



# SLMA NEWS

THE OFFICIAL NEWSLETTER OF THE SRI LANKA MEDICAL ASSOCIATION

AUGUST 2017, VOLUME 10, ISSUE 08

## DENGUE COUNT 2017



**ACTION AGAINST DENGUE!**



**STARTS AT HOME**

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# EFFICACY

The golden poison dart frog from Columbia, considered the most poisonous creature on earth, is a little less than 2 inches when fully grown. Indigenous Emberá, people of Colombia have used its powerful venom for centuries to tip their blowgun darts when hunting, hence the species' name. The **EFFICACY** of its venom is such that it can kill as much as 10 grown men simply by coming into contact with their skin.

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# PRESIDENT'S MESSAGE

Dear Members,

The past weeks witnessed the glorious celebration of reaching the half century milestone of two reputed professional medical institutions of Sri Lanka. The Ceylon College of Physicians held a simple ceremony to celebrate its Founder's Day on 24<sup>th</sup> July at the College premises following a highly successful Medical Exhibition for the general public. Meanwhile the Sri Lanka College of Obstetricians & Gynaecologists held a high level Golden Jubilee Congress at the BMICH in collaboration with many international organizations dedicated to women's health. These landmark events personified the very basis on which our profession is built. Both these colleges with their large membership, engaged in a multi-disciplinary approach to addressing current health priorities with wide participation of many fields of health. The SLMA extends its heartiest congratulations and applauds both colleges for looking to the future by learning from their past experiences.

In the meantime, we were all greatly relieved to learn that the statistics of the dengue epidemic had begun to ebb. However, this is simply not a reason for any degree of complacency for the prevention of Dengue in Sri Lanka. With this principle forming the basic foundation, the SLMA having obtained concurrence from the

Director General, arranged a round table meeting with several health authorities and colleges to discuss this matter with a group led by an expert who had international and local experience with vector borne disease. The Dengue Coordinating Unit and the Directorate assigned with public health activities were present. Having taken stock of the current situation, a meaningful discussion ensued on how to scale up prevention of dengue. The need to develop a pragmatic schema for a sustainable dengue prevention programme with community participation was unanimous. The mandatory requirement for a nationwide perennial approach, with a five-year plan, that takes into account the less recognized non-health sectors of our society were addressed in detail. It is the SLMA's sincere wish that the Presidential Task Force for Dengue Prevention would be able to take these important recommendations into consideration and pave the way in achieving these goals. These discussions also highlighted that Sri Lanka has every reason to win over this major health challenge successfully – given our excellent track record in maternal and child health, immunization and the effective prevention of outbreaks of contagious diseases in the midst of natural disasters.

The issue of CPD quantification was also discussed in detail with the

DGHS. There is much enthusiasm and hope on the part of the Ministry of Health, the SLMA Council, most professional colleges and the GMOA to formalize the process with all relevant authorities. I am very pleased that the participation and support of our sister colleges has been extremely proactive and constructive. It is hoped that a course in Cardio Pulmonary Resuscitation for all groups of doctors will be a good start. Quoting a local lead in Family Medicine, "as a minimum essential certification, all doctors who care for patients, even at primary care level in private or government sectors should have level 4 (Emergency first aid and Basic Life Supports) certified competency. Let us start with the basics without any compromise." On this positive note the SLMA with the Ministry of Health is committed to addressing and attaining quality through regular formal training and certification from the simple basics of CPR to acquiring and updating our knowledge and skills in managing common diseases.

Let us, as a responsible profession, not confine such important issues to 'talk' alone but take forward an effective action plan to improve our standards.

Yours truly,

**Chandrika Wijeyaratne**  
President SLMA

## JOINT REGIONAL MEETING

### SRI LANKA MEDICAL ASSOCIATION IN COLLABORATION WITH KEGALLE CLINICAL SOCIETY

Dr. Bhanuja Wijayatilaka  
Assistant Secretary / SLMA

It is my pleasure to report that the Sri Lanka Medical Association (SLMA) held its 4<sup>th</sup> successful Regional Clinical Meeting in collaboration with the Kegalle Clinical Society. The meeting was successfully conducted on 8<sup>th</sup> August, 2017 at the Auditorium

of the Teaching Hospital, Kegalle.

President, Sri Lanka Medical Association, Prof. Chandrika Wijeyaratne, and the President, Kegalle Clinical Society, Dr. Zaffarullah Wazeer welcomed the gathering.



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## JOINT REGIONAL MEETING...

President SLMA gave a brief overview about SLMA and invited all doctors to join its membership with a view to work collaboratively to address current health priorities in order to directly benefit our population. The sessions included six differing topics that were delivered by Dr. Zaffarullah Wazeer, Consultant ENT and Head and Neck Surgeon, Teaching Hospital Kegalle, Dr. Mahen Kothalawala, Consultant Microbiologist, Teaching Hospital Kandy, Dr. Ranjan Mallawaarachchi, Master Trainer in palliative care, Con-

sultant OMF Surgeon and Head, Palliative Care Unit, Base Hospital Kuli-yapitiya, Dr. Bhanuja S. Wijayatilaka, Consultant Community Physician, Nutrition Division, Ministry of Health, Dr. Sajitha Jayasekara, Medical Officer Nutrition, Teaching Hospital Kurunegala and Dr. Musriff, Acting Consultant Community Physician, Anti Malaria Campaign, Ministry of Health. The sessions were concluded with much appreciation of the excellent lectures delivered by resource persons. Both resource persons and participants

were handed over certificates by the president SLMA. The vote of thanks was delivered by the Secretary of the Kegalle Clinical Society.

The coordination and support provided by the Director, Teaching Hospital Kegalle, President, Kegalle Clinical Society and staff of the hospital including doctors and nursing officers as well as the kind sponsorship provided by the State Pharmaceutical Corporation and Anti Malaria Campaign of the Ministry of Health are greatly appreciated.

## SCREENING OF THE DOCUMENTARY MOVIE 'MERCHANTS OF DOUBT'

An interactive session, with screening of the documentary movie 'Merchants of Doubt' was held on Saturday 15<sup>th</sup> July 2017 from 9 am – 11 am at the Bougainvillea Room, Galadari Hotel Colombo. This was conducted by the Centre for Combating Tobacco (CCT), Faculty of Medicine, University of Colombo in collaboration with the SLMA Expert Committee on Tobacco, Alcohol and Illicit Drugs as a special symposium parallel to the 130<sup>th</sup> Anniversary International Medical Congress of the Sri Lanka Medical Association (SLMA). How the scientists and lobbyists lie for money on health issues was explained through this movie. Exposing how a handful of scientists obscured the truth on issues from tobacco smoke to global warming was discussed by this documentary. CCT director Dr. Mahesh Rajasuriya conducted this session followed by a panel discussion with the panellists: Dr. Diyanath Samarasinghe and Dr. Palitha Abeykoon (Chairman, National Authority on Tobacco and Alcohol). A large number of medical students, researchers and medical professionals attended this session.



