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October 2016, VOLUME 09, ISSUE 10





THE OFFICIAL NEWSLETTER OF THE SRI LANKA MEDICAL ASSOCIATION

# **Children and Adolescents** in Exercise and Sport

**Midwives use Smart Phones** to Monitor Malnourished Children

**Hepatoprotective Effects of Medicinal Plants** 

Winners of **Prizes and Awards-SLMA 2016** 



#### Foundation Sessions 2016









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# **SLMA President**



Dr. Iyanthi Abeyewickreme MBBS (Ceylon), Diploma in Venereology (London), MSc, MD (Colombo), FCVSL, Hon. Senior Fellow PGIM Consultant Venereologist

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#### Official Newsletter of The Sri Lanka Medical Association

No. 6, Wijerama Mawatha, Colombo 7. Tel: +94 112 693324 E mail: office@slma.lk

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# **PRESIDENT'S MESSAGE**

ctober was a very busy and an important month for the SLMA. The renovations and refurbishments taking place at Wijerama House may have inconvenienced many and I thank them for their support and patience. We managed to complete most of the work in time for the Foundation Sessions which was the highlight of the month. You may be aware that the Foundation Sessions were held outside Colombo during the past years. However, in 2015 the SLMA Council decided that in future, the Foundation Sessions should be held at the SLMA House itself. Hence, the Sessions were held in Colombo at the Wijerama House from 20<sup>th</sup> – 22<sup>nd</sup> October 2016.

The Foundation Sessions of the SLMA were held for the first time in 1997 during the presidency of late Dr. S. Ramachandran. At that time the Annual Anniversary Medical Congress was held during March and there were not many academic activities thereafter. Therefore, the aim of having the Foundation Sessions was to fill the vacuum in the academic calendar of

the SLMA during the second half of the year. The Dr. E.M. Wijerama Endowment Lecture which is an integral part of the foundation sessions was initiated to honour Dr. E. M. Wijerama who donated his magnificent mansion to the Sri Lanka Medical Association. The first E.M. Wijerama Endowment Lecture was delivered by Dr. C. G. Uragoda. This year, the E.M. Wijerama endowment lecture was delivered by Dr. Suriyakanthie Amarasekara, Consultant Anaesthetist and Past President SLMA who has served the Association with distinction and dedication.

There was a symposium on 'Safety in the health care setting' and an interactive session on 'Advertisements on healthcare products and cosmetics – are they misleading or not?' In addition, a workshop on 'Management of acute poisoning' was conducted as part of the academic programme.

The SLMA also signed a Memorandum of Understanding with the Chinese Medical Association during October for the purpose of exchanging information on continuing medical education, short-term training, exchanging meeting calendars of annual scientific meetings and/or international scientific meetings and for bilateral visits for the annual meetings.

The Social Activities Committee, which was responsible for the most memorable Doctors Concert this year, is busy planning and preparing for the Medical Dance which will be held on 9<sup>th</sup> December 2016 at the Cinnamon Grand Hotel. Please purchase your tickets from the SLMA office. I invite all doctors and their families to join us for an unforgettable evening of fun and fellowship.

The Annual General Meeting (AGM) of the SLMA will be held on 23<sup>rd</sup> December at 7.00pm at the N.D.W. Lionel Memorial Auditorium. It is important that SLMA members attend the AGM and I invite all members to be present on the 23<sup>rd</sup> of December.

With best wishes, Dr. Iyanthi Abeyewickreme

# CHILDREN AND ADOLESCENTS IN EXERCISE AND SPORT

Dr. B.J.C.Perera MBBS(Cey), DCH(Cey), DCH(Eng), MD(Paed), FRCP(Edin), FRCP(Lond), FRCPCH(UK),



FSLCPaed, FCCP, CGP(SL) Consultant Paediatrician and Senior Fellow, Postgraduate Institute of Medicine, University of Colombo Honorary Advisor, Sri Lanka Sports Medicine Association Past President, Sri Lanka Medical Association

hildren and adolescents are naturally active and exercise is generally considered to be a part and parcel of life for them. It is a well-researched and proven adage that a physically active childhood

is a sine gua non for a healthy childhood and, even more importantly, for a hale and hearty life into the future, way beyond childhood and adolescence. However, this age-old notion is being gradually eroded by a set of circumstances quite a bit beyond the control of children and young people themselves. The amazingly fast pace of life, the ubiquitous complaint of a woeful lack of time for them and their parents, academic needs in a rat race for continued educational superiority and plain laziness inculcated through sheer lack of peer pressures, are some of the constraints that have increasingly produced a set of 'couch potatoes'. Enter over-weightiness and frank obesity, with their attendant future complications, into the lives of the jewels of society, the next generation.

Experts tell us that, in some areas of our country, at least one in five children have these problems of being overweight and obese. In contrast to the times of today, several decades ago, finding a child or an adolescent at home, between the hours of 4 to 6 in the evening, would bring about visions and suspicions of a physical illness or even a psychological malady. Those youngsters were expected to be out in a playing field and being involved in some sort of sport. The weighty problems were extremely rare. Alas, how times have changed !!

Yet for all that, there is a rather small cohort of children and adolescents who, due to many a reason, take up to sports, just as ducks take to water.

Contd. on page 03



2

## Contd. from page 02 CHILDREN AND ADOLESCENTS...

They get involved in social level sports and the more talented even get into competitive sport. In fact, many of them are now being recruited into organised competitive sport from a very young age. The reasons for such occurrences are many. Material, financial and even scholastic privileges associated with winning performances at the elite level count very high in the list of compelling reasons that entice them to take up to organised competitive sport.

