Osteoporosis prevention should be started early
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Pank Jit Sin

Bone mineral density (BMD) peaks during adolescence, hence this is the best time to accumulate calcium, says a specialist. Discussing various studies on bone health and its associated factors, Professor Nikhil Tandon, of the department of endocrinology and metabolism, All India Institute of Medical Sciences, New Delhi, India, said peak BMD at certain important sites is achieved by the end of the second decade of life. Thus, pubertal years are critical for bone mass accumulation.

Speaking at the 3rd Asia-Pacific Osteoporosis Meeting held in Kuala Lumpur, Malaysia, recently, Nikhil said: “Eighty percent of peak bone mass is achieved from birth to adolescence. The annual increase in BMD and volumetric BMD is most marked in females at time of menarche and in males between 13 and 17 years of age.” [J Clin Endocrinol Metab 1992;75:1060-1065, Bone Miner 1993;23:171-182]

Physically active people have significantly higher mineralization rates compared with their sedentary counterparts, he said. A study by Jones and Dwyer revealed that sports participants have around 4 percent higher BMD in their femoral neck and lumbar spine compared with those who did not exercise. [J Clin Endocrinol Metab 1998;83:4274-4279] However, it was also noteworthy that increasing bone mass through physical activity wanes after puberty. [Acta Paediatr 1996;85:19-25]

Calcium is the most touted nutrient for healthy bones. Nikhil said most cross-sectional studies have identified a positive correlation between dietary calcium and childhood BMD. The threshold for calcium intake is between the ages of 9 and 17, with a daily intake of 1,500 mg [Am J Clin Nutr 1992;55:992-996] Peak calcium accretion rates are achieved in girls aged 12.5 years and in boys aged 14. Similarly, high calcium intake also has a protective effect against fractures in adolescents.

Looking at intervention studies utilizing exercise, calcium, vitamin D and other fortified foods, he said the effects are very apparent, especially in populations which were previously undernourished. Unfortunately, these benefits are not always sustained once intervention is stopped. He reiterated that the outcomes of intervention studies often depend on the baseline characteristics.

“If you look at the outcome of the same studies on a population in developed countries with adequate macronutrition, then the likelihood of such a study bringing benefits is going to be very low.” Conversely, the same intervention studies using the same macronutrients such as calcium and vitamin D carried out in a developing country with poorer nutritional status would yield more pronounced benefits.

But Nikhil said the transition from research projects to public health policy has yet to commence, although that is arguably the most important reason for research.
Radha Chitale

A joint policy statement from the American Academy of Pediatrics and the American College of Medical Genetics and Genomics definitively recommends against genetic testing for inherited adult-onset diseases during childhood.

The organizations argue that unless interventions during childhood can reduce morbidity or mortality, such predictive genetic testing can “have significant medical, psychological, and social implications, not only for the minor but also for other family members.” [Pediatrics 2013;131:620-622]

The authors note that genetic testing and screening should always be done in the context of the best interest of the child and together with professional guidance and counseling.

“This position prioritizes the child’s autonomy and privacy interest over his/her parents’ desire to know,” said Dr. Calvin Ho, assistant professor at the Centre for Biomedical Ethics at the National University of Singapore.

Similar recommendations were made in a 2005 report by Singapore’s Bioethics Advisory Committee, Ho said.

In the US, newborn screenings for metabolic, hematologic and endocrine abnormalities are common and these abnormalities can be treated early.

But advances in genetic testing and screening technology as well as increased consumer interest and the rise of home testing kits highlighted the need for clarity about when and if to conduct further tests on young children.

Previously, experts have pointed out that knowledge of adult-onset diseases for which there is no childhood intervention could compromise the child through diversion of family resources, stigmatization, child’s loss of self-esteem and discrimination by family or institutional third parties such as schools. [JAMA 1994;272:875-881]

Direct-to-consumer and at-home genetic test kits, such as 23andMe, are highlighted in the position paper as particularly problematic as they lack professional oversight for accuracy and interpretation and counseling.

The policy statement makes an exception to their recommendation in cases where “diagnostic uncertainty poses a significant psychosocial burden, particularly when an adolescent and his or her parents concur in their interest in predictive testing.”

“These exceptions are important for their recognition of the critical role of the family as caregivers,” Ho said, although he noted that in most cases, deferring genetic testing is ethically and legally sound.
Daring to Dream

A doctor recounts his humble beginnings and his determination to succeed.

Dr. Low Lee Yong has mastered changing cannot into can. In a new memoir called I Dare to Dream: Make Possible the Impossible, Low, the son of a goods hawker and homemaker, relates his childhood in a Bukit Timah kampong village in the 1970s and his journey to become a physician and eventually founder and CEO of the managed care organization MHC Asia Group, which links over 1,000 clinics in Singapore and Malaysia through a virtual administrative system.

Despite his mother’s urging to become a teacher, the sight of people seeking help from doctors in white coats impressed Low enough to choose medicine as a career, in spite of little encouragement from teachers and poor English and Mandarin language skills. Low’s book offers brief snapshots of the ups and downs of starting his own practice in Ghim Moh, expanding a medical conglomerate and a short but intense bout in politics. Now, Low, 49, spends the majority of his time overseeing MHC and will be writing more, including an account of MHC’s founding and a book of life lessons told through jokes. Radha Chitale sat down with Low to discuss his story.

Growing up poor had a consistent impact on you as you struggled for success, especially through school. What aspects of that life are you glad to have left behind and what do you wish you could have kept?

In the early 70s, growing up in the kampong, life was simple, there was no technology, everybody was happy and until you see people who are rich you don’t know that you are poor. Because it’s a simple life, running around without slippers, plucking fruits, chasing animals, innovating and improvising toys. But it’s difficult in the sense that every day there are lots of things to do like washing clothes, tending the farm, scooping sewage, chopping wood, and that’s not easy.

But it was not complicated like modern life where you have to worry about a thousand and one things, reply to emails and have lots of responsibility. It’s a tough life but you kind of miss it because it’s a simple life as well.

You took a lot of big financial risks throughout your career, sometimes without a safety net. What drove you to jump into big investments like that?

When you have nothing to lose, you really have nothing to lose. I wasn’t in to get anything in the first place, just to try to explore and learn, not knowing that I was taking risks. For example, I didn’t realize I was taking loans at 20 percent interest to buy out my [S$30,000 service] bond. I just wanted to get out.

When you are quietly thinking about it, yes, the amount of money borrowed is huge and to owe the bank S$30,000 and later on much more is quite scary. I think I knew it was a big thing but I didn’t feel the risk because the ideas of interest and cost didn’t really cross my mind. If you ask me, it was partly ignorance, partly guts and partly determination.
If I were to do it now, of course I would take risks but calculated risks. I know how to get in, how to get out and when to get out. I learned that, whatever you want to venture into, think what is the worst-case scenario and can you live with it? If you can, then ok, go for it.

You converted to Christianity during medical school and faith plays a large role in your life. How do your faith and your medical training inform each other?

As a doctor you see life and death situations. Obviously we all know that we don’t live forever so there’s this question of where are you going. So if you can get answers settled early in your life and in your career then it’s much easier to handle life and death situations.

As a business person, my faith helps me in my value systems. Many times you might be tempted to do things on the borderline when there is no straightforward right or wrong and your faith has to come in and tell you to do right, not what only benefits you or your company. I don’t think I ever got into business to get rich. I got into business because it’s a game... you’re going into the unknown and creating things and making a difference.

Why did you write this book?

People kept asking me, “why did you start MHC?” And Cecilia [Tan, Chairman of MHC Asia Group] has been pestering me to write it because she knows what I went through. I thought, yes, I should write it because if I don’t share the lessons I learned then other people cannot benefit from it.

I want to tell students, look it doesn’t matter what your teacher says, it’s not the end of the world, you can make a difference and you can prove they are wrong. If you have passion you can go forward. And I want to tell teachers that look, your words do make a difference in our lives. It’s not true that what you say comes in one ear and out the other because as it goes through, the brain can get damaged or inspired.

At any point, did you concede that your mother may have been right and you should have been a teacher?

To a certain extent, my mother is absolutely right. I should have been a teacher because I find myself educating everyone now – with my stupid mistakes! All the things I ever learned, I educate others by sharing my stories. You need to be a great educator to motivate and inspire patients to take charge of their health. To me, part of health education has to be when people can remember a story and they enjoy it.
DOH launches debate cup for Kalusugang Pangkalahatan

Dr. Lee Edson Yarcia

Xavier University won the championship title of The Secretary’s Cup, a nationwide debate competition sponsored by the Department of Health. After besting 15 other national finalists from all over the Philippines, the team composed of Lee Arvin Dy Gogo, Rene Gandeza and Giano Libot was awarded during the closing ceremonies held at Century Park Hotel last March 16, 2013.

The Secretary’s Cup is an awareness campaign initiative by the Universal Health Care (UHC) Study Group with the aim of sparking interest and discourse on DOH’s Universal Health Care agenda dubbed Kalusugang Pangkalahatan. Academic debating, which allows speakers to explore the pros and cons of an issue, was the platform used by DOH to engage the most vocal and eloquent Filipino youth at present. The motions used in the debate rounds were formulated from the most contentious issues in health today, including private investments in public hospitals and facilities, regulating fees of health professionals, and recentralizing health services to the DOH, among others. After winning in their respective regional elimination series, 16 finalists were flown to Manila to compete for the coveted championship title.

During the grandfinal round, Xavier University argued against the motion That the Philippines should shift to a tax-funded National Health Service as opposed to one funded by social health insurance. Dy Gogo, who was recognized as the finals best speaker, argued that PhilHealth must expand its coverage of the poor to make sure that quality health care is accessible even to the marginalized sector of the society.

Universal Health Care is defined as the provision to every Filipino of the highest possible quality of health care. Health secretary Dr. Enrique Ona, in his speech, emphasized that the three thrusts of Universal Health Care—facilities enhancement, financial risk protection, and the attainment of Millenium Development Goals—is gaining momentum.

“For the first time ever, we have an administration that is committed to the attainment of Universal Health Care,” says Secretary Ona.

The event was also graced with the presence of Dr. Alberto Romualdez of the UHC Study Group, Mr. Teodoro Padilla of the Pharmaceutical and Health Care Alliance of the Phillipines, Ms. Marites Vitug of the Journalism for Nation Building Foundation, Dr. Jaime Montoya for the Philippine Council for Health Research and Development, and Ms.
Suyin Liu Lee of Asia Society.

“The Secretary's Cup successfully familiarized me with the socio-economic realities of health in the country. It was an honor to get involved with the national advocacy for universal health care,” says Jake Bustos, one of the debaters from the University of the Philippines-Los Baños.

The debate cup is part of the series of information dissemination campaigns of the DOH, which includes Health Talk Series and Town Hall Meetings.

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Faster PhilHealth claims processing in Region 6

Dr. James Salisi

Faster processing of Philippine Health Insurance Corporation (PhilHealth) claims in Region 6 received plaudits from Dr. Elmer Pedregosa, concurrent president of Private Hospital Association in the Visayas and Philippine College of Hospital Administrators.

“PhilHealth’s efforts resulted in faster processing of benefit claims and also reduced the number of Return-to-Hospital claims thereby contributing to a successful relationship among private hospitals in Western Visayas as partners in the healthcare industry,” Pedregosa said.

