Clinical guidelines tackle driving risk in OSA

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Clinical guidelines tackle driving risk in OSA

Rajesh Kumar

All patients undergoing initial evaluation for obstructive sleep apnea (OSA) should be asked about daytime sleepiness and recent unintended motor vehicle crashes or near-misses due to sleepiness, fatigue or inattention, the American Thoracic Society (ATS) has recommended.

Patients with these characteristics are considered high-risk drivers and should be warned about the potential risk of driving until effective therapy is initiated, the society said in its latest clinical practice guidelines for sleep apnea, sleepiness and driving risk in non-commercial drivers. [Am J Respir Crit Care Med 2013;11:1259-1266]

“Up to 20 percent of crashes that occur on monotonous roads can be attributed to sleepiness, and the most common medical cause of excessive daytime sleepiness is OSA,” said Dr. Kingman Strohl, director of the center for sleep disorders research at Case Western Reserve University in Cleveland, Ohio, US and chair of the committee that drafted the guidelines.

“With these new guidelines, we’ve aimed to provide healthcare practitioners with a framework for the assessment and management of sleepy driving in the evaluation of OSA.”

Physicians should assess the clinical severity of OSA and find out any prior treatment the patient may have received, including behavioral interventions. Adherence and response to therapy should be assessed at subsequent visits and drowsy driving risk should be reassessed if it was initially elevated, the guidelines recommended.

In patients with a high clinical suspicion of OSA who have been deemed high-risk drivers, polysomnography should be performed and, if indicated, treatment initiated as soon as possible. If they have no co-morbidities, at-home portable monitoring is a reasonable alternative to polysomnography.

But continuous positive airway pressure (CPAP) should not be used for the sole purpose of reducing driving risk. For patients with confirmed OSA who have been deemed high-risk drivers, CPAP therapy to reduce driving risk is recommended rather than no treatment.

In those with suspected or confirmed OSA deemed high-risk drivers, stimulant medications for the sole purpose of reducing driving risk are not recommended.

“Clinicians should...inform patients and
their families about drowsy driving and other risks of excessive sleepiness, as well as behavioral methods that may reduce those risks,” said the authors.

“[They] should routinely inquire in patients suspected with OSA about non-OSA causes of excessive daytime sleepiness, comorbid neurocognitive impairments, and diminished physical skills, which may additively contribute to crash risk and affect the efficacy of sleep apnea treatment.”

Doctors are also urged to familiarize themselves with local statutes or regulations regarding the compulsory reporting of high-risk drivers with OSA.

“Addressing the issue of drowsy driving requires the combined effort of physicians, patients, and policy makers,” said Strohl. “The assessment for sleepiness before and with treatment of OSA, as outlined in these new guidelines, is an essential part of these joint efforts.”
Antibiotics a cost-effective option for treating back pain?

Alexandra Kirsten

An intensive course of relatively affordable antibiotics may help patients with back pain.

A recently published study suggests that specific chronic low back pain can be caused by bacterial infections and therefore responds to antibiotic treatment.

In the study, a total of 162 patients with chronic low back pain with symptoms of duration > 6 months after a previous disc herniation, with bone edema demonstrated as Modic type 1 changes on the MRI, were recruited from different spine centers in Denmark. Subjects had had either conservative or surgical treatment. [European Spine Journal 2013, doi: 10.1007/s00586-013-2675-y]

To test the efficacy of antibiotics to treat their back pain, the patients were randomized to either 100 days of amoxicillin-clavulanate medication or placebo. MRI scans, symptom questionnaires, clinical exams, and blood tests were blindly done at baseline, at end of treatment, and at a 1-year follow-up.

The antibiotic group improved statistically significantly on primary outcome measures of disease-specific disability and lumbar pain, as well as on secondary endpoints such as global perceived effect, leg pain, hours of lower back pain, sick leave days, bothersomeness, constant pain, MRI Modic grading, and physical exam measures (p=0.05 to 0.0001). Improvements continued until 1-year follow-up. Additionally, in the antibiotic group, there was a significant decrease in the volume of Modic 1 findings on the MRI scans but no reduction in the placebo group. Side effects were mostly gastrointestinal and reported by 65 percent in the antibiotic group and 23 percent in the placebo group.

“The antibiotic protocol was significantly more effective for this group of patients (chronic LBP associated with Modic 1) than placebo in all the primary and secondary outcomes,” the authors said.

Thus, the study results might justify antibiotics for patients with chronic low back pain and Modic 1 MRI changes following a herniated disc when they have failed to respond to all other treatment options. Nevertheless, the authors cautioned that they rely on their fellow colleagues to use clear evidence-based criteria and to avoid excessive antibiotic use.

Non-specific low back pain affects about 80 percent of people at some point in their lives. According to the National Institute of Health, in the US, low back pain is the most common cause of job-related disability, a leading contributor to missed work, and — after headache — the second most common neurologic ailment.
Improving cancer care in settings of poverty

Excerpted from a keynote address by Dr. Paul Farmer, chair of the Department of Global Health and Social Medicine at Harvard Medical School and chief of the Division of Global Health Equity at Brigham and Women’s Hospital in Boston, Massachusetts, US, during the annual meeting of the American Society of Clinical Oncology (ASCO), held recently in Chicago, Illinois, US.

Oncologists, hematologists and ancillary staff are increasingly interested in the challenges faced in care in the developing world.

But it’s very difficult to build the systems and platforms for care, things like hospitals and clinics, when they don’t exist. Think of leukemia deaths, or deaths from lymphoma or breast cancer. The outcome gap requires support from academic medical centers and practitioners in developed countries.

To silo-ize prevention and care activities is very often a mistake, even though we ourselves make that our task. We adhere to the rubric of prevention, diagnosis and care in cancer prevention campaigns.

Silo-izing the approach and funding and commitment to care delivery to the poor is a big mistake.

In the late 1990s, the public health community thought it would not be cost-effective or sustainable to use antiretroviral therapy to treat human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) in Africa. This kind of defeatism had to be challenged and the slope of that curve is being reversed by domestic staff.

Now the average cost of a therapeutic regimen for an adult is US$90 per year. Plus, people are able to go back to work.

Cancer is a huge problem in lower middle income countries; this is where the majority of malignancies are, yet the funding gap in these areas looks like what the funding gap for AIDS was.

In providing already proven cancer therapies to people who have great need of them, the role of academic medicine is central. This is a group who already know how to break down silos. People involved in cancer care are used to working with surgeons, anesthesiologists, social workers, and palliative care specialists and so on. We need that kind of approach to cancer prevention and care on a global stage.

Most of the people we see in poor settings have many primary care problems, like cancer. We can’t deliver the standard kind of care for chronic afflictions if you don’t have people helping you from the community. With AIDS care, we have trained such workers to recognize the symptoms of illness, the complications of therapy, and help patients with these services.

The outcomes are stunning, and when you compare the outcomes of AIDS care in a community-based model versus standard care where community health workers are not
working with doctors and physicians, you see that the only way to get such good outcomes is in a clinical trial.

So why can’t we do this with cancer? People say you can’t treat cancer without cancer doctors, but what if we’d said that about AIDS. If you think about how many AIDS specialists there are in rural Malawi, Rwanda or Kenya, I can tell you the answer back then was zero. Now, when there are millions of people on therapy, getting pretty good treatment, it is still zero or it is one or two and only growing slowly.

The challenges to effective care are straightforward. You need oncologists but they don’t have to be there all the time. When they are in local settings, they bring up the quality of care but there are ways to use technology platforms to achieve this in efficient and trans-regional ways.

You need staff but take a hard look at the human resources really needed to deliver health care. High quality care can have many definitions but the quality of effort should be very high. There should be ways to build in protocols for staff to make systems equitable and compassion functional.

From those in US centers who donate their time to work in poor settings, the consensus is that local partners can be taught to give very good quality of care. Doctors, nurses and lab technicians in poor settings want a chance to do what we do when we work in safe, clean hospitals with the tools we need.

With the success of AIDS treatments over the past 30 years, to see basic science, drug development and diagnostic development linked to real delivery for people living in poverty with the disease is an amazing victory for science and medicine. This is what we need to happen with malignancies, but we’re not there yet.

First, we can’t just talk of big plans to put in a lab or deliver care. We have to get pilot projects up and running and supported.

We need to start to codify and improve in-service training, and other kinds of training for local physicians and nurses.

And we need to formalize our training for subspecialists, like oncologists, since this need for subspecialists is never going to go away.

In modern medicine, attention is usually given to basic science discovery followed by the science of care around diagnosis, treatment and prevention. It’s messy, requires publication, and the time between discovery and proven effectiveness and actual delivery is very long. That time can stretch to an eternity in places where there are no existing platforms at all.

Building up good delivery science, documenting the work done, and disseminating progress through the internet, journals, or conferences is key, and is part of the important work of academic medical professional societies.

Also important will be to support drawing new talent to global cancer care. Lots of trainees want to do global oncology and global cancer care. Senior figures in oncology might think about new tracks of care that don’t replace a fellowship in, say, general surgery or oncology, but complement those tracks with a health equity track that is global. And global doesn’t mean international. Equity and global health equity are universal concerns.
Chronic obstructive pulmonary disease (COPD) should not prevent patients from enjoying sexual intimacy with their partners, according to Dr. Tomas Realiza, an expert on COPD from Cardinal Santos Medical Center in Greenhills, San Juan City.

The fear of shortness of breath during sex induces many patients with COPD and their partners to avoid sexual intimacy. Additionally, maintaining sexual arousal and or reaching climax further discourage some patients who reach sexual intimacy with their partners.

"Being diagnosed with COPD does not mean the end of your sex life," Realiza emphasized. He explained that this is true for as long as patients adhere to maintenance therapy, adjust their expectations and communicate well with their partners.

The WHO estimates that in 2002 there were 202 million people who suffered from COPD. It is a serious public health concern and life threatening if not properly managed; and, in most cases, it often goes undiagnosed.

"It is very important that we find out who among our patients have COPD. As with chronic diseases, the goals of therapy in COPD are to address the symptoms, future risks of exacerbations, limitations of DALY (disabilities-adjusted life-year), lead normal or near-normal lives; but among patients with COPD the last objective may not be attainable," Realiza said.

The decline in lung function is characteristic of COPD. The primary problem is small airway inflammation, which contribute to difficulty of breathing because once patients inspire, there is closure of the airway. This leads to hyperinflation, increased total lung capacity, increased residual lung volume and reduced inspiratory capacity. All of these...
will lead to hyperinflation and increased exertional dyspnea and reduced exercise tolerance.

The effect of COPD on sexual activity is negative, reducing couples to fear of shortness of breath and exacerbations.

To lessen the impact of the disease, maintaining the clinical stability in COPD patients is the primary goal of therapy. This is where long acting bronchodilators help improve symptoms and reduce exacerbations.

Bronchodilators work by airway stabilization, which reduces airway compression and in the long term may also reduce airway fibrosis. Long acting bronchodilators interrupt the vicious cycle of COPD. They reduce exercise symptoms throughout the day and help patients become more active.

“With bronchodilators, you increase the ventilatory ceiling, patients become more comfortable, the work of breathing is less, and they recover faster from the exercise. If we apply this to the sex life of patients with COPD, if they recover faster, then they may be able to do a second round,” Realiza said. This is why adherence to maintenance therapy makes sex or other forms of intimacy possible for COPD patients.

“Good sex is not automatic. To get things right, it is essential to talk with your partner and approach the subject openly and directly,” Realiza advised.

**Steroids improve outcome in leptospirosis**

**Dr. Carol Tan**

The use of steroids decreased the mortality rate of patients with leptospirosis presenting with pulmonary symptoms, according to a new study conducted by Dr. Diane Bernardo et al. from the Philippine General Hospital–Section of Infectious Diseases, Department of Medicine.

The authors discussed that pulmonary involvement of patients afflicted with leptospirosis is associated with rapid clinical deterioration and high mortality rate; hence, the role of steroids in ameliorating the pulmonary insult in leptospirosis was explored in this study.

In this meta-analysis, researchers collected all randomized and non-randomized studies conducted on patients aged 15 years and above, diagnosed with leptospirosis that manifested with pulmonary symptoms and treated with steroids. The primary outcome of interest was mortality rate. Studies that had different population groups, no pulmonary involvement, different outcomes, and no control groups were excluded. After screening all studies, a total of three non-randomized prospective cohorts and one randomized controlled trial were included in the meta-analysis.

Results of the study showed that in the non-randomized trials, the administration of methylprednisolone 500-1000 mg/day or dexamethasone 200 mg/day for 3 days,
followed either by oral prednisolone at 1 mg/kg/day for 7 days or oral methylprednisolone at 8 mg/day for 5 days decreased the mortality rate among leptospirosis patients with pulmonary involvement (odds ratio of 0.20, 95 percent CI 0.09-0.45). The mortality benefit was particularly apparent when steroids were given within the first 10 to 12 hours of presentation.