What is generally not appreciated is the notion that children and adolescents are not miniature adults, that they have unique features and that they need very special attention. These youngsters need expert care in coaching, training, dietetics and psychological interventions, to enable them to blossom out to their fullest potential. Growth, development, gender differences, talent, coaching and training are some of the important considerations in dealing with children in sport. Different types of training include specific technicalities of the particular sport as well as nonsports-specific training procedures to develop general fitness, endurance, speed, acceleration, agility, flexibility and strength.

Ken Doherty, the Irish Snooker player who had the rare distinction of being the World Champion in amateur as well as professional circuits once said "There are five **S**s in sport., **s**tamina, speed, strength, skill and spirit. The greatest of these is the spirit". The spirit of the game., the spirit of participation. This is very relevant today in this intensely competitive world. Everybody wants to win. It has often been said "never mind whether you won or lost but what matters is that you played the game". Sadly today, some may not even have heard of it or for that matter, even believe it.

However, it is paramount that these activities that are undertaken are appropriate for the age and stage of development of the child. Proper training will also help to mitigate against injuries. All these training procedures can be instituted from a very young age, provided that care is taken, under medical supervision, to make the schedules as suitable a possible for each individual child. Over enthusiasm and the culture of pushing the child too hard on the part of coaches and trainers should be carefully moderated and even curtailed. For example, if a child is made to swim so hard that at the end of the training session he or she is not even able to get out of the swimming pool, we are going way over the limits of endurance.

Precise selection of training procedures, use of correct equipment, expert advice and medical supervision are important in the makeup of a child or adolescent involved in sport. These are even more important for talented elite athletes. Care must be taken to avoid 'burn out' due to excessive training and unremitting competition. A proper balanced diet and adequate hydration are two other important components in the life of a child athlete. Contrary to popular belief, there are no magic foods or fluids that enhance performance. Many of the supplements that are bandied about as magic potions for excellence in sports performance have no scientific merit.

Young female athletes have special problems. These include menstrual difficulties, psychological aspects, vulnerability towards special injuries and the female athlete triad/tetrad. Many young girls involved in sports develop their own ways of dealing with their monthly problems. Some may need medical attention too for the menstrual disturbances. In certain types of sports, female athletes are more prone to develop specific injuries. A case in point is that young girl athletes are around six times more prone to develop anterior cruciate ligament injuries of the knee when compared to male athletes. The Female Athlete Triad/Tetrad consists of eating disorders. menstrual troubles, osteoporosis and cardio-vascular problems.

Young athletes with injuries need specialised attention. Certain injuries, if not handled with expert care, could lead to major problems in the future. Some of these may even have the potential to cut short a very promising athletic career. Some chronic diseases such as asthma, diabetes etc., are not specific contraindications to taking part in sports. In fact young people with these problems are well known to benefit by taking part in sporting activities. In point of fact, quite a few of the greatest and most famous athletes are known sufferers of some of these chronic maladies. A classic example is Jackie Joyner-Kersee. She is dubbed as the "Super Woman Athlete" of all time and considered by many to be the all-time greatest athlete in the women's heptathlon as well as in the women's long jump. She won three gold, one silver, and two bronze Olympic medals, in those two events, at four different Olympic Games. The 1987 Sports Illustrated magazine, in its front cover, labelled her as The Super Woman, However, SHE WAS A BAD ASTHMATIC, and she fought that too like a true champion.

Sports psychology is also of paramount importance to young sportspersons. Parents have a very special role to play in the case of children and adolescents in sport. It is necessary to realise that the making of a champion depends a lot on how these elite and talented children and adolescents are handled. They have to be able to handle victory as well as defeat in the most gracious of manners. For a young sportsperson, winning is ever so important. Pele the Brazilian star, the King of Football, once said "More difficult the victory, greater is the happiness in winning". Those who win trophies and medals may not have real gold in their acquisitions but they are made of determination, sweat and guts. Only those who are conversant with the sports scenario would know how much effort has gone into those winning ways.

Contd. on page 04

# Contd. from page 03 CHILDREN AND ADOLESCENTS...

Yet for all that, the immortal words of Rudyard Kipling at the entrance to the hallowed Centre Court of *Wimbledon "If you can meet with Triumph and Disaster and treat those two imposters just the same..., you'll be a man, My Son"* should be the guiding motto for all young sportspersons.

However, just to secure a victory, engaging in all kinds of malpractices, cheating and even resorting to various forms of doping, would definitely be classed as totally unacceptable behaviour patterns that are way below the level of an elite sportsperson. There generally is zero tolerance to all these forms of misconduct. In the normal course of events, retribution is a certainty, sooner or later. Perseverance and relentless trying are qualities that need to be nurtured in a young sportsperson. It was Michael Jordan, the American Basketball star, who won two Olympic Gold Medals, who said "Obstacles do not have to stop you. If you run into a wall don't turn around and give up. Figure out how to climb it, go through it or work around it". The motto should be "Win if you can, lose if you must, but NEVER EVER QUIT".

A frequently doled out excuse for not taking part in sporting activities is that there is no time. It is definitely not a valid excuse. The secret is to MAKE TIME. This has to be drilled into the minds of young people today. Never mind everything else, even exams come and exams go, make time for sport and exercise. It has been said that sport does not build character, it actually reveals your character. Sport shapes personality too. These are desirable attributes that go a long way towards the making of a balanced and pleasant disposition later on in life.

It was Muhammad Ali, the greatest heavyweight boxer of all time, who said "Champions are not made in the gyms. Champions are made of something they have deep inside them, a desire, a dream, a vision". It is imperative that in addition to all forms of training, dietary attention and psychological adjustments, young athletes learn that the more you dream, the further you get.