CCT Director Dr. Mahesh Rajasuriya, with the panelists: Dr. Diyanath Samarasinghe and Dr. Palitha Abeykoon



Participants.....



Prof. Jennifer Perera, Dean, UCFM

## IMPORTANT NOTICE

Any member of the SLMA who considers himself/herself suitable to guide the SLMA in the year 2019 as President is kindly requested to contact the SLMA Office to obtain the Application for President Elect 2018.

### TO STUDENTS IN THE IUSF AND TO DOCTORS IN THE GMOA

When we were young Medical Students in the late fifties, if any group of students in the Ceylon University wanted to strike, the Vice Chancellor of the Ceylon University made it clear that their names would be struck off the roll immediately. Our Parents would have not tolerated us if we refrained from attending classes for whatever reason.

When I was a member of the GMOA, we did not own even Duty Free Bicycles, but we continued to work and to be "On Call" 24 hours daily, despite the comparatively low salaries when compared to the Mercantile Sector. There was no Private Practice then and no overtime. There were no major epidemics like the present Dengue Epidemic. Even then, for **obvious reasons**, Token or Indefinite Strikes were not thought of by the Doctors.

Need I say more?

**Dr K Rajendra**

### A SNIPPET FROM HISTORY: THE CLASSICAL DESCRIPTION OF A DOCTOR

There are men, and classes of men, that stand above the common herd: the soldier, the sailor and the shepherd not infrequently; the artist rarely; rarely still, the clergyman;

He is the flower, such as it is, of our civilisation; and when that stage of man is done with, and only remembered to be marvelled at in history, he will be thought to have shared as little as any in the defects of the period, and most notably exhibited the virtues of the race.

Generosity he has, such as is possible to those who practise an art, never to those who drive a trade; discretion, tested by a hundred secrets; tact, tried in a thousand embarrassments; and what are more important, Herculean cheerfulness and courage.

So it is that he brings air and cheer into the sickroom, and often enough, though not so often as he wishes, brings healing.

**Robert Louis Stevenson**  
19<sup>th</sup> Century Scottish Author

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**Dr B J C Perera**

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# MICROBIOME AND POTENTIAL APPLICATIONS IN HEALTH AND DISEASE

Professor Jennifer Perera  
Senior Professor of Microbiology and Dean  
Faculty of Medicine  
University of Colombo

## Introduction:

The human body is home to 100 trillion (10<sup>14</sup>) bacterial cells and a quadrillion viruses and a significant number of eukaryotes and comprise ten times the number of cells in the human body. They live on and within us and form our **microbiota**. The genes they encode is collectively known as the microbiome. The **microbiota** is sometimes referred to as our “forgotten organ”. The human microbiota, especially the gut microbiota, has even been considered to be an “essential organ”. The body contains at least 1000 different species of known bacteria. They carry 150 times more microbial genes than are found in the entire human genome.

Microbes colonize all the surfaces of the human body that are exposed to the environment with the majority residing in the intestinal tract. If one considers the bacterial communities in a given body site they tend to resemble across individuals. However, there is also considerable inter-individual variability. Metagenomic studies have established that despite this inter-personal variability in composition, (the species types and their numbers), there is a shared core of functionalities, in the microbiome.

Host genetics play an important role in the establishment and shaping of the gut microbiota, and this is more so for bacterial communities compared to viral communities. Having said that it is reported that twins share less than 50% of their species level bacteria. Thus factors other than genetics are responsible for this variation.

How does the microbiota establish itself in the human body? Babies are exposed to a plethora of microbes from different environments immediately upon birth and are rapidly colo-

nized by the microbes they first encounter. Depending on the method of delivery the colonization varies. Infants born vaginally have communities resembling those found in the vaginal microbiota of their mothers. In contrast, those delivered by caesarean section harbor a microbiota characteristic of skin and dominated by taxa such as *Staphylococcus* and *Propionibacterium* spp.

The bacterial composition begins to converge towards an adult-like microbiota by the end of the first year of life and fully resembles the adult by two and a half years of age. Once the microbiota has reached maturity it remains mostly stable in adulthood. *However, this happens when general diet, disease, and environment, are also being held constant.* In the elderly, the composition is different from that of young adults, particularly in the proportions of *Bacteroides* spp. and *Clostridium* groups. Variability of bacterial composition is greater in this age group compared to that of adults, and this may be related to the wide range of morbidities in elderly and the subsequent use of medications.

If we are to understand the role of microbiota in disease, understanding the stability of the microbiota within

an individual through time (time series studies) is an important step to determine the norm. Deviations from norm which is known as dysbioses will allow prediction of disease and help to develop therapies to correct these imbalances through microbial transplantation.

Gut microbiota can be categorized into one of three variants or “enterotypes” based on the dominant genera (*Bacteroides*, *Prevotella*, or *Ruminococcus*). Interestingly, individuals on a diet high in animal fat have a *Bacteroides*-dominated enterotype, whereas a carbohydrate-rich diet is associated with the *Prevotella*-dominated enterotype. Differences in diet between children in Africa and Europe have also been shown to correlate with differences in the microbiota, with the African cohort being enriched in Bacteroidetes and depleted in Firmicutes, presumably to maximize energy uptake from their fiber-rich diet. The global trend toward a Western-like diet, which has high intakes of red meat, high-fat, and sugars, may result in a homogenization of the microbial communities in humans and this may lead to loss of “endangered microbes” that could play important roles in bacteriotherapy.