In addition, one of the non-randomized studies showed that the use of steroids decreased the need for mechanical ventilation. Only 18 percent of the patients who received steroids needed ventilator support, while 62 percent of the patients who did not receive steroids necessitated mechanical ventilation.

In contrast, the randomized controlled trial showed that there was no significant change in mortality rate among patients with pulmonary manifestations of leptospirosis who were given dexamethasone 200 mg/day for 3 days followed by prednisolone 1 mg/kg/day for four days compared to those who were given standard antibiotic therapy only. Steroids were also found to have no significant effect on length of hospital stay, duration of bleeding and duration of mechanical ventilation support.

The authors concluded that data from non-randomized studies suggest that steroids have a mortality benefit in leptospirosis with pulmonary involvement. Randomized trials are still needed to provide stronger evidence for the beneficial effects of steroids in decreasing the mortality rate of leptospirosis with pulmonary manifestations, as well as to evaluate other outcomes such as safety and tolerability.

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**Insufficient evidence for vitamin E use in non-alcoholic fatty liver**

**Dr. Nicolo Cabrera**

A meta-analysis by researchers from the Jose R. Reyes Memorial Medical Center including five randomized controlled trials of vitamin E versus different control interventions showed a statistically insignificant trend favoring controls in normalizing serum alanine aminotransferase levels.

With Dr. Deepak Shrestha and Dr. Rajendra Rijal as lead investigators, the research team carried out a systematic search for clinical trials on Google Scholar, Cochrane, GastroHep and PubMed as well as via a manual search of various relevant journals. Trials included patients with a history of minimal or no alcohol use and imaging findings of hepatic steatosis or compatible histology such as simple steatosis, fatty infiltration with non-specific inflammation, steatohepatitis, fibrosis or cirrhosis. Other causes of hepatic steatosis were considered exclusion criteria. The meta-analysis included 424 patients in total.
The first trial from 2004 compared 14 patients who received vitamin E and a low-calorie diet with 14 who received a low-calorie diet alone. The second study from 2005 was comprised of a 28-patient treatment group and a 29-patient control receiving ursodeoxycholic acid. The 2006 study administered placebo to the 43 patients randomized to control and vitamin E to the 45 patients assigned to treatment. The fourth study from 2008 had three arms: 19 patients receiving vitamin E, 19 patients undergoing lifestyle interventions and 38 patients without lifestyle interventions. The 2011 study assigned 58 patients to receiving vitamin E, 57 patients to receiving metformin and 58 patients to receiving placebo.

All five studies yielded statistically inconclusive results. The 2004 and 2008 trials showed a slight trend favoring vitamin E supplementation with odds ratios of 0.81 (95 percent CI, 0.23 to 2.89) and 0.93 (0.22 to 3.91) respectively, whereas the rest of the trials showed a slight trend toward their respective controls with 1.38 (0.47 to 4.03) in the 2005 study, 1.86 (0.74 to 4.68) in the 2011 study and 1.61 (0.66 to 3.91). The meta-analysis arrived at an odds ratio of 1.39 (0.87 to 2.23).

“Treatment with vitamins costs less than any other treatment and there are negligible side effects. However, there is no statistically significant data to recommend the use of vitamin E, researchers remarked. They felt that the presently available evidence can neither support nor refute the use of vitamin E or antioxidants in this patient population. Prospective randomized controlled studies with larger populations should be conducted to come to a more definitive conclusion on the question, the team recommended.

Multi-drug-resistant tuberculosis (MDR-TB) and extensive drug-resistant tuberculosis (XDR-TB) cases have epidemiologic significance worldwide, according to Dr. Arto Soeroto with the Hasan Sadikin Hospital–Department of Internal Medicine, Indonesia.

“Globally, 3.7 percent of new tuberculosis cases and 20 percent of previously treated cases are estimated to have MDR TB. … The proportion of XDR-TB in MDR-TB cases is quite high at 9 percent,” stated Soeroto.

The speaker added that the highest proportion of MDR-TB is found in Eastern Europe and Central Asia. In Indonesia, there have been 1,177 MDR-TB cases as of February 2013 and 27 cases of XDR-TB as of November 2012.

This year, WHO guidelines updated tuberculosis classification. Monoresistance is
defined as resistance to one first-line anti-TB drug. Polydrug resistance involves resistance to more than one first-line anti-TB drug, other than isoniazid and rifampicin. Multidrug resistance involves resistance to at least both isoniazid and rifampicin. Extensive drug resistance is resistance to any fluoroquinolone and to at least one of three second-line injectable drugs (capreomycin, kanamycin and amikacin), in addition to MDR. Rifampicin resistance is defined as resistance to rifampicin detected using phenotypic or genotypic methods with or without resistance to other anti-TB drugs.

There were also changes in the definition of treatment outcomes. Cure is defined as completion of treatment as recommended by the national policy without evidence of failure, and three or more consecutive negative cultures taken at least 30 days apart after the intensive phase.

Treatment failure is defined as treatment termination or need for permanent regimen change of at least two anti-TB drugs because of lack of conversion by the end of the intensive phase; bacteriological reversion in the continuation phase after conversion to negative; evidence of additional acquired resistance to fluoroquinolones or second-line injectable drug; or development of adverse drug reactions.

A new diagnostic tool, GeneXpert uses the principles of polymerase chain reaction to detect tuberculosis and gene mutations which cause drug resistance. Results of this test can be retrieved in two hours, so patients at high risk of MDR-TB can immediately start appropriate treatment while waiting for conventional culture and drug sensitivity tests, added Soeroto.

Validity studies done in England stated that GeneXpert had a sensitivity of 94.4 percent and a specificity of 98.3 percent, while studies conducted in Indonesia showed sensitivity of 92.3 percent and specificity of 75 percent.

Principles of treatment of MDR-TB include usage of at least four drugs with either certain or almost certain effectiveness and treating the patient for 18 months past culture conversion.

“Regimens should include at least pyrazinamide, fluoroquinolone, a parenteral agent, ethionamide or prothionamide, and cycloserine or p-aminosalycilic acid if cycloserine cannot be used,” explained Soeroto.

It is essential to promptly diagnose drug resistant tuberculosis and to design a treatment strategy that takes into consideration rates of drug-resistant tuberculosis, technical capacity and financial resistance, concluded the speaker.
Telmisartan may be superior to other ARBs for dyslipidemia

Dr. James Salisi

Telmisartan may be superior to other angiotensin receptor blockers (ARBs) in managing dyslipidemia and elevated fasting glucose in hypertensive patients at increased risk of cardiovascular morbidity and mortality, according to a meta-analysis conducted by Dr. Mary Joy Ordanza and colleagues at the Ospital ng Makati.

Ordanza and colleagues analyzed animal and human studies on telmisartan and other ARBs to compare their effects on metabolic parameters such as high density lipoprotein (HDL), triglycerides and fasting blood sugar of patients with hypertension and metabolic syndrome. They culled 12 studies that included a total of 762 participants that fulfilled the inclusion criteria.

Among the patients, 378 were allocated in the telmisartan group and 384 in the other ARB group who were treated for a minimum duration of 8 weeks. Intervention, control and treatment effects and modifiers such as trial duration, telmisartan dosage, gender, and comorbidities were collected. The researchers computed and used difference in the means and standard deviations of the variables at the end of the intervention period for telmisartan and other ARB from the baseline.

The study found that there were statistically significant reductions in levels of triglycerides and fasting blood glucose that proved the beneficial effect of telmisartan compared with other ARBs. Furthermore, the levels of HDL increased in the treatment group. The investigators noted significant difference on and heterogeneity between the two groups in fasting plasma glucose. Because of the heterogeneity, they conducted a sub-group analysis that eliminated the heterogeneity in the 40-mg dose but not in the 80-mg dose.

These findings support the idea that telmisartan may not be metabolically neutral or have little or no impact in carbohydrate and lipid metabolism like other ARBs. As representative of a subgroup of ARBs, telmisartan has been identified as a partial agonist for the peroxisome proliferators activated receptor (PPAR)-γ, which plays an important role in regulation of carbohydrate and lipid metabolism.

The activation of PPAR-γ by telmisartan may improve insulin sensitivity in addition to its antihypertensive effects. This suggests that ARBs could have an anti-metabolic potential for prevention and treatment of diabetes and...
cardiovascular diseases in high-risk populations. This study sought to confirm it by analyzing past studies on humans and animals.

The benefits of telmisartan not only as an effective antihypertensive but also as an agent to address insulin resistance and cholesterol metabolism are of considerable clinical value. Significant statistical heterogeneity found across studies and question on the most appropriate dose and treatment duration prompt further investigation.

Close monitoring of pregnancy with hep B recommended

Varios pregnancy complications have been associated with hepatitis B infection, which makes monitoring even after delivery important, according to Dr. Diana Alcantara-Payawal, the president of the Hepatology Society of the Philippines.

“Hepatitis B is a growing concern, especially in the Philippines, which is considered an endemic region for this virus,” she said. She noted that since treatment takes a long time, it becomes a burden both for the pregnant women and the unborn baby.

Alcantara-Payawal remarked that acute HBV infection during pregnancy did not show increased mortality to the mother and teratogenic effects to the infant. However, higher incidence of low birth weight and prematurity has been reported. Similar to acute infection, she said that chronic HBV infection is also associated with a higher risk of prematurity and low birth weight. In addition, chronic infection is associated with a higher incidence of gestational diabetes mellitus. Paradoxically, it was not associated with pre-eclampsia.

Touching on the issue of perinatal HBV transmission, Alcantara-Payawal said that the risk of transmission without immunoprophylaxis at birth is 70 to 90 percent in hepatitis B envelope antigen (HBeAg)-positive mothers. Worse, the infection can develop to chronic Hepatitis B infection in 90 percent of infected neonates. She noted that HBV transmission predominantly happens at birth and rarely in utero or during amniocentesis.

“Breastfeeding is not contraindicated for infants born to hepatitis B surface antigen (HBsAg)-positive mothers,” said Alcantara-Payawal. Even though HBsAg can be detected in breast milk, she explained that appropriate immunoprophylaxis of the infant using vaccination and hepatitis B immune globulin (HBIG) prevents additional risk of transmission. She also cited studies which showed that breastfed infants did not have a higher risk than formula fed infants in getting HBV infection. However, she emphasized that
there is limited data on the safety of lactation among newborns of HBsAg-positive mothers receiving antiviral therapy.

To address the issue of antiviral treatment during pregnancy, Alcantara-Payawal recommended considering early treatment at 32 weeks age of gestation with either lamivudine, tenofovir or telbivudine for mothers with high alanine aminotransferase (ALT) and high HBV DNA (10⁷ copies/mL). At birth, the baby receives HBIG and universal vaccination for HBV. If the mother chooses to breastfeed, Alcantara-Payawal recommended discontinuing antiviral treatment.

“Since they develop flares [after delivery], you have to continue monitoring your patients for flares with HBV DNA and ALT every one to 2 months for 3 months,” Alcantara-Payawal emphasized. For mothers with HBV DNA < 10⁷ copies/mL, she did not recommend antiviral treatment during pregnancy; but at birth, the baby should receive HBIG and universal HBV vaccination. Monitoring for maternal postpartum flares is also recommended in this group.
PhilHealth provides maternal and child benefits

Ian Carlos Achero

Department of Health (DOH) secretary Dr. Enrique Ona advised women who are Philippine Health Insurance Corporation (PhilHealth) members to make the most of their maternal and child care package benefits.

Due to complications of pregnancy like hemorrhage, hypertension and sepsis, the United Nations reported that 11 Filipino mothers die daily from complications of pregnancy or childbirth.

Through PhilHealth, mothers and their babies can avail of the medical attention needed for a safe and effective delivery, said Ona. The case rate packages of PhilHealth give members financial coverage which varies depending on the case and health institution.

All types of members are entitled to know how much of their health expenses can be shouldered by PhilHealth. To those giving birth in accredited non-hospital facilities (health centers, lying-in clinics, birthing homes or midwife-managed clinics) and Level 1 hospitals, PhilHealth members will be able to get a cost benefit of Php 8,000 for a maternity care package. Those undergoing normal spontaneous delivery in accredited Levels 2 to 4 hospitals are entitled to a cost benefit of Php 6,500. Coverage for cesarean section delivery in said facilities and performed by accredited health professionals amounts to Php 19,000.

Babies of members can also benefit from the newborn care package in accredited hospitals and lying-in clinics for a cost benefit of Php 1,750. This package includes physical examination, eye prophylaxis, vitamin K administration, Bacillus Calmette–Guérin (BCG) vaccination, first dose of hepatitis B immunization, newborn screening tests and breastfeeding advice.