The PhilHealth Region 6 Office has been able to reduce the average time to process a claim from an average time of 130 days in 2011 to just 5 to 7 days in 2012. This reduction came despite the increase in the number of claims received from 1,200 in 2011 to 1,700 in 2012.

The turn-around time for more than 15,000 case rate and 9,000 fee-for-service claims was shortened from the time the claims were received to the time checks for these claims were released without adding staff and even without additional working hours.

Furthermore, the regional office reduced by more than half from the number of claims it denied, from 3,000 in January 2012 to only 1,400 in December 2012. Claims may be denied in case the claim is incomplete, filed later than the prescribed period of 60 days after discharge from the hospital, or non-compliant to the requirements.

Mr. Dennis Mas, PhilHealth vice president for Region 6, attributed their achievements to a series of ICD 10 trainings and regular dialogues with hospitals in the Western Visayas Region.

Proper coordination with the hospital and training of 200 hospital billing clerks have also helped in reducing return-to-hospital claims from 9,000 in January 2012 to 2,600 in December of the same year. Return-to-hospital claims are claims that are incomplete or not properly filled and are returned to the hospitals that sent them.

PhilHealth Region 6 local health insurance offices have also done well and received an award from the Civil Service Commission for Citizen’s Satisfaction Center Seal of Excellence.
SC issues 120-day restraining order against RH law

Dr. Nicolo Cabrera

The Supreme Court (SC) of the Philippines voted, 10-5, to issue a status quo ante (SQA) order preventing the implementation of Republic Act (RA) 10354, the Responsible Parenthood and Reproductive Health Law of 2012—set for March 31, 2013—for 120 days. Dissenting were Chief Justice Lourdes Sereno and Associate Justices Antonio Carpio, Mariano del Castillo, Estela Perlas Bernabe and Marvic Leonen. Oral arguments on the constitutionality of the law will be heard by the SC on June 18, 2013.

Albay Rep. Edcel Lagman, a long-time proponent of the law, has been quoted saying the SQA is merely a “temporary setback” and that he predicts the SC will uphold the law in the end.

Health Secretary Dr. Enrique Ona signed the implementing rules and regulations (IRR) of Republic Act (RA) 10354, the Responsible Parenthood and Reproductive Health Law of 2012, in Baseco, Tondo, Manila, on March 15, 2013.

The signing marked Department of Health approval of the implementing framework for the new law. To draft the IRR, public consultations were held in the cities of Davao, Cebu and Manila where health care professionals, interest groups and civil society organizations attended and participated. The IRR draft committee was chaired by the health secretary and included representatives from the Department of Education, the Department of Social Welfare and Development, the Philippine Commission on Women, the Philippine Health Insurance Corporation (PhilHealth), Department of Interior and Local Government, the National Economic and Development Authority, Leagues of Provinces, Cities and Municipalities of the Philippines.

In accordance with RA10354 which required at least four non-government organizations to be included in the draft committee, the following organizations were invited to join the draft committee: the Philippine Medical Association, the Philippine Obstetrical and Gynecological Society, Inc., Likhaan Center for Women’s Health, Inc., the Reproductive Health, Rights and Ethics Center for Studies and Training, Women’s Health Care Foundation, Inc., the Alliance of Young Nurse Leaders and Advocates International, Inc., and the Bishops-Businessmen’s Conference for Human Development.

“The completion and signing of the IRR is vital in translating government’s Universal Health Care or Kalusugan Pangkalahatan into an operational framework to reduce maternal deaths and improve overall reproductive health outcomes,” declared Ona.

RA 10354 hopes to improve the access to family planning services through enhanced health service delivery, provision of mobile health clinics in remote and depressed areas, expansion of PhilHealth coverage to reproductive health services particularly for the poor, hiring and training of skilled health professionals as well as continuous monitoring and review of reproductive health programs.

“This is just the beginning of our continuing effort to ensure that no woman will die while giving life,” Ona stated prior to the restraining order.
Researchers find immune-boosting properties in invasive weed

Ian Carlos Achero

Chromolaena odorata (Lf.) King & Robinson, commonly known as hagonoy, was found by researchers to boost the immune system of Balb/C mice. Four aspects of the immune system, namely macrophage phagocytic activity, cellular proliferation, superoxide production and plasma lysozyme activity, were improved by intraperitoneal injection of C. odorata extract. Hagonoy is a problem weed infesting pasture areas that grows rapidly under almost any land area [Phil Journ Sci.2012;141(1):35-43].

Researchers discovered that Balb/C mice immunosuppressed with cyclophosphamide (Cy) improved their immune system when given whole extract. In the researchers’ experiment, 36 mice were equally divided into three groups. One of the three groups was injected with C. odorata extract intraperitoneally for ten days. For positive control, another group of mice was injected with cyclophosphamide, a chemotherapeutic drug, at days 1, 4, 7 and 10 of the treatment period. The researchers also gave Cy to the C. odorata-treated mice one hour after the plant extract was injected. The third group stood as negative control and was injected with sterile phosphate-buffered saline (PBS). The mice were sacrificed at the 11th day to perform immune response assays.

The researchers measured the four aforementioned immune responses by following published protocols. In order to know the macrophage phagocytic activity, opsonized yeast cells were mixed with splenic macrophages collected from the mice and percent phagocytic activity was computed. To measure cellular proliferation, lipopolysaccharide (LPS, a component of gram-negative bacterial wall) was used by the researchers to stimulate the proliferation of B lymphocytes. Superoxide anion production was measured by giving phorbol myristate acetate, an inducer of the respiratory burst, and computing the superoxide anion radical released. The researchers measured plasma lysozyme of mice by determining protein concentration through a colorimetric protein assay kit.

The phagocytic activity of macrophages from mice given the plant extract was significantly increased compared to Cy-treated mice. The mean percentage phagocytic activity was increased from the 4.33 percent of Cy-treated group to 21.42 percent of the extract-treated mice. As expected, mice given Cy had the lowest phagocytic activity. The extract also stimulated multiplication of LPS-sensitive cells. The researchers proposed that C. odorata may contain compounds that can improve the immune system.

Plasma lysozyme detected in extract-treated mice was higher compared with Cy-treated mice but their difference was not significant. In the superoxide anion tests, mice given the extract had higher production of the anion compared to Cy-treated mice but the difference was also not significant.

The authors noted that other species of Chromolaena like C. hirsuta and C. squalida possessed immunomodulatory effect as well. They concluded the study by saying C. odorata extract could potentially reverse the immunosuppressive effects of cyclophosphamide.
Alternative voice test found effective for Filipino newborns

Dr. James Salisi

‘Baah’ voice test may be a reasonable alternative test to objective physiologic examinations for newborn hearing screening, a study Teresa Luis Gloria-Cruz, Genereso Abes and Franc Louie Abes from the University of the Philippines-Manila concluded. They compared ‘Baah’ and ‘Psst’, two common Filipino words used to call or get the attention of a person to find which would be better for newborn hearing screening.

They found that test subjects can produce ‘Baah’ sound better than ‘Psst’ at threshold intensities that can screen for possible deafness. This is a step towards developing an inexpensive test procedure that can be used to implement universal newborn hearing screening as mandated by law.

The Newborn Hearing Screening Act mandated that all babies born in hospitals should be screened for hearing loss before discharge, while those born outside hospitals must be screened within the first three months after birth.

However, the internationally recommended objective physiologic examinations for universal hearing screening such as the otoacoustic emissions (OAE) test and acoustic brainstem response (ABR) are not widely available and accessible. Thus, there is a need for an inexpensive test that can be done in remote areas by trained health workers.

The investigators recorded the sounds ‘Baah’ and ‘Psst’ produced by two groups. One group consisted of 8 males and 8 females, with ages ranging from 20 to 30 years old. They were asked to produce the sounds three times. The investigators visualized and analyzed the range of frequencies of the recorded sound.

They found that the male ‘Baah’ sound stimulated sound frequency ranges from 100hz to 5000hz while the female sound ranged from 150hz to 5000hz. The frequency range for ‘Baah’ sound indicated sound stimulation from low to high frequencies. This is important because although newborns may not have high frequency sound perception, they may still retain residual low frequency sound perception.

The other group consisted of randomly selected 50 males and 43 females whose ages ranged from 16 to 75 years old. They were asked to produce the same sounds thrice at one- and two-meter distances in a quiet room. The investigators compared and analyzed the computed mean of the three trials done from both distances for ‘Baah’ and ‘Psst’ tests.

The ‘Baah’ sound produced from one meter was not significantly different from that produced at two meters. In contrast, the ‘Psst’ sounds were significantly different at one-meter and two-meter distances.

Majority of the test subjects could produce the ‘Baah’ sound at 90db and above but the majority could not produce the word ‘Psst’ at 90db. Babies who cannot perceive sound from a cutoff of 90db in both the low and high frequencies may be classified as profoundly deaf.
A pilot systematic review of 33 articles on robot-assisted neuromotor rehabilitation for upper limbs and 30 for lower limbs showed a trend toward superior functional recovery compared to usual therapy—but was not statistically significant.

Investigators searched the electronic databases of MEDLINE via PubMed, Embase and Google Scholar for controlled trials with article in English from 2001 through 2010. Short and long-term motor control as well as motor strength was improved. Some cases of reduction in spasticity were found, but pain was unchanged. The experimental intervention had no consistent impact on the performance of functional tasks such as activities of daily living (ADL) in multiple sclerosis, cerebral palsy or spinal cord injury.

With respect to the upper limb, results varied according to the greater intensity of the treatment as measured by the higher number of repetitions of task-specific exercises. In stroke patients, bilateral therapy resulted in better motor recovery than unilateral therapy. In patients undergoing therapy for lower limbs, achievement of the sitting position in the wheelchair during the early phase and achievement of the standing position later were seen.

Biofeedback, the use of instrumentation to make covert physiological processes overt, may be clinically applied to improve a patient’s motor control through “re-educating” that control using visual or audio feedback with the help of electromyelogram, positional and force parameters “in real time.”

Precise mechanisms are unclear, but previous review of studies suggested that new pathways may develop or an auxiliary loop recruits existing pathways that are unused or underused in the execution of motor commands. [J Neuroeng Rehabil 21 Jun 2006; DOI:10.1186/1743-0003-3-11]

Continued training could then later establish “new sensory engrams” that would al-
allow the patient to later engage in improved motor activity without feedback, according to the review. One of the current developments in the area of biofeedback for neurorehabilitation is a shift from static to task-oriented feedback, which may have an advantage in improving functional ADL tasks.

In the same review on biofeedback therapy, its limitation was recognized in patients with severe motor deficits, with patients unable to initiate any functional movement at all, leaving them with no biofeedback to capitalize on. Rehabilitation robots address this issue by providing mechanical assistance for movement. The review awaited new studies that will pursue the combination of robotics and advanced biofeedback as an approach for sensorimotor rehabilitation.

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**Interactive learning styles provide optimal learning opportunities**

**Dr. Carol Tan**

Interactive teaching strategies can improve medical education in rehabilitation medicine, according to Dr. Ian Cameron, chairman of the Department of Rehabilitation Medicine, Sydney Medical School - University of Sydney.

“There is a scientific literature between education and learning in health care, and it finds lectures are not particularly effective as a learning medium … Overall, a more interactive style is better,” said Cameron.

