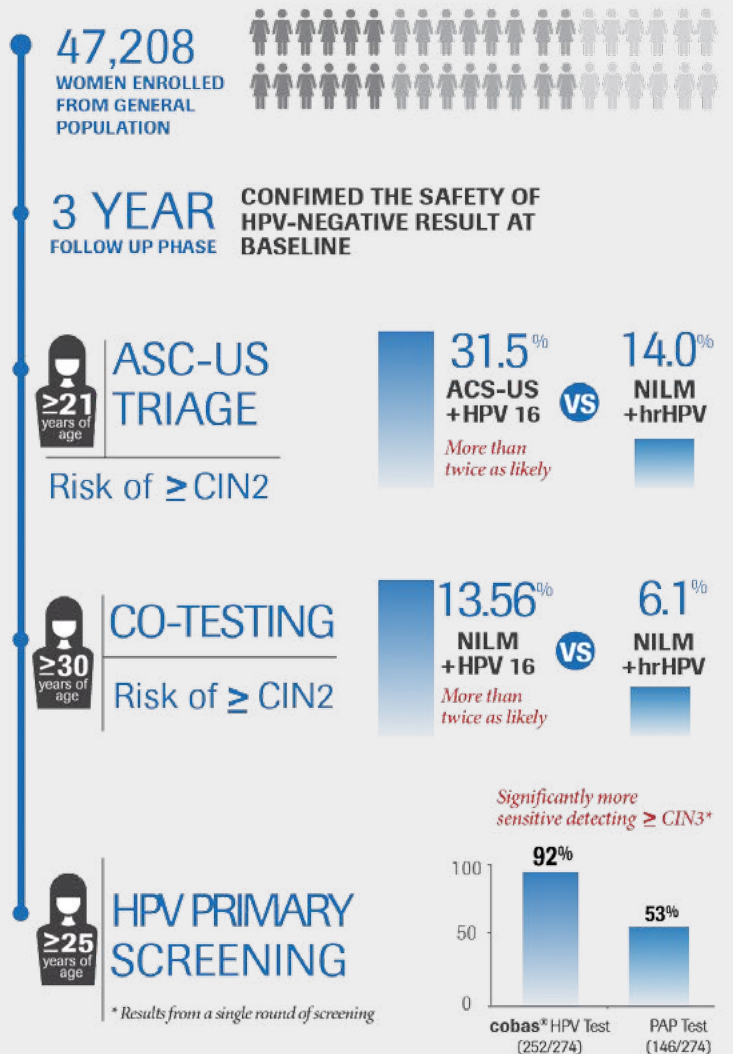
Since the early 2000s, Dr. Wright has been working to bring together societies and organizations to push the model of consensus guidelines for the screening and management of cervical diseases. This is an important part of his legacy as is the work he has put in to developing cervical cancer screening programs.

"I've been working for almost 20 years in Sub-Saharan Africa, trying to develop screen and treat approaches for people who don't have access to what we consider routine cervical cancer screening. The next step is to implement what we've learned, in terms of vaccination and HPV testing, in order to be able to prevent cervical cancer where the burden is greatest."

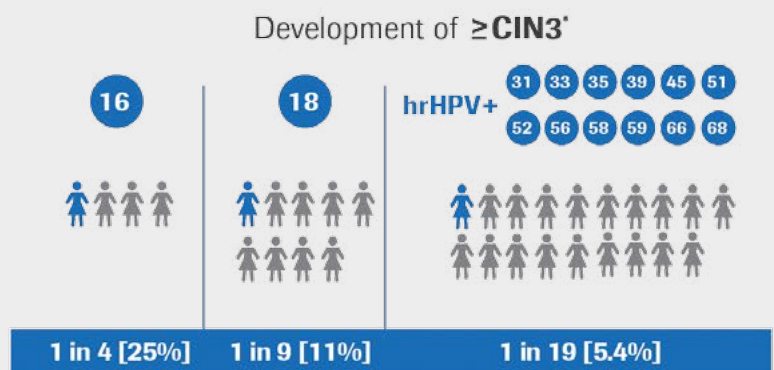
Dr. Wright says one of the most important tasks is to get cervical cancer screening on national healthcare agendas: "Even if globally we were able to get high vaccination coverage of girls, you've got a whole population of women who are older than the vaccination age who will need screening. Vaccination is great for preventing cancer 20 or 30 years from now, but you don't want to tell a whole generation of women that they don't have prevention."

<sup>1</sup>Ferlay, J., et al. (2014). GLOBOCAN  
<sup>2</sup>Bosch, F.X., et al. (2008). *Vaccine* 43:S52-60  
<sup>3</sup><https://www.hpv16and18.com/hcp/HPV-Test-FDA-Approval-Final.html>. Last accessed 10 October 2016  
<sup>4</sup><https://www.hpv16and18.com/hcp/athena-hpv-clinical-trial/background-study-design.html>. Last accessed 10 October 2016  
<sup>5</sup>Wright TC Jr, et al. Primary cervical cancer screening with human papillomavirus: End of study results from the ATHENA study using HPV as the first-line screening test. *Gynecol Oncol.* 136 (2015) 189-197  
<sup>6</sup>The American College of Obstetricians and Gynecologists. (2012). ACOG Practice Bulletin. Clinical Management Guidelines for Obstetrician-Gynecologists: Screening for Cervical Cancer  
<sup>7</sup>Fahey, M.T., Irwig, L., Macaskill, P. (1995). *AM J Epidemiol* 141(7):680-689  
<sup>8</sup>Castle, P.E., et al. (2011). *Lancet Oncol* 12(9):880-90  
<sup>9</sup>Tay, SK. Presentation at AOGIN, Singapore. 2016

# The Largest Prospective Study To Evaluate HPV & Pap Screening Strategies



## HPV RISK STRATIFICATION within 3 years



Ref: 1. Stoler MH, et al. High-Risk Human Papillomavirus Testing in Women With ASC-US Cytology. *135 (2011) 468-475.* 2. Wright TC Jr, et al. Evaluation of HPV-16 and HPV-18 Genotyping for Triage of Women With High-Risk HPV+ Cytology-Negative Results. *136 (2011) 578-586.* 3. Wright TC Jr, et al. Primary cervical cancer screening with human papillomavirus: End of study results from the ATHENA study using HPV as the first-line screening test. *Gynecol Oncol.* 136 (2015) 189-197.

# When every minute counts

Saving time to diagnose acute myocardial infarction with troponin T high-sensitivity test

PROF. CHRISTIAN MÜLLER

## **Professor Christian Müller**

of the University Hospital of Basel, Switzerland, is actively involved in cardiovascular biomarker research and is the Principal Investigator of the TRAPID-AMI study. He is a professor at the Swiss National Science foundation, won several awards for his achievements in cardiology research and is an editor of the European Heart Journal as well as the Journal of the American College of Cardiology.



Acute myocardial infarction (AMI) is a condition where minutes count, with delays to treatment as short as half an hour having a measurable effect on a patient's chance of long-term survival. The TRAPID-AMI (High sensitivity cardiac troponin T assay for RAPID rule-out of Acute Myocardial Infarction) study<sup>1</sup> was published in the *Annals of Emergency Medicine* earlier this year, confirming a novel approach for a more rapid diagnosis of heart attack in patients with acute chest pain. The strategy is based on the cardiac troponin T high-sensitivity test and reduces the observation time needed to rule-in or rule-out a heart attack from 3-6 hours to just 1 hour.

The European Society of Cardiology adopted this accelerated diagnostic concept at their annual meeting held in London (UK) in August 2015. Their new clinical practice guidelines (2015 ESC NSTEMI) now support the 1-hour diagnostic algorithm with high-sensitive troponin testing validated in the TRAPID-AMI study<sup>2</sup> and other studies such as APACE<sup>3</sup>.

Professor Christian Müller of the University Hospital of Basel, Switzerland, Principal Investigator of TRAPID-AMI study, gave us insights into how patients and physicians in the emergency department (ED) will benefit.

*“This is of critical help in the allocation of resources in emergency departments.”*



**How do the results of the TRAPID-AMI study have the potential to change clinical practice?**

With conventional assays, guidelines recommend measurements at presentation and after six hours. So everybody would have to wait for six hours in the ED for the second measurement to make sure the patient was not having an AMI. With the use of high-sensitivity assays, the guidelines of the European Society of Cardiology recommend that the second measurement can be done after three hours.

But that still means we have to wait for three hours to do the second measurement, and only then can we be sure whether or not the patient has had an AMI. The beauty of the one-hour algorithm is that we can accelerate our diagnostic procedure and in 75% of patients obtain the same information after one hour. This tells us whether or not the patient can be ruled out for AMI or has a very high likelihood of having AMI.