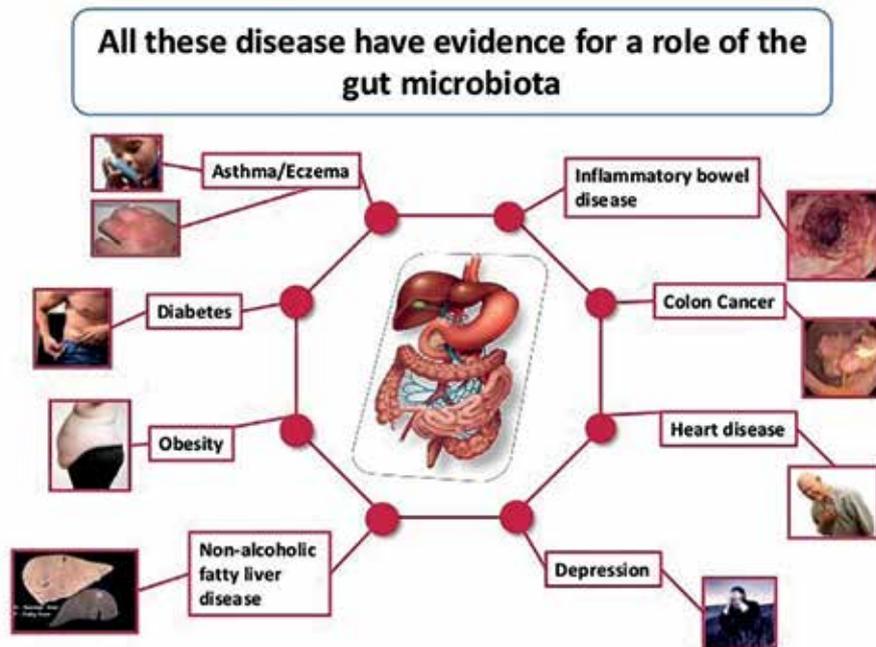


Figure 1: Gut microbiome. Reference: <http://allergiesandyourgut.com/2017/05/22/get-gut-microbiome-sequenced-free/>

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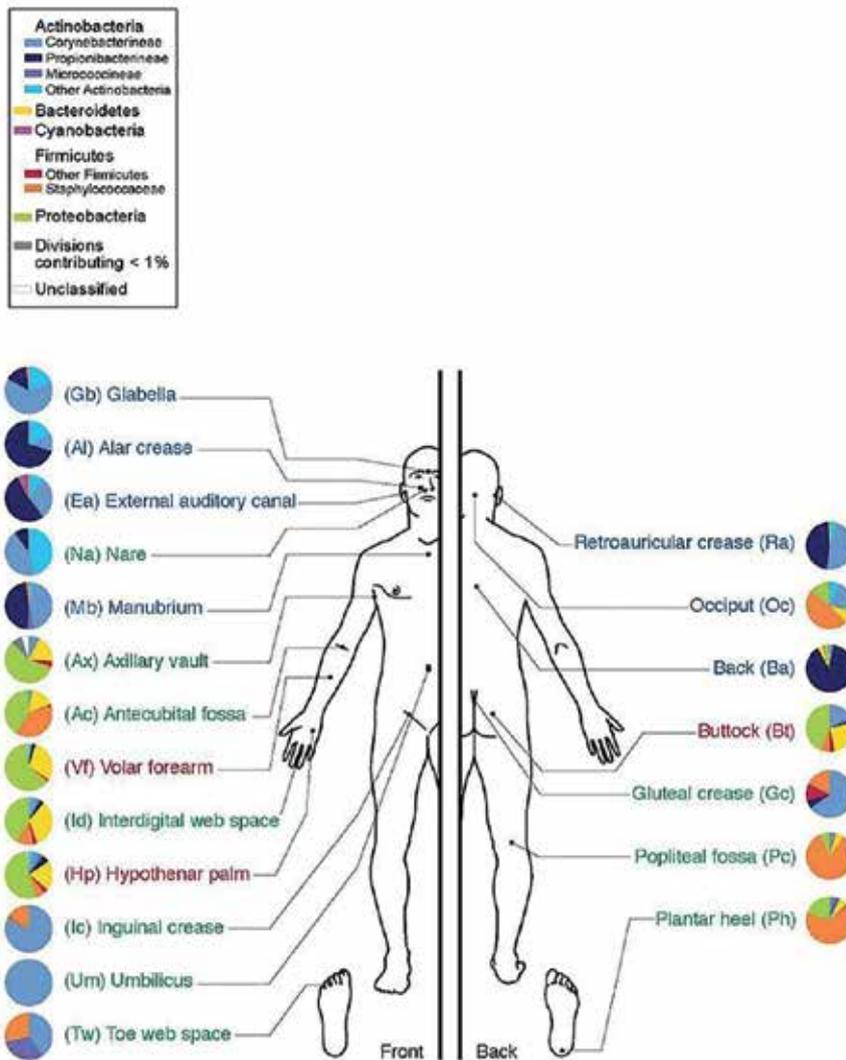
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# MICROBIOME & APPLICATIONS...



**Figure 2:** Microbiota of skin  
Reference: Human Microbiota – Wikipedia

## Impact on Health:

How do they impact on maintaining normal health and physiology? The microbes interact with one another and with the host, and contribute to basic biological processes. To explain this further,

A) the microbiota contains far more versatile metabolic genes than are found in the human genome. These provide humans with unique and specific enzymes and biochemical pathways. These can help in absorbing undigested carbohydrates. This trait has probably acted as a strong evolutionary force for establishing bacteria as human symbionts. If we examine the energy and nutrition component processes of the body, these genes increase energy extraction from food, harvest nutrients, and alter appetite signaling.

B) Second, the human microbiota also provides a physical barrier, protecting its host against foreign pathogens through competitive exclusion and the production of antimicrobial substances.

C) Studies have clarified the role of the gut microbiota in lipid and protein homeostasis. The normal gut microbiome also produces short-chain fatty acids. They can be quickly absorbed in the colon and help in regulating gut motility, inflammation, glucose homeostasis, and energy harvesting.

D) Furthermore, the gut microbiota has been shown to deliver vitamins to the host, such as folates, vitamin K, biotin, riboflavin (B2), cobalamin (B12), and possibly other B vitamins too.

E) Perhaps even more importantly, the gut microbiota interacts with the immune

system, to promote the development of immune functions. The innate immune system recognizes microbe-associated molecular patterns (MAMPs) and these are present across diverse lineages of bacteria. These are mostly components of the bacterial cell wall and flagella proteins. The bacteria are also important in suppressing inflammatory response and promoting immunological tolerance, and this interaction occurs through their toll like receptors (TLRs). Not only the innate immune mechanism, but the adaptive immune system is also programmed by microbiota. They impact the differentiation of T cell populations, which determine self-/non-self-discrimination mechanisms also get educated by commensal microbiota

## Impact on Disease:

Traditionally the study of diseases, has been classically approached from a “one microbe-one disease” viewpoint. Viruses, eukaryotes, and bacteria were traditionally studied under conditions in which they were believed to cause disease. Just as the “one gene-one enzyme” outlook proved to be an oversimplification that failed to explain complex phenotypes, we need to appreciate the fact that humans are colonized with numerous microbes, and that some diseases might result from dysbiosis rather than the presence of a single disease-causing microbe.

Microbial dysbiosis is shown to impact in the development and progression of a wide variety of human diseases such as infectious diseases, liver diseases, gastrointestinal cancers, metabolic diseases, respiratory diseases, obesity, inflammatory bowel disease (IBD), and diabetes, mental or psychological diseases, allergies and autoimmune diseases.