The speaker presented some strategies that he found effective in teaching various rehabilitation medicine topics. One strategy discussed was case-based learning, in which a brief case is given to the students to serve as a trigger. The students will then develop their own learning paths by formulating individual diagnostic and management plans for the case. This strategy is particularly useful in areas where there are a limited number of rehabilitation medicine tutors.

Another strategy that Cameron discussed was entitled SCORPIO, which stands for Structured, Clinical, Object Referenced, Problem-based, Integrated and Organized. In this strategy, a short introductory lecture is given before students rotate among different stations in small groups. The stations are strategically set-up to provide the students with a problem-based integrated learning experience. Assessment stations may be included before, during or after the teaching circuit. This strategy has been found to be very effective as a teaching medium; however, it requires a large number of rehabilitation medicine teachers and is more expensive.

The trend towards employing more interactive teaching strategies is observed not just among medical schools, but also in residency programs and continuing medical education for medical professionals. Interprofessional learning is a form of learning activity that is widely used internationally.
In this strategy, discussions are conducted by a group of professionals so that more insights can be garnered from each of the health professional participants. It has been found to be an effective strategy to promote learning among adult participants.

Cameron explained that adult learners tend to be internally motivated, self-directed, practical, goal oriented and relevance oriented. Adults like to be respected and prefer to take responsibility for their own learning. This characterization would explain why lectures, wherein learners are passive recipients, are not as effective as interactive teaching strategies in which adult learners can participate and form their own learning paths.

“There are a number of different adult learning styles. It is important to recognize this because each of us learns a different way … so we need flexibility,” added Cameron. Learning styles can be classified visual, aural, written or kinesthetic. The speaker concluded that to promote effective learning, it is important to know your own learning style, to be aware of the learning styles of others, and to design appropriate strategies to enhance the learning of all the participants involved.

Playing Nintendo Wii™ may help rehabilitate stroke patients as an adjunct to conventional therapy, a recent study revealed. The investigators conducted a randomized controlled trial on the effectiveness of virtual reality using Nintendo Wii™ Sports (Tennis) as an adjunct to the conventional therapy in upper limb stroke rehabilitation in a tertiary hospital. They determined and compared the upper limb gross motor responses among patients with upper limb weakness post-stroke treated with Nintendo Wii™ tennis as an adjunct to physical and occupational therapy versus conventional therapy alone.

Patients were diagnosed with a first episode of stroke less than 6 months duration and upper limb weakness at the out-patient department from May to December 2012. They screened 107 stroke patients; 16 of which qualified but only 12 gave their consent. Eight completed the conventional therapy of physical and occupational therapy twice a week for 8 weeks. They were randomized either to the conventional therapy and the Nintendo Wii™ group, which had to play Wii tennis for 30 minutes after the conventional therapy.

The mean age of the conventional treatment group was 56.0 years old while the Nintendo group was 57.5 years old. The investigators tested for the effects of treatment across time as well as the interaction of treatment and time by using the repeated measures analysis of variance on the change in scores of the Fugl-Meyer Arm Scale (FMA), Box and Bloc Test (BBT), Barthel Index (BI) and grip strength scores of the two groups.
Both conventional therapy and treatment with Nintendo Wii™ showed statistically significant improvement in Barthel Index, which is a measure of a person’s functioning, specifically the activities of daily living and mobility. In both groups the arm motor function as measured by indices such as FMA, BBT and grip strength improved across time, however the changes were not statistically significant across time and between treatment groups. Similarly, no evidence was found that there was significant difference between the two groups in their Barthel Index scores.

Nevertheless, the investigators concluded that playing Nintendo Wii™ sports may be a potential adjunct to the conventional stroke rehabilitation to promote motor recovery and to improve independence in performing activities. Because the virtual reality game was fun, easy to understand and easy to set up, it encouraged the stroke patients to do task-specific and intensive training.

Android and Java app introduced for amputee profiling

Ian Carlos Achero

An application for Android and Java enabled phones called ASCeNT or Amputee Screening through Cellphone Networking was developed by Ateneo Java Wireless Competency Center and Smart Communications, Inc. With a mobile solution for amputee profiling, people from distant areas can be assessed through submitted reports from the application and referred to specialists when necessary; which also makes follow-up care is more convenient. A version for iOS devices is being developed.

Dr. Jose Alvin Mojica, chairperson of the Department of Rehabilitation Medicine, Philippine General Hospital (PGH) and Dr. Josephine Bundoc, head of the Prosthetics and Orthotics Unit, PGH, discussed the crucial role of the application in giving amputees better care by paperless and user-friendly methods. A demonstration of the mobile application was held with volunteer patients and physicians at the conference.

The main difference between the Android and Java version is that the Android version uses a touch-screen input while the Java version uses keypad input. Both require password to prevent unwanted access. By default, upon downloading the Android application from Google Play, the password is the lowercase letter “a”. Password settings, similar to other applications, can be changed by the user. All of the essential features for patient management like sending reports and viewing patient data are present in both versions.

Upon opening the application, two actions, Reports and Options, are presented to the user. Options contain settings such as password change, while Reports contain prosthesis and patient records. Upon pressing or selecting Reports, four options appear, namely...
Send Prosthesis Report, View Saved Patient Info, View Sent Reports and View Pending Reports. The app is able to take pictures of the prosthesis and the patient to be sent to a database for storage and analysis.

ASCeNT influenced the Philippine Health Insurance System to include prostheses in its reimbursement benefits.

“Because of the database we have via ASCeNT, we were able to convince PhilHealth to reimburse prostheses. So, starting June 2013, PhilHealth will now pay P15,000 for every prosthesis of an amputee,” Bundoc said. ASCeNT also received the Galing Kalusugan Awards from the Health Market Innovations in the Philippines in 2011.

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**UK center presents rehab measures for SCI**

**Dr. Nicolo Cabrera**

Prof. Chinnaya Asari Thiyagarajan, MD, an associate specialist with the National Spinal Injuries Center of the Stoke Mandevuil Hospital in Aylesbury, Buckinghamshire, UK, outlined the respiratory support and rehabilitative measures carried out at his center for patients with high cervical spinal cord injuries (SCI).

Thiyagarajan centered his message on respiratory care, both in the acute and long-term settings, to address respiratory complications as the leading cause of mortality after high SCI. Respiratory failure owing to acute injury ranges from 22.6 to 57 percent.

The speaker emphasized exercise training, particularly cardiac and aerobic conditioning, due to poor general status of paraplegics. At their medical center, software is used to facilitate programmable contraction of muscles. An example would be putting a patient on a stationary bicycle with electrodes on the quadriceps to cause them to contract. Exergaming was introduced as a new field that looks into the applications of video games for rehabilitation and conditioning.

Respiratory muscle training using spring-loaded devices and biofeedback would target expiratory or inspiratory muscles or both, depending on the level of SCI. Secretion clearance, important in all types of high SCI but most especially at levels C6 to T1, would be achieved through techniques such as air stacking in long volume recruitment, manual assistive cough, maximum insufflation-exsufflation and glossopharyngeal or “frog” breathing.

Acutely, respiratory muscle paralysis leads to hypoventilation, atelectasis, increased work of breathing and possibly death. Loss of sympathetic activity and effective hypersensitivity of the parasympathetic system increases respiratory secretions, aggravating lung status. Respiratory instability and critical care would delay rehabilitation, argued the speaker.

At their center, SCI patients would be categorized under group I with C1 to C3 injuries, group II with C3 to C5 and group III with C6...
to T1. SCI proximal to C3 would lead to loss of both inspiratory and expiratory muscles. Thiyagarajan noted, “Above that [C3 level], you require lifelong [mechanical] ventilation.” Group II patients’ need for support would vary, with many initially requiring mechanical ventilation but would eventually be weaned and sent home breathing independently. In group III, with intact inspiratory but weak expiratory motor strength, secretion clearance would be most crucial.

Thiyagarajan emphasized respiratory support specific for SCI, stating that a clinician with little experience with SCI “will ventilate the patient with the specific guidelines defined for acute respiratory distress syndrome that is up to 10 mL per kilogram body weight. But these patients require very high tidal volume which is about 30 mL per kilogram body weight [or] about 1000 or 1200 mL.”

Physiologically, patients with high SCI would have reduced inspiratory capacity, forced vital capacity (FVC) and total lung capacity. Clinically, however, FVC and peak cough flow would be sufficient in monitoring the patient's long-term respiratory rehabilitation.

Home-based rehabilitation technologies gain ground

Dr. James Salisi

Innovations in home-based rehabilitation technologies are gaining popularity now as alternative solutions to providing health care services to an aging population are being sought. One such innovation is telerehabilitation or the practice of providing rehabilitation services over a distance through the use of information and communications technology such as the Internet. Consultative, preventive, diagnostic and therapeutic services are provided to patients via two-way interactive telecommunication technology.

“There is a paradigm shift in healthcare. The consumer now is at the center of the orbit of various healthcare strategies. Health providers or doctors are not anymore the center of healthcare system. Therefore, we need a new approach,” said Dr. Nam Jong Paik, a telerehabilitation expert from Seoul National University, Bundang Hospital.

In Korea, patient co-payment was around US$600 in 2008. However, since medical care is given free to citizens, the trends show that people, especially the elderly, tend to overuse the available health services. As such, there is a clear need for an alternative approach to clinic-based and healthcare provider-centred health services delivery system.

“With limited resources and experienced people we still need increased productivity without sacrificing quality. Healthcare system shifts from recovery from illness to maintaining wellness. The focus is on fully individualized and mobile concern, getting support people at home or in care facilities to improve the delivery of health and social
care,” said Paik as he explained the need for telemedicine and telerehabilitation.

As technology advances in the field of remote sensing and the cost of broadband technology goes down, opportunities to do telerehabilitation and telemedicine in general are ripe for the picking, according to Paik. Telerehabilitation overcomes the distance barrier and the insufficient number of skilled health workers. It fills the need to decongest hospitals, maximizing limited resources to serve a greater number of people. With it, patients can be discharged earlier and be monitored continuously for care and follow-up.

Telerehabilitation can be applied in various aspects of healthcare such as consultation, home and activity monitoring, assessment, motor relearning via robot and biofeedback, diagnosis and evaluation, and education and training. Remote Speech-language and Cognitive Treatment or RESPECT, developed in the US, helps patients to do speech therapy remotely.

Virtual reality has been used for gait-rehabilitation for post-stroke patients, cognitive training and neglect training. Paik and his colleagues have developed a game of catch-the-rabbit using mobile phones and tablet to rehabilitate stroke patients through exercises and movements that are simulated by the game.

While Paik is optimistic about the advantages of telerehabilitation, he also pointed out that a Cochrane review emphasized the need for more studies on telemedicine applications to clearly establish its benefits.

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**Dry needle technique relieves chronic upper back pain**

**Dr. Carol Tan**

The dry needle technique is an effective treatment modality for alleviating chronic upper back pain, new research has shown.

This technique involves the insertion of solid filiform needles into myofascial trigger points, which are composed of multiple contraction knots that produce pain. This technique is hypothesized to relieve pain by activating endogenous opioids.

In a study conducted by researchers from the University of Health Sciences-Department of Rehabilitation Medicine in Laos, the dry needle technique was found to be more effective than the use of non-steroidal anti-inflammatory drugs (NSAIDs) in relieving pain among patients with chronic upper back pain.