Additional benefits to sponsored members are available in government hospitals. Sponsored members are entitled to a “no balance billing” policy where no other fees or expenses shall be charged to or paid for by the sponsored member above and beyond the package rate for maternity care.

Mismanagement on the part of some childbirth attendants such as “manghihilots” and “comadronas” can also contribute to maternal and infant deaths, according to Roland Eric Macanas, a maternal and child health specialist from the Japan International Cooperation Agency-DOH partnership. The DOH issued an order authorizing only skilled and trained midwives, physicians and nurses to help pregnant women in delivery.

The solution to maternal and neonatal deaths lies not only in the government but also in educating pregnant women who remain uninformed of the risks of childbearing. Through the case rate packages of PhilHealth, it is expected that correct information and proper management from healthcare professionals will improve maternal and childbirth survival rates.
DOH launches ‘healthy lifestyle movement’

Dr. Nicolo Cabrera

The Department of Health formally launched nationwide ‘healthy lifestyle movement’ PilipinasGo4Health on June 6, 2013, to control rates of non-communicable diseases (NCDs) that the department reports to be on the rise due to improper diet, insufficient exercise and excessive drinking and smoking.

PilipinasGo4Health encourages Filipinos to commit to physical activity, proper nutrition and cessation or prevention of tobacco and alcohol consumption citing “abundant scientific and social evidence” that habits like these comprise the “path to better health,” articulated health secretary Dr. Enrique Ona.

The worldwide toll of cardiovascular disease, respiratory disease, diabetes and cancer is 36 million lives annually, established the DOH press release on launch day. It further specified that 10 Filipinos die every hour due to cigarette smoking-associated diseases such as lung cancer, emphysema and bronchial disorders.

Ona also called out to drinkers and would-be drinkers, describing the effect of alcohol as “complex,” possibly leading to impairments in judgment and risky behavior that could later on result in road accidents or violence.

The Global Adult Tobacco Survey (GATS) in 2007 showed that 57.8 percent of youths live with smokers and 67.9 percent are exposed to smokers outside their homes. The 2009 GATS found that 17.3 million Filipinos ages 15 years and older are tobacco smokers. The Food and Nutrition Research Institute informed DOH that only seven out of 100 adult Filipinos get “vigorous exercise” at least three or four times a week.

Ona explained, “GATS data show that a number of smokers accessed tobacco when they were very [sic] young to make informed choices. By the time they are old enough, they find it very hard to quit and some may already suffer consequences.” He cited “misinformation or lack of information, indifference and careless practices and habits” among Filipinos when it comes to their health.

“We believe that every Filipino has the right to a healthy family, community and country. As lead advocate for the nationwide healthy lifestyle movement, we work hand-in-hand with different sectors to provide options for healthy living and make it accessible to as many people as
possible,” pledged the movement’s webpage at www.go4health.ph.

The web page provides lifestyle suggestions for various age groups such as kids, youth and adults as well as roles or settings such as parenting, education, health care and the workplace. Web page visitors may also download documents containing information on tobacco, alcohol, diet and exercise.

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**Possibility of harm stops VCO trial on infant nosocomial infection**

**Dr. James Salisi**

Investigations at the Neonatal Intensive Care Unit (NICU) of the Philippine General Hospital cancelled a randomized controlled trial of topical application of virgin coconut oil (VCO) in the prevention of nosocomial infections in neonates born less than 34 weeks gestational age because of possibility of harm. Dr. Resti Ma. Bautista, Dr. Jacinto Blas Mantaring III, and Dr. Anna Lisa Ong-Lim decided to stop the study because of increased incidence of nosocomial infection in the topical VCO treatment group according to a paper published by Acta Medica Philippina, the Philippines’ National Health Science Journal.

The investigators carried out a prospective, randomized, non-blinded, controlled clinical trial at the NICU of PGH to determine the efficacy of the topically applied VCO in the prevention of nosocomial infection in neonates born less than 34 weeks gestational age. The preterm infants received either 4g/kg of topical VCO twice daily for 14 days or routine skin care. They were followed up until 28 days or discharge.

The investigators used need for double volume exchange transfusion (DVET) for sepsis, all-cause mortality rates and length of hospital stay as outcome measures.

A total of 52 infants had been randomized with 24 to topical VCO and 28 to routine care, when the trial was terminated due to increased incidence of nosocomial pneumonia in the topical VCO group. The incidence of nosocomial pneumonia went up to 17 percent in the topical VCO group while it was only 7 percent in the control group.

There were four cases of pneumonia in the treatment group and two in the control group, which represented an increase of 9.5 percent in the risk occurrence of nosocomial pneumonia in topical VCO group. While this was insufficient to state whether harm truly existed, the difference was considered by the investigators as already clinically significant to warrant termination of the trial before desired sample size was reached.

The mortality rate in the topical VCO group
was 12 percent versus 14 percent in the control (RR=0.875 [0.217, 3.258]; p=0.851); however, this was not statistically significant. A trend that showed decreased need for DVET for sepsis was also found in infants treated with topical VCO (RR=0.166, [0.009, 3.056]; P=0.098). There was no significant difference between the lengths of hospital stay in the two groups.

The groups were comparable in terms of baseline characteristics. No cases of meningitis, necrotizing enterocolitis and urinary tract infection were recorded in either group.

Jumping off from other studies that proved the efficacy of VCO as an anti-microbial agent, the investigators wanted to determine whether VCO could be used as a cheap alternative to prevent nosocomial infection in premature infants. If proven, it would help stave off cost from medical care in developing countries like the Philippines where VCO is cheap and readily available. However, the initial findings that showed possibility of harm were enough to prompt the investigators to stop the trial.

Despite these findings, future studies on effectiveness and safety of VCO given orally rather than via topical administration may still be carried out, according to the investigators.
## CONFERENCE CALENDAR

### JULY

**2013 Annual Postgraduate Course of the Foundation for Reproductive Care Inc.**

**July 2-4, 2013**  
Venue: Sofitel Philippine Plaza Manila, Pasay City  
Info: The Foundation for Reproductive Care Inc. in cooperation with University of the Philippines - Philippine General Hospital Department of Obstetrics and Gynecology  
Telephone: (+632) 524 3518 or 554 8400 loc 2300  
Email: up_pghpostgrad2013@yahoo.com  
Website: [http://www.facebook.com/2013Postgrad](http://www.facebook.com/2013Postgrad)

**16th Midyear Convention of the Philippine College of Chest Physicians**

**July 26-27, 2013, 2013**  
Venue: Grand Caprice, Lim Ket Kai Mall, Cagayan de Oro City  
Info: Philippine College of Chest Physicians  
Telephone: (+632) 924 9204  
Email: secretariat@philchest.org  
Website: [http://www.philchest.org](http://www.philchest.org)

### AUGUST

**4th Annual Postgraduate Course of the Asian Hospital and Medical Center Department of Anesthesiology**

**August 10, 2013**  
Venue: Palms Country Club Ballroom, Filinvest City, Muntinlupa City  
Info: Asian Hospital and Medical Center Department of Anesthesiology  
Telephone: (+632) 876 5724  
Email: aainc08@yahoo.com  
Website: [http://www.asianhospital.com](http://www.asianhospital.com)

### SEPTEMBER

**19th Annual Convention of the Philippine Association for the Study of Overweight and Obesity**

**September 6, 2013**  
Venue: Crowne Plaza Galleria Manila, Ortigas Center, Pasig City  
Info: Philippine Association for the Study of Overweight and Obesity  
Telephone: (+632) 632 1533 or 359 9268  
Email: sec@obesity.org  
Website: [http://www.obesity.org.ph](http://www.obesity.org.ph)

**25th All-in-one (All Subspecialties) Postgraduate Course of the Philippine Children’s Medical Center**

**September 17-18, 2013**  
Venue: Crowne Plaza Galleria Manila, Ortigas Center, Pasig City  
Info: Philippine Children’s Medical Center  
Telephone: (+632) 924 6601 loc 338 or 240  
Email: pcmcpedmed@yahoo.com

### OCTOBER

**Midyear Convention of the Philippine Society of Nephrology**

**October 4-6, 2013**  
Venue: L' Fisher Hotel, Bacolod City  
Info: Philippine Society of Nephrology  
Telephone: (+632) 687 1198  
Email: psnmanila@gmail.com  
Website: [http://www.mypsn.org](http://www.mypsn.org)
Disclosure, euthanasia discussed in ethics symposium

Ian Carlos Achero

Two deans of medical colleges, Dr. Angeles Tan Alora and Dr. Brigido Carandang Jr., gave their stand on key ethical issues in the ETHICS (Educators Tackle Health Issues in Case Studies) Symposium 2013 held at the Philippine College of Physicians’ 43rd Annual Convention. Alora is a former dean of the University of Santo Tomas-Faculty of Medicine and Surgery (UST-FMS) and coauthor of the book “Beyond a Western Bioethics.” Carandang is the current dean of the St. Luke’s College of Medicine-William H. Quasha Memorial Center.

The practice of medicine entails making moral and ethical decisions. These decisions affect patient’s lives as well as doctors themselves. In the symposium, audience response was collected using hand-held clickers. A button was pressed by the audience for each choice on the screen. The choices made were compared to a survey conducted by Medscape to American physicians.

Providing unnecessary measures

The first ethical issue discussed was giving life-sustaining measures that proved futile. According to Alora, generally if an intervention is futile, it is unnecessary. Because of scarce resources, especially in the Philippines, giving something unnecessary is useless and potentially wasteful.

There could be conditions or circumstances where, for example, if the family has not accepted death yet. To help them accept, you might do something to prolong life. So, I can understand it, but I cannot recommend it,” explained Alora. The will of the patient must also be taken into account. Alora added that the choice would also depend on what the patient would have chosen if he were able to choose.

Another issue tackled is devoting scarce or costly resources to a younger patient rather than to one who is older but not facing imminent death. Carandang did not agree prioritizing the younger patient. “The mere fact that you’re younger doesn’t mean that you
have the right to use resources," he answered. Alora agreed completely.

Two opposing viewpoints were given on the question “Is it ever acceptable to perform ‘unnecessary’ procedures due to malpractice concerns?” An example of this in practice is a patient with ample resources deciding to have a CT scan for simple headaches. Carandang, a neurologist, answered, “I don’t necessarily agree with the patient. However, since you insist, it’s your right to have a scan.” This stance assumes that the risks of the procedure have been fully explained to the patient, such as unnecessary radiation from a head CT scan.

The question in ethics is not whether it’s popular or not. The question is, is it right or not?

Alora disagreed, saying, “If you do it for malpractice, that means you’re worried about your popularity. The question in ethics is not whether it’s popular or not. The question is, is it right or not?” She added that doctors are not slaves to the wishes of patients. For example, she mentioned that if a patient decides to commit suicide, we ought not to help the deed. According to her, if the patient insists on doing an unnecessary procedure, especially in the Philippine setting where resources are limited, she will withdraw from the patient.

The reason for doing a procedure must also be taken into account as well. As stated by Alora, if a procedure is done to look for something, it’s a necessary procedure. However if the sole reason is to satisfy the patient, the procedure is unnecessary. Carandang maintained his position that if doing the procedure helps the patient sleep better, especially if the patient is neurotic, he will agree to the procedure.

Ensuring full disclosure

A difficulty facing physicians is whether or not to report a colleague who seems impaired by addicting substances or illness. One example is a colleague going into the operating room drunk or performing surgery with parkinsonian tremors. Alora expressed that in this scenario, it is our obligation to maintain a professional standard. If a colleague harms a patient due to sickness, standards go down. She recalled a famous personality accusing physicians as a “brotherhood of silence,” wherein if one makes a mistake, everyone tries to cover it up or remain silent.

“It is your duty to report him to the correct authorities. It is not your duty to go to media,” Alora emphasized.

Non-disclosure of mistakes that did not cause harm was talked about. For example, multivitamins were supposed to be given by a nurse but an antimicrobial was given instead, without any adverse effects.

Carandang responded that it is not acceptable to cover up anything even if the said measure did not cause harm. He said that if such happens, he will apologize and reassure the patient that such will not happen again. Alora joked that telling lies might lead one to become a politician. In the United States, consistent with the speakers’ view, the most common cause of lawsuits to physicians is nondisclosure. Patients would often say they just want an explanation to be given from the start.
Some doctors might hide a terminal or preterminal diagnosis from patients because they believe hiding the information can boost their spirit. Family members might also request the physician to hide the diagnosis from their loved ones in the hope of a better outcome. Similar to the preceding dilemma, this also entails not disclosing information.

Alora reacted that disclosing a terminal or preterminal diagnosis depends on the context and emotional state of the patient. This is because there are some patients who will get more depressed with the information, commit suicide and die. However this is a rare case, she clarified, because most patients know they are seriously sick and are only looking for confirmation through the doctor. Carandang agreed, adding that such an act deceives the patient and gives them false hope.