**Who will benefit from the results of this study? Patients, emergency departments, cardiologists?**

Ultimately, I strongly hope everybody. It's a great benefit for the patient, we think using the algorithm in clinical practice will allow improvement in patient care. It will be of huge operational benefit in the ED. If a patient with a benign, non-cardiac disease occupies a room in the ED

for six hours then that room cannot be used for other patients with acute life-threatening disorders. And of course we cardiologists will have a substantial benefit because the algorithm really makes best use of the diagnostic information provided by the cardiac troponin assay. However, while the algorithm does a fantastic job, it must always be applied in conjunction with the proper clinical assessment including a 12-lead electrocardiogram (ECG).

*“The beauty of the one-hour algorithm is that we can accelerate our diagnostic procedure.”*

**Could the introduction of this one-hour algorithm to clinical practice help reduce overcrowding in the emergency department?**

Overcrowding is a major issue in many EDs all over the world. I really think that the application of this one-hour algorithm will help to reduce overcrowding because it reduces the time to diagnosis, particularly for those patients who are at extremely low risk and do not have an acute life-threatening disorder but a benign disorder.

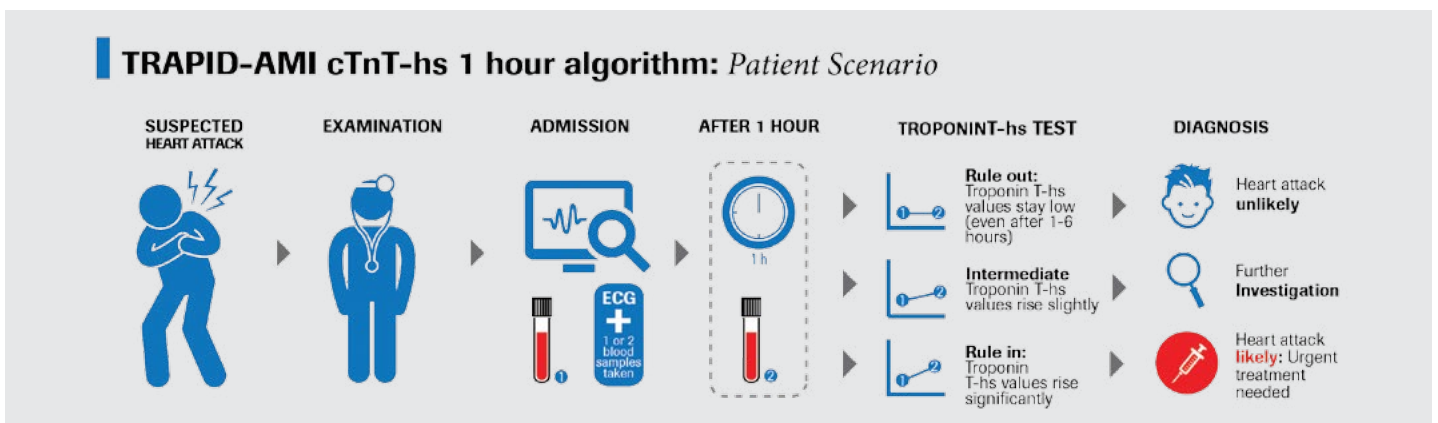
**At the hospital level, could we anticipate any financial impact associated with the application of the TRAPID-AMI one-hour algorithm?**

It is extremely likely that the clinical application of the one-hour algorithm will be associated with a substantial reduction in treatment cost because the most important driver of treatment cost in the ED is the duration of stay. ■

<sup>1</sup>Mueller, C., et al. (2015). *Ann Emerg Med* 68(1): 76-87.e4

<sup>2</sup>Roffi, M., et al. (2016). *Eur Heart J* 37(3):267-315

<sup>3</sup>Reichlin, T., et al. (2015). *CMAJ* 187(8):E243-E252



Ref: Mueller, C., et al. (2015). *Ann Emerg Med* 68(1): 76-87.e4



# Surviving preeclampsia

Why women need to be their own advocate

BRIDGIT O'DONOVAN

**Dia:gram** catches up with *Bridgit O'Donovan*, a mother of two, who shares what it's like to survive eclampsia. Her experience embodies the urgent, unmet need for better predictive diagnostics in preeclampsia to save lives of both mothers and their unborn babies.



**B**ridgit O'Donovan woke up early on a Sunday with a feeling that something was very wrong. She was almost 30 weeks pregnant. She woke her husband up and tried to tell him she was feeling unwell. But the words came out garbled. "I wasn't making any sense. I lost my eyesight. I remember Alan saying, 'I'm over here' and I said, 'I can't see you.' My daughter came into the room calling for me and I couldn't see her either." Her husband drove her to the hospital where the doctors found her blood pressure had ratcheted up to 171/106: she was having a seizure. Bridgit was diagnosed with eclampsia and rushed in for an emergency C-section, which saved her life.

Preeclampsia is a complex and multisystem pregnancy disorder that causes 15 per cent of all premature births<sup>1</sup> and 42 per cent of all maternal deaths worldwide<sup>2</sup>. The condition involves reduced blood flow from the placenta and inadequate oxygen and nutrients to the foetus which, if left undetected, can lead to serious health consequences for both mother

and baby. In developing countries, the disease kills nearly 70,000 women each year<sup>3</sup>.

"I was lucky that we got to the hospital when we did because they stabilised me quickly." Bridgit lives in Singapore, a highly developed country well known for its healthcare infrastructure. Bridgit's undetected preeclampsia progressed rapidly to eclampsia, a rare complication marked by seizures and sometimes, a fatal coma. An MRI showed no brain damage from the seizure. Her son, Leo, who was born premature and a little bigger than her palm, was also fortunate. "He looked like a kitten, his skin was translucent and his eyes had yet to form pigments but he was just a perfect, tiny person," Bridgit said.

Preeclampsia is notoriously difficult to diagnose. Many of the early symptoms resemble the normal effects of pregnancy on the body like nausea, vomiting and rapid weight gain. This is why preeclampsia has earned the nickname, 'the great

imitator.' Other symptoms include severe headaches, abdominal pain and vision changes. Standard diagnosis involves detecting high blood pressure after 20 weeks and protein in the urine<sup>4</sup>. Approximately 80 per cent of pregnant women with signs of preeclampsia do not develop the condition<sup>5</sup>. So physicians face the dilemma of unnecessarily hospitalising a woman and causing stress and alarm. Left undetected, preeclampsia causes complications such as haemorrhaging, multiple organ failure and stroke.

As a healthy and active 36-year-old, Bridgit noticed that her second pregnancy seemed nothing like her first. "My first was so normal I didn't even have morning sickness." But with the second, she just didn't feel well. At 14 weeks, she was diagnosed with placental notches and Intrauterine Growth Restriction (IUGR). This means the foetus is behind its gestational age in terms of size and development.

Bridgit's doctor prescribed mini aspirins and told her the goal was to get to 26 weeks for a viable pregnancy. She had weekly check-ups to monitor that the baby was growing normally. "At every check-up, there was nothing to suggest any serious issues. My blood pressure was higher than normal at 140/90. My doctor said it was stable and I didn't need to worry," she added.

Bridgit was working full-time as a communications professional. She had headaches but they'd come and go. Just before week 29, Bridgit stopped working as she felt too tired and had experienced a sudden pain in her diaphragm while pushing her daughter's stroller to school. In retrospect, there were many symptoms that she attributed to normal pregnancy discomfort in Singapore's muggy heat. She regrets that she wasn't more confident in her own instinct that things weren't quite right: "I was embarrassed to ask too many questions. We rely on our doctors to tell us when something is wrong but they only know when you tell them. If I had asked, what should I look out for given that I have an IUGR baby? Then, my doctor could have said, 'If you have any of these symptoms, come straight to the clinic.' Nurses have a role to play too. When I called and said I had a headache, they should have said, she has an IUGR baby and she should come to the clinic and check it out."

These sort of missed signals underline the urgent need to expand current diagnostic criteria and reduce the number of preeclampsia-related deaths. Over the last two decades, scientists have identified two new biomarkers with the potential to transform how the disease is detected, monitored and treated. Based on the discovery, Roche has developed a new preeclampsia test that measures

a ratio of two proteins found in the mother's blood. The test can predict which pregnant women with suspected preeclampsia will and will not develop the condition, with greater certainty than standard diagnostics<sup>5</sup>. It gives doctors the confidence to send healthy women home safely and to prioritise treatment for women who are more likely to develop the condition.

Bridgit wishes that her risk had been detected earlier and that she had been able to avoid a major traumatic event



***“There is an urgent need to expand current diagnostic criteria and reduce the number of preeclampsia-related deaths.”***

in her life. "People say that premie babies will catch up but I know that Leo will always be on the smaller side. He was born with a hole in his heart that solved itself. But he still needs a lot of care and a kind of high-intensity parenting," she said.

Bridgit recently celebrated her 40th birthday but the frightening experience of eclampsia stays with her. "I'm still quite emotional about it. It took me a while to share the joy of a normal pregnancy with my friends who got pregnant around the same time as I did. I was grieving for the loss of my pregnancy and the fact that my child is not 100% healthy." Bridgit stopped working for about two years to focus on building back her strength and caring for Leo. Seeing her son get better, stronger and grow into

a talkative three-year-old has been a healing experience, she said.