The study involved 400 adult patients who consulted at Setharthirath Hospital from January to December 2007 and were diagnosed with chronic myofascial pain syndrome. The patients’ age ranged from 30 to 50 years old, with an average age of 41 years. There were 200 male and 200 female patients; half of each sex group were farmers and the other half were officers.
The patients were separated equally into two groups based on sex and occupation. One group was given NSAIDs 7.5 mg once a day and muscle relaxants 500 mg thrice a day. The dry needle technique was applied in the other group. The patients were treated for seven days, and their pain levels were assessed daily.

In the group treated with dry needle technique, 68 percent of the patients achieved pain relief on the first day. The remaining 32 percent achieved pain relief on the second day. The patients did not report any adverse side effects. In contrast, among the patients treated with NSAIDs and muscle relaxants, 52 percent reported pain relief on the second day of treatment, 37 percent on the third day, and the remaining 11 percent on the fourth day. In addition, among the patients who reported pain relief on the fourth day, 89 percent complained of dizziness and 67 percent complained of fatigue.

The authors concluded that dry needle technique is an excellent treatment modality for patients with chronic upper back pain caused by myofascial pain syndrome. They found that this technique not only alleviates pain more quickly than NSAID use, but it also has no side effects and is much cheaper. However, it has not been proven to be effective for other causes of chronic upper back pain, such as disc herniation, osteoarthritis, spondylosis, spondylitis, fractures and bone neoplasms.
Physical medicine and rehabilitation (PM&R) is a recent field that prevents disability and restores the quality of life of patients. “It’s about the quality of life. I would say physical medicine and rehabilitation is focused on that, returning patients to their function, or doing modifications to achieve better functioning,” said Dr. Bonifacio Rafanan, president of the Philippine Academy of Rehabilitation Medicine (PARM).

Aside from usual pharmacologic agents like antispasticity drugs and pain relievers, the usual practice of PM&R specialists includes Botox administration, fluoroscopic spine and joint injections, ultrasound imaging of muscle and ligaments and electrodiagnostics (eg, electromyography). According to Rafanan, combining the different modalities to restore patients to their optimal function inspired him to the specialty.

“Rehabilitation medicine is a new field. We can still develop, further explore, the scope of the specialty. And that’s something that fascinates me,” he shared.

Rehabilitation medicine goes beyond what the layperson’s concept of medicine is. “In medical school, we were taught about the diagnosis and treatment but not much about return to the normal or highest functioning of a person. That actually interested me and it would also be better for the patient. You are going beyond the traditional treatment,” he added.

PM&R aims to correct common misconceptions about disability and its management. Prevention of disability is also important. Before a disability starts or becomes worse, intervention should be done.

“Our concept of disability is usually about people using wheelchairs, wearing crutches and those with cognitive problems like cerebral palsy and stroke. But now, disability is a much bigger concept. If you are unable to do a particular function, you have a disability.” He further elaborated saying, “If you are supposed to do this thing and you are not
able to do that, like a basketball player that can’t run, then there’s a disability already.”

From admitted stroke and spinal injury patients, the usual practice of most PM&R specialists is also spent in an outpatient clinic. “We mostly see musculoskeletal injuries, neck pain and back pain. We also see developmental problems in children such as spasticity in cerebral palsy patients,” said Rafanan. Early inpatient rehabilitation is important because neurologic problems such as traumatic brain injury and stroke require early rehabilitation for optimal outcomes. “Studies show that the earlier the functional intervention on the patient, the better the outcome and the faster the recovery,” he mentioned.

Recent guidelines for the rehabilitation of low back pain and stroke were formulated by PARM. These are among the few clinical practice guidelines done by PM&R practitioners worldwide.

“The unique thing about these guidelines is the functional approach to diagnosis and management. Not just the anatomical defect, but functional assessment should be done as well. Modalities such as heat and cold, physical therapy (PT), occupational therapy (OT) and speech pathology are included. The outcomes of functional interventions are evaluated too like patients’ range of motion,” Rafanan mentioned.

In a fracture patient, after the bone heals the affected limb is assessed for restoration to its optimal function. “If we do an intervention like PT what is the endpoint? Can the patient do these things? After a fracture heals, the function of the limb needs to be corrected,” added Rafanan.

Rafanan said that current challenges to PARM include standardization of residency training among countries and increasing the number of fellowship programs. According to him, PARM and the ASEAN Rehabilitation Medicine Association (ARPAC) are organizing more conferences that include national and international content to update practitioners’ knowledge of variations in PM&R practice.

“Subspecialization and the multimodality approach to rehabilitation are among the directions of PARM and ARPAC,” he added.

WHO drafts action plan for noncommunicable diseases

Ian Carlos Achero

Representatives from 18 countries gathered at the WHO Regional Office for Western Pacific at UN Avenue, Manila City last March 2013. The representatives drafted an action plan for prevention and control of noncommunicable diseases (NCDs). The NCDs are principally composed of cardiovascular diseases, chronic respiratory diseases, cancer and diabetes and account for 80 percent of deaths in the Western Pacific region. Several objectives were projected to be attained by each member state for the period
of 2013 to 2020.

“NCDs are the deadliest epidemic you’ve never heard of,” said Mr. Timothy O’Leary, Public Information Officer of WHO Western Pacific. In the whole world, NCDs account for 63 percent of deaths, the WHO press release stated. “This is the second time the general assembly convened for a health topic - the other health topic is AIDS. This raised the status of NCDs to a very important matter,” he added.

Dr. Susan Mercado, director of Division of Building Healthy Communities and Populations of the WHO, emphasized that NCDs prematurely kill more people than infectious diseases which usually grab media attention.

“Cardiovascular disease is the leading cause of death in the Philippines. One out of four Filipinos is hypertensive. Close to half of all males are smoking. Half of all women and children in the country are exposed to second-hand smoke. Six out of ten Filipinos do not have adequate physical activity. The list goes on and on,” said Mercado. According to WHO, NCDs can be prevented and controlled by modifying four major risk factors: tobacco, unhealthy diet, alcohol and physical inactivity.

Dr. Hendrik Bekedam, director of Division of Health Sector Development of the WHO, said that NCDs are the ultimate challenge for a health system.

“In the past, the health system is great in addressing acute diseases. You treat them and it’s over. The chronic nature of NCDs is an enormous challenge,” Bekedam noted. He also mentioned key areas the meeting must address. First is to make sure the people have access to services. He added that consistent access is also needed because NCDs take years of treatment.

“Out-of-pocket expenditure reaches up to 50 percent here in the Philippines; much of it is related to NCDs. We must make sure people access it not by out-of-pocket,” Bekedam said.

Dr. Mark Jacobs, director of Public Health of the Ministry of Health, New Zealand, explained that NCDs seem like a technical term for doctors but it just simply means heart disease, cancer, diabetes and lung disease. A multisectoral solution is also needed.

“The best way to illustrate multisectoral involvement is that no amount of information to people about how they should eat more healthy food or exercise will work if they don’t have access to healthy food or they don’t get enough physical activity because they don’t feel safe in their communities,” Jacobs emphasized.

In order to strengthen the capacity of each member state to prevent and control NCDs, the draft action plan recommends creating a national unit dedicated to NCDs and assessing the impact of public policies on the epidemiology of these diseases. To reduce the exposure of people to the four major risk factors of tobacco, unhealthy diet, alcohol and physical inactivity, the action plan urges the member states to control these through legislation as exemplified by the Sin Tax Law. Research and development to prevent NCDs is also important. Monitoring trends and determinants of NCDs is another objective stated in the action plan.
MARKET WATCH

Proton pump inhibitor with new dual delayed release technology

Dexilant (dexlansoprazole) is a proton pump inhibitor (PPI) with a new Dual Delayed Release Technology (DDR) that combines two different granules in one pill. Within an hour, the first batch of medicine is released. Another release happens around four to five hours later. Dexlansoprazole is also among the PPIs with the highest bioavailability (85 percent).

Dexilant is commonly prescribed for heartburn, a symptom of gastroesophageal reflux disease (GERD). The DDR enables it to provide 24-hour relief from heartburn due to GERD as seen in clinical studies. As a result, it showed best control of intragastric pH among present PPIs. [J Neurogastroenterol Motil. 2013;19(1):25-35.] Dexilant is also prescribed for healing and maintenance of erosive esophagitis (EE).

Common adverse effects include diarrhea, stomach pain, gas and nausea and vomiting. Dexilant (dexlansoprazole) is manufactured by Takeda Pharmaceuticals and is available in stores nationwide.

Combination pill may improve diabetic patients’ adherence

AstraZeneca recently launched Kombiglyze XR (saxagliptin + metformin extended-release), a once-a-day pill that can help patients with Type 2 diabetes adhere to treatment. Held at Best Western Premiere F1 Hotel, Taguig City last March 11, 2013, the event featured Professor Nancy Bohannon, director of Clinical Research at the Cardiovascular Risk Reduction Program at St. Luke’s Hospital in San Francisco, California who emphasized the benefit of combination therapy for diabetes. Emphasis for combination is due to the results of the United Kingdom Prospective Diabetes Study (UKPDS), which showed that many patients on metformin monotherapy eventually failed to achieve optimal blood sugar control.

Medication adherence is difficult because of multiple pills needed for diabetes and other associated conditions such as hypertension, high cholesterol and heart disease. Failure to adhere to prescribed therapeutic regimen can result in diabetic complications.

“Along with lifestyle modification, innovative therapies such as saxagliptin + metformin XR are needed to fight the diabetes epidemic,” said Dr. Joey Miranda, the secretary of the American Association of Clinical Endocrinologists, Philippine Chapter.
**MARKET WATCH**

**New technology utilizes microcurrents**

The launch of Biological Cell Regulation (BCR) Therapie, a new German breakthrough for pain management, was held last February 27, 2013 at EDSA Shangri-la Hotel. The tag “German acupuncture without needles” was made because of its non-invasive technology for pain management. Dr. Rudiger Schellenberg, the founding President of the International Society of Medical Microcurrent Therapy, explained how the technology works with live demonstration to the audience.

“Microcurrents are applied by a device to closely resemble the body’s natural energy or ‘chi’ to help regenerate cells at a faster rate thus healing the source of pain,” said Dr Schellenberg. BCR Therapie machines are attached to the patient using color-coded wires. The wires carry microcurrents below 700 microamperes.

Two BCR Therapie machines, the Clinic Master Professional and the Vital Master, are simple to operate with minimal training necessary. Both machines are ISO-certified and will be available in the Philippines thru Castro Maternity Hospital and Medical Center.

**March celebrated as rabies awareness month**

Various parts of the country offered free rabies vaccination to dogs in celebration of Rabies Awareness Month last March. The National Rabies Prevention and Control Program, an interagency effort led by the Department of Agriculture, aims to create and focus the attention of the public to this highly fatal disease. The Philippines has the sixth highest number of human rabies cases worldwide. Rabies also has the highest case fatality rate of any infectious disease.

Rabies remains a public health problem. It affects the nervous system and is characterized by paralysis, hydrophobia and aerophobia. According to the DA, one third of rabies deaths come from children less than 15 years old. The DA reports that most of the cases are due to dogs (98 percent), with some infections from cats (1.3 percent) and other animals (0.001 percent) such as cattle, carabao and pig.