**Fulfilling a death wish**

Three states in the United States, Oregon, Washington and Vermont, legalized physician-assisted suicide. Some countries are considering legalizing it.

Alora clarified the difference between physician-assisted suicide and euthanasia. In euthanasia, the patient asked to end his life and another individual (ie, physician) gives the lethal intervention. In physician-assisted suicide, it is the patient who administers the lethal intervention to himself. Alora opposes physician-assisted suicide for the reason that it is still suicide on the patient’s part and the doctor cooperated in the wrongdoing. “So if the patient goes to hell, you go to hell with him,” she joked.

“In the Philippine scenario, some families wish to end treatment because they have run out of resources even if a family member still has a chance to recover. Carandang emphasized that lack of funds does not entail stopping treatment. He believes the obligation is on the physician to look for resources and try to help the patient. Alora agreed with Carandang, adding that physicians, especially the Catholic physician, should provide free service, share resources and fight for a just policy so such situations never occur.

> "The most common cause of lawsuits to physicians is nondisclosure"

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To cut, or not to cut: Evaluating surgical prophylaxis in at-risk patients

Dr. Nicolo Cabrera

A discussion that had largely been confined to medical circles spilled over into broader public consciousness last May when multi-awarded Hollywood actress Angelina Jolie explained her decision to undergo bilateral prophylactic mastectomy (BPM) in a New York Times op-ed piece.

“My doctors estimated that I had an 87 percent risk of breast cancer and a 50 percent risk of ovarian cancer. [...] I decided to be proactive,” Jolie wrote. Her mother had ovarian cancer and died with the disease in 2007 at the age of 56. Her aunt died with breast cancer several weeks after Jolie’s op-ed piece had gone to print. Jolie and her aunt discovered had both tested positive for a mutation of \textit{BRCA1}, a tumor suppressor gene, increasing their risk of developing these two cancers plaguing women worldwide. Jolie completed a three-step process—including reconstruction—over three months at the Pink Lotus Breast Center in California last April.

She acknowledged that surgery may not be the appropriate option for every woman, but she addressed female readers, “I hope it helps you to know you have options.” She added, “I can tell my children that they don’t need to fear they will lose me to breast cancer.”

In the wake of Jolie’s personal health decision, more patients are asking about undergoing prophylactic surgery to cut their own risk of developing cancer. Among the prophylactic procedures discussed in this article with a review of their indications and evidence are oophorectomy, mastectomy, hysterectomy, prostatectomy and colectomy.

Prophylactic mastectomy, oophorectomy and hysterectomy

In 2008, the PROSE (Prevention and Observation of Surgical End Points [breast cancer]) Study Group reported findings from a prospective cohort of 483 women with disease-associated germline \textit{BRCA1/2} mutations. Bilateral mastectomy reduced breast cancer risk by approximately 95 percent in women with prior or concurrent bilateral prophylactic oophorectomy (BPO) and by approximately 90 percent in women with intact ovaries \cite{J Clin Oncol 2004; DOI: 10.1200/JCO.2004.04.188}.

A Cochrane review of 39 observational
studies published in 2010 found that BPM effectively reduced the incidence of and death from breast cancer, particularly among BRCA1/2 gene mutation carriers, but rigorous prospective studies such as randomized trials are still required. The review recommended the procedures for those at very high risk of disease [Cochrane Database Syst Rev 2010; DOI: 10.1002/14651858.CD002748.pub3].

"Randomized, controlled trials of surgical interventions to prove mortality benefits are not likely to be feasible"

Ovarian cancer has also been associated with gene mutations for Lynch syndrome or hereditary nonpolyposis colorectal cancer (HNPCC). Along with malignancies of the ovary and the colon, the endometrium and peritoneum may also be involved. Findings from a prospective cohort of 315 women suggested that prophylactic hysterectomy and bilateral salpingo-oophorectomy effectively prevented endometrial and ovarian cancer in mutation-positive women [N Engl J Med 2006; DOI: 10.1056/NEJMoa052627].

Drs. Mark Robson and Kenneth Offit of the Clinical Genetics Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, in New York noted the absence of trial data, “Randomized, controlled trials of surgical interventions to prove mortality benefits are not likely to be feasible.”

The remaining areas of uncertainty make it difficult to recommend these procedures without reservation. Specifically on breast cancer, they articulated, “Even if preventive mastectomy reduces the risk of breast-cancer mortality, the degree to which it improves survival beyond that achieved with RRSO (risk-reducing salpingo-oophorectomy) and surveillance (including MRI), with or without tamoxifen or raloxifene, is not clear.”

Despite Jolie’s confidence that her children “don’t need to fear,” Robson and Offit pointed out that the BPM and BPO do not entirely prevent the risk of subsequent breast or ovarian cancer, stating the residual risk of primary peritoneal cancer after BPO is 0.2 percent annually and the absolute risk after BPM has not been clearly defined.

**Prophylactic prostatectomy**

Also this year, a 53-year-old British businessman underwent the first prophylactic prostatectomy after discovering his BRCA2 gene mutation. Initially, his doctors were reluctant to perform the procedure because he had normal prostate-specific antigen levels and MRI findings. The decision was made in light of recent research showing that BRCA1/2 gene mutation carriers tend to have Gleason scores of 8 and higher, T3/T4 staging, nodal involvement and metastasis at diagnosis compared to non-carriers [J Clin Oncol 2013; DOI: 10.1200/JCO.2012.43.1882].

Similar to the above prophylactic surgeries, no data from controlled trials demonstrating survival benefit are available to guide clinical decisions.

**What’s the catch?**

Shouldn’t we be testing all men and women for these risky gene mutations? Why are some doctors reluctant to support these prophylactic surgeries? It might work—isn’t it worth a try? Isn’t doing something better than
doing nothing? The quick answer to most, if not all, of these questions is not necessarily.

*BRCA* gene mutations are performed only by Myriad Genetics at a list price of close to USD 4,000. And the rarity of the mutation means that it may not be worth it for every person to get tested. Dr. Sandra Adamson Fryhofer, Clinical Associate Professor of Medicine at Emory University School of Medicine, wrote for Medscape in Internal Medicine about the importance of genetic counseling as helpful and informative.

“Women of Ashkenazi Jewish descent should consider testing if any first-degree relative—their mother, daughter or sister—has had breast or ovarian cancer or if two second-degree relatives on the same side of the family have been diagnosed with them,” noted Fryhofer.

Fryhofer outlined some family patterns for women of any ethnic background that may indicate need for *BRCA* testing: having (1) a male relative with breast cancer, (2) a first-degree relative with bilateral breast cancer, (3) two first-degree relatives with breast cancer at or before age 50 years, (4) at least three first- or second-degree relatives with breast cancer at any age or (5) at least two relatives with ovarian cancer and (6) first- and second-degree relatives with breast or ovarian cancer particularly if with both, regardless of age at diagnosis.

Prophylactic surgery is not the only option. Less drastic options—those that do not subject the patient to surgical risks such as bleeding or postoperative risks such as early menopause and decreased overall satisfaction—include cancer surveillance and screening such as mammography, clinical breast exams and MRIs for breast cancer as well as clinical exams and transvaginal ultrasound for ovarian cancer. Reliability of CA125 in finding early ovarian cancer is uncertain.

Fryhofer also points out chemoprevention with oral contraceptive pills and tamoxifen are also available.

Surgery cannot remove all at-risk tissue. Whatever tissue may remain may still be a site for the development of cancer, Fryhofer reiterated misgivings of Robson and Offit.

**Personalized, tailored medicine**

All the study data in the world—even from randomized trials or meta-analyses—can only make broad conclusions about patient populations. It is impossible to determine with 100 percent certainty what outcomes await any individual patient who chooses any particular treatment option. Some uncertainty remains even with treatments based on trial data with hard clinical outcomes. An even greater degree of it becomes unavoidable with treatments based on surrogate outcomes or observational data.

Every patient is unique, not only biologically but also socially and psychologically. The patient’s preferences should ultimately shape the treatment plan. However it is the physician’s duty to educate his or her patient about what we know about the disease and the diagnostic and treatment modalities available as well as, or perhaps particularly, what we do not know. Otherwise a patient opting for one treatment path or the other could be laboring under misconceptions or false hopes—an unwitting betrayal of his or her own preferences. And that could be the greater tragedy.
Acne Board of the Philippines launches treatment guidelines

Last May 29, 2013, Galderma held a dinner symposium at Makati Shangri-La Hotel highlighting the launch of Multidisciplinary Treatment Guidelines for Acne, a book of treatment recommendations expertly reviewed and compiled by the Acne Board of the Philippines.

Dr. Flordeliz Abad-Casintahan, chairperson of the board, talked about the group’s history, activities and goals. The Acne Board of the Philippines was formed in 2005 by dermatologists from different regions of the Philippines. The development of a set of guidelines was a part of the objectives of the group to disseminate information to physicians and improve the outcome of the acne treatment in Filipino patients.

Acne can affect up to 51 percent of women and 43 percent of men in their 20s and continue on throughout adulthood. It is a condition that can cause significant psychosocial burden to patients.

Remarkable radiant complexion with Lab46 Skincare

The Lab46 Skincare Remarkable Face Radiance product line gives way to a younger, healthier complexion by taking away old, blemished skin. Rich in antioxidants and age-reducing components, the product line helps the skin attain a white, healthy glow.

The Remarkable Face Radiance Toner contains 5 percent glycolic acid which enhances skin texture, clears acne scars, washes follicles and whitens skin tone. A Pore-Minimizing Toner minimizes the appearance of pores while improving skin texture. The Remarkable Face Radiance Soap smoothens skin tone, normalizes oil production and renews the skin.

The Remarkable Face Radiance Cream helps tighten the skin leading to a more even skin tone. Remarkable Face Radiance Gel gives a healthy luminosity to the skin and helps in moisture retention. Lab46 Skincare Remarkable Face Radiance is manufactured and distributed by Holistix Inc.
Nobel Prize-winning scientist discusses nitric oxide

A Nobel Peace Prize-winner and a distinguished Professor of Pharmacology at the UCLA School of Medicine in California, Prof. Louis Ignarro discussed nitric oxide and cardiovascular health in a Menarini Philippines-sponsored lecture held at the 44th Annual Convention of the Philippine Heart Association (PHA) at the EDSA Shangri-La Hotel in Mandaluyong City.

“His extensive research on cardiovascular health and discovery of the role of nitric oxide have contributed significantly to the effective treatment of cardiovascular diseases,” said PHA president Dr. Saturnino Javier.

Menarini recently introduced nebivolol, the only beta blocker known to induce vascular production of nitric oxide. It is indicated for the treatment of essential hypertension and mild and moderate chronic heart failure.
Candesartan and amlodipine combination benefits elderly

In a dinner symposium held in One Esplanade, Takeda Philippines introduced Unisia, a fixed-dose combination pill consisting of candesartan plus amlodipine. Dr. Alan Gradman, professor of medicine at Temple University School of Medicine in Pittsburgh, Pennsylvania, gave a lecture during the event. Blood pressure control in the elderly is essential to reduce cardiovascular events which translate to increased life quality and expectancy.

“From an endpoint perspective, amlodipine has never been bested in any major clinical trial,” said Gradman. Citing the Study on Cognition and Prognosis in the Elderly (SCOPE) trial, Gradman added that candesartan showed 32 percent risk reduction in the occurrence of major cardiovascular events in the elderly. Candesartan was also shown to have positive effects on cognitive function, quality of life and new-onset diabetes. With the combination, major adverse cardiovascular events were reduced by 39 percent, he said.

Gradman highlighted that each agent has proven endpoint reduction with minimal metabolic side effects.

Azilsartan provides best hypertensive control among ARBs

Edarbi (azilsartan), an angiotensin II type 1 receptor blocker (ARB), was shown to provide superior blood pressure control compared to other ARBs in the market. Dr. Hermann Haller, director of the Department of Nephrology at Hannover Medical School in Germany, discussed the need for a new ARB in a dinner symposium hosted by Takeda Philippines.

According to Haller, studies have shown that azilsartan provides better 24-hour blood pressure control than other ARBs such as valsartan and olmesartan. He said that the greater antihypertensive effect of azilsartan can be attributed to its persistent ability to inhibit binding of angiotensin II to its receptor compared to others. Even with its better BP lowering effect, the side effect profile of azilsartan is similar to other ARBs.

Haller added that azilsartan was also shown to have pleiotropic effects in preclinical studies such as improved insulin sensitivity and reduced proteinuria.
Nutramedica, manufacturer and exclusive distributor of Novuhair, introduces the Novuhair 3-in-1 Pack which now comes with a herbal conditioner to complement the herbal shampoo and topical scalp lotion.