Thus information on microbiota has changed the focus from **individual agents** that are implicated in disease toward a **community view** and has already precipitated paradigm shifts in diagnosis and management.

Contd. on page 10



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# MICROBIOME & APPLICATIONS...

## ***The human microbiota and infectious diseases***

Numerous studies have demonstrated that infection is associated with the type of microbiome. For example, the intestinal microbiota of patients with *Clostridium difficile* infection which causes a post antibiotic pseudomembranous colitis is significantly altered. Disturbance of the microbiota has also been associated with the progression of human immunodeficiency virus disease.

## ***Metabolic diseases***

In animal models of obesity, the interplay between the two dominant gut microbes *Bacteroides* is significantly reduced and *Firmicutes* is increased. Also this energy harvest phenotype is transmissible simply by transplanting the obese microbiota into healthy, lean donors.

## ***Chronic Inflammatory diseases***

There is evidence to show that chronic inflammatory disorders such as Chron's Disease and autoimmune diseases such as rheumatoid arthritis and multiple sclerosis are also a result of inappropriate action of the adaptive immune system mediated by the gut microbiota.

## ***Psychiatric disease is another area that has been highlighted***

"Microbiota-gut-brain axis" is now seen to involve a number of systems, including the endocrine system, neural system, metabolic system, and immune system, all of which are engaged in constant interaction. Gut microbiota dysbiosis may increase the transfer of gut bacteria across the intestinal wall and into the mesenteric lymphoid tissue. This could provoke an immune response that releases of inflammatory cytokines, which in turn can activate the vagus nerve and spinal afferent neurons. Autism spectrum disorder (ASD) has been reported as correlating with an altered gut microbiota.

## ***Antibiotic use and microbiome***

Although the particular taxa affected by antibiotic treatment vary among individuals, some taxa do not recover even months after antibiotic treatment, and in general, there is a long-term decrease in bacterial diversity. The repeated use of antibiotics in humans has been hypothesized to increase the reservoir of antibiotic-resistant genes in our own microbiome

## ***Impact on management of diseases***

Restoring a healthy microbial community by transplantation of a foreign gut microbiota has proven to be a valuable tool in the treatment of certain diseases such as *C. difficile* infections. This may be the ultimate goal that needs to be achieved in the many diseases that would be identified as causally related to a specific microbiome phenotype through research studies.

## ***Future research needs***

The completion the human genome sequence was a "crowning achievement" in biology. However, the same scientists believed that it would be incomplete until the synergistic activities between humans and microbes living in and on them are understood. They called for a "second human genome project" of "Human Microbiome Project" that would entail a comprehensive inventory of microbial genes and genomes at the four major sites of microbial colonization in the human body: mouth, gut, vagina, and skin. Large-scale sequencing projects such as the Human Microbiome Project and the Earth Microbiome Project will ultimately be critical for providing a unified and all-encompassing view to better understand the link between the microbiota and health and disease.

Prior to designing therapeutic strategies for the variety of diseases expected to be caused by microbiota dysbioses, there is a need for more complete time-series analysis of microbial communities at higher resolution and lon-

ger time ranges to assess normal variability. Also there should be studies to study disturbance events such as antibiotic use to diet shifts. This should yield better understanding of both the normal levels of variability through time and what amounts of change the microbiota can withstand before becoming diseased or disbiosed. There is also a need for more integrative studies that examines the interaction between the microbiota, the host, and the environment to produce a specific phenotype.

It is even more important to consider the nature of the evidence supporting a relationship between the microbiota and the predisposition to disease as associative, correlative, or causal. Currently the associative evidence dominates the evidence base. The handful of cause-and-effect performed show that this form of evidence is increasing. The results of such studies are expected to be useful in monitoring disease development, in providing a basis for personalized treatments, and in determining future therapeutic possibilities. The ethical, legal, and social implications of such research are being systematically studied concurrently.

## ***Technological developments***

Only a small minority of these bacterial types in the human body can be cultured. The culture-independent high-throughput sequencing has greatly expanded the repertoire of known microbes and has made it possible to characterize and compare many samples rapidly. This has enabled the detection of disease-associated patterns in the human microbiota.

Transforming the vast amounts of data that these projects will generate into useful and applicable knowledge requires novel approaches of interpretation such as "machine reading". The application of these methods will hopefully more accurately predict disease states and appropriate therapies.

**Contd. on page 12**



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# MICROBIOME & APPLICATIONS...

New technologies are coming into focus such as I chips/ I tips and micro-fluidic studies, gut on a chip constructions, colonic stem cell constructions and are already in use in research laboratories.

## Conclusion

It is believed that future advances in science in the field of microbiome

would hopefully demonstrate that there are opportunities to improve human health through monitoring or manipulation of the human microbiota.

1) Jose C Clemente, Luke K Ursell, Laura Wegener Parfrey, Rob Knight. The Impact of the Gut Microbiota on Human Health: An Integrative View. Cell 148, 16 March 2012.

2) Baohong Wang, Mingfei Yao, Longxian Lv, Zongxin Ling, Lanjuan Li. The Human Microbiota in Health and Disease. Engineering 3 (2017) 71–82.

3) Christina Tobin Kährström, Nonia Pariente & Ursula Weiss. Intestinal Microbiota in Health and Disease. 7 July 2016, Vol 535, Nature 47.

## DELAYED DIAGNOSIS OF MALARIA RISKS REINTRODUCING THE DISEASE TO SRI LANKA

Munas M Muzrif<sup>1</sup>, M Weerasena<sup>1</sup>, A D Ranaweera<sup>1</sup>, M N Danansuriya<sup>1</sup>, S D Fernando<sup>2</sup>

<sup>1</sup>Anti Malaria Campaign, Ministry of Health, Sri Lanka

<sup>2</sup>Department of Parasitology, Faculty of Medicine, University of Colombo

**S**ri Lanka received global recognition for eliminating malaria in September 2016. The last case of indigenous malaria was reported in October 2012. With imported malaria cases being reported in the country, and the vector mosquito being prevalent here, malaria could be re-introduced to Sri Lanka unless precautions are taken. This comprises a major challenge to the health care personnel of Sri Lanka. A case of a recent patient with imported malaria who failed to be diagnosed for 25 days, and was instead repeatedly treated for various other conditions in several hospitals, illustrates the major

challenge facing the country in keeping it free of malaria.

A 39 year old Sri Lankan male, building construction worker who was working in Guinea, Africa, developed fever in March 2017, and was diagnosed with malaria and treated appropriately in Guinea.