Bridgit is also channeling her trauma into creating more awareness for preeclampsia. When she reads an interesting article about the disease, she shares it through her Facebook and Twitter accounts. "Many pregnant women and their partners are told not to be paranoid. I want women to feel

powerful in knowing their bodies and asking questions when something feels wrong." She shared that women have reached out to her and discussed what to ask their doctors and what to look out for. "This is great - because being pregnant is serious business. Enjoy the baby shower but do your homework and be prepared to be your own advocate," she said. ■

<sup>1</sup>Goldenburg, R.L., Rouse, D.J. (1998). *NEJM* 339:313-320.

<sup>2</sup>Verlohren, S., et al. (2010). *Am J Obstet Gynecol* 202(161):e1-11.3.

<sup>3</sup><http://www.who.int/mediacentre/news/releases/rel-lease44/en/>. Last accessed in September 2016.

<sup>4</sup>Wagner, L.K. (2004). *Am Fam Physician* 70(12):2317-2324.

<sup>5</sup>Zeisler, H., et al. (2016). *NEJM* 374:13-22.



*“Today, students are no longer satisfied with just a graduate degree and the majority go on to pursue post graduate studies.”*

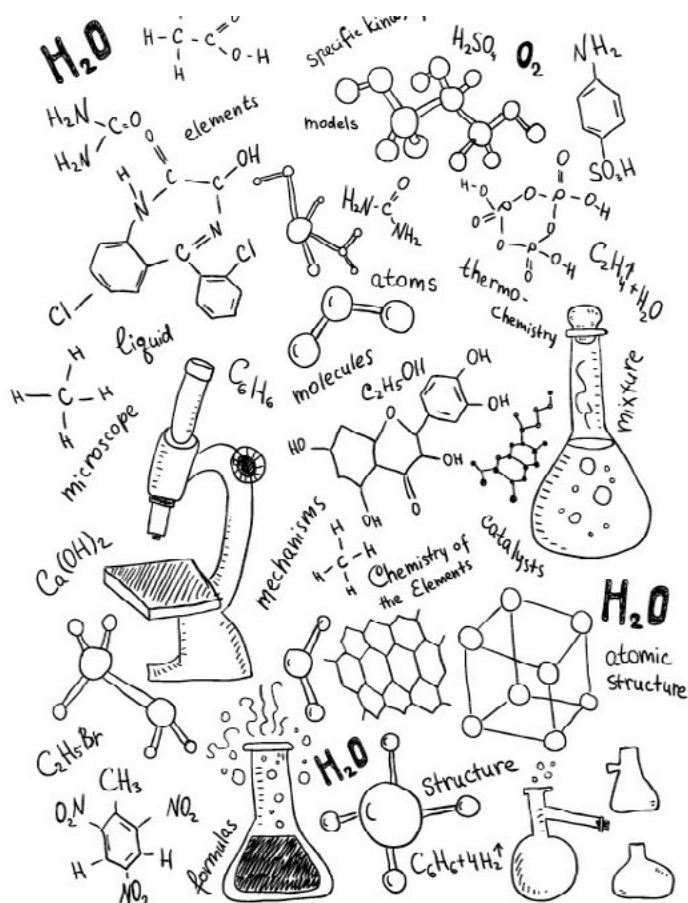
## Lessons from the lecture hall

Teacher, mentor and master chemist, Prof. Fang talks about the evolution of laboratory medicine in Taiwan.

PROF. WOEI-HORNG FANG

When his former thesis advisor, Paul Modrich won the Nobel Prize for Chemistry in 2015, **Prof. Woei-Horng Fang** was invited to the ceremony. Prof. Fang, who is the associate professor at the Department of Clinical Laboratory Sciences and Medical Biotechnology, College of Medicine, National Taiwan University (NTU), was a PhD student in Dr. Modrich's laboratory at Duke University in North Carolina in the early 1990s. He recalled exciting and grueling times as a 34-year-old completing a thesis on DNA mismatch repair. “I was working 70-hour weeks: 10 hours a day, seven days a week. It was amazing to have seen ground-breaking research on familial colorectal cancer and see the impact on medicine,” he said.

Today, Prof. Fang guides both undergraduate and graduate students at NTU in molecular biology and clinical chemistry research and practice. “It is fantastic when you have students who are talented and interested in research. I also experienced the new generation of students who are very distracted by their devices. My approach is to treat them as adults and I'll mention it once at the beginning of class that they need to exercise self-control. My job is to figure out the experiments to engage their interest,” he said.



In many ways, Prof. Fang's professional journey is intertwined with the evolution of laboratory medicine as an educational discipline in Taiwan. Standing in the laboratory where he graduated with a Master's degree in Biochemistry nearly 30 years ago, Prof. Fang talked to **Dia:gram** about the changes he has seen over the years.

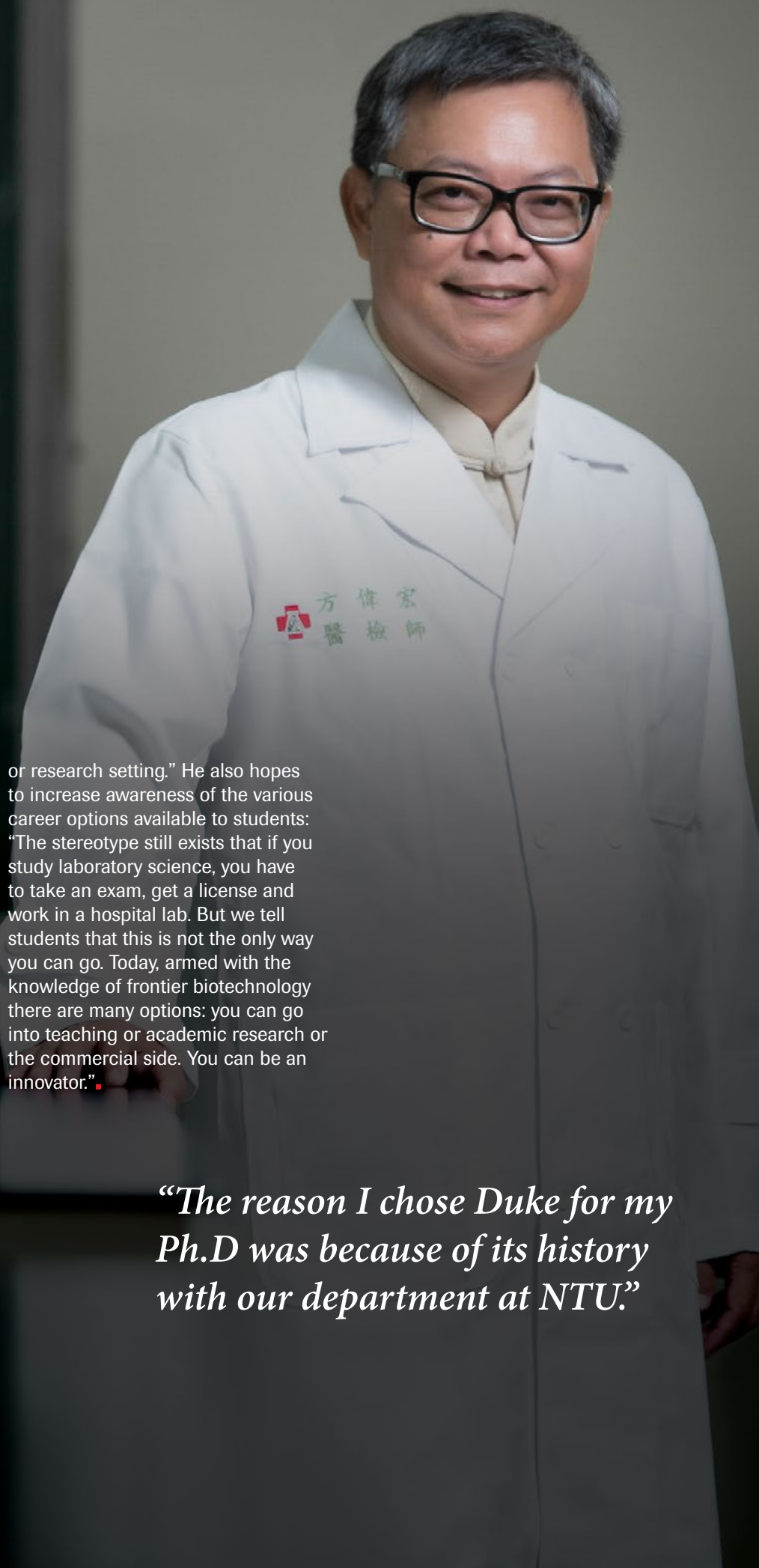
It was in 1950 that the National Taiwan University Hospital first established a central laboratory to provide clinical diagnostics support for the hospital. "Those days, the lab personnel were high school graduates, who after a brief period as trainees, took on basic lab work," he said. This changed after the hospital invited Dr. Davison, the Dean of Duke University's medical school as a visiting consultant. As part of a complete reform of medical education in Taiwan, Dr. Davison recommended that NTU create a separate School of Medical Technology to train students in clinical laboratory science.