The Novuhair brand rejuvenates hair follicles and improves blood circulation to the scalp to stimulate hair growth. It also provides optimum nutrition to combat hair loss and hair thinning.

A clinical trial conducted last year by Dr. Ma. Rica Silva-Mallari, dermatologist from St. Luke’s Medical Center in Quezon City, showed 100 percent success rate among the volunteers. All subjects experienced no progression of hair loss with decreased hair shedding. More importantly, no side effects were experienced by the subjects.
Different definitions of gastroesophageal reflux disease (GERD) have been used in literature. The current definition and classification of GERD is a global and evidence-based construct developed by patients, physicians and regulatory agencies. *1* According to this definition, GERD is a condition that develops when the reflux of gastric contents causes troublesome symptoms and/or complications. It is further subclassified into esophagitis and extraesophageal syndromes. GERD symptoms become troublesome when they adversely affect an individual’s well-being. Mild symptoms occurring on 2 or more days per week or moderate/severe symptoms occurring on more than 1 day per week are often considered troublesome by patients. *1*

In the Western world, the prevalence of GERD is around 20% to 40%. *2* According to the Asia Pacific Consensus on the Management of GERD, the incidence in Asia has increased in recent years. The prevalence of GERD in individual Asia Pacific nations ranges greatly from 3.5% in Korea to 30% in Taiwan. *3* In the Philippines, using 15,981 upper endoscopy results, a local study showed that the prevalence of erosive esophagitis (EE) increased from 2.9% in 1994-1997 to 6.3% in 2000-2003. *4*

The American Gastroenterological Association (AGA) surveyed 1,064 patients with GERD and found that almost 40% of them experienced recurring symptoms. The patients surveyed were receiving once-daily proton pump inhibitors (PPIs) for 13 months. Nighttime symptoms were the most common bothersome problem, with 65% reporting they experienced breakthrough symptoms at night and 28% while sleeping. Only 23% of patients taking PPIs said they were completely satisfied with their current therapy. Because of the finding that PPIS, patients used adjunctive medications like antacids, H1 receptor antagonists, or other over the counter (OTC) PPIs. The AGA concluded the study by stating that current once-a-day and even twice-a-day PPI therapy fell short of relieving GERD symptoms. *5*

The GERD in Asia Pacific Survey (GAPS) assessed the impact of GERD on patients’ quality of life. *6* It found that 94% of PPI-treated patients experienced breakthrough symptoms. Sixty one percent of PPI-treated patients had breakthrough symptoms at night. The breakthrough symptoms were severe enough that 23% of PPI-treated GERD sufferers did not enjoy a good night’s sleep. *7* Only 24% of patients on PPI therapy felt that their pain or discomfort was completely under control. *8* When the respondents were asked for a “wish list” for a new medication, answers reported from five countries were similar, including elimination of nighttime symptoms and 24-hour symptom relief (Figure 1).
Getting HIV drugs to the masses – the conflict between commercial and public health interests

Leonard Yap

Nothing prepared the world for HIV’s virulence when it was first discovered in 1981. For the first few years post-discovery, the world was on its knees, with no idea what HIV and AIDS was, and no treatment to fight the illusive disease.

Today, though the AIDS pandemic continues to plague humanity, it has become less of a death sentence and more of a manageable disease like diabetes. This impressive turn-around can be attributed to advancements in antiretroviral treatments (ART), improved access to medications, and an unprecedented amount of cooperation between the scientific community, media and the highest corridors of power.

Unfortunately, there remains conflict between commercial and public interests when it comes to equitable access to high-quality, affordable ART for the masses, said Dr. Jennifer Cohen, assistant professor of medicine at the Hospital of the University of Pennsylvania, Philadelphia, US, and medical advisor to Médecins Sans Frontières (MSF, or Doctors without Borders).

Pharmaceutical companies have been accused of abusing the current patent system to extend their monopoly and to obtain additional patents on drugs, and combinations that include it, through a process known as ‘evergreening,’ whereby manufacturers can extend the life of a patent by making a small alteration to an existing compound, Cohen told Medical Tribune.

Asked what incentive big pharmaceutical companies have to create new, innovative
medicines if they cannot have control over their patents, Cohen said, “Pharmaceutical companies have really recouped all of their cost many times over, plus a very large profit margin by selling their drugs under patent monopolies in wealthy markets. However, the ostensible incentive given by a patent should be time limited. Eventually, generic companies can come in and reduce costs. In the US, the patent for most of the medications contained in this branded fixed-dosed combination, have actually run out.”

“The generics we currently use are a key component. There has been no possibility of treatment scale-up for the current 8 million people on treatment without the use of affordable, high-quality generics.”

A study by Massachusetts General Hospital in Boston has muddied the efficacy of generic ARTs, which have been used extensively worldwide, claiming that switching patients from the branded version of ART to its generic equivalent could be less effective and endanger patients’ lives. The study chose to let slide that intellectual property patents prevent the use of more affordable patient-friendly combination drugs, Cohen said. [Ann Intern Med 2012;156(11):817-33]

The article compared the efficacy of a single-tablet fixed-dose of tenofovir/emtricitabine/efavirenz on adherence compared to a multi-tablet regimen that was previously used in first-line ART in a cohort of US patients who were primarily homeless or marginally housed. Scientifically, that comparison would be like comparing apples to oranges, Cohen said.

“What the study showed is that fixed-dose combinations seemed to be easier to take for patients and improved adherence. This makes sense because one pill once a day is much easier to remember compared to combination therapy that has multiple pills or pills twice a day. This also helps to ensure that the complete regimen of ART is taken by the patient because it is all contained in a single pill. As adherence is the most important predictor of treatment success, fixed-dose combinations are really an important part of our toolbox for adherence.”

The study concluded that switching to

“Unfortunately, there remains conflict between commercial and public interests when it comes to equitable access to high-quality, affordable ART

“Evergreening not only hurts patients, because it disallows access to the drug at an affordable price, but it actually hurts the motivation to create truly innovative drug products because it grants a very important commodity [patents] in our current system of patents based on something that may not be truly innovative.”

Cohen added that innovation is alone meaningless without access to medications, noting that MSF’s interests are primarily patients who live in low- and middle-income countries (LMICs). These patients desperately need affordable, effective and easy-to-take medications to live long, healthy and productive lives, and to decrease HIV transmission within the population.
generic regimens in the US could result in savings of US$1 billion in the first year alone, but this important and hard-hitting conclusion is obscured by the fact that the quality and efficacy of generic medicines is erroneously questioned.

"The generics we currently use are a key component. There has been no possibility of treatment scale-up for the current 8 million people on treatment without the use of affordable, high-quality generics"

Fixed-dose combination ARTs were first developed by generic manufacturers in India because the individual medicines were not patented there, allowing them to be combined into one pill. MSF’s experience providing HIV treatment and a number of studies have shown that fixed-dose combinations make adhering to treatment easier for patients. MSF, in collaboration with the University of Montpellier’s Research Institute for Development in France, conducted a clinical trial in 2004 and found that generic fixed-dose combinations were as effective as the branded version. [Lancet 2004;364:29-34]

As asked about the consequences of the Massachusetts General Hospital study on LMICs and the world, Cohen said, “Physicians in LMICs are very well aware of the concept of fixed-dosed combinations and, in fact, fixed-dosed combinations are recommended by the WHO as an important part and preferred regimen for ART. Physicians and patients in LMICs have actually had access to single-pill fixed-dosed combinations for quite a long time, starting with stavudine-based regimens and now the tenofovir-based regimens. In fact, LMICs have had to use generic fixed-dosed combinations before those in the US had access to branded fixed-dosed combinations.”

“The US first-line treatment is a one-pill once-a-day regimen of tenofovir, emtricitabine and efavirenz. Those in LMICs have had access to these for quite a while. In LMICs, we have access to these regimens for under US$200 per patient/year. This makes it a very affordable regimen and these sorts of fixed-dosed combinations are one of the major drivers that have allowed us to put over 8 million people on treatment and really begun to show decreases in mortality and morbidity and decreases in HIV transmission in LMICs,” Cohen said.

Although two of the three drugs in the combination will be available as generics in the US, the third drug, tenofovir disoproxil fumarate (TDF), remains patented. However, the basic patent for tenofovir has expired. The patents on this drug are what block the production of combinations of TDF with the two generics and prevent patients in the US from accessing generic versions of the branded combination.
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Iodine deficiency in pregnancy can affect child’s cognitive development

Alexandra Kirsten

Even a mild lack of iodine during pregnancy may be harmful to the brain development of the child.

This was the main finding of a recent large-scale trial including more than 1,000 women and their children in the UK.

“Although iodine deficiency is often thought to be a problem of developing countries, industrialized countries are not immune,” said the study authors, led by Professor Margaret Rayman of the University of Surrey in Guildford, England.

As part of the study, the researchers analyzed samples and data from the Avon Longitudinal Study of Parents and Children (ALSPAC), a long-term UK health research project involving more than 14,000 women who were pregnant in 1991 and 1992 which has followed the health and development of their children till today. [Lancet 2013, doi: 10.1016/S0140-6736(13)60717-5]

By measuring urinary iodine concentration in stored samples from 1,040 first-trimester pregnant women from the ALSPAC cohort, the researchers could categorize them as being iodine deficient or sufficient. According to WHO guidelines, an iodine-to-creatinine ratio of ≥ 150 μg/g is considered adequate. However, over two-thirds of the women in the cohort studied (67 percent) were found to be iodine deficient.

To evaluate how iodine deficiency might affect the childhood cognitive development, each of the women’s children were assessed at age 8 for IQ and age 9 for reading ability.

After adjusting for potential confounding factors such as parental education and breastfeeding, children of women with an iodine-to-creatinine ratio < 150 μg/g were more likely to have scores in the lowest quartile for verbal IQ (95% CI 1.09-2.30; p=0.02), reading accuracy (95% CI 1.15-2.49; p=0.007), and reading comprehension (95% CI 1.06-2.23; p=0.02) than those of mothers with higher ratios. Moreover, a negative ratio-dependent correlation was found between the iodine-to-creatinine ratio of the mother during pregnancy and the cognitive scores of the children. The lower the mother’s concentration of iodine was, the lower the IQ and reading ability in the children seemed to be.

“Our results clearly show the importance of adequate iodine status during early pregnancy, and emphasize the risk that iodine deficiency can pose to the developing infant, even in a country classified as only mildly iodine deficient,” said Rayman.

Iodine, a crucial micronutrient which is consumed mainly via dairy products and seafood, is essential for thyroid hormone production and for normal in utero neurodevelopment. During pregnancy, iodine intake must be increased by 50 percent because of physiological increases in maternal thyroid hormone production. The results of the trial “raise concerns that the iodine status of pregnant women is a public health issue that needs to be addressed,” the researchers concluded.
Low-cost rotavirus vaccine shows good efficacy

Rajesh Kumar

A low-cost rotavirus vaccine (Rotavac®, Bharat Biotech) developed and manufactured in India has shown good efficacy and safety in a randomized, double blind phase III clinical trial.

The vaccine reduced severe diarrhea caused by rotavirus by 56 percent in the first year of life in 6,799 infants aged 6 to 7 weeks. The trial results also showed clear evidence of protection across different rotavirus strains and continued efficacy in the second year of life, said the researchers.

"With its low price and strong efficacy, [the vaccine] has the potential to significantly reduce the incidence of severe diarrhea due to rotavirus among children in India.

Infants enrolled at three sites in India received the vaccine along with others under the Universal Immunization Programme, including oral polio vaccine (OPV). Subsequent assessment of immune responses to OPV showed that infants receiving Rotavac® and OPV together generated comparable immune responses to all three polio serotypes as the infants receiving OPV without Rotavac®.

The vaccine was developed through a unique social innovation partnership that brought together the Indian government and Hyderabad-based private company, Bharat Biotech, with the expertise of National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC) and the Stanford University School of Medicine in the US, the Research Council of Norway, the UK Department for International Development and the non-governmental organizations – Programme for Appropriate Technology in Health (PATH) and Bill & Melinda Gates Foundation.

“This public-private partnership is an exemplary model of how to develop affordable technologies that save lives,” said the foundation co-chair Mr. Bill Gates in a statement.

Bharat Biotech had earlier offered to provide the vaccine for US$1 per dose and a spokesman said the company has an installed capacity of 300 million doses and will start production once it gets the license. If licensed, the vaccine will be a hugely affordable alternative to the rotavirus vaccines already on the market, but will need WHO approval before it can be given to children in other resource poor countries.

“With its low price and strong efficacy, [the vaccine] has the potential to significantly reduce the incidence of severe diarrhea due to rotavirus among children in India,” said Dr. M. K. Bhan, advisor to the Indian Academy of Pediatrics, adding that the virus kills more than 100,000 children in India every year.