# THE MONTHLY CLINICAL MEETING OF THE SLMA FOR SEPTEMBER 2016

Dr.Kushlani Jayatilleke, Assistant Secretary-SLMA

he monthly clinical meeting of the SLMA for September 2016 was held on 20<sup>th</sup> of



September from 12 noon to 1.30pm at the SLMA Auditorium in collaboration with the Sri Lanka College of Obstetricians & Gynaecologists. The topic for discussion was "Post-partum Haemorrhage". The case presentation was done by Dr C. G. Maggonage, Senior Registrar in Obstetrics and Gynaecology. Apresentation on "Visual Estimation of Blood Loss in Post Partum Haemorrhage (PPH)" was made by Dr A. K. P. Ranaweera, Consultant Obstetrician & Gynaecologist, Profesorial Unit, De Zoysa Hospital for Women. This was followed by a Picture guiz on "Visual Estimation of Blood Loss" by Dr. M. R. M. Rishad, Consultant Obstetrician & Gynaecologist, Castle Street Hospital for Women. There was a discussion of MCQs by Dr U. D. P. Rathnasiri, Consultant Obstetrician & Gynaecologist, Castle Street Hospital for Women. The meeting was chaired by Dr.Dennis J. Aloysius.



SLMANEWS

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# 600 MIDWIVES IN POLONNARUWA, MATALE AND NUWARA ELIYA DISTRICTS USE SMART PHONE TO MONITOR MALNOURISHED CHILDREN!

Professor Vajira H. W. Dissanayake

President Designate, Commonwealth Medical Association, Past President, Sri Lanka Medical A sociation (2012) President, Health Informatics Society of Sri Lanka



\_ \_ \_ \_ \_ \_ \_ \_ \_ \_ \_ \_ \_ \_ \_ \_ \_ \_ \_ n my column of September 2015 of Sunday Times Business, I presented a scenario where health care workers in the field will be using smart phones to monitor patients in the future. This lead to a flurry of 'internet chatter' questioning when this would really happen and whether it is really possible in Sri Lanka. Well folks, we are on our way there. Within a year of that article we now have 600 midwives in Polonnaruwa, Matale, and Nuwara Eliya districts using smart phones to monitor malnourished children in their districts and we can monitor them from Colombo! The app that we developed to do so even won an international award - the mBillionth Award awarded by the Digital Endowment Foundation, India and Google. Yes, if there is a will there is a way, real progress is possible in this country. This column written with contributions from my team, illustrates this system.

In spite of substantial performance in many aspects of the preventive healthcare sector (you may have heard that Sri Lanka was certified as having eradicated Malaria recently) sadly nutrition indicators in our country continue to fail to stay on par with the rest of the health indicators. A significant proportion of Sri Lankan children are victims of various forms of malnutrition which has reflected negatively on the country's development agenda. Scientific evidence has shown that nutrition in the first 1000 days of life is decisive for the level of physical and cognitive development of the individual and hence has an impact on national productivity.

The District Nutrition Monitoring System (DNMS) was proposed as a solution to this challenge and the information system development and training were entrusted to the Health Informatics Society of Sri Lanka by the Nutrition Secretariat of the Presidential Secretariat. The task was undertaken by Dr. Pamod Amarakoon, a Medical Doctor who was reading for his MSc in Biomedical Informatics under the supervision of Dr. Roshan Hewapthirana, CEO, HISSL and myself. We collaborated with the Ministry of Health. The collaborators from the Ministry during the crucial final stages of the project implementation were: Dr. Rasanjali Hettiarachchi, Director, Nutrition Co-ordination Unit, and Dr R. R. M. L. R. Siyambalagoda, Deputy Director General, Public Health Services II. The team at the Family Health Bureau lead by Dr. Sapumal Dhanapala also played a crucial role. The funding for the project came from the UNICEF with Dr. Renuka Jayatissa and Dr. Gamini Jayakody playing a key role in this aspect. Our software development partner was k-soft.

The DNMS consists of two components: (1) data collection by midwives using a mobile application for Android based smart phones and storage of the data on a central server and (2) monitoring and evaluation by administrators using a web portal.

The mobile application component of DNMS is capable of gathering information of malnourished children categorizing the severity of the nutritional problem to facilitate nutritional interventions. At the same time, the system has a facility to record the underlying causative factors and facilitate channelling this information to multi-sector stakeholders based at the Divisional Secretariat of the area so that they can take corrective action at the house hold level – such corrective action may include providing nutrition supplements to the family, financial assistance to begin a home garden, etc.

In villages, malnourished children are identified at community health facilities and weighing centres. Malnourished children identified at these clinics will be registered in the DNMS using the smart phone by the midwives. At the same time, they will identify the risk factors in the household of the child that contributed to this situation and enter them into the system. The children entered into the system will be followed up in subsequent visits at a field clinic or at their homes. The data collected through the mobile device is transferred to the central server in real time. The data transferred to the central server is verified and approved by the supervising officers, such as Supervisory Nursing Sisters and Medical Officers of Health. Once validated by the supervising officers in the field, the data is available to higher level health authorities for analysis and decision making.



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# Contd. from page 06 600 Midwives in...



A DNMS training session at Matale



#### The DNMS Mobile Interface



The DNMS web interface where using GIS the exact location of the houses of malnourished children can be visualised on a map





Dr. Pamod Amarakoon, Dr. Rasanjli Hettiarachchi, and Dr. Roshan Hewapathirana Receiving the mBillionth Award for the best early stage mobile App in South Asia



The mBillionth Award

#### **RESPONSE FROM HEALTH STAFF**

Public Health Midwives positively accepted collecting data using the DNMS mobile application. They provided valuable input to improve the mobile application and the quick start manual. It was observed that within several hours the Public Health Midwives grasped the core concepts of DNMS. During the training sessions, they enthusiastically attempted to register children from the field allocated to them.

Q.

Some of the Medical Officer of Health areas were using a similar approach to identify malnourished children using paper records. Hence the DNMS concept was welcomed by Medical Officers of Health as a means to improve the current process.