Dr. Davison also helped establish a 'Duke University Fellowship Program' to enable Taiwanese medical technology students to pursue advanced studies in the United States. Taiwan's ministry of education also instituted grants to support systematic training for advanced research. "The reason I chose Duke for my PhD was because of its history with our department at NTU," Prof. Fang said.

When Prof. Fang returned to Taiwan after his PhD, he went back to NTU to teach students. He said that in the early years, the School of Medical Technology was not very successful. "They enrolled maybe 10 students per year in the first few years. Being a doctor or surgeon was very prestigious and when people heard the term 'medical technology' they thought the degree would train them to become doctors. Most of the graduates would go to the US or Japan to study medicine or dentistry. Very few of the original graduates actually stayed in laboratory science."

Today, students are no longer satisfied with just a graduate degree and majority go on to pursue postgraduate studies. The department started offering a Master's program in 1997 and established a PhD program in 2002. These developments kept pace with technological advances such as molecular diagnostics, nuclear assays, real-time PCR and next generation sequencing. "Every time a new technology became practical, we quickly adopted it into our teaching materials." In recognition of these developments, the department changed its name to include biotechnology in 2005. "We felt that medical technology was an obsolete term and the name we have now is more reflective of the training we provide to our students."

Graduates of the program pursue teaching, research or work in hospital labs. "Today, a very high percentage of our graduates choose to go back to clinical laboratory science. In



this hospital itself we have several graduates from our department. Our PhD students go on to become professors at other universities,” Prof. Fang said.

The department too has grown from less than 10 junior faculty to 15 full-time faculty today. “When I was an undergraduate student here, the Department was short of faculty and dominated by doctors who had done some lab work. Few people had a Master’s degree and almost nobody had a PhD. Now, all of our faculty hold PhDs and across different disciplines like biochemistry, microbiology, tumor biology and haematology,” Prof. Fang said.

Prof. Fang has recently been re-elected for the second term as the President of the Chinese Association for Clinical Biochemistry in Taiwan and hopes to improve collaborative efforts across biomedical disciplines. “There is always more need for better diagnostics within a hospital

or research setting.” He also hopes to increase awareness of the various career options available to students: “The stereotype still exists that if you study laboratory science, you have to take an exam, get a license and work in a hospital lab. But we tell students that this is not the only way you can go. Today, armed with the knowledge of frontier biotechnology there are many options: you can go into teaching or academic research or the commercial side. You can be an innovator.”

*“The reason I chose Duke for my Ph.D was because of its history with our department at NTU.”*



## Ten questions with Lance Little

Lance Little has served as Managing Director of Roche Diagnostics Asia Pacific since 2012. Prior to this, he was the Managing Director of a number of Roche Diagnostics affiliates, including India, Thailand and New Zealand. In this wide-ranging interview with **Dia:gram**, Lance shares his mission to promote the true value of diagnostics, his leadership philosophy and his daily inspiration.



## **1** *What keeps you in this line of work?*

Through all the roles I've had at Roche, I discovered that it's the passion for bringing people together, where they feel empowered to make a difference. I joined Roche in 1995 as an Application Specialist supporting Boehringer Mannheim's clinical chemistry portfolio, before moving into sales and marketing roles. I already had 10 years of experience working in both public and private labs in New Zealand. My passion at that point was a technical one. I loved having the ability to complete an installation and see how it transformed the workflows and the environment for the better. Right now, it's really about building teams that people love being part of. It's also about having the ability to create an environment that delivers benefits to patients, clinicians and our customers – that is what keeps me going.

## **2** *What role can diagnostics play in designing for better patient experience and outcomes?*

Diagnostics has a central role to play in transforming patient experience and outcomes. I see diagnostics as an enabler, helping healthcare professionals provide truly personalised care for their patients. Across Asia Pacific, we have worked with many different types of laboratories, from new green-field labs to well established labs to improve quality, speed and processes. A well-run laboratory cuts waiting time for patients as well as the anxiety associated with not knowing a test result. Effective screening diagnostics programs can have a dramatic impact on the health of entire populations through early detection and prevention.

## **3** *What healthcare challenges does the region face and how can diagnostics help?*

One fundamental challenge is that even though diagnostics influences over 60 per cent of clinical decision

making, it receives approximately 2% of healthcare funding. Depending on the country and its stage of development, you have a range of challenges. The emerging markets are striving to achieve a basic level of healthcare for the entire population. Once they've achieved that successfully, there is the flip side of managing the costs associated with care. In emerging markets, diagnostics can shape best practice, particularly because healthcare systems are still being established. In the developed space, smart use of diagnostics can have a profound impact on reducing downstream costs.

*“Labs now realise that they need to be much more proactive in the fight for funds. It's important to tell their story, show the evidence and advocate for the value they hold.”*

## **4** *What hurdles do you face in communicating the value of diagnostics in healthcare?*

Diagnostics provides answers and clarifies specific health-related questions that enable clinicians and individuals to act and take control of their own health. With advancements in science and technology, diagnostics is no longer just a stepping stone to treatment. It is about intervention. It is about better disease management and better patient care. It is about preventing disease from getting worse or detecting it before it even starts. The first hurdle is articulating the value of complications that have been prevented as a result of diagnostic testing – the case of

diabetes that is detected and well managed; the heart attack detected within the hour; the cervical cancer caught while it is still pre-cancerous – these interventions save lives and cut healthcare costs. But that's only the first hurdle. The second hurdle is taking that into a healthcare environment where people are prepared to bet long-term and put a little more money into diagnostics. The modeling shows that they will save money down the road this way. But it's difficult, frankly, to find the people and the environment that will take that long-term bet.

## **5** *How could laboratories take the lead in driving conversation around the value of diagnostics?*

Laboratories are still seen as a support function. But labs now realise that they need to be much more proactive in the fight for funds. It's important to tell their story, show the evidence and advocate for the value they hold within the healthcare environment. I think labs need to collaborate more and become a stronger voice. One of the most visible groups in the region is IVD Australia. They've been relatively successful in telling their story, being involved in policy-making and leading discussions on the value of diagnostics.

## **6** *What impact has the opening of the Centre of Excellence in Singapore had on the region?*

I saw within our organization a significant variation in the skill levels of specific functions. For example, an engineer in one country may be much more developed than an engineer in another country, for all sorts of reasons. This is also the case when it came to marketers and salespeople and it has a lot to do with the maturity of the industries in those countries, the different operating environments and business models. Through the Centre of Excellence, we want to lift standards in a consistent manner. There's no cut-down version for Asia and we're training everyone

to a global standard. We're also imparting a lot of knowledge beyond the analyser, and therefore our people add tremendous value to the lab. We trained over 400 salespeople last year. We also completed 186 technical trainings in Singapore apart from the training that's happening in other countries.

We're also working with various partners, including industry bodies such as APFCB, who are trying to lift standards of laboratory practice. We work with them in running quality programs and Lean Six Sigma programs to improve standards.

### **7 What are the biggest lessons you've learned about doing business in the region?**

I've reflected on these lessons a lot. You have the same product that is used the same way. But the journey from Roche to the customer lab is unique in every country. It is driven by the fact that people in different countries will make decisions differently depending on their environment. Drivers for decision-making are not only scientific or commercial, but also influenced by culture, and all our cultures in Asia Pacific are quite different.

So, for me, the lesson is to seek and understand the culture and why people make the decisions they make. If I was sending a manager to a new country tomorrow, my first instruction is to understand the cultural drivers, as this would be one of the core pillars by

which people make decisions. Learning and seeking to understand, being open minded – these are the big lessons I've learned.

### **8 If there is one leadership lesson you could share, what would it be?**

If it comes down to one thing, it might sound clichéd, but I believe it's about building trust. Without trust, people will not truly embrace the direction you

***“Diagnostics is the backbone of healthcare providing value beyond just diagnosis. It is an enabler, helping healthcare professionals provide the best guidance for patients.”***

want to take the team. The ultimate question to ask is “does the team trust enough to follow the leadership with complete commitment, and equally does the leadership trust the team to

execute and bring their creativity to the table.” The role of a leader within our organisation in Asia Pacific is essentially to create the direction, smooth the pathway, then allow our teams to execute. This is where I believe authenticity is critical. People may not always agree with you or like your decisions, but if you are consistent and truly authentic, then the teams have a reason to get behind you as a leader.

### **9 What are you reading right now?**

Right now I am reading two books. One called "Shift" which is a book about the historic turnaround that Carlos Ghosn achieved with Nissan in Japan. The other is the classic work from the Roman philosopher Seneca, "Letters from a Stoic". Both are great reads and challenge my thinking which I think is valuable.