Rotavac® is an oral vaccine administered to infants in a three-dose course at the ages of 6, 10, and 14 weeks, alongside other routine immunizations recommended at these ages.
Chinese researchers have reported promising efficacy and safety results from a phase III study of a newly developed enterovirus 71 vaccine against hand, foot, and mouth disease (HFMD) in young children.

In the multicenter trial, a total of 10,245 healthy children aged 6-35 months from four centers across China (three in Jiangsu province and one in Beijing) were randomly assigned to double-blind treatment with either the vaccine or placebo, administered as two doses 28 days apart.

The results showed that the vaccine provided 90 percent protection (95% CI 67.1-96.9) against clinical EV71-associated HFMD (p=0.0001) and 80.4 percent (95% CI 58.2-90.8) against EV71-associated disease, including neurologic complications (p<0.0001) for at least 12 months. Additionally, the vaccine demonstrated 100 percent efficacy against EV71-associated hospitalization.

The vaccine was also reported to be well tolerated. Rates of adverse events were similar between the vaccine and placebo groups and no vaccine-related serious adverse events were recorded.

HFMD is a common viral illness that usually affects infants and children younger than 5 years old. Symptoms include fever, herpangina and skin rash.

The novel vaccine against EV71 was developed for use in the Asia-Pacific region where the greatest number of serious cases, that can cause potentially fatal meningitis and encephalitis, occur.

“A vaccine for EV71 is urgently needed to prevent and control epidemics of EV71,” commented the study authors. The virus has caused major outbreaks of HFMD worldwide, accounting for more than 6 million cases and over 2,000 deaths in the past decade.

Nevertheless, the researchers pointed out that the vaccine has only an impact on EV71-related diseases and there are many viruses that can cause HFMD. Therefore, “despite its high efficacy for preventing EV71-associated HFMD, the EV71 vaccine might have little part in reducing the overall incidence of HFMD, even by universal mass immunization of children.”
Regeneration of spinal cord nerves helps in stroke recovery

Alexandra Kirsten

Regenerative processes of damaged nerves in the spinal cord contribute to neurologic recovery after stroke.

Data from a study conducted by an US research team demonstrated that voluntary motor recovery is associated with outgrowth of the axons in the corticospinal tract (CST) and synaptic formation in the denervated side of the spinal gray matter.

Until now, there are no efficacious therapies available for the majority of patients with stroke, in part because it is not completely understood how the brain and nerves repair themselves.

“Because the behavioral improvement after stroke involves many processes and multiple neural pathways between the motor cortex and the spinal cord, the specific contribution of the CST to neurological recovery after stroke requires investigation,” explained lead author Dr. Yi Li and colleagues from the Henry Ford Hospital in Detroit, Illinois, US.

To examine the role of axonal remodeling in the spinal cord to motor behavioral recovery after stroke, the researchers used transgenic mice with yellow fluorescent protein labeling in the CST. The animals were trained for 5 days to foot-fault and single-pellet reaching tests to assess their dexterity and possibility to walk on an unevenly spaced grid.

After the training, the carotid arteries in all mice were blocked with a suture in the middle cerebral artery for 1 hour to simulate a stroke. Next, the mice were divided into four groups. After the suture was removed and blood flow was restored, one group was given a bilateral pyramidotomy (BPT) to severe CST axons. The other groups were either given no surgery or “sham” bilateral pyramidotomy.

The mice then underwent single-pellet and foot-fault tests 3 days after surgery, then weekly for 14 to 28 days to reassess dexterity, the amount of “stroke” damage to voluntary movements, and the degree of recovery from the lab-induced “stroke.” Functional improvements could be seen during the initial 14 days in all animals (p<0.01 vs day 3). Progressive recovery was present during the subsequent 14 days in sham-BPT mice (p<0.001 vs day 14) but not in BPT mice.

The stroke-affected cervical gray matter of the sham-BPT mice showed a significantly higher amount of growth-associated proteins at day 14 after stroke compared with normal mice (p<0.001). Additionally, CST axonal density and Synaptophysin-Cy3 staining of the axonal terminals were significantly increased at day 28 compared with day 14 in these animals. [Stroke 2013 2013; doi: 10.1161/STROKEAHA.113.001162]

Stroke is still the leading cause of long-term disability in adults.
term disability in adults. Although most patients have some spontaneous behavioral improvements during the first several months after stroke, the recovery of motor function is generally incomplete.

“The present study provides substantial evidence that the CST axonal remodeling in the denervated spinal gray matter contributes to re-establishment of functional corticospinal connections and to voluntary motor behavioral recovery after stroke,” the authors explained. In future “enhancing CST axonal remodeling in the spinal gray matter may provide a therapeutic opportunity to improve neurological recovery during the later phase after stroke,” they added.

Gonorrhea now a challenge due to antibiotic resistance

Leonard Yap

Gonorrhea used to be relatively easy to treat and required just a single-class antibiotic. Unfortunately, this is no longer true as the antibiotic arsenal against gonorrhea is rapidly dwindling, says an expert.

Not long ago, a single dose of ciprofloxacin was all that was required to win the battle against gonorrhea, said Mr. David Livermore, a professor of medical microbiology at the University of East Anglia, and lead researcher on antibiotic resistance for the Health Protection Agency, UK.

A decade ago, there were reports of resistance against ciprofloxacin among sex workers in the Philippines. In addition, the cephalosporins were beginning to lose ground against the bacteria. By 2010, ceftriaxone resistance was detected in patients in Japan, France and Spain, Livermore said. [J Antimicrob Chemother 2010;65:2141-8]

The byword for antibiotics in the current situation of resistance is ‘antibiotic stewardship.’ The treatment of gonorrhea has been exemplary because only patients who require antibiotics receive them and the treatment regime is extremely simple – one dose of oral ciprofloxacin. Genitourinary medicine physicians have exercised extreme restraint in prescribing antibiotics and have followed guidelines to the letter. Yet, resistance has become a serious issue, he said.

Livermore suggested that treatment regimens could have been approached differently ie, cycling the antibiotic options to enhance the fight against gonorrhea by utilizing cefixime, ciprofloxacin and spectinomycin, all of which were available and active against gonorrhea. This strategy, instead of using a single antibiotic agent, may have stemmed the tide of resistance. In addition, using a multi-dose regimen may have also slowed the progression to resistance.

Livermore said the lack of new antibiotic
agents is exacerbating the problem of antimicrobial resistance. This can be attributed to the fact that antibiotic discovery is difficult, particularly those targeting gram-negative bacteria like gonorrhea. New classes of agents that target different sites of the body are difficult to come by, and this is further hampered by the fact that antibiotics are not very profitable for big pharmaceuticals, which restrict the amount of funds channeled into research for these drugs.

In 1943, penicillin was 100 percent effective against *Neisseria gonorrhoea* at a dose of 72 mg, but by 1969 it took 3 g of penicillin plus probenecid to be fully effective. Then ciprofloxacin in 1984, a single pill dosed at 250 mg, became the standard prescription. [J Antimicrob Chemother 2010;65:2141-8]

An estimated 448 million new infections of curable, sexually transmitted infections (STIs) like syphilis, gonorrhea, chlamydia and trichomoniasis occur yearly worldwide. Some STIs exist without symptoms. It is estimated that up to 70 percent of women and a significant proportion of men with gonococcal and/or chlamydial infections experience no symptoms at all. Both symptomatic and asymptomatic infections can lead to the development of serious complications. [Sexually transmitted infections. Available at: www.who.int/mediacentre/factsheets/fs110/en/ Accessed on 27 May]

Livermore was speaking at the 9th International Symposium on Antimicrobial Agents and Resistance (ISAAR) 2013 held in Kuala Lumpur, Malaysia.
Iron and zinc supplements for low birthweight babies

Amanda Cameron

Underweight babies can benefit from early supplementation with iron and zinc, new research shows.

Zinc supplements in the first weeks of life improve the health, survival and growth of very low birthweight (VLBW) infants, while iron supplements for the first 6 months prevent anemia and improve the later behavior of marginally low birthweight (MLBW) infants.

Zinc is known to be important for the development of the brain and the respiratory and intestinal tracts, but few data exist on its use as a supplement in preterm infants.

Italian researchers therefore conducted a double-blind randomized controlled trial in 193 preterm infants weighing under 1500 g at birth.

When they were 7 days old, these VLBW infants began receiving a daily multivitamin tablet, one ingredient of which was either zinc 9 g or placebo.

Babies in the zinc group were more than twice as likely to survive to hospital discharge and had a significantly higher discharge weight, Dr. Gianluca Terrin from the University La Sapienza, Rome, told delegates.

They were also less likely to become very sick before discharge, Professor Terrin said. Altogether 44 percent of zinc-supplemented babies suffered late-onset sepsis, necrotizing enterocolitis, bronchopulmonary dysplasia, intraventricular hemorrhage, periventricular leucomalacia or retinopathy of prematurity, compared with 62 percent in the placebo group (p=0.017).

In particular, no zinc-supplemented babies had necrotizing enterocolitis whereas it occurred in 6.3 percent of the placebo group (p=0.014).

More research is needed to find the optimal dose of zinc supplements for VLBW infants, Professor Terrin noted.

Optimal dosing was precisely the reason
for Swedish researchers investigating the use of iron supplements in MLBW infants, who are at risk for iron deficiency.

Although iron is important for neurodevelopment, too much of it can cause problems and there are no clear recommendations for the dose and duration of supplements in newborns weighing less than 2,500 g.

The researchers had previously found in a randomized placebo-controlled trial that giving daily iron supplements to otherwise healthy MLBW babies during the first 6 months of their life not only protected against iron deficiency and iron deficiency anemia at 6 months but reduced behavioral problems at 3.5 years, without any short-term adverse effects on morbidity or growth. [Pediatrics 2010;126:e874-83 and 2013;131:47-55]

To explore whether giving zinc for longer might result in even greater benefits, they checked those same children for iron deficiency and its associated anemia at 12 months and 3.5 years of age, Dr. Staffan Berglund from University Umeå, Sweden, told delegates.

They found that children were still protected against iron deficiency and iron deficiency anemia at age 1, having a significantly lower prevalence of both compared with the non-supplemented group (p≤0.035), but that the protective effect had disappeared by age 3.5 years.

“We see no reasons to prolong the supplements until 12 months considering the possible risks of adverse effects during that phase of life,” Dr. Berglund said.

The trial involved 285 otherwise healthy newborns weighing 2,000-2,500 g who, at 6 weeks of age, were randomized to receive placebo or iron supplements at a dose of 1 or 2 mg/kg/day until they were 6 months old. The protective effects were associated with the higher dose only.

Laxatives only real option for constipated children

Amanda Cameron

Nothing other than laxatives works for children with constipation, not even fluid, fiber and exercise, according to updated guidelines from ESPGHAN.

Produced in tandem with the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN), the latest guidelines on functional childhood constipation were presented at ESPGHAN 2013 ahead of their finalization and publication in May.

Italian pediatrics professor Annamaria Staiano told delegates that polyethylene glycol (PEG), with or without electrolytes, is recommended as first-line treatment for children with fecal impaction, with once-daily enema as a useful add-on.

PEG without or without electrolytes is also
the recommended first-line maintenance therapy for children with constipation, said Professor Staiano, who works at the University of Naples “Frederico II”.

Evidence does not, however, support the routine use of milk of magnesia, mineral oil or stimulant laxatives as maintenance therapy for constipation.

Neither does it support using most treatment options for chronic constipation or any new treatments for intractable constipation, said Professor Staiano, who is also president of the Italian Society of Paediatric Gastroenterology, Hepatology and Nutrition.

Unfortunately, there is no evidence to support the use of any non-pharmacological treatments for childhood constipation either, said Dr. Marc Benninga from the Academic Medical Centre in Amsterdam, the Netherlands.

Contrary to accepted wisdom, children who get fiber supplements, extra fluid, and more exercise are no better off, and neither are those who get behavioral therapy or anorectal biofeedback.

Acupuncture is ineffective too, as are other alternative medicines such as homeopathy, osteopathy, chiropracty and yoga.

The guidelines simply recommend children with constipation should have a normal fiber and fluid intake with normal daily physical activities, and that demystification, explanation and toilet training are useful in children with a developmental age of at least 4 years.

Professor Benninga explains that, until there is more evidence, the guidelines cannot recommend prebiotics or probiotics for functional constipation, or two promising new therapies for refractory constipation, transcutaneous and sacral nerve stimulation.

As for diagnosing functional constipation, the guidelines suggest using the definition provided by the ROME III criteria, NASPGHAN president-elect Carlo Di Lorenzo told delegates.

A history should be taken and a physical examination made, but digital rectal exam is not recommended unless needed to check for faecal impaction when only one ROME III criterion has been met.

The consensus guidelines contain two algorithms, one each for infants and older children. They were last published in 2006.
A yeast extract from lychee fruit can reduce the duration of antibiotic-associated diarrhea, Chinese researchers have discovered.