The mobile interface was simple and easy to understand. It was observed that Public Health Midwives learnt the DNMS data entry process quickly. Health staff highly appreciated the on-site, hands on nature of the training. According to some of the Public Health Midwives, DNMS training was a motivation for them to use ICT for their routine work.

#### CHALLENGES AND SOLUTIONS

• Smart phones were seen as a challenge initially. However, we learnt that due to the very focused nature of mobile applications, training Public Health Midwives to use smart phones and mobile data entry were less time consuming than giving them general ICT training.

Similarly, we noted that the learning curve for using mobile phones was steeper than for desktop applications, especially for less IT savvy health care workers. This included creating Gmail accounts for them to register to the Google App store to download the DNMS application.

Lack of mobile coverage in some Public Health Midwives areas was a challenge to the DNMS design. However, we used a storeand-synchronize approach to overcome the issue and Public Health Midwives were able to successfully use this in areas with low mobile internet coverage.

٠ The after-sales support was negotiated with the smart phone vendor. We were able to devise a service model which can be replicated island-wide.

Providing a monthly mobile internet data bundle for Public Health Midwives was another challenge.

> Contd. on page 10 SLMANEWS

October 2016

# Contd. from page 08 600 Midwives in...

Currently, UNICEF provides a monthly internet allowance of Rs. 200 per Public Health Midwife.

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# **SLMA FOUNDATION SESSIONS 2016**



Contd. from page 09 **SLMA Foundation...** 



SLMANEWS

# *EMEDICAL* Contd. from page 10 DANCE **SLMA Foundation...** 9<sup>TH</sup> OF DECEMBER 8.00 PM ONWARDS @ Cinnamon Grand Hotel **Open to Doctors & Their Guests** Tickets to be purchased through a doctor Bands: "Flame" & "Misty" 🕀 Gift vouchers & gift packs for **TICKETS: RS. 6000/=** everyone **Dress: Lounge / National** Airline tickets & many more prizes Tickets available at SLMA office to be won No 6, Wijerama Mawatha, Colombo 7 Tel 0112 69 33 24 Sumptuous dinner Email: office @ slma.lk

# **MICROCEPHALY AND ZIKA**

Dr.Kapila Jayaratne MBBS, MSc, DCH, MD (Community Medicine) Consultant Community Physician, National Program Manager



Maternal & Child Morbidity & Mortality Surveillance,

Family Health Bureau – Ministry of Health, President – Perinatal Society of Sri Lanka.

In the new born, is a rare condition. This condition has recently gained much media and public focus because of its association with the Zika virus (ZIKV). On 1<sup>st</sup> of February 2016, WHO declared a Public Health Emergency of International Concern (PHEIC) in response to the reports of clusters of microcephaly cases and neurological disorders in the areas affected by the ongoing ZIKV outbreak especially Latin America. Microcephaly is a clinical sign and not a disease. Until recently, there was no standard surveillance case definition for microcephaly. At present microcephaly is broadly defined as a small head size, typically greater than two standard deviations below normal.

To assess whether a baby has microcephaly reliably WHO advocates measuring head circumference 24 hours after birth, comparing the value with WHO growth standards, and continuing to measure the rate of head growth in early infancy.

The head circumference <-2SD according to INTERGROWTH standards for gestational age and sex is preferred by many experts. The head circumference is measured as occipital frontal circumference.

**Incidence:** Birth defects registries in USA have estimated that microcephaly ranges from 2 - 12 babies per 10,000 live births. Many countries, including Sri Lanka, have no valid data on microcephaly and its causality.

Even the estimated incidence of microcephaly has wide variation due to differences in the definition and subjects under study.

#### How does it happen ?

The foetal skull is made of six bones that are not fused at birth. Head size of the baby in the womb increases in size because of brain growth, exerting physical force on the skull bones and causing them to expand as well. The rate of expansion is highest in the first few months and gradually plateau over time.

There are two mechanisms resulting in a 'small head' to occur; premature fusion of cranial sutures (i.e., craniosynostosis) or poor brain growth;

1. If the sutures between skull bones fuse prematurely, the head circumference will grow at a much slower rate results in an abnormal shape –Craniosynostosis.



# Contd. from page 11 Microcephaly and Zika...

2. When the foetal brain has a lower volume than normal, it may not grow as expected normally. Decreased brain growth exerts decreased outward force on the skull thus resulting in decreased expansion of the head circumference. This process may result in a normally shaped or symmetric head.

Microcephaly can present at various ages and can be either static or progressive, depending on the cause.

#### Causes of microcephaly:

Various aetiologies can lead to decreased brain volume and microcephaly but, often the cause remains unknown.

The most common causes are given in this table:

mosquito can result in a devastating malformation."

Zika virus is transmitted primarily by Aedes mosquitoes – this is the same mosquito that transmits dengue, chikungunya and yellow fever. Persons with Zika virus disease can present with mild fever, skin rash, conjunctivitis, muscle and joint pain, malaise or headache.

Zika virus is primarily transmitted to people through the bite of an infected mosquito. Evidence is emerging of sexual transmission of Zika virus even up to 6 months.

Genetic 40%	Perinatal brain injury 30%	Postnatal brain injury 30%
Syndromic	Congenital infections (TORCH)	Severe malnutrition
Trisomy (21, 18, 13)	CMV	Meningitis/Encephalitis
Continuous gene deletion	Rubella	Trauma
5p- deletion*	Toxoplamosis	Severe chronic diseases
Monogenic	Teratogens	Hypothyroidism
Rett syndrome	Alcohol, cocaine	Chronic renal insuffisiancy
Cornelia de Lange	Anti-epileptic, lead, mercury	Toxins
Rubinstein-Taybi	Radiation	Lead poisoning
Smith-Lemli-Opitz	Hypoxic-ischemic encephalopathy	
Isolated	Maternal disease	
Autosomal dominant	Hyperphenylalaninemia	
Familial (autosomal recesive)	Diabetis, hypertension	
X-linked	Severe maternal hypothyroidism	(Craniosynostosis)
Micro-deletions/duplications	Folate deficiency	
Inborn error of the metabolism	Placental insuffisiency	

Trisomy = Down syndrome

As such microcephaly has many causes, of which Zika is potentially just one, in addition to viruses such as Rubella, Cytomegalovirus (CMV) and Lymphocytic Choriomeningitis Virus (LCMV).