The National Rabies Prevention and Control Program aims to eliminate rabies in the Philippines by 2020. There was a 56 percent reduction in number of cases from 2001 to 2006 and 57 percent reduction from 2006 to 2011. Several rabies-free zones have been declared like Camiguin and Marinduque. Although there is a large drop in number of cases, 200 to 400 Filipinos still die per year from it.
MARKET WATCH

Triple therapy for hepatitis C increases cure rate

MSD Philippines launched the oral protease inhibitor boceprevir, a new treatment for hepatitis C. Triple therapy, consisting of boceprevir, peg-interferon and ribavirin, on naïve patients showed that the chance of achieving virologic cure rates double. Hepatitis C can enter the body through a simple needle prick or through blood transfusions and organ transplants, without presenting symptoms. Lack of treatment can lead to liver cirrhosis and death.

Dr. Ena Lyn Ang, gastroenterologist and medical adviser of MSD, said that treatment of Hepatitis C is difficult because of low response rates. “Hepatitis C has six genotypes. Genotype 1 is very difficult to treat,” she said. “The standard of care for hepatitis C treatment, whatever genotype, is always peg-interferon plus ribavirin, the combination. But as we go along, we’ve noticed that genotype 1 has a very low response rate.”

In addition to naïve patients, those who had previously failed therapy and considered harder to treat had an almost triple chance of achieving cure when boceprevir was added to standard treatment. The virologic cure rate, or sustained virologic response (SVR), is defined as undetectable HCV-RNA 24 weeks after the completion of therapy.

Cost-effectiveness of quadrivalent anti-HPV

Professor Margaret Anne Stanley, the Director of Research of the Department of Pathology, University of Cambridge, visited Manila to discuss the efficacies of human papillomavirus (HPV) vaccines and emphasized the cost-effectiveness of the quadrivalent vaccine. HPV-associated diseases are a significant health concern because specific genotypes (HPV 16 and 18) have a known oncogenic potential.

Two types of vaccines are currently available against HPV. The bivalent vaccine offers protection against the two most common causes of HPV-related cancers, HPV-16 and HPV-18. The quadrivalent vaccine (Gardasil) protects against HPV-16 and HPV-18 as well as HPV-6 and HPV-11, the most common causes of genital warts. Both consist of virus-like particles (VLPs) that are capable of eliciting an antibody response that is much stronger than that obtained from a natural infection. It can persist for up to 8 years after vaccination.

The additional protection given by the quadrivalent vaccine rendered it cost-effective, which was an important consideration for the health policy makers in the UK. In September 2012, the quadrivalent vaccine (Gardasil) replaced the bivalent vaccine in the national immunization campaign of the UK.
APRIL

2013 Midyear Convention of the Philippine Obstetrical and Gynecological Society
April 10-12, 2013
Venue: The Oriental Hotel Legazpi City, Bicol
Info: Philippine Obstetrical and Gynecological Society
Telephone: (+632) 921 7557 or 435 2384
Email: pogs@pldtdsl.net
Website: http://www.pogsbicol.com

50th Annual Convention of the Philippine Pediatric Society
April 14-17, 2013
Venue: Philippine International Convention Center, CCP Complex, Pasay City
Info: Philippine Pediatric Society
Telephone: (+632) 926 6758 or 926 6759
Email: ppsinc@pps.org.ph
Website: http://www.pps.org.ph

20th Annual Scientific Meeting of the American College of Chest Physicians-Philippine Chapter
April 17-19, 2013
Venue: Baguio Country Club, Baguio City
Info: American College of Chest Physicians-Philippine Chapter
Telephone: (+632) 687 7510
Email: accp_philchap@yahoo.com.ph
Website: http://www.accp.org.ph

21st Annual National Convention of the Philippine Academy of Pediatric Pulmonologists
April 30, 2013 to May 1, 2013
Venue: Taal Vista Hotel, Tagaytay City
Info: Philippine Academy of Pediatric Pulmonologists
Telephone: (+632) 332 8855
Email: papp_office@yahoo.com
Website: http://www.papp.org.ph

MAY

Midyear Convention of the Philippine Orthopaedic Association
May 1-3, 2013
Venue: Subic Bay Traveler’s Hotel, Subic Pampanga
Info: Philippine Orthopaedic Association
Telephone: (+632) 667 3926 or 667 3946
Email: celia@philortho.org
Website: http://www.philortho.org

39th Midyear Convention of the Philippine College of Surgeons
May 3-4, 2013
Venue: Avenue Plaza Hotel, Naga City
Info: Philippine College of Surgeons
Telephone: (+632) 927 4974 or 928 1083
Email: pcs@pcs.org.ph
Website: http://pcs.org.ph

43rd Annual Convention of the Philippine College of Physicians
May 5-8, 2013
Venue: SMX Convention Center, Pasay City
Info: Philippine College of Physicians
Telephone: (+632) 910 2250 or 910 2252
Email: secretariat@pcp.org.ph
Website: http://www.pcp.org.ph

43rd Annual Convention and Scientific Event of the Philippine Heart Association
May 23, 2013
Venue: Crowne Plaza Hotel, Quezon City
Info: Philippine Heart Association
Telephone: (+632) 470 5525 or 470 5528
Website: http://www.philheart.org
The ‘rising tide’ of cardiovascular disease in Asia includes patients who do not always fit into standard Western calculations for high cardiovascular or diabetes risk, but who should nevertheless be targeted for surveillance and preventive measures, says one expert.

“They represent a unique profile of skinny diabetics who are not obese but have higher blood glucose levels than their Western counterparts,” said Associate Professor Carolyn Lam, consultant, National University Heart Centre, Singapore.

Asian women have greater central adiposity (higher waist-to-hip ratio, higher truncal fat and visceral fat) than Caucasian women, which may explain their greater metabolic risk, Lam said. This suggests that Asians need not weigh >100kg to become diabetics.

Clinicians should also recognize that the left ventricular mass index (LVMI) cutoffs recommended by the American Society of Echocardiography for the diagnosis of left ventricular hypertrophy (LVH) may need to be lowered in Asians as research has shown that Asian patients, particularly Chinese, Malays and Indians, have consistently lower LVMI values than Western patients.

“If we are to use cutoffs derived from Western populations, there is a potential to underdiagnose LVH and under-recognize the transition of stage A to stage B HF,” Lam said. Ethnicity-specific cutoffs should then be used to assess for structural changes (left ventricular remodeling and dysfunction) which are strongly associated with heart failure (HF).

She also highlighted that stage C or overt congestive HF, characterized by increased breathlessness, fatigue and fluid retention, occurs at a younger age in Asian patients and is associated with a high prevalence of diabetest despite relative lack of obesity compared with Western cohorts.

Important inter-ethnic differences may exist which may affect management. Endothelial dysfunction, which is linked to renal dysfunction, is also highly prevalent among Asian patients with HF. It therefore represents a particularly attractive therapeutic target.

When it comes to medical therapy, use of disease-modifying HF agents (beta-blockers, ACE inhibitors, ARBs, vitamin K antagonists) was also lower in the Asia Pacific region compared with the US and Europe, which represents a potential opportunity for improving treatment outcomes, she said. Device therapy is also underused and poorly accepted.

Lam is optimistic that three ongoing studies, the Singapore Heart Failure Outcomes and Phenotypes (SHOP), the Asian Sudden Cardiac Death in HF (ASIAN-HF) and the Outcome in Patients with Heart Failure with a Preserved Left Ventricular Ejection Fraction (PEOPLE) study, will fill the knowledge gaps in HF in Asia.
GRACE score underestimates ACS mortality risk in Asians

Monika Stiehl

The commonly used Global Registry of Acute Coronary Events (GRACE) underestimates in-hospital mortality risk score for Asian patients with acute coronary syndrome (ACS), according to the results of a Singapore study.

“You can’t say that one [score] fits all,” said lead study author Assistant Professor Mark Y. Chan from the National University Heart Centre, Singapore. “We have to be specific and sensitive to differences in both ethnicity as well geographical location, when we are performing risk stratification for acute coronary syndrome.”

In the study, Chan and colleagues evaluated the performance of GRACE in a large Singaporean cohort which included 10,100 Chinese, 3,005 Malay, and 2,046 Indian patients hospitalized in Singapore’s public healthcare system for acute myocardial infarction from 2002 to 2005. [Am Heart J 2011;162:291-299]

The GRACE mortality risk model was initially calibrated based on data from 11,389 patients with acute myocardial infarction or unstable angina admitted to hospitals around the world from 2002 to 2003. These patients were predominantly of European descent; no Asian patients were included. The model takes into account eight major patient risk factors – age, serum creatinine levels, systolic blood pressure, heart rate, initial cardiac enzyme elevations, heart failure severity, ST elevation or depression ≥1mm, and cardiac arrest at presentation.

The Singapore researchers reported that, in reality, in-hospital mortality rates in the three different ethnicities tested were much higher than the rates predicted using the GRACE score. According to the GRACE score, predicted in-hospital mortality rates were 2.4 percent for Chinese, 2.0 percent for Malays, and 1.6 percent for Indians. However, the corresponding actual observed in-hospital mortality rates were 9.8 percent, 7.6 percent and 6.4 percent, respectively.

“External risk scores for coronary heart disease should be tested and recalibrated in all unique, previously untested populations before used”, said Chan.

Using a recalibrated GRACE score, taking into account risk factors for Singaporeans, the researchers showed a lower mismatch, but there was still an underestimation of risk.

“Good accurate risk stratification facilitates appropriate healthcare allocation and is associated with better outcomes”, concluded Chan, adding that more Pan-Asian risk-stratification studies are needed to adapt externally developed risk scores for Asian populations.
Personal Perspectives

"It is indeed a very interesting experience for us cardiologists from the Philippines. Especially the sessions and discussions about heart failure patients and coronary artery disease – [these] were very informative – as well as the summary of the European Society of Cardiology of their recommendations. That will be very helpful for our patients back home."

Dr. Diana Jean Roxas, cardiologist, St. Lukes Medical Center, Quezon City, Philippines

"It was very interesting for me to be at the APSC. One of the main important topics for me was hypertension. I have learnt a lot about new drugs and treatments against high blood pressure and in our country hypertension is currently a very serious problem."

Dr. Evy Febriane, cardiologist, Royal Hospital Surabaya, Surabaya, Indonesia

"I was very impressed by the enthusiasm of the Asian Pacific [Cardiology] Society to set up such a huge congress here in the region. And what especially is notable, that the Asian Pacific countries collaborate so well to organize international congresses in the area which I believe is very important especially when you look at the prevention efforts that need to be made in this area."

Professor Stefan Gielen, deputy director of cardiology, University Halle-Wittenberg, Halle, Germany
Interview with new ESC President

The European Society of Cardiology (ESC) was well represented at the recent Asian Pacific Society of Cardiology (APSC) Congress and even hosted its own stream of lectures in the scientific program, under the theme of ‘ESC in Asia Pacific’. The new ESC president, Professor Panagiotis Vardas (PV), was in attendance and Medical Tribune (MT) had the opportunity to interview him. Monika Stiehl reports.

MT: What were the main tasks of the ESC at the APSC Congress?

PV: We are here supporting the huge strategic project named Global Scientific Activities. This project includes countries which are not regular members of ESC like China, India, Saudi Arabia, Brazil and Argentina, to name a few. And in this context we are visiting some bigger congresses, like the APSC, and of course participating in the scientific program. The general part of ESC here at the APSC was to give a summary and five take-home messages from the ESC Congress last year in Munich.

MT: What in your opinion were the most important topics here at the APSC Congress?