### **10 What inspires you at work and outside of work?**

The common theme that threads through both arenas is a desire to be valuable to others. At work, I am inspired when I can bring people together as a team and watch them grow through that experience. At home, I want to contribute to the journeys that my family members are on. Being able to contribute positively to all these people in my life inspires and motivates me every day. ■



# Reinventing blood testing for the digital age

How one doctor, his co-workers and even his family are set to transform blood testing for patients and the medical profession alike.

DR. DAVID ZAHNISER

*Dr. David Zahniser PhD* is a pioneering medical scientist best known for his work developing new ways of collecting samples and reading slides automatically for Pap smears. But that's about to change. In the works since 2004, Bloodhound technology is his groundbreaking new innovation and is at the core of the new cobas m 511 integrated haematology solution. The technology is set to revolutionise haematology and blood testing, not only for patients, but for medical professionals who can now get faster results and state of the art images to work with. Dr. Zahniser speaks about Bloodhound, what's inspired his journey and how his children have been integral in the development of this pioneering technology.



**B**loodhound is the catchy name for the technological brainchild of Dr. David Zahniser, which is about to change the world of hematology. Dr. Zahniser always had an enthusiasm for physics and technology and started his career in medical science at the Massachusetts Institute of Technology (MIT). At the end of his senior year at the school, he started using computer imaging systems to measure cells at a time when no one else was doing it. “We were looking at cancer cells at the time, and I got excited about applying my technological knowledge to something that would be good for biology and medicine,” he explains. Dr. Zahniser admits that MIT was challenging and when he was invited to finish his PhD in the Netherlands, he jumped at the chance. It was when he returned to the United States to work as a research professor at Tufts Medical School in Boston that he first started looking into how imaging could help in the field of hematology.

In 1989 he founded a company called Cytoc, where he developed automated ways to prepare and analyse pap tests. When this company grew too big, he left and founded a consulting firm and started working on automated reading for blood cells for malaria.

“It was in 2004 when two doctors from Brigham and Women’s Hospital approached me, telling me that they had an idea of how to do a complete blood count with a single drop of blood. They asked if I could help them to make it reality. I took on the project in my basement and set up the technology.”

“I pricked my finger dozens and dozens of times to get that little drop of blood. Problem was, I just couldn’t get it working and reproduce the pictures they showed me from an experiment they had done,” Dr. Zahniser admits.

“One day, the sun was shining through the window in the basement and I saw the images the doctors had seen before. It was due to the angle of the

light,” he says. “Like a lot of good inventions, a little luck goes a long way.”

It was after successfully applying for a grant from the National Institute of Health that Dr. Zahniser, his MD colleagues, and his consulting team got to the next level with the project... a successful proof of concept. The next major step occurred by chance when he caught up for dinner with his old colleagues from Cytoc. It just so happened they had received some money from a single venture capital firm looking to help out an existing company, or start a new company. “As they say, the rest is history and we set up Constitution Medical, Inc. in 2009.”

According to Dr. Zahniser, the uniqueness of the bloodhound technology is that it automates the quantitative and qualitative process of which has been a major challenge in haematology that many people have tried to tackle for some time. Bloodhound has two main advantages. Firstly, it requires a lot less blood for a sample. 30 microliters is enough for detailed cell analysis, whereas traditional ‘flow’ sampling technology requires around 100 microliters and preparing a slide requires another 100 microliters. In fields such as paediatrics, this is ground breaking because taking samples from infants, particularly those born prematurely, or with illnesses, is difficult to say the least. The same goes for people with chronic conditions who require ongoing blood counts.

The advantages to medical professionals are also significant. With Bloodhound technology, the morphology of blood cells are clearly recognisable and if there is something abnormal they immediately have computer digital images available for the medical technologist to review. Abnormalities can be identified without the need to prepare a blood smear as a second step since the complete CBC analysis is done from images. Even if nothing abnormal is flagged in the blood sample, the images are

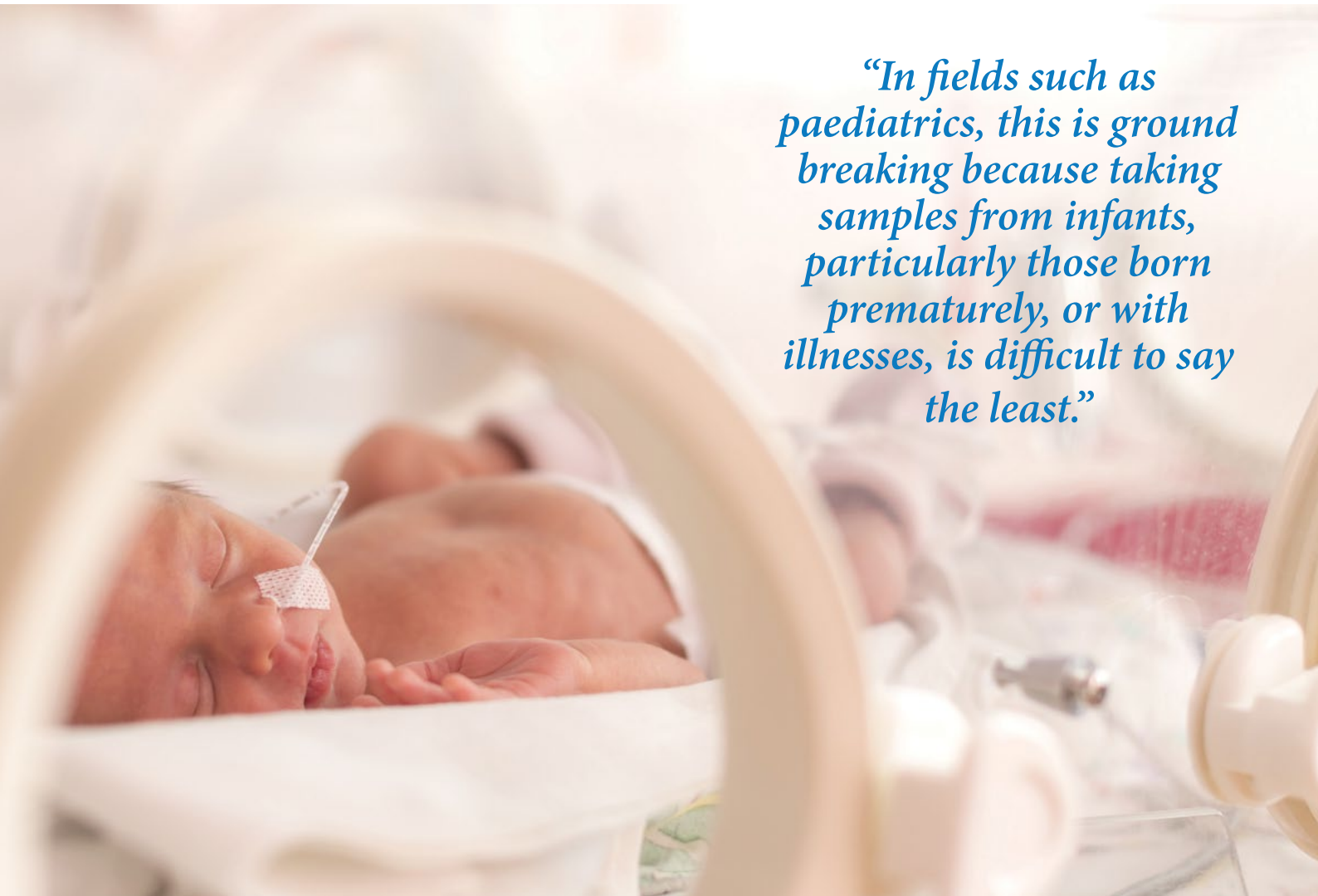


still available afterwards. This isn’t the case with flow technology where more samples may need to be taken.

More than anything, what Bloodhound offers medical professionals is fast and standardised results.

The Bloodhound technology operation and viewing software runs on an iMac. “I’ve been using Apple since the Apple II series was launched. I was using that to do some digital imaging, playing around with it and some algorithms and muscle biopsies. The evolution of the computer really fascinates me,” he says.

Results from blood samples are shown in clear, sharp images that can easily be classified by size and shape of cell. “The days of looking at cells under microscopes may be over,” says



*“In fields such as paediatrics, this is ground breaking because taking samples from infants, particularly those born prematurely, or with illnesses, is difficult to say the least.”*

Dr. Zahniser. “The lab technician can work from the screen and if a message appears saying ‘suspicious white blood cells,’ you click on this message and the pictures pop up. It’s fun!”

Dr. Zahniser credits some of the lecturers during his early years of PhD study in the Netherlands and his tutors at MIT with ingraining a sense of optimism into his love of science. “At MIT, what they train you to do is to believe you can solve any problem,” he says. “They give you confidence and an appreciation for breadth of knowledge. I can combine different fields and use my common sense to be a good inventor.”

Dr. Zahniser’s family has also played an integral part in the development of the Bloodhound technology and

early life. His twin boys, Russell and Michael, helped design the technology for interaction on the computer screen and algorithms for the digital imaging respectively, while his daughter Anne has helped with marketing and graphics. They all have a natural ease with technology. “It didn’t dominate our family but it infused our life,” says Dr. Zahniser. “Computers were always around, they all had one. I have about 30 computers in my basement, I’m just afraid to get rid of them!”