On 13<sup>th</sup> April, US Centre for Disease Control (CDC) announced Zika virus as the cause of a surge in birth defects across Latin America and the Caribbean, linking Zika infection during pregnancy not only to microcephaly but also to congenital blindness, stillbirths, and other foetal abnormalities (Dyer 2016). CDC states "There is no longer any doubt that Zika causes microcephaly. We believe the microcephaly is likely to be part of a range of birth defects." The CDC remarked "Never before in history has there been a situation where a bite from a

#### Diagnosis

During pregnancy, early diagnosis of microcephaly can sometimes be made by foetal ultrasound. The possibility of diagnosis is higher if ultrasound scanning is done at the end of the second trimester, around 28 weeks, or in the

third trimester of pregnancy.

Often diagnosis is made at birth or at a later stage by measurement of head circumference.

For the confirmation of the cause of microcephaly various laboratory investigations and imaging tests need to be done both in the mother and the baby;

- Serology/molecular testing for Zika, CMV, Rubella, toxoplasmosis, LCMV
- Cranial USS
- Karyotyping
- · Histopathological studies

#### Microcephaly Surveillance:

Sri Lanka is considered a country at possible risk of Zika virus transmission due to the presence of the transmitting mosquitoes.

After WHO declared a Public Health Emergency of International Concern in February 2016, and provided advice on standardising and enhancing surveillance for microcephaly and GBS, particularly in areas of known Zika virus transmission and areas at risk of such transmission, an expert working group including community physicians, paediatricians, neonatologists, geneticists, virologists and administrators, emphasized the need of microcephaly surveillance in neonates and developed a surveillance format.

The Ministry of Health, Sri Lanka initiated microcephaly surveillance from the 2<sup>nd</sup> week of February 2016 covering the entire country. The surveillance programme covers 77 specialized hospitals where 95% of births take place.

#### **References:**

Dyer, O, US agency says Zika virus causes microcephaly, BMJ 2016;353:i2167



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## HEPATOPROTECTIVE EFFECTS OF MEDICINAL PLANTS AGAINST CHEMICALLY INDUCED HEPATOTOXICITY

Professor N. D. W. Lionel Memorial Oration of SLMA 2016

By Dr. R. P. Hewawasam (BSc, MIChem C, MPhil, PhD) Department of Biochemistry Faculty of Medicine, University of Ruhuna



iral hepatitis is the most common cause of liver inflammation worldwide. According to the World Health Organization, Hepatitis B (HBV) affects as much as 10% of the adult population in endemic areas and causes approximately 780,000 deaths per year. An estimated 130 million to 150 million people globally are chronically infected with Hepatitis C virus (HCV). In addition, approximately 75-80% of newly infected patients will become chronically infected either by not being treated or by failure to respond to treatment. Long-term complications of chronic HCV infection develop over several years, including continued hepatic inflammation, cirrhosis, end-stage liver disease and hepatocellular carcinoma (HCC). The ultimate long-term goals of therapy are to achieve a sustained viral response (SVR) and to clear the surface antigen, thus preventing or reducing the development of hepatic decompensation, cirrhosis, or HCC as well as to prolong survival. Seven agents have been approved by the Food and Drug Administration (FDA), USA to treat chronic hepatitis, which include two immunomodulators (conventional IFN- $\alpha$  and PEGylated IFN- $\alpha$ ) and five nucleoside/ nucleotide (NA) analogs (lamivudine, telbivudine, entecavir, adefovir and tenofovir).

Unfortunately, side effects preclude the use of IFN- $\alpha$  in large numbers of patients, and prolonged maintenance therapy to suppress HBV is not feasible. Furthermore, combination therapy costs approximately 10,000/- to 18,000/- USD per year. Although interferon, nucleotide analogue combination therapy has been the standard of care in developed countries regardless of which genotype of HCV the patient was infected with, the overall

sustained virologic response (SVR) rate is 50-60% with this treatment. The search for new drugs continues to improve the SVR rates in patients infected with certain HCV genotypes as well for those who do not respond well for the combination therapy. Since most of these advanced therapies are not affordable to the patients in the developing world, the search for new therapeutics remains a higher priority. For many of the chronic conditions including liver cirrhosis no cure currently exists, despite progresses in understanding the mechanisms of fibrosis and pinpointing a number of possible drug targets and anti-fibrotic drug leads. The only anti-fibrotic drug currently registered in Europe and the US, pirfenidone, has shown some beneficial effects, but its clinical efficacy on fibrosis remains equivocal. A number of herbal medicinal products such as those used in traditional Chinese medicine have been reported to have some effect on fibrosis, but robust scientific evidence of these botanicals as safe and effective antifibrotic therapeutics is lacking.

Therefore, despite enormous advances in modern medicine, there are no completely effective drugs that stimulate hepatic function, offer complete protection to the organ, or aid in regenerating hepatic cells. Thus, it is necessary to identify alternative pharmaceuticals for the treatment of hepatic diseases, with the aim of these agents being more effective and less toxic.