PV: Here ... we had a number of important issues to discuss related to cardiovascular medicine. In my opinion, in invasive cardiology, [for example, one of the issues is] transcatheter aortic valve implantation, which means repairing aortic valves through the arteries without operation. Our experience in this technique is getting better and the effectiveness of this therapy is proven. [We also discussed] mitral clips and the field of mitral valve repair also without any operation. This is a hot and evolving new topic in cardiovascular medicine.

MT: At the end of August this year we will have the ESC Congress in Amsterdam. What can we expect?

PV: [The ESC Congress in] Amsterdam is expected to be a huge success. We have the first indications about the size of the congress. It was really a pleasant surprise for us, to see that in spite of the economic crisis in Europe the number of abstract submissions was a new record. It is much higher than in Munich last year – about 10,500 abstracts. This is a strong indication that the number of delegates will be large as well. And the [number of] satellite symposia is expected to be more than in Munich. We are going to organize a great event in Amsterdam with around 27,000 to 30,000 participants.

MT: Can we expect some changes in the ESC guidelines this year?

PV: Yes, in Amsterdam we are going to announce a number of new guidelines. We expect new guidelines for example in pacing and in arterial hypertension, to name two of them. We have to see how many of them are ready but at least three or four new guidelines will be announced.
Much has been learned about heart failure with preserved ejection fraction (HF-PEF), but there remains no clear pharmacologic treatment for this syndrome. “HF-PEF may be as common and as incapacitating as heart failure with reduced ejection fraction (HF-REF), however the value of pharmacologic therapy in HF-PEF is uncertain,” said Dr. Karl Swedberg from the Sahlgrenska Academy, University of Gothenburg in Gothenburg, Sweden. “Diuretics may be used to control sodium and water retention... angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blockers (ARBs) and a beta-blocker seem reasonable, but no treatment has been shown convincingly yet to reduce morbidity and mortality in patients.”

In the ALLHAT* study involving hypertensive patients, risk of new-onset HF was higher in the amlodipine and lisinopril arms compared with the chlorthalidone arm. After a diagnosis of HF, the subsequent 5-year mortality rate was similar between subjects with HF-PEF and HF-REF. [Circulation 2008;118:2259-2267] Current ESC guidelines for HF-PEF therapy focus on optimizing blood pressure control, use of lowest dose diuretics to control fluid overload, control of HR extremes (chronotropic failure or rapid atrial fibrillation), managing comorbidities, weight loss and exercise training. However, the guidelines do not provide information on how to specifically achieve these goals. Many studies looking at the effect of ACEIs/ARBs and beta-blockers on HF hospitalization or CV death (the PEP-CHF, the CHARM-preserved trial, I-PRESERVE) have been conducted with conflicting results.

In practice, most patients receive an RAAS inhibitor. Clinical trials however have failed to show any significant benefit of RAAS blockade in the prevention or treatment of HF-PEF. The use of RAAS inhibitors was associated with lower all-cause mortality in a large national registry involving 41,791 patients in the Swedish Heart Failure Registry. However, the study included patients with ejection fractions (EFs) of >40 percent. The results were non-significant when the study was limited to patients with EFs of >50 percent. [JAMA 2012;308:2108-2117]

Although inhibitors of the RAAS and sympathetic nervous system should continue to be used in patients with HF-PEF who have comorbidities (hypertension, diabetes or coronary artery disease), the use of these drugs for the primary treatment of HF-PEF remains unsupported by the available evidence.

Treatment of HF-PEF remains empirical and centered around blood pressure control and volume control. Clearly, new therapies should improve quality of life and increase mortality benefit, said Swedberg.

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*ALLHAT: Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial
Some doctors still fail to prescribe life-saving beta-blockers to heart patients in favor of symptom-relieving drugs, especially among the elderly, said Dr. Michel Komajda, a cardiologist at the Pitié Salpêtrière Hospital in Paris, France, and former president of the European Society of Cardiology (ESC).

The trend against providing beta-blockers, which reduce the stimulating effects of stress on cardiac and other tissues, and reduce the risk of secondary heart attack and hypertension, was identified in a survey from the ESC’s EURObservational Research Programme. \[Eur J Heart Fail 2010;12:1076-1084\]

“There are some good reasons [to not prescribe beta-blockers] but in some other instances, it is simply the reluctance of prescribers to provide life-saving drugs and we therefore need to continue to provide education programs,” Komajda said.

According to the survey, the rate of beta-blocker prescription was 86.7 percent.

However, Komajda pointed out that the proportion of patients enrolled in this registry is about 40 percent at best.

“The situation is even worse when you look at the proportion of patients who reach the target dose of beta-blockers,” he said.

The survey showed that less than 40 percent of patients reached target dosing for beta-blockers.

Prescribing beta-blockers or other renin-angiotensin-aldosterone system (RAAS) inhibitors can be problematic in elderly people. Most of these drugs are cleared through the kidneys, which can become dysfunctional with age. Consequently, the half-life of these drugs in the body can double or triple.

For the elderly, prescribing symptom-relieving drugs may be becoming a trend, Komajda said, which is unfortunate because the Euro Heart Failure Survey showed that in-hospital mortality was significantly influenced by patients not receiving beta-blockers and other RAAS blockers. \[Eur Heart J 2007;28:1310-1318\]

“Age is not a good reason not to provide life-saving drugs to these patients,” Komajda said.

Consistent education about the use of beta-blockers pays dividends.

In three surveys of about 2,000 patients each, given after an updated version of the ESC guidelines for heart failure were released, beginning in 2004, the rate of prescriptions for beta-blockers increased (from 65 to 78 percent) and so did the proportion of patients who reached the target dose (18 to 26 percent), or at least half of the target dose (47 to 60 percent). \[Eur J Heart Fail 2009;11:85-91\]

Komajda noted this trend had positive impacts on overall patient survival as, over the last 15 years, Europe has seen a significant decline of hospitalization and of mortality among heart failure patients.
Industry Update brings you updates on disease management and advances in pharmacotherapy based on reports from symposia, conferences and interviews as well as the latest clinical data. This month’s Industry Updates were made possible through an unrestricted educational grant from Servier.

- Blood pressure control with perindopril-amlodipine is cardioprotective • • • • • • • • • • • • • • • • • • • • • • • • • • • Pg 33
- Optimizing treatment options for HF with ivabradine • • • • • • • • • • • • • • • • • • • • • • • • • • • Pg 36
High blood pressure, or hypertension, is a leading cause of death and disability globally, across developing and developed regions. Meta-analyses have shown that systolic blood pressure is linked to cardiovascular disease (CVD) mortality. The higher the systolic blood pressure, the greater the risk of CVD mortality, even compared with ischemic heart disease. [Lancet 2002;360:1903-1913]

**CVD epidemiology in Asia Pacific**

In the Asia Pacific region, stroke is more prominent than even coronary heart disease; prevalence ranges from 20-45 percent, averaging at about 30 percent. However, despite improvement in awareness and control, a large proportion of patients remain suboptimally controlled. [J Hypertens 2012;30:1734-1742]

Studies have also shown that Asian populations are more intensely affected by changes in blood pressure compared with Caucasians.

The Asia Pacific Cohort Studies Collaboration, which included about 500,000 people from around Asia and about 100,000 people from Australasia, showed that for every 10 mm Hg decrease in systolic blood pressure the risk of stroke decreased 37 percent among Asians and 28 percent among people from Australia and New Zealand. This is more obvious in hemorrhagic stroke but still true for ischemic stroke. [J Hypertens 2003;21:707-716]

“If we control blood pressure well, we will reduce stroke better than heart attack,” said Dr. Piyamitr Sritara, professor and chairman of the Department of Medicine at Ramathibodi Hospital and Mahidol University in Bangkok, Thailand. “Every millimeter of mercury matters.”

A meta-analysis of 61 prospective, obser-
vational studies including 1 million adults showed that for each 2 mm Hg decrease in mean systolic blood pressure there was a 7 percent reduction in the risk of ischemic heart disease mortality but a 10 percent reduced risk of stroke mortality. [Lancet 2002;360:1903-1913]

Sritara noted that the most common reasons for not achieving blood pressure goals are lack of patient compliance, ineffective monotherapy and intolerable side effects from therapy.

**Choice of antihypertensive regimen**

There are a variety of antihypertensive drugs available to control blood pressure, including beta-blockers, thiazide diuretics, angiotensin receptor antagonists (ARBs), calcium antagonists and angiotensin-converting enzyme (ACE) inhibitors.

Although there remains debate about what the first-choice drug should be, some trials have shown that the ACE inhibitor perindopril plus amlodipine offer superior benefits.

**Clinical trial evidence**

The ASCOT-BPLA\(^1\) trial was a multicenter, randomized, prospective, controlled trial of 19,257 hypertensive patients with additional risk factors. It showed a significant benefit in all-cause mortality for patients randomized to amlodipine plus perindopril as required compared with those given the beta-blocker atenolol plus bendroflumethiazide as required (hazard ratio [HR], 0.89; 95% CI, 0.81-0.99; p=0.025). With an 11 percent relative risk reduction (RRR), p=0.0247, the trial was stopped early after a median follow-up of 5.5 years. [Lancet 2005;366:895-906]

Professor Fausto Pinto, of the Lisbon University Medical School in Lisbon, Portugal, said ACE inhibition has been shown through different trials to have a continuum of benefits from lowering blood pressure, improving vasodilatation, and reducing cell proliferation and migration and atherosclerotic plaque stabilization.

Among patients with stable coronary artery disease, two trials, HOPE\(^2\) and EUROPA\(^3\) demonstrated improvement in primary outcome measures of cardiovascular death, myocardial infarction (MI), cardiac arrest, and stroke among treatment groups given ACE inhibitors compared with a placebo group. [N Engl J Med 2000;342:145-153; Lancet 2003;362:782-788]

Both trials showed a RRR of 20 percent in primary endpoint measures using active therapy compared with a placebo – ramipril in the HOPE trial (p=0.001) and perindopril in the EUROPA trial (p=0.0003).

Two other trials, PEACE\(^4\) and QUIET\(^5\) showed no difference between ACE inhibitor treatment groups (trandolapril and quinapril, respectively) and placebo groups. [N Engl J Med 2004;351:2058-2068; Am J Cardiol 2001;87:1058-1063]

Trandolapril had a 4 percent RRR for the primary endpoints of cardiovascular death, MI and revascularization compared with placebo (p=0.43) while quinapril had a 4 percent relative risk increase in the primary endpoints of cardiovascular death, MI, cardiac arrest, revascularization and hospitalization for unstable angina compared with placebo (p=0.6).

The EUROPA trial further demonstrated no heterogeneity between groups of patients at various levels of risk – that perindopril had the same effects for relative cardiovascular death, non-fatal MI and cardiac arrest risk reduction among low (RRR, 17 percent), medium (RRR, 32 percent) and high (RRR, 12
percent) risk groups of patients (p=0.15). [Eur Heart J 2006;27:796-801]

Perindopril is also successful at improving outcomes in patients on other preventive therapies. A subgroup of patients on antiplatelet agents, beta-blockers and lipid-lowering drugs (n=2,087) showed a significant relative risk reduction with perindopril compared with placebo (RRR, 28 percent; p=0.004). A comparison showed that the overall EUROPA population (n=12,218) reduced their relative risk on perindopril versus placebo similarly (RRR, 20 percent; p=0.0003).