- He arrived in Sri Lanka on the 10th of April 2017 and started working in his company.
- Developed fever on the 19<sup>th</sup> of April 2017
- Consulted a General Practitioner in the Colombo District and received treatment for viral fever
- Got himself admitted to Base Hospital X in the Colombo District on the 23<sup>rd</sup> of April due to continuing fever
  - o Treated for fever from 23 - 30<sup>th</sup> of April at this Base Hospital (BH X) where malaria was not considered in the differential diagnosis

- o Treated for typhoid fever with Cefuroxime, Ceftriaxone, Doxycycline,
- o Left against medical advice on the 30<sup>th</sup> of April due to persisting fever.

• Admitted to a Private Hospital in the Colombo District (PVT A) on the same day (30<sup>th</sup> of April) and the same treatment initiated at BH X, was continued. Fever subsided temporarily. A past history of malaria was noted on the BHT.

- o U/S abdomen done at PVT A: showed acute parenchymal liver disease.

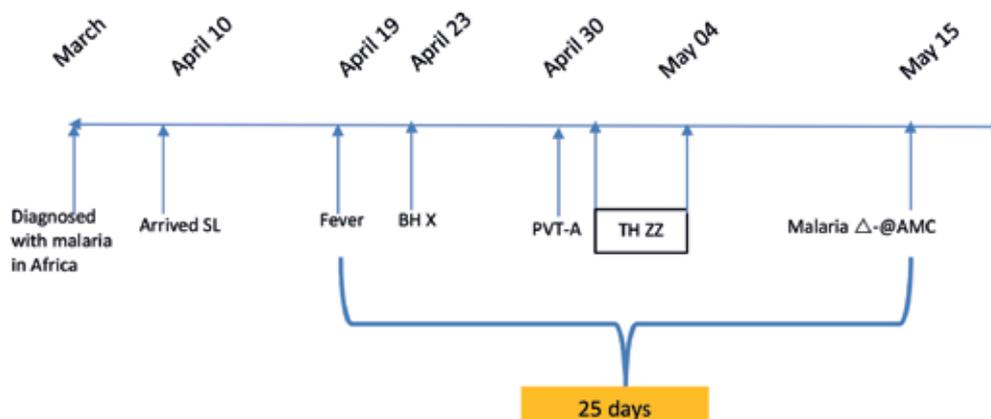
• Transferred to a Teaching Hospital in the Colombo District (TH Z) for further management on the 1<sup>st</sup> May 2017 and investigated for hepato-splenomegaly until he was discharged on the 4<sup>th</sup> of May 2017.

- o During the stay a blood smear for malaria was requested but the result was reported as negative for parasites.

o Patient presented for clinic visit on 15<sup>th</sup> May 2017 to TH Z – Senior Registrar referred patient to the Anti Malaria Campaign (AMC).

- Patient came to AMC on 15th May 2017 afternoon: diagnosed with Plasmodium falciparum Malaria.

• After a delay of 25 days, treatment with anti-malarial medicines was started on the 15<sup>th</sup> of May immediately after diagnosis and the patient was re-admitted to BH X for inpatient-treatment as a requirement.



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## DELAYED DIAGNOSIS OF...

### Comment:

- Of the many contacts the patient had with the health system, only in one (private hospital) was a past history of malaria and a travel history was elicited.

At none of the points of contact was a malaria diagnosis sought through blood examination.

- Treatment being delayed for 25 days could have threatened the life of the pa-

tient. Secondly, over the 25 days the patient could have transmitted the infection to vector mosquitoes and begun a cycle of transmission in the country again.

- Having been certified by the World Health Organisation as malaria-free, the country needs to report on indicators which include the responsiveness of the health system to suspect and diagnose imported malaria cases promptly. The present case history critically shows that our health

system needs fuelling with sufficient training and a positive attitude amongst healthcare providers with regard to malaria diagnosis.

### Acknowledgements

We would like to thank Dr H D B Herath, Director Anti Malaria Campaign for his continuous support and Dr Kamini Mendis for all the assistance she has provided on writing up this article.

## WHAT WOULD PEOPLE SAY ABOUT YOU AFTER YOUR DEATH?

### The legacy of Alfred Nobel

Can you imagine reading your own obituary in the newspaper? What would people say about you? Alfred Nobel got the chance to read his own death notice, and he didn't like what he saw.

Alfred Nobel was a very wealthy and successful man. He had become an expert in chemistry and invented three of the most commonly used explosives in the world - dynamite, gelignite (used in mining) and ballistite, which is still used as a rocket propellant today. With the huge fortune he made from these inventions, Nobel bought an engineering company called Bofors and turned it into an arms manufacturer. He made another enormous fortune designing cannons and guns and selling them around the world.

Then, in 1888, Alfred's brother died while visiting France. A French newspaper thought it was Alfred who had died and they published an obituary that began like this:

#### **THE MERCHANT OF DEATH IS DEAD**

*Dr. Alfred Nobel, who became rich by finding ways to kill more people faster than ever before, died yesterday....*

Alfred Nobel was shocked. Was this what people thought of him? Was this the legacy he would leave to the world?

That's when he decided to use his vast wealth to make a positive difference. Nobel set up a foundation with 250 million dollars in funding. Every year the foundation would consult the leading experts in the world and hand out prizes to people who had made great contributions to humanity. There would be prizes for sciences, for literature, and for promoting peace.

Today the Nobel Prizes are probably the best known and most prestigious awards in the world. They have been awarded to great scientists, authors and activists and helped draw attention to many outstanding works and worthy causes.

Nobel set up his foundation in 1895; just in time to influence his own obituary. He died only a year later.

The Nobel Prizes accomplished his wish; they created a very different legacy for him than a reputation as "The Merchant of Death." He is not remembered as an explosives inventor or arms dealer any more but as one of the greatest philanthropists of all time.

He is also a great example of how it is never too late to change your life and help make the world a better place.

What will you be remembered for?

*Content provided by Dr B J C Perera from an electronic mail forwarded to him by Professor Sanath P Lamabadusuriya*

# MS WALK

Dr Enoke Corea  
President,  
Multiple Sclerosis Association of Lanka

**W**orld Multiple Sclerosis (MS) Day is celebrated on the final Wednesday in May. This year, World MS Day was held on Wednesday, 31<sup>st</sup> May with the theme "Living with MS". In Sri Lanka, the MS Association of Lanka (MSAL) has held commemorations of this day ever since the very first World MS day in 2009. This year, MSAL held a Walk to raise awareness on MS among the general public on Saturday June 10th at the Viharamahadevi Park. The Chief Guest was the SLMA President, Prof Chandrika Wijayarathne and the Guest of Honour was the President of the Association of Sri Lankan Neurologists (ASN), Dr Udaya Ranawaka.