Many plant derived drugs used in modern medicine are developed by ethnomedical leads and subsequent ethnopharmacological studies. There are more than 120 drugs of known structure such as digoxin, L-dopa, morphine, codeine, methyl salicylate that are extracted from higher plants and used in allopathic medicine. Historically, herbals have been used for a number of liver conditions, particularly chronic hepatitis C and alcohol-induced liver disease. Recent progress in the study of traditional drugs has resulted in the isolation of a number of active principles, including antihepatotoxic constituents, after evaluating the hepatoprotective effect of the plant using several animal (in vivo) model systems. Their pharmacological and biochemical actions have been examined and the clinical effects of some of them have been evaluated for liver protective activity on a scientific basis.

Carbon tetrachloride and acetaminophen, widely used hepatotoxins, have been used extensively to screen medicinal plants with hepatoprotective activity. Carbon tetrachloride (CCI,) is certainly the best known example of a chemical whose hepatotoxicity is presumably the consequence of the formation of free radicals, especially trichloromethyl radical by the hepatic cytochrome P450 system with subsequent production of centrilobular necrosis. Histopathological changes observed in CCI, toxicity are similar to that of viral hepatitis. Acetaminophen (paracetamol), the widely used analgesic is hepatotoxic when overdosed. 5-10% of the dose is excreted as glutathione-derived conjugates (3-cysteinyl conjugate, 3-mercapturate, and 3-methylthioconjugate). These thioethers are detoxification products of the reactive, putative toxic metabolite of acetaminophen, N-acetyl-p-benzoquinone imine (NAPQI).



SLMANEWS

## Contd. from page 14 Hepatoprotective Effects...

After overdoses of paracetamol, the normally adequate detoxification of the reactive metabolite of paracetamol by glutathione is overwhelmed and hepatic glutathione levels are depleted allowing the reactive metabolite to damage the liver cell. Synthesis of new glutathione is inadequate to cope with the rate of depletion.

Therefore, the main objective of this study was to investigate the protective effect of five medicinal plants, Asteracantha longifolia (neeramulliya), Asparagus falcatus (Hathawariya), Epaltes divaricate (Heen mudamahana), Vetiveria zizanioides (Sewenna) and Corriandrum sativum (kottamalli) on CCI, and paracetamol induced acute hepatotoxicity in ICR mice. Detailed studies on three medicinal plants were carried out to investigate their antioxidative activity. An attempt was also made to study the phytochemical profile and toxicological effect of each plant extract used.

Hepatotoxicity was induced by the administration of a single intraperitonial dose of CCI, (0.5 mL kg<sup>-1</sup> CCI, in olive oil) in one model and in the other by the administration of paracetamol (300 mg kg<sup>-1</sup> in saline) orally, after a 16 h fast. An aqueous extract of each plant (0.9 g kg<sup>-1</sup>) was used on pre and post-treatment basis. Mice were sacrificed at the end of the study and blood and liver tissue were collected and were used for the assessment of liver damage by the estimation of serum levels of ALT, AST, ALP, liver reduced glutathione level and histopathological assessment of liver damage. The ability of all plant extracts to protect the liver against the changes mediated by carbon tetrachloride and paracetamol confirmed that all plants possessed antihepatotoxic properties at least against the two hepatotoxins used. Both pre and post-treatment decreased the CCl<sub>4</sub> and paracetamol mediated increase in serum enzyme activities and increased the liver reduced alutathione concentration. Histopathological studies also provided supportive evidence for the biochemical analysis. The magnitude of hepatoprotective properties varied among the five plants used.

Results of the preliminary study provided confirmatory evidence for the ability of all plant extracts to act as hepatoprotective agents. However, when both biochemical analysis and histopathological assessment of liver damage were considered together, the three plants *Asteracantha, Asparagus* and *Vetiveria* could significantly hasten the recovery of damage due to  $CCl_4$  or paracetamol. Therefore, they were selected for the determination of antioxidant enzyme activities and lipid peroxidation in the serum and liver cytosolic fraction.

All three extracts improved the activity of antioxidant enzymes, glutathione peroxidase, glutathione reductase and glutathione-S-transferase and reduced the malondialdehyde formation, hence lipid peroxidation in the liver homogenate and serum significantly. Although magnitude of antioxidant activity varied in the three plants used, *Vetiveria* was considered as having the highest activity compared to the other two plants.

It is established that in several plants with antihepatotoxic properties, the crude drug effect is known to be mediated by the action of a number of separate active components, the potencies of the individual active principles being less than that of the crude extract. Tannins, phenolic compounds, cardiac glycosides and flavonoids were present in all five plant extracts but alkaloids were present only in Epaltes, Asteracantha and Corriandrum. Reducing sugars and cyanogenic glycosides were absent in all five plant extracts. Results indicated that the antioxidative activities observed in respective plant extracts could be due to the presence of phenolic compounds, mainly flavonoids.

The therapeutic efficacy of any plant extract depends not only in its pharmacological potency but also in its lack of toxicity. The plants extracts used in the present study had no effects on the biochemical parameters (ALT,AST,ALP), haematological parameters (Haemoglobin concentration, RBC count, WBC count, PCV) and histopathology of body organs (heart, lung, liver, spleen, intestine and kidney) after administering them daily for one month in mice. General conditions of the animals did not change and they remained in good health throughout the experiment.

The antioxidative effect of plant extracts was higher against the paracetamol induced hepatotoxicity. The ability of Vetiveria extract to increase the hepatic GSH activity significantly in the control animals may be the reason for its observed highest effect in the experimental groups. Both CCI, and acetaminophen must be microsomally metabolized before their toxic properties are manifested. In addition, the cascade of cellular injury involving free radicals is a complicated process involving multiple activities of enzymatic and non-enzymatic antioxidants. Therefore, plant extracts may exert their action against CCI, and acetaminophen induced liver damage by impairing the metabolism of toxins through inhibition of the activities of microsomal enzymes or by modulating the activity of a variety of enzymatic and non-enzymatic antioxidants.