ACE inhibitors not one-trick pony

“Then, if you look at the duration of the effects of the ACE inhibitors, they are not all the same,” Pinto said. “In perindopril for instance, the trough to peak ratio is about 75 percent to 100 percent, which is probably the highest one when compared with some of the other ACE inhibitors.”

Among the various ACE inhibitors represented in the analysis – lisinopril, enalapril and perindopril – perindopril had the only statistically significant reduction in all-cause mortality (HR, 0.87; 95% CI, 0.81-0.93; p<0.001). [Eur Heart J 2012;33:2088-2097]

The same meta-analysis showed no significant reduction in all-cause mortality or MI among patients using ARBs (n=82,383; HR, 0.99; 95% CI, 0.94-1.04; p=0.683). [Eur Heart J 2012;33:2088-2097]

In a meta-analysis comparing the benefits of ACE inhibitors and ARBs it was shown that a composite outcome of CV death, MI and stroke was reduced by only 7 percent by ARBs (p=0.012), while ACE inhibitors produced a 14.9 percent (p=0.001) reduction of the risk. [J Am Coll Cardiol 2013;61:131-142]

“ACE inhibitors are not a one-trick pony,” said Dr. Frank Ruschitzka, director of the Heart Failure/Transplantation Clinic at the University Clinic in Zurich, Switzerland. “ACE inhibitors are like a Swiss army knife. They lower angiotensin II... and they halt breakdown of bradykinin.”

“Because of the high prevalence of hypertension, the widespread use of ACE inhibitor-based strategies may result in an important gain in lives saved,” Pinto said.

Ruschitzka noted that perindopril is the only drug that has ever lowered mortality among hypertensive patients, and three trials in particular, which included a total of 34,282 patients, showed this effect.

Compared with placebo, all-cause mortality was reduced by 21 percent (p=0.02) in the HYVET\textsuperscript{6} trial, which combined indapamide and perindopril in elderly hypertensives, and by 14 percent (p=0.025) in the ADVANCE\textsuperscript{7} trial, which combined perindopril and indapamide in diabetic patients, in addition to the 11 percent reduction in all-cause mortality (p=0.025) seen in the ASCOT-BPLA trial. [N Engl J Med 2008;358:1887-98; Lancet 2007;370:829-40]

All together, these trials demonstrated that perindopril results in a 13 percent reduction in all-cause mortality (p<0.001).

“Perindopril hit the mortality target and that has not been shown with any other drug in the hypertension field,” Ruschitzka said.

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1. ASCOT-BPLA: Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm
2. HOPE: The Heart Outcomes Prevention Evaluation Study
3. EUROPA: EUropean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease
4. PEACE: Prevention of Events with Angiotensin Converting Enzyme Inhibition
5. QUIET: QUinapril Ischemic Event Trial
6. HYVET: Hypertension in the Very Elderly Trial
7. ADVANCE: Action in Diabetes and Vascular disease: PreterAx and DiamicroN MR Controlled Evaluation
Heart failure (HF) is a debilitating disease requiring lifelong management. Despite standard therapy, a significant proportion of patients remain symptomatic. At a Servier-sponsored symposium held in conjunction with the Asian Pacific Society of Cardiology 2013 Congress in Pattaya, Thailand, experts highlighted the benefits of adding ivabradine (Coralan®, Servier) in patients in sinus rhythm whose heart rate (HR) remains elevated despite optimal treatment with beta-blockers, or when beta-blockers cannot be tolerated.

“HR is the main focus of manipulations for HF as elevated HR at rest suggests higher risk of death,” said Associate Professor Sarana Boonbaichaiyapruck, head of the pediatric cardiology unit at Ramathibodi Hospital in Thailand and chairman of the symposium.

Standard therapy for HF involves a combination of neurohumoral antagonists (an ACE inhibitor/ARB, a beta-blocker and a MRA) and a diuretic. When attempting to reduce HR, the recommendation is to maximize the dose of beta-blockers before adding another drug. Many patients however are not able to tolerate higher doses of beta-blockers.

Ivabradine, a selective If current inhibitor, is a novel option in pure HR reduction. “The beauty of ivabradine is that it is devoid of any pharmacological action but HR reduction,” said Professor Michel Komajda, head of the cardiology department, Pitié Salpêtrière Hospital in Paris, France, and former president of the European Society of Cardiology. Unlike beta-blockers, ivabradine has no effect on myocardial contractility and blood pressure.
The SHIFT evidence

In the primary analysis of SHIFT (Systolic Heart failure treatment with the If inhibitor ivabradine Trial), the addition of ivabradine to optimal therapy reduced the primary endpoint of cardiovascular death or HF hospitalization by a significant 18 percent (p<0.0001) during a median follow-up of 2 years. This was driven by a 26 percent reduction in the risks of hospitalization for worsening HF and death from HF. Ivabradine’s effect on HR was greater among patients with the highest HR at baseline. [Lancet 2010;376:875-885]

The beauty of ivabradine is that it is devoid of any pharmacological action but HR reduction

The trial involved 6,558 patients with systolic HF, already treated with guideline-recommended therapies (including beta-blockers) and randomized to ivabradine or placebo. Ivabradine was well-tolerated although 5 percent of patients had bradycardia. “There was no evidence of third degree AV block or pro-arrhythmia which was reassuring,” said Komajda.

An ivabradine trial in post-myocardial infarction patients with reduced systolic function (BEAUTIFUL) also provided good safety data for ivabradine although the study did not show any improvement in outcome. [Lancet 2008;372:807-816]

Additionally, quality of life (QoL) improved significantly in ivabradine-treated patients. [Eur Heart J 2011;32:2395-2404]. “By contrast, beta-blockers have not been shown to improve QoL while ACE inhibitors only showed modest improvement,” said Komajda.

In an echocardiography sub-study, ivabradine reversed cardiac remodeling as shown by reductions in LV volumes, which resulted in improved heart function. [Eur Heart J 2011;32:2507-2515]

Ivabradine effects dependent on baseline HR

A sub-study of SHIFT confirmed that ivabradine’s effect on the primary endpoint was significant regardless of the background beta-blocker dose. [J Am Cardiol 2012; 59:1938-1945].

“Thus, it’s the baseline HR and not the beta-blocker dose that matters … the magnitude of HR reduction with ivabradine beyond what was achieved with beta-blockers primarily determines the subsequent outcomes in HF,” he added.

Ivabradine exerts the same beneficial effects in patients with systolic HF (NYHA II-III) regardless of whether or not they’re taking aldosterone antagonists. [Eur J Heart Fail 2013;15:79-84]

Improved survival

This was supported by data from a recent analysis which showed that the addition of ivabradine substantially reduced HF death by 39 percent (HR 0.61, p<0.0006) and HF hospitalization by 30 percent (HR 0.70, p<0.0001). In patients with baseline HR ≥75 bpm, the effect was maximal in patients who achieved HR reductions of >10 bpm. [Clin Res Cardiol 2013;102:11-22]

Fewer rehospitalizations

Conversely, total hospitalizations were less frequent with ivabradine compared with placebo (p=0.0002). The risk of sec-
ond or third hospitalization for worsening HF was also significantly reduced (p<0.001 and p=0.012, respectively). [Eur Heart J 2012;33:2813-2820]

“Reducing total burden of HF hospitalizations to the extent seen with ivabradine in SHIFT would likely reduce the cost of care for patients with HF,” Komajda said.

Guideline-recommended therapies are underutilized in clinical practice, depriving patients of a tremendous benefit.

Ivabradine enters ESC guidelines

Based on the results of SHIFT, ivabradine by name has been included in the latest ESC guidelines for chronic symptomatic systolic HF. It is recommended in patients in sinus rhythm, with ejection fraction ≤35 percent and HR remaining ≥70 bpm despite optimal therapy with ACE inhibitors/ARBs, beta-blockers and MRAs.

The UK National Institute for Health and Clinical Excellence (NICE) also recommended ivabradine as an option for patients with chronic systolic HF (NYHA class II-IV) in sinus rhythm with HR ≥75 bpm and ejection fraction ≤35 percent. The NICE committee said “ivabradine is a cost-effective use of NHS resources for HF treatment after optimized initial therapies have been achieved and patients remain symptomatic or when beta-blockers are contraindicated or not tolerated.”

Patients at the core of HF management

Associate Professor Patrick Jourdain, cardiologist from Rene Dubos Hospital in Pontoise, France, however said guideline-recommended therapies are underutilized in clinical practice, depriving patients of a tremendous benefit.

“Titration to targeted dosages with proven beneficial effects is lacking partly due to patient comorbidities and medical inertia... widespread use of HR-lowering agents would have a significant impact on outcomes.”

Physicians should involve patients in disease management. There should be a one place, one team, and one message concept. Games and home-based interventions should be employed and expert-patient self-management programs should be integrated to quickly identify high-risk patients and optimize therapy, he added. Development of HF units/clinics has proven its utility for improving therapy optimization, developing patient self-management programs and reducing HF hospitalizations.

Conclusion

When HR reduction is not feasible despite beta-blocker therapy at the maximally tolerated dose, the addition of new heart-rate reducing agent ivabradine should be considered. Achieving HR between 50 to 60 bpm could minimize cardiovascular risk and substantially reduce HF hospitalizations and death in patients with chronic symptomatic systolic HF.
The Changing Panorama of Women’s Health: Navigating New Frontiers

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Dear Colleagues,
The Obstetrical & Gynaecology Society of Singapore (OGSS) extends a warm invitation to you to join us at the 9SICOG 2013 on 22-24 August 2013.

An island city of fast-paced movements, Singapore is emerging as a regional referral hub for tertiary care involving high-risk obstetrics cases, complex gynaecological cancer treatment, urogynaecological problems and neonatal care. Leading the way with Asia’s first test-tube baby in the 1980’s, Singapore pioneered the world’s first micro injection baby in the 1990’s and in 2010, the world’s first emergency operation for cornual ectopic pregnancy via a single navel incision. The country is the chosen host of the Joint Commission International (JCI)’s headquarters in the Asia Pacific; the Asian base of UK Imperial College, and US Duke University Medical Schools. Singapore also has the only specialist training system outside of the US to be recognized by the US Accreditation Council of Graduate Medical Education International (ACGME-I). Against a backdrop of rapid developments, the bi-annual SICOG started convening in 1994 to help members of Asia Pacific’s O&G community keep abreast with a fast-changing panorama of women’s health in our societies.

With the aim of sharing O&G treatment outcomes from the regions that we serve, the 9SICOG 2013 has designed a programme to address new learnings in O&G. We cordially invite you and colleagues to engage in interactive discussions at the 9SICOG 2013 which will provide a professionally rewarding forum to share experiences and best-practices, aimed at improving clinical practice of the O&G community. We look forward to welcoming you.

Yours Sincerely,

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Dr Devendra Kanalingam
9SICOG 2013 Organising Vice-Chairperson

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Eribulin: Antitubulin agent for the treatment of metastatic breast cancer

Eribulin (Halaven®, Eisai), a synthetic antitubulin agent derived from natural marine sponge, has been approved in North American markets for use in the treatment of patients with metastatic breast cancer. Clinical trials leading to eribulin’s registration showed net benefits of the drug in improving overall survival in this indication.