The MSAL was founded by Dr Hithaishi Perera, a doctor and MS patient, who realised that her fellow MS patients needed a support group to combat the stigma and isolation they felt and the lack of knowledge and awareness among their families and communities. She mobilised a group of her classmates and launched MSAL as its first President. Unfortunately, due to increasing ill health she was unable to continue day to day running of the Association but remains as the first contact for patients.

The MSAL is an association bringing together persons with MS, their doctors, caregivers and other well wish-



ers with a view to promoting optimum health and improving the lives of persons with MS. MSAL was started in year 2006 and is a registered company with audited accounts. It is affiliated to the Multiple Sclerosis International Federation and is a voluntary organization funded by donations and fund raising activities of the Association.

The main aim of the Association is to provide support to persons living with MS. Activities of the Association include providing moral support to patients and caregivers through home visits, organizing talks by experts to help patients understand and cope with their disease and by providing financial assistance, where necessary, for wheelchairs, physiotherapy, purchase of drugs and disposables, for travel to MS meetings and for daily living especially in cases where

the bread winner has been affected. The association serves as a support group for patients and their families where they can share their day to day problems and solutions. Through the association, people round the country could be made aware of Multiple Sclerosis and know that something can be done about preventing permanent disability. The association hopes to raise funds to build awareness, train nurses, attendants and family members, provide rehabilitation accessories, counseling, and support and effect infrastructure changes in patients' homes to aid in improving mobility and self-sufficiency.

MS meetings are held in Colombo and Kandy. These meetings provide an opportunity for MS patients to share their experiences and coping mechanisms with other patients and are open to anyone interested in MS. We have had many speakers addressing our meeting including national and international specialists in MS, neurologists, urologists, rehabilitation physicians, speech therapists, physiotherapists and nurses, including nurses specializing in rehabilitation.

We have published articles on MS and interviews with MS patients in the newspapers, in both English and Sinhala, in our effort towards creating greater public awareness and are hoping to have some publicity in the Tamil language newspapers as well.



Contd. on page 16

# MS WALK...

The latest venture of the association is a programme to conduct a needs assessment of each patient in their own home environment to generate recommendations for patient care, physiotherapy, assistive devices and alterations of home infrastructure needed to improve the quality of life of MS patients and their caregivers.

The MSAL would like to invite all persons with MS to join the MSAL and contribute to its activities. We will be grateful if doctors who care for MS patients would inform patients of this Association and its activities and refer them to the association or send us names and addresses of patients. MSAL can be contacted at msalinfo@slnet.lk or MS Association, 144 Vipulasena Mawatha, Colombo 10 or at the following number 0777319333. More information can be found on our website [www.mssrilanka.org](http://www.mssrilanka.org).

The MSAL is a voluntary organization funded by donations and fund raising activities. Fund raising activities are held regularly and include benefit show and movies, jumble sales, sale of Christmas cards and key tags etc. The Association would welcome donations which will be used to further the objectives of the Association. Donations could be made to The Multiple Sclerosis Association of



Lanka, Commercial Bank A/c Number 1100037477.

*“Getting the MoSt out of life!”*

## MINIMIZING PRE-ANALYTICAL ERRORS FOR A COMPREHENSIVE PATHOLOGICAL EVALUATION OF TUMOURS: THE SURGEON’S ROLE

Dr A A H Priyani  
Consultant Histopathologist,  
Senior Lecturer in Pathology  
Department of Pathology,  
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Convener for National  
Immunohistochemistry  
Laboratories 2011-2016  
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**H**istopathological evaluation of a malignant tumour extends beyond its diagnosis. It also includes assessment of factors for

prognostication and post-operative management of patients that include tumour staging and grading, completeness of excision with resection margin clearance to the closest millimeter. In the current era, immunohistochemical (IHC) evaluation has become a mandatory investigation for most of the cancers. IHC is used to determine the tissue of origin and the expression of tumour specific molecular markers determining the prognosis and personalized therapy of a patient.

Optimal fixation of tissue in a suitable fixative and preservation of anatomical relations without distortion of the specimen are fundamental requirements for a pathologist to assess a specimen and issue a comprehensive pathology report that determines the subsequent management of the patient. Similarly, if a biopsy is sent for pre-operative diagnosis of a tumour, the sample obtained should be adequately representative of the lesion.

Contd. on page 18

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## MINIMIZING PRE-ANALYTICAL...

### Tissue fixation:

Proper tissue fixation is of paramount importance to preserve tissue architecture and cellular morphology of a tumour that is required for its diagnosis and histological grading. Studies have shown a progressive fall in mitotic index of tumours (a loss of 30 to 50% by delay in fixation for 2 to 6 hours) introducing errors in the grading of breast carcinoma <sup>(1)</sup>. Optimum tissue fixation is also required for retrieval of tissue specific antigens assessed by IHC stains. Suboptimal tissue preservation due to both under or over fixation in formalin may result in false negative and false positive staining in IHC, impacting the specific therapy and the assessment of prognosis.

As per the guidelines of the American Society of Clinical Oncologists and the College of American Pathologists (ASCO/CAP), specimens should be fixed in 10% neutral buffered formalin as early as possible ensuring the cold ischemia time (total time from excision to placement in formalin) of less than 60 minutes. The duration of tissue fixation should be for a minimum of 6 hours and should not be more than 72 hours <sup>(2)</sup>.

The rate of penetration of formalin into a tissue is approximately one millimeter per hour, therefore, penetration of formalin to a deep-seated tumour located within a large specimen takes several hours. By then, the tumour has started the process of autolysis. To ensure uniform penetration of the fixative, it is important to fix small volumes of tissues (5 mm to 1 cm) <sup>(1)</sup>. The best way to overcome this problem is to send the specimen immediately to the laboratory, thereby enabling the pathologist to cut the specimen into thin sections, ensuring rapid and uniform fixation of the tumour.

Suboptimal tumour preservation is a significant problem in our settings where the specimens are not received immediately to the laboratory. A study done at a tertiary care setting

in Sri Lanka has shown that 14% of mastectomy and wide local excision specimens of breast have suboptimal tumour preservation irrespective of the type of surgery. None of the specimens received to the laboratory on the same day of the surgery has showed suboptimal tumour preservation <sup>(3)</sup>. The suboptimal tumour preservation also has shown a positive correlation with the delay in transporting specimens to the laboratory for more than one day <sup>(3)</sup>.