Further studies are required to determine the active components of the plants under study and the exact mechanism that underlie their protective effect against liver damage. Based on the biochemical and histopathological evidence, it can be concluded that out of the five plant extracts used, Asteracantha longifloia (neeramulli whole plant), Asparagus falcatus (Hathawariya tubers) and Vetiveria zizanioides (Sewenna roots) can be considered as having significant hepatoprotective activity and antioxidant activity can be considered as one mechanism of action where Vetiveria zizanioides showed the highest effect compared to Asteracantha and Asparagus.



# **ANNUAL GENERAL MEETING: 23<sup>RD</sup> DECEMBER 2016**

The Annual General Meeting of the Sri Lanka Medical Association will be held at 7.00 p.m. on Friday, 23<sup>rd</sup> December 2016, at the Lionel Memorial Auditorium, "Wijerama Mawatha, Colombo 7. All members are cordially invited to be present.

Any proposals/ resolutions to be taken up at the AGM should reach the Honorary Secretary, SLMA on or before 25<sup>th</sup> November 2016.

The agenda of the meeting is given below.

Dr. Neelamanie Punchihewa Honorary Secretary, SLMA

## Agenda for the Annual General Meeting: 23 - 12 - 2016

- 1. Reading of the notice calling for the Annual General Meeting
- 2. Observation of I minute silence for departed members of SLMA
- Adoption of the minutes of the last Annual General Meeting held on 17<sup>th</sup> December 2015.
- 4. Confirmation of new members of the SLMA who joined in 2016
- 5. Resolutions
- 6. President's address
- 7. Secretary's Report for 2016
- 8. Treasurer's Report for 2016
- 9. Election of Office Bearers and Council members for the year 2016.
- 10. Appointment of Auditors
- 11. Address by the new Presidents
- 12. Any other business

# WINNERS OF PRIZES AND AWARDS-SLMA 2016

Winners at 129th Anniversary International Medical Congress and research grants of the SLMA 2016

Awards for Oral Presentations

#### **1. E. M. WIJERAMA PRIZE**

**OP008:** Effect of non-steroidal anti-inflammatory drugs (NSAID) on bleeding and Liver in Dengue infection

Wijewickrama A, Abeyrathna G, Gunasena S, Idampitiya D

#### 2. S. E. SENEVIRATNA PRIZE

OP018: Incidence and risk factors for non-alcoholic fatty liver disease in an urban, adult Sri Lankan population – a community cohort follow-up study

Niriella MA, Kasturiratna A, De Silva ST, Perera KR, Subasinghe SKCE, Kodisinghe SK, Piyaratna TACL, Vithiya K, Dassanayaka AS, De Silva AP

#### 3. H. K.T. FERNANDO PRIZE

OP069: Human epidermal Growth Factor Receptor-2 (HER2) expression in gastric adenocarcinoma and relevant clinic-pathological features in a cohort of Sri Lankan patients

Subasinghe D, Sivaganesh S, Samarasekera A, Kumarasinghe MP, Samarasekera DN, Lokuhetty MDS

#### **4. SIR NICHOLAS ATTYGALLE PRIZE**

OP048: Knowledge on low birth weight among pregnant women and their partners in Anuradhapura District Guruge GND, Perera KMN, Dharmaratne SD, Gunatunga W

Contd. on page 17



# WINNERS OF...

#### 5.WILSON PEIRIS PRIZE

# OP043: Development of a Snakebite risk map for Sri Lanka

Ediriweera DS, Kasturiratne A, Pathmeswaran A, Gunawardena NK, Wijayawickrama BA, Jayamanne SF, Isbister GK, Dawson A, Giorgi E, Diggle PJ, Lalloo DG, de Silva HJ

### 6. DAPHNE ATTYGALLE PRIZE FOR THE BEST PAPER IN CANCER

OP066: Components of the leptin system as risk factors for sporadic breast cancer in Sri Lankan women and their modulation by menopausal status

Rodrigo HACIK, Tennekoon KH, Karunanayake EH, Amarasinghe IY, De Silva GKS

### 7. SIR FRANK GUNASEKERA PRIZE FOR THE BEST PAPER IN COMMUNITY MEDICINE & TUBERCULOSIS

OP072: Knowledge, attitudes and practices of army soldiers on prehospital trauma care in Matara district

Chathurika H.L.S

#### 8. KUMARADASARAJASURI-YA PRIZE FOR THE BEST PA-PER IN TROPICAL MEDICINE

OP001: The prevalence of cirrhosis in adults with evidence of immunity against Hepatitis A

Kobbegala KGVJ, Karalliyadda HN, Ranawaka C, Niriella M, De Silva AP, Dassanayake AS, De Silva HJ

### 9. SPECIAL PRIZE IN CARDIOLOGY

OP004: Are we recognizing the correct state of blood pressure control of our patients in out-patient set-

#### ting?

Bandara HGWAPL, Kogulan T, Kodithuwakku NW, Hewarathna UI, Karunaratne RMSP, Jegavanthan A, Hathalahawatta C, Ralapanawa DMPUK, Jayawickreme KP, Ambagaspitiya AW

### 10. S. RAMACHANDRAN PRIZE FOR THE BEST PAPER IN NEPHROLOGY

#### OP051: Risk factors and outcome of primary urinary stones in children: a single centre experience

Gunasekara W D V N, Wijesinghe S W M N S, Ekanayaka E M S S, Jasinge E A, Hemachandra D K M N

### 11. SPECIAL AWARD FOR BEST ORAL PRESENTATION IN PHARMACOLOGY

#### OP056: Metformin: use as a pharmacological agent in management of childhood obesity

Warnakulasuriya LS, Fernando MAM, Adikaram AVN, Thawfeek ARM, Anurasiri WML, Silva KDRR, Sirasa MSF5, Samaranayake D, Wickramasinghe VP