In 2013, Roche Diagnostics bought Constitution Medical, Inc. (CMI) to bring this breakthrough technology to the market. The system is officially called the cobas m 511.

Dr. Zahniser, who now works for Roche Diagnostics, says he’s looking forward to getting out into the field

and talking to potential customers about the Bloodhound technology and how it might change the medical landscape. Not least, he feels it could aid future developments in researching other diseases, and potentially making advanced academic hospital services available in community settings.

Despite all these advancements, adoption in practice might take some time “We went through the same things in other areas and we managed to change the way people look at things”, says Dr. Zahniser. “Bloodhound technology is such a huge change for hematology. I know some people will need persuading but in the end they love it.” ■

# Lean thinking and the hospital laboratory

A laboratory functions as the nerve centre of a hospital, enabling thousands of critical diagnoses and treatment decisions each day. **Dia:gram** explores how lean thinking has helped transform processes at Far Eastern Memorial Hospital in Taipei.

DR. FANG-YEH CHU



The laboratories at the Far Eastern Memorial Hospital (FEMH) in Taipei process anywhere between 11,000 to 12,000 tests a day. Just a few years ago, the hospital was running less than half the number of tests. Instead of being daunted by this dramatic increase in workload, **Dr. Fang-Yeh Chu**, the man in charge of quality management, was inspired to overhaul established ways of working and pursue radical improvements in quality, speed and efficiency

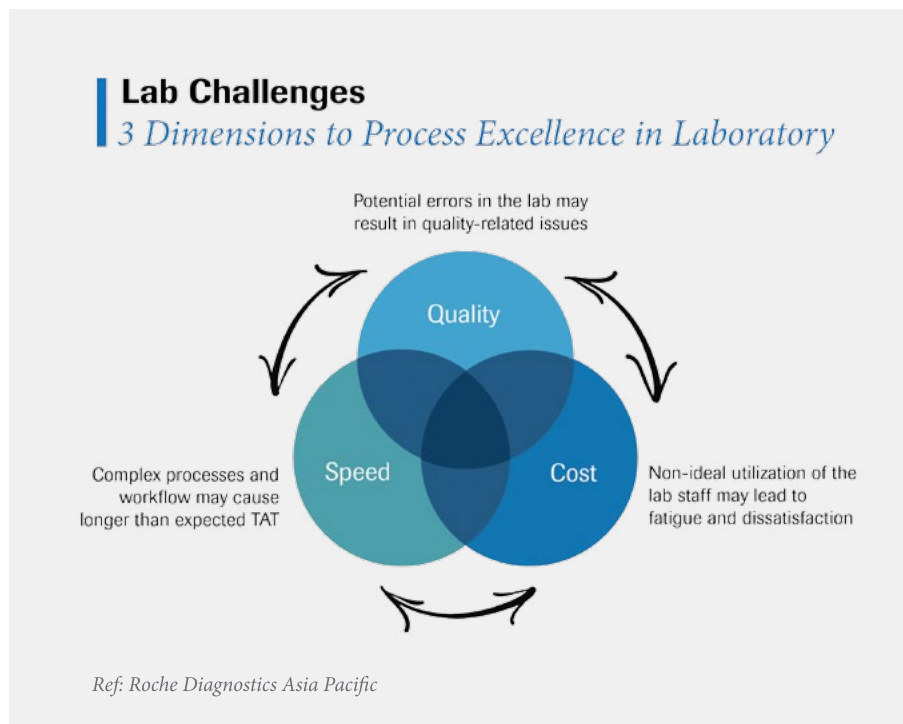
When **Dia:gram** visited FEMH in August 2016, Dr. Chu was supervising a comprehensive renovation of laboratory services - from the way patients are registered to where their blood is drawn and when the result is issued. The plan was set in motion two years ago, when he brought in Roche's Workflow Solutions team to improve processes. "Our workload had nearly tripled in a short time but we had the same number of employees. Often, we even had a shortage of staff because turnover was high. I wanted to spend some time and effort to understand how we could boost efficiency," Dr. Chu said.

The Roche Workflow Solutions team spent three months analysing the situation. "We found many, many problems," Dr. Chu said. The team applied a methodology called Lean Six Sigma, known for its success in helping teams accelerate process improvement. One of the fundamental principles of Lean thinking is that the fewer the steps to perform any given task, the less room there is for error. As the Roche team applied this principle to the labs at FEMH, they found ways to dramatically reduce the number of steps and improve key performance indicators of quality, speed and operational costs.

A key problem was the complexity of managing the workload between the hospital's three different labs on three separate floors. Each lab had its own operating hours, workflow and responsibilities. There was the STAT lab for emergency tests, the routine lab and the outpatient lab. Staff turnover was high, especially at the STAT lab. "We found that the STAT lab received and analysed more than half of the total samples, even though only 16% are classified as emergency room patients," Dr. Chu said. The Roche team's solution was to combine the STAT and routine labs into a centralised lab in the basement, leading to massive gains in a streamlined workflow and reduced number of steps.

Three months ago, the STAT and routine groups started to work together in a newly constructed area. "When the employees from the different labs came together in the same environment, they encountered similar problems and they offered to help each other. This year, the STAT lab has become stable. People did not like working there before because they had to bear the imbalanced workload. Now, they are much happier," Dr. Chu said.

The next problem that the Roche Workflow Solutions group targeted was speed or Turnaround Time (TAT). "Our core competence is cardiovascular disease. Many physicians rely on the cardiac marker tests to make decisions and these need to be issued within 30 minutes," Dr Chu said. The analysis found that while 84% of emergency



room blood samples were processed in under 30 minutes, about 3% of samples took twice as long. It was not clear whether the bottlenecks in the process occurred during pre-analysis, during or after it. So the Roche team recommended a manual 'Timestamp Study Analysis' where they installed scanners at key laboratory locations. Every step was recorded in painstaking detail – from the time it took to register the patient, to collecting the sample, sending it to the lab, result validation, quality control and issuing the result. The timestamp study found several pre-analytical and post-analysis steps that were causing delays. "Some of the steps where the delays occurred were so unbelievable to me. We think we are the experts but unless you have

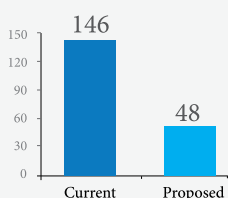
an objective analysis of the workflow steps, you don't even know and cannot improve," Dr. Chu said. The timestamp study identified that test validation was a source of significant delay. "We introduced auto-validation and we shortened the average TAT from 35 minutes to 25 minutes," Dr. Chu said.

Dr. Chu is also looking at automating processes by integrating IT solutions with the lab. "People will often say that you've got a new device with high speed and great throughput and that will solve all your problems. This is not true. The truth is that you have to go beyond the device to have a very good process to reduce the number of steps and leave less room for error," he said.

### Current Vs Proposed: Outpatient Department (OPD)

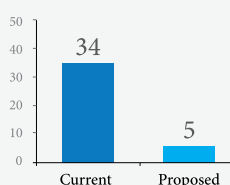
95 steps and 29 decision making points eliminated

Total Process Steps



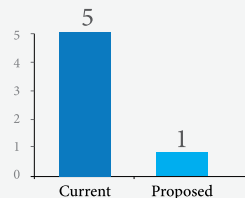
204% improvement

Total Decision Making Points



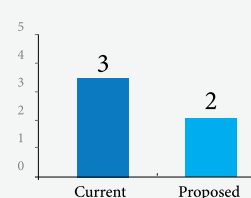
580% improvement

Number of Times Sample Transported To Another Lab



400% improvement

Number Of Levels Involved



50% improvement

Ref: Roche Diagnostics Asia Pacific



Dr. Chu said the entire exercise has served to dispel many myths around automation, including fears that it will decrease the need for trained lab technicians. “When we had some early success with lean processes and automation, it gave my people more time to focus on the unusual results. If you are pushing a button 1,000 times a day to validate results, you don’t have time to call the physician. You cannot have the conversation where you say: “Do you think this data is consistent with your patient? I think something is wrong.” This is where we can help the physician and truly add value.”

In order to facilitate continuous learning, Dr. Chu initiated diagnostic grand rounds in 2008 where the lab invites physicians and nurses to discuss interesting cases each month. In the beginning, he faced a lot of resistance. “When I launched it, people really hated me for making them do it. Some said it was a good idea but they just don’t have the time. Now, it’s different. People are eager to call the physician to discuss an unusual result. We have had over 100 case discussions from across 30 disciplines. This really adds to our knowledge and improves outcomes for our patients,” he said.

Dr. Chu said that another big myth to dispel is in relation to return on investment. FEMH invested NT\$20 million in overhauling their Point-Of-Care systems last year. “My boss, colleagues and experts from

other hospitals all asked me the same question about ROI. The assumption is that you lose money because with the new devices, IT system, training of personnel and QC, you effectively double the expense of each test. But at the end of the year, we found we actually earned money. How did this happen? We did not know that we were doing at least a fifth of the tests for free because somebody forgot to charge it. Now with IT, you can’t forget. Sure, we have higher expenses, but we also have higher income.”