Therefore, if a delay is unavoidable, the surgeon should by arrangement with the pathologist, make a controlled single incision into the lesions, preserving the integrity of key resection margins. The specimen should then be put into a fixative immediately. If such an incision is made, the resection margins should be inked using India ink or a suitable water insoluble ink (fabric paint).

Fixation of the specimen in adequate quantity of formalin is also important. Ideally the container should have formalin more than 10-20 times the volume of the tissue <sup>(1)</sup>. Specimens contaminated with blood tend to autolyse quickly therefore the specimen should be clean before transferring into formalin. Light specimens like lipomatous tissue and lung tissue tend to float in formalin hindering fixation of the surface, hence can be covered with a large piece of gauze that will get soaked in formalin.

### Specimen orientation:

The specimens should be retained intact with proper anatomical relationships. Distortion of the specimens hinders precise identification of tumour infiltration to adjacent structures and accurate measurements of distance of the tumour to its resection margins.

The main reason for distortion of specimens is usage of inappropriate specimen containers. Usage of a small container and squeezing the specimen into a container with a nar-

row opening can result in distortion and sometimes fragmentation of the specimen. Wide-mouth adequate volume containers with well-fitting lids are suitable to transport tissue specimens for histopathological evaluation.

Unnecessary cutting into specimens after surgery also causes specimen distortion. Over enthusiastic surgeons sometimes cut the specimen to see how the tumour looks like, but this will distort the specimen, making identification of resection margins and anatomical relationships difficult.

Organ conservative procedures like wide local excisions in breast cancer are now popular than radical surgeries. These specimens lack normal anatomical relationships for tissue orientation; hence at least three anatomical directions (superior, lateral and deep) should be marked to orient the specimen. The tags used for the orientation should be properly written in the request form unless those were done per a standard protocol previously agreed by both parties. If multiple biopsies have been obtained from different locations of an organ, the specimens should be sent in appropriately labeled separate containers.

### Representative biopsy for pre-operative diagnosis:

Tumours have heterogenous morphology. It may contain areas with necrosis, cystic change, haemorrhage, degenerative changes and inflammatory reaction in addition to tumour proper. Viable tumour tissue also can show different morphological patterns in different areas. Hence a biopsy obtained for pre-operative diagnosis should be adequately representative of the tumour. General rules include obtaining multiple biopsies from a lesion, avoiding biopsying the periphery of a solid tumour, the centre of a cystic tumour and the base of an ulcerated tumour, which can show necrotic tissue and or inflammatory tissue.

## MINIMIZING PRE-ANALYTICAL...

The edge of an ulcer and the solid area of a tumour with cystic change are the best areas to biopsy. The surgeon also put the hands into trouble by sending two different biopsies of the same lesion to two different pathologists, hence receiving two different reports based on the morphological patterns present in different areas of the tumour.

### Labeling the container and filling the request form:

Patient identification to avoid specimen mixed up is a fundamental rule not only in tissue specimens but also for any specimen sent for investigation. The surgeons should make sure that the specimen containers are labeled with the investigation requested, patient identification details, specimen type and the site and the date of collection of specimen, prior to transferring the specimen to the container. If time of collection of the specimen is also specified, rapid processing of urgent biopsies is possible on the same day, as minimum time of fixation of six hours is adequate for small biopsies.

Most histopathology laboratories have developed their own request forms, which should be properly filled by the clinician. Details of previous biopsy or cytology reports and other concurrent tissue or cytology investigations requested should be included in the request form. Then the pathologist can issue a comprehensive report considering the findings of other tests and previous reports.

### Conclusion:

Specimens collected for histopathological evaluation are unique for several reasons. Firstly, obtaining a second sample is technically difficult and sometimes impossible if total excision of the lesion concerned has been done. Secondly, there is no guarantee that the findings to be

seen in the first biopsy will be seen in the subsequent biopsies. Further, the specimen collected is used not only for routine histopathology, but also for IHC and molecular assays as and when required.

Unlike other laboratory tests routinely done in a hospital laboratory, histopathology testing is costly. If a full panel of IHC markers were to be done on a tumour, the total cost may exceed LKR 100,000 - 200,000. A significant number of IHC tests are repeated in hospital IHC laboratories due to difficulties in antigen retrieval because of suboptimal fixation of tissue.

Therefore, proper collection, handling, fixation and transport of specimens are of paramount importance for the benefit of the patient and for the health budget.

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## MALARIA COUNT

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## The mysteries of type 2 diabetes in developing countries

More research is needed in low- and middle-income countries where the epidemic of type 2 diabetes is on the rise. KM Venkat Narayan talks to Fiona Fleck.

**Q: How did you become interested in type 2 diabetes research?**

**A:** When I was a physician and public health person working largely on cardiovascular diseases (CVD) in the early 1990s, a leading cause of death in Scotland at the time, I was invited to join a study of people with type 2 diabetes. This study included a work group to develop standards of care and I got to attend the Cambridge Diabetes Epidemiology Seminar. I met Peter Bennett, who was leading the Pima Indian Study at the National Institutes for Health in the United States of America. He invited me to join his team for two years. It was a difficult decision. My wife and I had to leave tenured jobs and move to Phoenix, Arizona. But those two years have extended to 24 years. Spending time with the Pima Indians and studying the disease and the suffering it was causing was a defining experience for me. I sensed that what was happening in the Pima community could happen to the rest of the world.

**Q: And it did happen. As a cause of death, diabetes jumped from number 15 in 1990 to number nine in 2010. Which countries now have a high burden of type 2 diabetes and which are tackling this disease in the most effective way?**

**A:** Countries in the Middle East have a very high prevalence. The countries with the largest number of people with type 2 diabetes are China, India and the United States of America (USA). A major concern today is the increasing numbers of people with type 2 diabetes – not just in China and India – but also in other middle-income and low-income countries. The greatest success in the last 10 to 15 years has been in reducing deaths and complications in people with diabetes, such as heart attacks, stroke, amputations and kidney failure, particularly in Finland, the USA and other high-income countries. High-income countries now have effective tools for the control of blood glucose, blood pressure, lipids and screening for early complications and have done useful research to find ways to implement good quality of care.



Courtesy of KM Venkat Narayan  
KM Venkat Narayan

KM Venkat Narayan is one of the world's leading researchers on type 2 diabetes. He directs the Emory Global Diabetes Research Center. Prior to joining Emory University in 2006, he spent 10 years at the United States Centers for Disease Control and Prevention, leading the science efforts in his role as Chief of the Diabetes Epidemiology Section and later the Epidemiology and Statistics Branch. Narayan worked on the first diet-exercise intervention study as part of the Pima Indian Study of diabetes at the National Institute of Diabetes and Digestive and Kidney Diseases from 1992 to 1996, where he helped to develop the Diabetes Prevention Program (DPP). Before that, he worked in India, the United Arab Emirates and the United Kingdom of Great Britain and Northern Ireland as a tenured public health physician. He graduated in medicine in 1980 from St John's Medical College, Bangalore, India and subsequently qualified in geriatric medicine, public health and management. He is a member of several international and national committees on type 2 diabetes and other noncommunicable diseases. In 2015 he won the American Diabetes Association's Kelly West Award for outstanding achievement in epidemiology and is the Danish Diabetes Academy visiting professor at the University of Copenhagen.