Saccharomyces boulardii is known for its anti-diarrheal properties but its therapeutic effect against diarrhea provoked by antibiotic treatment has not been demonstrated before now.

The researchers, from Shengjing Hospital of China Medical University, tested S. boulardii in 283 hospitalized children given intravenous antibiotics for acute lower respiratory tract infection.

The researchers found that the average duration of antibiotic-associated diarrhea was nearly four times shorter with S. boulardii treatment.

Not only that, but children who received S. boulardii as a preventive measure were nearly 80 percent less likely to develop antibiotic-associated diarrhea in the first place.

In the two-part study, children were randomized to receive S. boulardii with their antibiotic therapy or to get antibiotics alone. The children were aged 6 months to 14 years.

The 139 in the S. boulardii group were significantly less likely to develop diarrhea, whether caused by antibiotics or not.

Only 4 percent of them developed antibiotic-associated diarrhea, compared with 19 percent of the control group.

Broken down by individual antibiotic, the effect was statistically significant for cefuroxime and for the combination of amoxicillin plus clavulanic acid.

In the second part of the study, the 42 children in the control group who developed diarrhea were randomized to oral rehydration with or without S. boulardii.

In this group of children, S. boulardii treatment significantly reduced the mean duration of diarrhea by more than 6 days. Diarrhea lasted an average of 9 days in children who did not get the probiotic, compared with just over 2 days in the treated group.

By day 5, children treated with S. boulardii were also passing significantly fewer stools per day (one rather than four), and showing better stool consistency, than those who received oral rehydration solution only.

“This is the first study suggesting that the administration of S. boulardii reduces the duration of antibiotic-associated diarrhea,” the lead researcher, Dr. Li-Shen Shan, told delegates.

“S. boulardii offers an appropriate and safe therapeutic intervention to treat diarrhea and antibiotic-associated diarrhea,” she concluded.
Diabetic nephropathy (DN) is expected to become a leading cause of chronic kidney disease (CKD) in China in the next 20 years, according to the findings of a recent national survey.

“Glomerulonephritis [GN] is currently the leading cause of end-stage renal disease [ESRD] in big cities such as Beijing and Shanghai, accounting for around 50 percent of all cases,” said Dr. Lu-Xia Zhang of the Institute of Nephrology, Peking University First Hospital, China. [Am J Kidney Dis 2013;61:918-922]

“However, DN has been on the rise since 2003, and is expected to become a leading cause of ESRD in China 10-20 years later,” she continued.

Interestingly, consumption of herbs containing aristolochic acid (AA) has been shown a distinct cause of CKD in China. [Am J Kidney Dis 2013;61:918-922] Many cases in China, as well as Taiwan, are linked to AA-containing herbs commonly used in traditional Chinese medicine. [Lancet 2013; e-pub May 31; doi: 10.1016/S0140-6736(13)60687-X]

The national survey, which included 47,204 respondents, also revealed an overall CKD prevalence of 10.8 percent. “This means there are about 120 million CKD patients in China,” said Zhang. “Unlike Western countries, our rate of advanced CKD is low. Stage 1 and 2 CKD account for about 85 percent of our CKD population.” [Lancet 2012;379:815-822]

“Recent studies in China also showed that CKD is correlated with cardiovascular dis-
ease [CVD] and stroke, particularly ischemic stroke,” she continued. [J Am Soc Nephrol 2006;17:2617-2621; J Hypertens 2012;30:901-907] “Other chronic complications of CKD in Chinese patients include cognitive decline [odds ratio, 2.73], incident dementia [hazard ratio, 1.41], and infection-related mortality [hazard ratio, 1.41 and 1.91 for CKD stage 3b and 4-5, respectively].” [Am J Nephrol 2010;32:117-121; BMC Nephrol 2012;13:129]

In Hong Kong, DN is the main cause of ESRD (48 percent), followed by GN (18 percent), according to 2012 data from the Hong Kong Renal Registry. “IgA nephropathy is the focus of attention in GN as it affects 47 percent of local patients aged 25-34 years, and symptoms are nonspecific at presentation in 68.4 percent of the cases,” said Professor Philip Li of the Division of Nephrology, Chinese University of Hong Kong. Thirty-six percent of local patients with IgA nephropathy progress to ESRD within 20 years.” [Nephrol Dial Transplant 2012;27:1479-1485]

“Early intervention can effectively delay CKD progression. Individuals at high risk of CKD are recommended to have regular urine and renal function tests,” Li added.
Limitations of current therapies have prompted significant basic and clinical interest in the use of traditional medicines for the treatment of diabetic nephropathy (DN).

Natural and traditional herbal medicines may potentially reverse kidney damage at the onset of proteinuria and may prove to be complementary, if not alternative, to the existing allopathic therapies, said Dr. Basil Roufogalis of the faculty of pharmacy at University of Sydney in Sydney, Australia.

Diabetic patients progressively develop clinically significant DN. Current therapy for this condition includes dietary protein restriction, blood pressure control, ACE inhibitors and angiotensin receptor blockers. However, a large number of patients still develop intractable disease, which is prompting the search of natural options, said Roufogalis.

Scores of randomized controlled trials involving traditional Chinese medicines such as gingo biloba, dogbane, astragalus, dan-shen and cordyceps mushroom; Ayurvedic medicines derived from fenugreek spice, curcumin (turmeric), ekanayaka and bark of the Arjuna tree and western herbal medicines based on milk thistle, north American ginseng, hawthorn and mango have shown different modes of action imparting nephro protection and reversing damage through up- or down-regulation of various molecular mechanisms.

Fenugreek, for instance, is believed to restore kidney function through decreased activities of superoxide dismutase (SOD) and catalase, increased concentrations of malondialdehyde in the serum and kidney, and increased levels of 8-hydroxy-2’-deoxyguanosine in urine and renal cortex DNA. Gingko biloba extract has shown to decrease blood and plasma viscosity in patients with early DN.

Dogbane is believed to have protective effects on renal function through the inhibition of renal cortex SOD and glutathione activity while Arjuna bark is believed to cause significant reduction in lipid peroxidation, increased superoxide dismutase, catalase, glutathione peroxide etc. in clinical trials.

However, some of these trials suffered from poor methodological quality and lack of blinding while others were in rats, said Roufogalis. That is why long-term, double-blinded randomized controlled trials with large human sample sizes involving such medicines need to be conducted to provide stronger clinical evidence, he added.
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Robotic Surgery Does Not Confer Additional Advantages Over Conventional Laparoscopic Surgery

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Proponents: Dr Jason TAN (Australia) & Dr LOH Foo Hoe (SG-MIE)
Opponents: A/Prof Jan PERSSON (Sweden) & Dr Peter BARTON-SMITH (SG-SGH)
On Fri 23 August 2013 at 9SICOG 2013

Prof Frank CHERVENAK
Weill Cornell Medical College (USA)

- Plenary 2: "Ethics in Obstetrics and Gynaecology: Past, Present, and Future"
- Obstetric Symposium: Fetal Medicine - "Applications of the Professional Responsibility Model of Obstetric Ethics to Cesarean Delivery"
- Medico Legal Symposium: "Ethics of Informed Consent and Directive Counselling"
Thu 22-Sat 24 August 2013 at 9SICOG 2013

Prof Sir Sabaratnam ARULKUMARAN
St George’s Hospital London (UK)

- Plenary 3: "Management of PPH: Lessons from The Confidential Enquiries"
- Debate: "Robotic Surgery Does Not Confer Additional Advantages Over Conventional Laparoscopic Surgery"; Moderator
- Medico Legal Symposium: "Managing Adverse Outcomes After Delivery"
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Obstetrical and Gynaecological Society of Malaysia (OGSM)

- Plenary 4: The Malaysian Lecture - "Anti-angiogenesis Therapy in Ovarian Cancer"
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<td>and Dr Edwin Chandracharan, St George's Hospital London</td>
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<td>Reproductive Medicine: Innovations to Improve ART Outcomes</td>
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Transdermal buprenorphine for chronic non-malignant pain

There is accumulating evidence and a growing consensus that opioid medications, which are widely used for the treatment of acute pain and cancer pain, may also be appropriate for some patients with chronic non-malignant pain. A transdermal formulation of buprenorphine (Norspan®, Mundipharma), a synthetic opioid analgesic derivative, has been shown to be effective for alleviating pain in such patients. The current report profiles this drug and its place within treatment guidelines for chronic non-malignant pain.

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

Introduction
Chronic non-malignant pain is a very widespread problem that is often not properly treated. One survey of patients attending primary care practices in the UK (n=5,036) found that around half report having chronic pain. The two most common causes of chronic pain are back pain and osteoarthritis. [Lancet 1999; 354:1248-1252] Another large survey of the general population in 15 European countries (n=46,394) found that 19 percent of adults suffer from some form of moderate-to-severe chronic pain (≥6 months’ duration). [Eur J Pain 2006;10:287-333]

Importantly, chronic pain has serious effects on quality of life, work productivity and social functioning. More than two-thirds of chronic pain sufferers have sleep disturbances; depression is present in about a fifth and nearly half do not receive adequate pain management. [Eur J Pain 2006;10:287-333] Among the elderly, osteoarthritis is the leading cause of pain and disability; four in five sufferers experience constant pain and/or limitation to their activity. [OA Nation. www.arthritiscare.org.uk/PublicationsandResources/Forhealthprofessionals/OANation.]

These statistics underline the need for effective analgesic medications for common chronic pain conditions. Opioids are widely accepted for the treatment of severe acute pain and chronic pain related to active cancer. There is a growing consensus that opioid therapy is also appropriate for some patients with chronic non-cancer pain. [J Pain 2009;10:113-130] However, there are limitations that prevent dose escalation with many currently used opioids (eg, fentanyl, oxycodone, morphine, hydromorphone, methadone) including nau-
sea, vomiting and cognitive dysfunction. Other more unusual adverse effects include hypogonadism (and consequent loss of libido) and, with long-term use, osteoporosis and loss of muscle mass. Furthermore, some opioids are associated with a risk of liver and kidney toxicity. [J Supp Oncology 2012;10:209-219] Buprenorphine can potentially address some of these problems.

Buprenorphine

Pharmacology

Buprenorphine is a synthetic opioid analgesic derivative of the morphine alkaloid thebaine, with a complex and unique pharmacology. [BuTrans (Buprenorphine transdermal system) Product Monograph] The antinociceptive action of buprenorphine is due to its properties as a partial agonist at μ-receptors and as a kappa (κ) antagonist. It is also a full agonist at orphanin (nociceptin) receptors. Buprenorphine binds to μ-receptors with high affinity and dissociates slowly, which results in a slow onset but relatively long duration of analgesia. [Eur J Pain 2008;13:219-230]

Earlier studies of the drug in animal models created a misconception that there is a ceiling effect with regard to analgesic efficacy; however a linear dose-response relationship has been demonstrated in humans in the therapeutic dose range. [J Supp Oncology 2012;10:209-219; Eur J Pain 2008;13:219-230; Pain Pract 2008;10:238-250] Buprenorphine has been reported to have about 25-100 times the potency of morphine, depending upon the pain model and route of application used. [J Supp Oncology 2012;10:209-219; Eur J Pain 2008;13:219-230]

Pharmacokinetics

Buprenorphine is highly lipid soluble and has a relatively small, compact molecule. These characteristics impart physicochemical properties that allow for good skin penetration. Combined with its potent analgesic action, this means that buprenorphine is ideal for transdermal delivery.[J Pain Symptom Manage 2005;29:297-226] Buprenorphine patches (BuTrans®, Norspan®) are available in three strengths: 5, 10 and 20 μg/h. The composition of these is identical, only the size varies, with the higher doses being delivered by a larger patch. Each patch provides a steady delivery of the active ingredient for 7 days, with steady state concentrations achieved after the third day of an initial application. With long-term use, there is no accumulation and following patch removal, plasma concentration of buprenorphine declines rapidly (approximately 50 percent in 12 hours). [BuTrans (Buprenorphine transdermal system) Product Monograph]

Clinical efficacy

A number of clinical studies have provided evidence of the efficacy of buprenorphine patches to alleviate chronic non-cancer pain conditions. For example in patients whose osteoarthritic pain was not controlled with non-opioids (ibuprofen 400 mg qid), the buprenorphine transdermal patch provided significantly better rates of treatment success and pain control than placebo over 28 days. [J Pain 2002;3(Suppl 1):12. Abstract 645] Another study in patients with chronic, moderate-to-severe osteoarthritic pain compared buprenorphine with twice-daily prolonged-
release tramadol tablets. The efficacy of the transdermal patch was non-inferior to that of prolonged-release tramadol tablets. At the end of the study, the majority of patients in both treatment groups (70 percent) said that they would prefer a 7-day patch to a twice-daily tablet for future pain treatment. [Clin Ther 2009;31:503-513]