Dr. Chu joked that his boss now actively encourages him to spend more money for such type of process improvements. “If you believe in it, you can make it happen. You need to persuade people that when they streamline processes, they don’t lose money,” he said.

In 2016, Dr. Chu has spent NT\$30 million to reconstruct the blood collection service at FEMH. Patients can use auto-registration booths to register themselves for the tests. “Many of the current lab processes are designed for the employee’s convenience not the patients. For instance, why do we make the patient go to the blood collection area to collect a urine cup? My vision is to have a very fast tracked service for patients with lab processes oriented towards ultimately benefiting the patient.” ■



*“If you are pushing a button 1,000 times a day to validate results, you don’t have time to call the physician.”*



5-6F 麻辣诱惑  
4F 康磁 Congen Massage  
2-3F SILK KING 真丝大王  
B1 麦当劳

江苏阳光集团公司

上海珍珠城展览  
7 观景咖啡餐厅 COFFEE RESTAURANT  
6 FUTURE STORE  
5 陶瓷精品商场  
4 SHANGHAI PORCELAIN EXPO  
3 珍珠城 PEARLS CITY  
2 工艺礼品 ART & CRAFTS  
1 新世界  
B1 KFC

BALENO  
7 观景咖啡餐厅 COFFEE RESTAURANT  
6 FUTURE STORE 世博未来商店  
5 陶瓷精品商场  
4 SHANGHAI PORCELAIN EXPO  
3 珍珠城 PEARLS CITY  
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# Cardiovascular risk in China

The biggest threat to China's healthcare is on the rise.

DR. DETLOFF RUMP



Non-communicable diseases (NCDs) kill 38 million people across the world each year. Cardiovascular disease accounts for the majority of these deaths, especially in developing countries<sup>1</sup>. In 2013, Swiss Re, one of the largest reinsurance companies in the world partnered with the Harvard School of Public Health to better understand and predict the future impact of cardiovascular disease in the rapidly evolving economies of Brazil, China, India and Russia. **Dia:gram** speaks with **Dr. Detloff Rump**, Chief Underwriter, Asia, Swiss Re who examines the potential for diagnostics and private insurance to partner and reduce the burden of the disease.

**I**n China, it is estimated that one life is lost to cardiovascular disease every 10 seconds<sup>2</sup>. According to the Systematic Explanatory Analyses of Risk factors affecting Cardiovascular Health (SEARCH) project, a joint research project undertaken by Swiss Re and the Harvard School of Public Health (HSPH), cardiovascular disease now accounts for 41 per cent of all deaths in China<sup>2</sup>.

Dr Rump, who has over 27 years of experience in risk assessment and is a trained physician says: "The SEARCH study showed that risk factors for cardiovascular disease

(CVD) such as hypertension, tobacco smoking, alcohol use and an unhealthy, westernised diet have trended upwards over the last 20 to 30 years. China's health profile has changed very quickly and NCDs now pose a considerable public health challenge and socioeconomic burden."

To reduce the economic burden of medical expenses for its citizens, the Chinese government announced nationwide healthcare reforms in 2009, with a view to achieving universal access to healthcare services by 2020<sup>3</sup>.

However, heart attack and stroke remain expensive to treat and survivors tend to have long-term medication and monitoring needs<sup>4</sup>. Dr. Rump explained that CVDs are a significant contributor to "catastrophic health expenses" where 40 per cent or more of total annual income of a family is spent on healthcare<sup>3</sup>. For instance, researchers looked at the direct cost components of atrial fibrillation (AF) related stroke in China. They found that about 60 per cent of the cost incurred after a stroke was during the acute hospitalisation phase, and 40 per cent was during the first year after discharge<sup>4</sup>. Medicines were

the biggest driver of costs but indirect costs such as a loss of income due to early retirement are also a factor. “The financial burden on medical costs continued to be significant for many months after patients are discharged from the hospital. This is unfortunate as almost all of the risk factors are modifiable with early detection and intervention,” Dr. Rump said. “But healthcare systems around the region, including China, are grappling with providing acute care and are not yet sufficiently geared towards preventing disease,” Dr. Rump noted.

“This is where the private sector including insurance companies can play a larger role. For instance, they can provide incentives such as reduced premiums to customers who maintain healthy lifestyles,” Dr. Rump said. He added that to be successful, an incentive model would require continuous and real-time monitoring. “Investing in the diagnostic infrastructure to screen the population and pick out those at higher risk to be placed into a lifestyle program can make a huge difference. Both public and private sectors should work together to provide tests and risk stratification at reasonable costs,” he said.

Another important private sector stakeholder is the employer. Dr. Rump cites the example of Japan, which he credits with having a robust preventative system. “It is partly linked to the fact that a majority of the

population is employed by the same company for a long time. They get regular annual check-ups as part of an employer-paid health program. Part of the longevity we see in Japan can be ascribed to it,” he said. Dr. Rump added that it makes sense for employers to play an active part in prevention of cardiovascular disease because they bear the secondary costs of the disease such as absenteeism, disability and premature death.

But what happens in rural areas where there is no employer? The study found that in rural areas, people were more vulnerable after being hit by CVD. Hospital stays were longer among urban residents compared to rural residents. Researchers said this is an indication that rural residents may receive inadequate treatment as they experience more financial hardships in meeting the costs of treatment. The study also revealed that the average annual cost increase for acute myocardial infarction, congestive heart failure and cerebral haemorrhage were around 8 per cent to 11 per cent, which were higher than the annual inflation rate of 4 per cent<sup>5</sup>.

This makes it all the more important that prevention is made a priority. “In rural areas, a simple and low-cost test kit can make a difference, something accessible such as a mobile health clinic to identify people at risk and provide actionable advice,” Dr. Rump said.

Risk certification would also enable more people to purchase insurance cover. Citing the example of diabetes, Dr. Rump recalled that just over a decade ago, it was challenging for people with diabetes to obtain insurance cover. “Now, with HbA1c monitoring, it is possible for diabetics to establish that their condition is under control and to purchase insurance,” he said. As more diagnostic data becomes available, he sees approaches to screening and intervention programmes changing to create greater impact on public health.

For Dr. Rump, the key to change is helping people understand their risk factors. “We can only create change if people are better educated about risk factors and are empowered to manage them.” ■

For more details on the SEARCH Study, please visit [http://cgd.swissre.com/risk\\_dialogue\\_series/](http://cgd.swissre.com/risk_dialogue_series/)

<sup>1</sup><http://www.who.int/mediacentre/factsheets/fs355/en/>. Last accessed in September 2016.  
<sup>2</sup>Report of Cardiovascular Diseases in China. (2012). National Center for Cardiovascular Diseases, China  
<sup>3</sup>Meng, Q., et al. (2012). *Lancet* 379(9818):805-814.  
<sup>4</sup>National Bureau of Statistics of China. *China Statistical Yearbook 1996-2012*.  
<sup>5</sup><http://www.inflation.eu/inflation-rates/china/historic-inflation/cpi-inflation-china.aspx>. Last accessed in September 2016.

## Cardiovascular Risk Factors in China over Time

### Hypertension

1991 – 13.6%

2010 – 33.5%

Source:  
 National statistics yearbook (2010).  
 National Bureau of Statistics of China,  
 Beijing [in Chinese].

### Diabetes

1980 – 0.67%

2010 – 11.6%

Source:  
 Zuo H, Shi Z, Hussain A (2014). *Diabetes Research and Clinical Practice*. 104:63-72.

### Overweight/obesity

Males:

Females:

1989 – 13.6%

1989 – 17.6%

2009 – 39.6%

2009 – 40.5%

Source:  
 China Health and Nutrition Survey (CHNS)  
 (1996-2012)

## Predicting the Risk of Preeclampsia

### Predictive value of the sFlt-1:PIGF ratio in women with suspected preeclampsia

In January this year, the *New England Journal of Medicine* published the results of PROGNOSIS, a groundbreaking clinical study demonstrating the prognostic value of the sFlt-1/PIGF immunoassay ratio test in predicting which pregnant women are at highest risk of developing preeclampsia<sup>1</sup>, one of the leading causes of death and complications for mothers and their unborn babies<sup>2</sup>.

PROGNOSIS was a multi-center, prospective, double-blind, non-interventional trial evaluating the short-term prediction of preeclampsia, eclampsia and HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome in pregnant women who were 18 years of age or older (24 weeks 0 days to 36 weeks 6 days of gestation at the first visit) with suspected preeclampsia. Between December 2010 and January 2014, more than 1,270 pregnant women were enrolled at 30 sites in 14 countries<sup>1</sup>.