# Award for Poster Presentations

### 12. SLMA PRIZE FOR THE BEST POSTER

PP065: Prevalence and clinicopathologicalcharacterization of triple negative and basal like breast carcinoma in Sri Lanka

Wijesinghe HD, Fernando J, Senarath U, Wijesinghe GK1, Lokuhetty MDS

#### Research Grant Awards

#### • GLAXO-WELCOME RESEARCH GRANT 2016

Severity, duration, treatment response and motor complications, and the association between these variables among patients with Parkinson's disease attending movement disorder clinics of two major hospitals in Jaffna

Dr.Ajantha Kesavaraj

#### • Dr. Thistle Jayawardena Research Grant for Intensive Care 2016

Antimicrobial activity of selected oral disinfectants against Acinetobacter causing ventilator associated pneumonia

Dr.Bimal Prabodha Kudavidanage

# • SLMA Research Grant 2016

A study on the associations between metabolic syndrome and abnormalities in seminal fluid parameters among men with infertility

Dr. Thilina Palihawadana

CNAPT Award

CNAPT (Ceylon National Association for The Prevention Of Tuberculosis)

#### An Award in Memory of Richard And Shella Peiris 2016

Joint winners

"Metformin for treatment of antipsychotic induced weight gain in a south Asian population with Scitzophrenia or schizoaffective disorder: a double blind randomized, placebo controlled study"

Professor Varuni de Silva

and

"Platelet activating factor contribution to vascular leak in Acute Dengue infection"

Dr.Chandima.Jeewandara

#### • G. R. Handy Award

"Association of Metabolic syndrome with testosterone and inflammation in men"

Dr. C. M.Wickramatilake

# THE COMMONWEALTH ADVISORY COMMITTEE ON HEALTH (CACH) MEETING

he Commonwealth Advisory Committee on Health (CACH) met today at the Cinnamon Grand Hotel. Colombo ahead of the Commonwealth Medical Association's 24th Triennial Conference 2016 which will beheld from 14 to 16 October 2016. CACH is the highest level advisory committee that advises the Commonwealth Secretariat in London on the policy direction for the health sector in the commonwealth. The members deliberated on a wide range of issues that affect the health and wellbeing of citizens of commonwealth countries. The members congratulated Sri Lanka for its excellent health achievements

and said that they want to learn from Sri Lanka. The meeting was chaired by Dr. Lakshmi Somathunga, Deputy

Director General (Medical Services) of the Ministry of Lanka. Sri The members of CACH come from the Pacific region, Asia, Africa, Europe, and North America. The commonwealth medical association conference on the theme 'Digital health for health and wellbeing' begins on 14 October 2016 and goes on till 16 October 2016 at the Cinnamon Grand.



The Members of the Commonwealth Advisory Committee on Health Dr.Lakshmi Somathunga (Deputy Director General Medical Services, Sri Lanka) and Dr. Joanna Nurse (Head of the Health and Education Unit of the Commonwealth Secretariat are in the center of the picture.

# COMMONWEALTH MEDICAL ASSOCIATION: 24<sup>TH</sup> TRIENNIAL CONFERENCE 2016

he Commonwealth Medical Association (CMA) is made up of National Medical Associations of commonwealth countries. The Commonwealth Medical Association's 24th Triennial Conference 2016 was held from 14<sup>th</sup> to 16<sup>th</sup> October 2016, at Hotel Cinnamon Grand, Colombo, Sri Lanka. Professor Vajira Dissanayake from Sri Lanka was elected as the President of the CMA at this event to serve for the period 2016 to 2019. Highlights of the inauguration ceremony are given below.









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## Contd. from page 18 Commonwealth Medical...



# JOINT CME PROGRAMME OF SLMA AND FMS-USJP - OCTOBER 2016

By Dr. Sajith Edirisinghe Council member –SLMA



Dr.Sumithra Tissera, Assistant secretary-SLMA

he fifth SLMA's joint Continuing Medical Education Programme (CME) was held at the Anatomy auditorium, Faculty of Medical Sciences (FMS), University of Sri Jayewardenepura (USJP), Nugegoda on 13<sup>th</sup> of October 2016 with an attendance of over 100 participants. The programme commenced with a joint welcome address by Dr. Malik Fernando, Past President of the SLMA, and Prof. Surangi Yasewardene, Dean, Faculty of Medical Sciences, USJP.

The first lectures were delivered by Prof. Nelika Malavige, Professor in Microbiology and

coordinator, center for dengue research on "Efficacy of rupatadine in treatment of dengue, a randomized placebo controlled Phase II trial". Dr.Bimalka Senevirathna, Senior Lecturer, Department of Pathology and coordinator, center of cancer research delivered the second lecture on "Early detection of pre-cancerous lesions".

After the tea break the first lecture was delivered by Prof. Hemantha Peiris, Senior professor of Bio Chemistry and the coordinator, center for kidney



research. He elaborated the novel findings of "Biomarkers of kidney disease". Dr. Samitha Ginige, consultant epidemiologist, Epidemiology Unit, Ministry of Health, Nutrition and Indigenous Medicine Sri Lanka delivered a timely valid topic as the 4<sup>th</sup> lecture on "Think you've been exposed to Zika"?

Contd. on page 22



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# Contd. from page 20 Joint CME Programme...

Final lecturer of the 5<sup>th</sup> CME was conducted by Prof. Varuni A. de Silva, Professor in Psychiatry, Consultant Psychiatrist, Faculty of Medicine, University of Colombo highlighting the important facts on "Publication and Research Ethics"

The meeting concluded with Dr. Sajith Edirisinghe, lecturer, Department of Anatomy, FMS-USJP delivering the vote of thanks.

All participants were awarded a certificate of participation.







# Cartoon of the Month



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