Naomi Adam, MSc (Med), Category 1 Accredited Education Provider (Royal Australian College of General Practitioners)

In the search for novel medicinal compounds, pharmacognocists have undertaken chemical analyses throughout the plant and animal kingdoms. More recently, these researchers have turned their attention to the marine environment, where a number of potential new drugs have been uncovered. One example of these is the antitubulin agents, derived from marine sponges. The first compound in this class to be isolated was halichondrin B [NSC 609395]. Discovered in 1985, this large polyether macrolide was found to have potent antimitotic and anticancer properties in vitro, apparently through a distinct and novel mechanism involving microtubules. Initially, further studies were hampered by the difficulty obtaining sufficient quantities for investigation. In 1998, the development of a synthetic method to produce halichondrin B enabled further work on this promising compound. The structural moiety responsible for the compound’s action was discovered (the macrocyclic lactone C1–C38), and this facilitated the development of synthetic analogues, including the drug E7389 – now known as eribulin mesylate. [Crit Rev Oncol Hematol 2012;81:163-183]

Microtubules are involved in a number of cellular functions, such as organization of internal structure, intracellular transport and cell division. Their role in mitosis makes them an important target for anti-cancer therapies. A number of chemical substances are known to disrupt microtubule dynamics, including taxanes, vinca alkaloids, and now, eribulin. [Cancer Treatment Rev 2012;38:143-151]

Eribulin
Mode of action

Eribulin (Halaven®) suppresses microtubule polymerization. Furthermore, eribulin sequesters tubulin into non-functional aggregates at clinically relevant concentrations. This disruption of mitotic spindle formation inhibits the cell cycle transition from ana-
phase to metaphase and ultimately leads to apoptotic cell death after prolonged mitotic blockade. [Halaven Product Monograph]

In preclinical studies, eribulin was shown to inhibit cell growth in a variety of cell lines, including breast cancer, colon cancers, non-small cell lung carcinomas, small cell cancer, prostate cancers, histiocytic lymphoma, pharyngeal squamous cell carcinoma (head and neck cancer), ovarian cancer, uterine sarcoma, promyelocytic leukemia and LOX melanoma.

**Pharmacokinetics**

The pharmacokinetics of eribulin is linear over the dose range of 0.25 mg/m$^2$ to 4.0 mg/m$^2$. Following IV administration there is a rapid distribution phase followed by a prolonged elimination phase, with a mean terminal half-life of approximately 40 hours. Exposure after multiple doses is comparable to that following a single dose and no significant accumulation of eribulin is observed on weekly administration.

Although there is some negligible metabolism of eribulin by cytochrome P450 3A4 (CYP3A4), it is unlikely that eribulin will have any substantial effect upon plasma levels of other drugs metabolized via CYP3A4. Eribulin is not metabolized by any of the other CYP enzymes, and is excreted primarily unchanged (82 percent in the feces and 9 percent in urine).

**Clinical efficacy**

The clinical trial program for eribulin commenced with four phase I dose-finding studies in patients with advanced solid tumors. These revealed neutropenia to be the most common dose-limiting toxicity. As it generally appeared after the third weekly dose, this established that the optimal protocol for eribulin was to give it on days 1 and 8 of a 21-day chemotherapy cycle. The phase I tumor response data were encouraging and these prompted phase II studies in patients with advanced breast cancer or metastatic breast cancer. In all of these, the patients had already received a median of three or four prior chemotherapy regimens. Objective response rates with eribulin in these trials were 11.5 percent, [J Clin Oncol 2009;27:2954-2961] 9.3 percent [J Clin Oncol 2010;28:3922-3928] and 21.3 percent. [J Clin Oncol 2010;28:1081]

Following on in the clinical study program was the phase IV EMBRACE (Eisai Metastatic Breast Cancer Study Assessing Physician’s Choice Versus E7389) trial, on the basis of which registration of the drug was gained. EMBRACE enrolled patients who had previously been treated with at least two and a maximum of five (median four) chemotherapy regimens for metastatic breast cancer. Eribulin was given at a dose of 1.4 mg/m$^2$ on days 1 and 8 in a 21-day cycle. The comparator was any single-agent chemotherapy, hormonal treatment, or biological therapy approved for the treatment of cancer; or palliative treatment or radiotherapy, chosen by the treating physician according to local practice. (In the comparator arm, 97 percent received chemotherapy and 3 percent hormonal therapy.) Patients were treated with a median of five cycles (range 1-23) of eribulin and this was associated with a significant improvement of a median of 2.5 months in overall survival. At 1 year, survival rates were 54 percent with eribulin and 44 percent in the comparator arm. [Lancet 2011;377:914-923]

**Adverse reactions**

According to the prescribing informa-
tion for eribulin, the most common adverse events (AEs, occurring in 25 percent or more recipients) were neutropenia, anemia, asthenia/fatigue, alopecia, peripheral neuropathy, and nausea and constipation. In terms of serious AEs, the most common were febrile neutropenia (4 percent) and neutropenia (2 percent). The most common AE resulting in discontinuation of eribulin was peripheral neuropathy (5 percent). Development of severe peripheral neuropathy occurred in 8 percent of patients. Eribulin is also associated with QT/QTc interval prolongation.

"There are currently dozens of ongoing trials of eribulin, in breast and many other cancers including lung, head and neck, colon and prostate cancer. ... As these outcome data become available, the role of eribulin in clinical practice will become clearer"

**Dosing**

The recommended dose of eribulin is 1.4 mg/m² IV over 2 to 5 minutes on days 1 and 8 of a 21-day cycle. Patients should have absolute neutrophil count (ANC) values ≥1,500 cells/mm³ and platelets >100,000/mm³ at the initiation of treatment. Prior to each dose, patients should be assessed for peripheral neuropathy and complete blood cell counts should be obtained.

**Place within treatment guidelines**

Expert opinion is divided regarding the role of eribulin in clinical practice. On the one hand, the assessment of the pan-Canadian Oncology Drug Review was that there is a net overall clinical benefit to eribulin in the third-line or greater treatment of women with incurable locally advanced or metastatic breast cancer previously exposed to anthracyclines and taxanes. This was particularly important given that metastatic breast cancer is the second leading cause of cancer death in women and in this heavily pre-treated population there are limited efficacious options available. [Pan-Canadian Oncology Drug Review. Final Clinical Guidance Report: Eribulin (Halaven) for Metastatic Breast Cancer. August 2, 2012]

In contrast, the guidance of the UK’s National Institute for Health and Clinical Excellence (NICE) is that eribulin is not recommended, within its licensed indication, for the treatment of locally advanced or metastatic breast cancer that has progressed after at least two chemotherapy regimens for advanced disease. The NICE Committee noted the novel mechanism of action and acknowledged that eribulin is the first drug of its class to demonstrate in a trial an overall survival benefit in heavily pre-treated patients with metastatic breast cancer. However, the Committee was concerned about the lack of information about health-related quality of life with eribulin, and were unconvinced as to its cost-effectiveness.

There are currently dozens of ongoing trials of eribulin, in breast and many other cancers including lung, head and neck, colon and prostate cancer. [Clinical Trials Gov http://www.clinicaltrials.gov/ct2/results?term=eribulin&Search=Search] As these outcome data become available, the role of eribulin in clinical practice will become clearer.
April

21st European Congress of Psychiatry
Location: Nice, France
Info: European Psychiatric Association
Tel: (33) 3 8823 9930
Email: hq@europsy.net
Website: www.epa-congress.org

European Congress on Osteoporosis and Osteoarthritis
17/4/2013 to 20/4/2013
Location: Rome, Italy
Info: International Osteoporosis Foundation
Tel: (32) 4 254 1225
Email: info@iofbonehealth.org
Website: www.ecceo13-iof.org

5th International Congress of Prediabetes and Metabolic Syndrome
18/4/2013 to 20/4/2013
Location: Vienna, Austria
Info: Kenes International
Tel: (41) 22 906 0488
Fax: (41) 22 906 9140
E-mail: prediabetes@kenes.com
Website: www.kenes.com/prediabetes

48th Annual Meeting of the European Association for the Study of the Liver
24/4/2013 to 28/4/2013
Location: Amsterdam, Netherlands
Info: European Association for the Study of the Liver
Tel. (41) 22 807 03 60
Fax. (41) 22 328 07 24
Email: easloffice@easloffice.eu
Website: www.easl.eu

5th Association of Southeast Asian Pain Societies Conference
28/4/2013 to 5/5/2013
Location: Singapore
Info: Pain Association of Singapore
Tel: (65) 6292 4710
Fax: (65) 6292 4721
Email: aseaps2013@kenes.com
Website: www.aseaps2013.org

MAY

American Urology Association (AUA) Annual Meeting
4/5/2013 to 8/5/2013
Location: San Diego, California, US
Info: AUA
Tel: (1) 410 689 3700
Fax: (1) 410 689 3800
Email: customerservice@AUAnet.org
Website: www.aua2013.org

Diabetes Preventing the Preventables Forum
24/5/2013 to 26/5/2013
Location: Kuala Lumpur, Malaysia
Info: Asia Diabetes Foundation
Tel: (852) 2637 6624
Fax: (852) 2647 6624
Email: enquiry@adf.org.hk
Website: www.adf.org.hk/dpp2013

12th Congress of the European Association for Palliative Care
30/5/2013 to 2/6/2013
Location: Prague, Czech Republic
Info: European Association for Palliative Care
Tel: (49) 89 548234 62
Fax: (49) 89 54823443
Email: eapc2013@interplan.de
Website: www.eapc-2013.org

World Congress of Nephrology
31/5/2013 to 4/6/2013
Location: Hong Kong
Info: ISN World Congress of Nephrology 2013
Tel: (852) 2559 9973
Fax: (852) 2547 9528
Email: registration@wcn2013.org
Website: www.wcn2013.org
JUNE

23rd Conference of the Asian Pacific Association for the Study of the Liver
6/6/2013 to 9/6/2013
Location: Singapore
Info: APASL Secretariat
Email: apaslconference@kenes.com
Website: www.apaslconference.org

International Digestive Disease Forum 2013
8/6/2013 to 9/6/2013
Location: Hong Kong
Info: UBM Medica Pacific Limited
Tel: (852) 2155 8557
Fax: (852) 2559 6910
Email: info@iddforum.com
Website: www.iddforum.com

3rd World Congress of Thoracic Imaging
8/6/2013 to 11/6/2013
Location: Seoul, Korea
Info: WCTI Secretariat
Tel: (82) 2 3452 7245 / (82) 2 3471 8555
Fax: (82) 2 521 8683
Email: wcti2013@insession.co.kr
Website: www.wcti2013.org

17th International Congress of Parkinson’s disease and Movement Disorders
16/6/2013 to 20/6/2013
Location: Sydney, Australia
Info: MDS Congress Staff
Tel: (1) 414 276 2145
Fax: (1) 414 276 3349
Email: congress@movementdisorders.org
Website: www.mdscongress2013.org

JULY

9th Asian Dermatological Congress
10/7/2013 to 13/7/2013
Location: Hong Kong
Info: ADC 2013 Secretariat
Tel: (852) 3151 8900
Email: adc2013@swiretravel.com
Website: www.adc2013.org

UPCOMING

13th International Workshop on Cardiac Arrhythmias - VeniceArrhythmias 2013
27/10/2013 to 29/10/2013
Location: Venice, Italy
Info: VeniceArrhythmias 2013 Organizing Secretariat
Tel: (39) 0541 305830
Fax: (39) 0541 305842
Email: info@venicearrhythmias.org
Website: www.venicearrhythmias.org
In this Series, find out about what these leading medical experts have to say about the latest updates in the management of asthma and COPD.

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