The PROGNOSIS study has demonstrated that low ratios of the proteins sFlt-1 and PIGF in the blood of women showing the signs and symptoms of preeclampsia can predict the absence of the condition within a period of one week (the rule-out claim). The data show that an sFlt-1/PIGF ratio of 38 and below can rule out the development of preeclampsia within the next week with a very high confidence level of 99.3%<sup>1</sup>.

PROGNOSIS also demonstrated that an sFlt-1/PIGF ratio greater than 38 may help predict whether women with suspected preeclampsia will develop the condition within four weeks (the rule-in claim)<sup>1</sup>, allowing doctors to identify at-risk patients who need close monitoring.

These important new findings represent a step-change in the prediction of preeclampsia in the clinical setting, where the gold standard has traditionally relied on the measurement of proteinuria and blood pressure<sup>3</sup>. Unfortunately, both are sub-optimal predictors of which women will develop preeclampsia and how the disease will progress<sup>4</sup>. As a consequence, many women with signs and symptoms of the disease are unnecessarily admitted to hospital for intensive observation and monitoring, resulting in worry for them and their families, and additional costs to the health provider.

Model 1 included age and sex. Model 2 was additionally adjusted for systolic blood pressure, hypertension treatment, current smoking, diabetes, cardiovascular disease and atrial fibrillation<sup>1</sup>.

The study looked at 15 different biomarkers in 3,224 participants. Out of the 15, higher levels of four biomarkers of inflammatory, endothelial and oxidative stress – C-reactive protein (CRP), total homocysteine (tHcy), tumour necrosis factor 2 (TNFR2) and vascular endothelial growth factor (VEGF) – were found to increase risk of IIS. In model 1, CRP, TNFR2, tHcy and VEGF were associated with higher risk of IIS<sup>1</sup>. In model 2, three of the biomarkers remained significantly associated with stroke risk except for CRP, which was no longer significant<sup>1</sup>.

In exploratory analyses, the researchers also found a significant relationship between CRP and a subtype of ischemic stroke: atherosclerotic brain infarction (HR 1.31, 95% CI 1.06 to 1.33). They also saw a relationship between cerebral embolism and both interleukin 6 (HR 1.11, 95% CI

As well as potentially saving lives, the more accurate diagnosis of preeclampsia may also have positive economic impacts on healthcare systems. In 2005, the average cost of preeclampsia, excluding normal delivery costs, was an estimated GBP 9,009 per pregnancy<sup>1</sup>. With an estimated 8.5 million women affected by preeclampsia every year, the annual cost of preeclampsia worldwide is estimated to be GBP 76.6 billion (based on the 2005 estimate), representing a major financial burden<sup>5</sup>. The addition of the sFlt-1/PIGF ratio measurement to proteinuria and blood pressure measures gives better prediction of preeclampsia. This could reduce by 50% the number of women hospitalized prior to preeclampsia diagnosis, leading to a cost savings of approximately GBP 400 per patient<sup>6</sup>. ■

<sup>1</sup>Zeisler, H., et al. (2016). *NEJM* 374:13-22

<sup>2</sup>Verlohren, S., et al. (2010). *Am J Obstet Gynecol* 202 (161): e1-11

<sup>3</sup>Wagner, L.K. (2004). *Am Fam Physician* 70(12):2317-2324

<sup>4</sup>Verlohren, S., Stepan, H., Dechend, R. (2012). *Clin Sci* 122(2): 43-52

<sup>5</sup>Anderson, U.D., et al. (2012). *Placenta* 33(suppl), S42-7

<sup>6</sup>Strunz-McKendry, T., et al. (2014). 20th COGI World Congress 2014

## Biomarkers May Help Predict Stroke

### Circulating biomarkers and incident ischemic stroke in the Framingham Offspring Study

People with high levels of four biomarkers in their blood may be more likely to develop a stroke than people with low levels of the biomarkers<sup>1</sup>, according to an observational study published in August 2016 in the online issue of *Neurology*, the medical journal of the *American Academy of Neurology*.

The study followed 3,224 participants, 54% of whom were women, for an average of nine years. During this period, 98 participants had a stroke<sup>1</sup>. The participants were an average age of 61 at the start of the study. Cox proportional hazard models were used to calculate the hazard ratios (HRs) of incident ischemic stroke (IIS) per SD increment of each biomarker.

1.06 to 1.33) and fibrinogen (HR 1.40, 95% CI 1.06 to 1.86)<sup>1</sup>.

Conditions that may affect vascular and systemic inflammation, such as chronic inflammatory diseases and infections, and long-term use of medications that have anti-inflammatory properties, were a limitation of the study and were unaccounted for. Also, the biomarkers were measured at single time points and not repeated over time.

The addition of these four biomarkers to the clinical Framingham Stroke Risk Profile score could potentially improve the ability to predict who might be at risk of stroke. However, given its observational nature, the results do not mean that elevation of these markers cause strokes, neither does it provide thresholds for clinicians to consider increased risk. Further research is needed to explore the role of these biomarkers as potential therapeutic targets<sup>1</sup>. ■

<sup>1</sup>Shoamanesh, A., et al. (2016). *Neurology* 87(12):1206-11.

# Upcoming Events *(January - June 2017)*

## JANUARY

### *Arab Health, Dubai*

30 January – 2 February

Dubai, UAE

[www.arabhealthonline.com](http://www.arabhealthonline.com)

## FEBRUARY

### *3rd Thailand Ian Donald Advanced Course of Ultrasound in O&G*

1 – 3 February

Bangkok, Thailand

### *13th Singapore ISUOG Course and 8th Scientific Congress of the College of O&G, Singapore 2017*

10 – 12 February

Singapore

[www.isuog-2017.com](http://www.isuog-2017.com)

### *Clinical Laboratory & Diagnostics Expo Japan*

15 – 17 February

Osaka, Japan

[www.scherago.com/clinical-japan/2016](http://www.scherago.com/clinical-japan/2016)

### *The 26th Conference of Asian Pacific Association for the Study of the Liver (APASL)*

15 – 19 February

Shanghai, China

[www.apasl2017.org](http://www.apasl2017.org)

### *CardioRhythm 2017*

24 – 26 February

Hong Kong

[www.cardiorhythm.com](http://www.cardiorhythm.com)

## MARCH

### *3rd Microbiome Asia Forum co-located with 2nd Probiotics Asia Congress*

1 – 2 March

Hong Kong

[www.globalengage.co.uk/microbiomeasia.html](http://www.globalengage.co.uk/microbiomeasia.html)

### *Highlights of ASH® Asia Pacific*

10 – 12 March

Hong Kong

[www.hematology.org/Highlights/Asia.aspx](http://www.hematology.org/Highlights/Asia.aspx)

### *American College of Cardiology*

17 – 19 March

Washington, DC, USA

[www.acc2017.org](http://www.acc2017.org)

### *6th Conference of The International Union Against Tuberculosis and Lung Disease Asia Pacific Region, 2017*

22 – 25 March

Tokyo, Japan

[www.aprc2017.jp](http://www.aprc2017.jp)

### *The 7th Congress of the Asia Pacific Initiative on Reproduction*

30 Mar – 2 April

Kuala Lumpur, Malaysia

[www.aspire2017.com/](http://www.aspire2017.com/)

### *labtechMED Eurasia*

30 March – 2 April

Istanbul, Turkey

[www.scherago.com/labtechmed](http://www.scherago.com/labtechmed)

## APRIL

### *MedLab Asia Pacific*

3 – 5 April

Singapore

[www.medlabasia.com](http://www.medlabasia.com)

### *The 10th Congress of Asia Pacific International-Academy of Pathology (APIAP) & Asia Pacific Society of Molecular and Immunohistology (APSMI)*

24 – 27 April

Bali, Indonesia

[www.apiap2017.com](http://www.apiap2017.com)

## MAY

### *China International Medical Equipment Fair (CMEF) Spring Edition 2017*

15 – 18 May

Shanghai, China

[www.scherago.com/cmef-ivd](http://www.scherago.com/cmef-ivd)

### *ICC 2017: The 19th International Conference on Cytology*

25 – 26 May

London, United Kingdom

[www.waset.org/conference/2017/05/london/ICC](http://www.waset.org/conference/2017/05/london/ICC)

## JUNE

### *EuroMedLab 2017*

11 – 15 Jun

Athens, Greece

[www.athens2017.org](http://www.athens2017.org)



What's causing it  
**will it get worse**  
*is my diagnosis correct*  
**am I sick** how can we prevent strokes  
and save millions  
which woman is  
at highest risk of  
cervical cancer  
how can I reduce  
my post-operative  
hospitalisation costs  
**Is something  
wrong with me**  
do I have cancer  
Am I at risk  
what diseases do I have  
who should manage  
her heart disease  
who is the best candidate  
for treatment  
**is he suffering  
a heart attack**  
did my pap miss  
something  
is he HIV+  
will this patient  
**recover quickly**  
after surgery  
**Is my baby  
in danger**  
is my treatment  
working  
**can I  
still get  
pregnant**

*I know I  
am not at risk  
we caught it early  
I know I am ok  
I know the treatment  
will work*  
I am in control  
my baby is  
fine

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