**“ I sensed that what was happening in the Pima community could happen to the rest of the world. ”**

**Q: So more people are living with type 2 diabetes than two decades ago?**

**A:** Yes, more people are surviving longer with the disease, but that means there are more and more people with costly complications. For example, diabetes is the leading contributor to the rise in inflation-adjusted health-care costs in the United States.

**Q: If it's so expensive to manage the disease and its complications, why isn't more done to prevent it?**

**A:** In the last 20 years several large randomized controlled trials in people at high risk for developing diabetes showed that aggressive life-style interventions (24 weeks of structured counselling,

individually or in groups to modify diet and activity) can reduce progression to diabetes by 30–60%. That's huge. The challenge is to implement that approach across national health systems and, even if implemented, the overall impact on prevalence would be modest, as it would only target people at high risk. Effective type 2 diabetes prevention must target people much earlier, but we still don't know how to do this.

**Q: How can we prevent diabetes across whole populations at an earlier stage?**

**A:** There is a huge knowledge gap at two levels. One, some countries [see news feature on previous page] have introduced taxation on sugar and soft drinks, so people are buying less and shifting consumption to other drinks. But we don't know which drinks they are shifting to or, importantly, whether this measure is helping to reduce obesity. Two, many countries subsidize the wrong foods, such as refined grains and highly processed foods, and while they recommend five portions of fruit and vegetables a day, the global supply of fruit and vegetables is currently unable to provide this. That shortfall in fruit and

vegetables is even greater in developing countries. We need to know how best to incentivize the industrial and agricultural sectors to produce more healthy food at affordable prices. We also need to get to know how best to motivate people to engage in more physical activity and to make their diets healthier.

*Q: Much of your recent research has been in low- and middle-income countries, why?*

A: Information from high-income countries does not necessarily apply to low- and middle-income countries. In south-east Asia and sub-Saharan Africa many thin people are developing type 2 diabetes. So there may be other important factors for the disease apart from being overweight. We have good data on how to treat diabetes and prevent it in high-risk groups, but we need to seek more knowledge on how to do this in developing countries. There is a huge dearth of prospective epidemiological data in low- and middle-income countries and a lack of intervention studies in these settings, and we need to invest in understanding the biology across the populations that are most affected. Why are so many thin people developing type 2 diabetes in low- and middle-income countries, does this suggest a different phenotype? We need to take the research and the epidemiology to where the epidemic is.

*Q: What should low- and middle-income countries be doing to tackle their diabetes epidemics?*

A: They should deliver good quality care for people with diabetes and they should identify people at high risk of developing diabetes and implement proven life-style interventions. These are the two immediate priorities. If we can reduce the rates of diabetes complications in high-income countries, why not in low- and middle-income countries? The big question is: can these countries afford to scale-up treatment and prevention? We can learn from the experience of other fields. For example, you can capitalize on: task-shifting to non-physician health-care professionals, low-cost medications, technology and telemedicine. In the vaccine and HIV research fields, the costs of interventions and technology have been reduced by shifting research hubs to low- and middle-income countries. We also need to collectively study the

effectiveness of the policies that work and get them implemented. We are not going to win the war on diabetes without more research and better data systems in the countries where many people have diabetes and where the diabetes epidemic is growing fast.

*Q: How can good quality care be delivered in low- and middle-income countries?*

A: We need to find ways of delivering noncommunicable disease (NCD) prevention and care, regardless of the socioeconomic constraints. India has a fantastic infrastructure for tuberculosis through the DOTS programme. A lot of people with tuberculosis also have diabetes, so why don't we integrate prevention and care into the tuberculosis clinic network or through primary care? In Africa we can do the same with HIV clinics. Just because a country lacks health resources does not mean good quality programmes cannot be implemented. We are talking about task-shifting to help to achieve this. There are many community health workers working in maternal child health who can be deployed for NCD care also, and patient groups have to be empowered.

**“ We need to take the research and the epidemiology to where the epidemic is. ”**

*Q: What contribution does WHO's Global action plan for the prevention and control of NCDs 2013-2020 have the potential to make?*

A: WHO has enormous power as a convener and whatever WHO says has a lot of credibility across the world, especially in low- and middle-income countries. There is extremely strong evidence for the effectiveness of better treatment and we should push harder for good quality diabetes care and management and access to essential medicines for diabetes. Developing countries need better monitoring of quality of care, better governance, better health financing models and more standards that governments can use. It's tempting to argue for large social and policy measures, but

they need to be evidence-based. We need a process of trial and error, where we implement national policies but also evaluate them so that we can learn as we go and avoid mistakes. WHO could argue for greater investment in surveillance and research, including basic research, in low- and middle-income countries.

*Q: What contribution can the sustainable development goals (SDGs) make?*

A: A lot. The SDGs cannot be achieved without addressing NCDs such as type 2 diabetes. The international community needs to rally for investment in global NCD prevention and control, in the same way as for HIV. It's a matter of strengthening primary health systems in low- and middle-income countries, where a good package for NCD and cardiovascular disease management costs about US\$ 400 per person per year.

*Q: Type 2 diabetes is increasingly appearing in young children. How can we stop this?*

A: The first cases of young onset were noted in the Pima Indians in the 1970s. At that time it was thought to be a Native American problem, then it appeared in Japanese people and it was thought to be a minority problem, until it occurred in the white population. In the late 1990s at CDC, we found that type 2 diabetes in youth was occurring in all ethnic groups, and that's how the SEARCH study started. The study has shown that type 2 diabetes is rare in children aged under 10 years, but not uncommon in the 10-to-20 years' age group. Studies have also shown that young-onset type 2 diabetes is linked to childhood obesity, and to maternal obesity and glucose levels during pregnancy. We published a paper in the *NEJM* in 2014 tracking a nationally representative sample of 7000 kids in the United States aged between five and 14 years. We found that by five years 27.5% of the kids were overweight, including 12.5% who were obese, and that some factors for childhood obesity and diabetes are rooted in pre-school age and maybe in utero. It's not surprising that the results of large studies of school-based interventions have not been encouraging, because some of the factors driving young-onset type 2 diabetes start in very early life. ■



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