In the setting of chronic back pain, transdermal buprenorphine has also been shown to be effective. In one study of patients whose pain was not controlled with non-opioids, the pre-study dose of NSAID was maintained, and either transdermal buprenorphine, oxycodone 5 mg / paracetamol 325 mg tablets every 6 hours, or equivalent placebo was added. Patients assigned to the patches reported a significant pain reduction relative to placebo and comparable to oxycodone/paracetamol. [Anesthesiology 2001;95:A-826]

Importantly, buprenorphine has been shown to treat a broad array of pain types (eg, bone pain, heat pain, pain related to nerve growth-factor injections, cold pressor pain). It also appears to produce less tolerance compared with other μ-agonist opioids. [J Supp Oncology 2012;10:209-219]

**Adverse effects**

Transdermal buprenorphine has a side effect profile typical of opioid analgesics and transdermal delivery systems. The most common adverse events reported in clinical trials (occurring in >10 percent of patients) are gastrointestinal (constipation, nausea, vomiting, dry mouth); central nervous system (dizziness, somnolence, confusion); skin and appendages (pruritus, pruritus at the application site, erythema, ie, application site reaction); and headache. [BuTrans (Buprenorphine transdermal system) Product Monograph]

Some evidence suggests that buprenorphine is associated with lower rates of constipation than with equipotent doses of morphine. This may be due in part to the fact that unlike other opioids, buprenorphine does not cause spasm of the sphincter of Oddi. [J Supp Oncology 2012;10:209-219]

Respiratory depression is potentially fatal and, therefore, one of the most concerning potential side effects of opioids. However, a number of animal and human studies have shown that buprenorphine has a lower propensity to cause respiratory depression than other opioids (methadone, fentanyl, and morphine). Buprenorphine is unique in that it has a dose-ceiling effect on respiratory depression, but not on analgesia. If respiratory depression does occur, it can be ameliorated with naloxone. [J Supp Oncology 2012;10:209-219; Pain Pract 2008;10:238-250]

Impairment of cognitive function, psychomotor function and driving ability is another consideration with the use of opioids for pain relief, although this does tend to decrease with prolonged use. Various studies have shown that, on average, buprenorphine does significantly impair performance of complex tasks; however, there is large individual variation in cognitive effects and each patient should be assessed individually. [J Supp Oncology 2012;10:209-219; Pain Pract 2008;10:238-250]

With regard to the effect on sex hormones and hypothalamic-pituitary-adrenal pathway, the available evidence suggests that buprenorphine has a minimal influence on these systems. There is less reduction in testosterone levels in men compared with methadone, and in women it does not influence menstrual cycles, testosterone or estrogen levels. [J Supp Oncology 2012;10:209-219]

Buprenorphine may have a lower potential for abuse than full receptor agonists because it does not produce a maximal response at
μ-opioid receptors. In addition, the slow dissociation from the μ-opioid receptor may result in fewer signs and symptoms of opioid withdrawal upon treatment cessation than with full μ-opioid agonists (eg, morphine). [J Supp Oncology 2012;10:209-219; Pain Pract 2008;10:238-250]

Dosing
When starting therapy with transdermal buprenorphine, the individual needs of the patient should be considered, including pain intensity and previous use of analgesics. Treatment should be commenced at the lowest dose (5 μg/h) and supplemental short-acting analgesics used until pain control is achieved. Patches should be applied to non-irritated intact skin on the flat surfaces of the upper outer arm, upper chest, upper back, or the side of the chest. The skin should be clean, dry, hairless or relatively hairless, and without large scars. [BuTrans (Buprenorphine transdermal system) Product Monograph]

The full analgesic effect of the initial dose should be achieved (ie, 3 days) before up-titrating dose, if required. Up to two patches can be used simultaneously, and combinations of the three different patch strengths allow a gradual and flexible increase in dose. The maximum dose is 40 μg/h, that is, two 20 μg/h patches. [BuTrans (Buprenorphine transdermal system) Product Monograph]

Place within treatment guidelines
The WHO three-step analgesic ladder was originally developed for cancer pain management; however, this approach is also used with chronic non-cancer pain. The first step of the ladder is a non-opioid with or without adjuvant analgesic. If pain persists or increases, step two is an opioid for mild-to-moderate pain added to the step one regimen with or without an additional non-opioid analgesic. If pain continues to persist or increase, the opioid is changed in step three to one for moderate-to-severe pain. [Cancer Pain Relief With a Guide to Opioid Availability, 1996] A review by the American Pain Society–American Academy of Pain Medicine Opioids Guidelines Panel found that long-term opioid therapy can be effective for carefully selected and monitored patients with chronic non-cancer pain. [J Pain 2009;10:113-130] The American Geriatrics Society guidelines for the pharmacological management of persistent pain in older persons (≥75 years) state that all elderly patients with moderate-to-severe pain, pain-related functional impairment, or diminished quality of life due to pain should be considered for opioid therapy (while NSAIDs should be used rarely and with caution in this population). [J Am Soc Geriatrics 2009;57:1331-1346] The European consensus guideline for the primary care management of chronic osteoarthritic pain also recommends a three-step scheme for pain treatment. Step one is intermittent or continuous paracetamol (≤4 g/d) ± topical NSAIDs; step two is a weak opioid or a low-dose strong opioid ± paracetamol ± topical NSAIDs; and step three is an oral or transdermal high-dose strong opioid. Low-dose strong opioids are preferred to high-dose weak opioids in the second step, specifically buprenorphine transdermal patch. [European consensus guideline for the primary care management of chronic osteoarthritic pain. 2008. Available at: www.eguidelines.co.uk]
Treating common skin infections in children

Skin infections commonly affect children of all ages. Although more common in those with underlying skin disorders such as atopic dermatitis, the infections can also occur in children without a history of skin disorders. Some skin infections are self-limiting (eg, molluscum contagiosum) and resolve even without treatment. Others such as impetigo may be managed in the primary care setting.

Rarely, skin infections may lead to morbidity and even mortality in children (eg, eczema herpeticum and staphylococcal scalded skin syndrome). The role of a primary care physician is to not only be able to treat simple skin infections but also to identify more dangerous conditions in time for tertiary referral. Outlined below are some common skin infections seen in children, along with suggestions for their diagnosis and treatment.

**Viral infections**

**Molluscum contagiosum**

Molluscum contagiosum (MC) is caused by a member of the poxvirus family. It is a common skin infection in children and adolescents. Spread by direct contact, it presents with single or multiple skin-colored, dome-shaped papules, commonly with a central umbilication (Figure 1).

MC is usually a self-limiting condition and can be left to self-involute over 6-12 months. An eczematous rash appearing around the lesions usually heralds self-involution over the next few weeks or months.

Treatment options, if required, include topical applications (eg, tretinoin or imiquimod), curettage, cryotherapy, pricking and expressing, and electrocautery.¹²

**Viral warts**

Viral warts, caused by the human papillomavirus (HPV), are a very common skin condition in children and adults.³ Warts are spread by direct contact, and can occur on almost any area of the skin, but most commonly occur on the hands and feet. On the palms and soles, they appear as papules with overlying thickened skin, punctuated by thrombosed capillaries and loss of overlying skin lines. Plane warts, most commonly occurring on
the face, present as skin-colored, flat-topped papules, sometimes in a linear configuration (Koebner’s phenomenon). Warts on other areas of the body can appear as filiform tumors (Figure 2).

A simple home-based treatment is the nightly use of a keratolytic agent, such as Duofilm or Verrumal. After application, the wart can be covered by a strip of duct tape which is removed in the morning. This should be done for 4 to 6 weeks before assessing treatment response. Other treatment options in the clinic include cryotherapy, electrocautery and ablative laser therapy.

However, these procedures may cause significant pain and distress to a young child. The use of a topical anesthetic cream before treatment may reduce the severity of pain. In children, warts may resolve spontaneously, although this may take up to 2 years.4

**Herpes simplex virus infections**

Herpes simplex virus (HSV) infections in children are most commonly caused by HSV I, and less commonly by HSV II. Herpes gingivostomatitis is the most common type of primary herpes in children, presenting as multiple, grouped, small blisters and erosions over an erythematous base.

It can involve the lips, gums and tongue. Associated systemic symptoms include fever, lethargy and irritability. Severe infections can lead to poor food intake and dehydration in a young child. Herpes labialis (“cold sores”) are common in children and adults and present as a localized, small-grouped, painless or painful blisters and erosions on the lips and around the mouth. Eczema herpeticum is herpes infection occurring in patients with underlying skin disease, most commonly atopic dermatitis.5

Patients present with worsening of their underlying skin disease, accompanied by small, punctate, grouped erosions and blisters (Figure 3). Lesions can become generalized. Mild herpetic infections can be treated with saline or potassium permanganate soaks, and application of an anti-bacterial or anti-septic cream to prevent secondary bacterial infection. Severely affected patients may require inpatient supportive treatment and treatment with systemic anti-virals (eg, acyclovir or valacyclovir). Topical acyclovir cream can be used to shorten the duration of cold sores.6
**Varicella-zoster virus**

The varicella-zoster virus causes chickenpox and herpes zoster (shingles). Chickenpox is a common childhood exanthema and is highly contagious. Early symptoms include fever, chills, myalgia and arthralgia. Skin lesions initially appear as red macules and papules, but quickly become vesicular and crusted. Lesions first appear on the face and trunk, before spreading to the extremities. New lesions continue to appear for the first week and spontaneously resolve after 2 weeks. Children immunized with the varicella vaccine may still develop chickenpox, although the disease is usually mild.7

Zoster is uncommon in children and presents with painful, grouped vesicles and erosions in a dermatomal distribution. Uncomplicated varicella infection can be managed conservatively. More severe infections can be treated with systemic anti-virals such as acyclovir and valacyclovir.

**Bacterial infections**

**Impetigo**

Impetigo is a common bacterial skin infection caused by Staphylococcus aureus, and less commonly, Streptococcus spp. It can occur on normal skin but also secondarily affects patients with underlying skin disease, especially patients with atopic dermatitis and discoid eczema.

Patients present with crusted, oozy, honey-yellow scaly papules and plaques. Lesions commonly occur around body orifices, such as the nose and mouth, and flaccid, soft blisters filled with clear or purulent fluid that easily rupture may also be seen. Young infants can develop staphylococcal scalded skin syndrome as a complication of impetigo. Treatment for impetigo includes normal saline or potassium permanganate soaks and topical anti-bacterial creams for mild, localized cases. More widespread involvement requires a 1-2 week course of oral antibiotics eg, cephalexin, cloxacinil or erythromycin.8

**Parasitic infestations**

**Scabies**

Scabies is caused by the Sarcoptes scabiei mite. It can be contagious within families and close contacts, and can occur in all age groups, even in young infants. Patients develop extremely itchy, crusted and excoriated papules. Scabetic burrows may also be seen. Common sites include the web spaces, axillae, peri-umbilical region and genitalia. For infants, scabies can also affect the scalp. Topical permethrin is recommended for the treatment of scabies in infants less than 1 year of age. For the treatment of older children and adults, topical malathion or topical permethrin is recommended. All treatments should be repeated 1 week after the first cycle of treatment. It is important to treat all family members staying in the same household, even if they are asymptomatic. All bed linen should be thoroughly washed.9

**Fungal infections**

**Dermatophyte Infections**

Dermatophyte infections, known more
commonly as “tinea” or “ringworm”, are uncommon in children but may be seen in adolescents. Predisposing factors include obesity, poor hygiene and diabetes. Classification is based on the site of infection eg, tinea cruris (groin), tinea capitis (scalp), tinea pedis (feet) and tinea corporis (trunk). Patients present with annular patches or plaques with a central hyper-pigmented area surrounded by erythematous, scaly papules at the periphery. Lesions are usually pruritic.

Diagnosis can be confirmed by skin scrapings for microscopic examination with potassium hydroxide mount or by fungal cultures. Treatment options include anti-fungal shampoos (eg, selenium sulfide shampoo, ketoconazole shampoo), anti-fungal creams (eg, miconazole, clotrimazole) and oral anti-fungals (eg, itraconazole, griseofulvin, terbinafine).

**Tinea versicolor**

Tinea versicolor (TV) is caused by a fungus, Malassezia furfur, which is part of the normal skin flora. It is uncommon in children but can occur in adolescents. Patients present with well demarcated, round-to-oval, scaly macules and papules most commonly over the chest, back, neck, arms and cheeks (Figure 4). Lesions may be hypo or hyper pigmented or skin-colored.

Patients may complain of itch. Microscopy of skin scrapings will reveal the fungus in a “spaghetti and meat-ball” configuration. Patients may be treated with anti-fungal creams (eg, clotrimazole, miconazole), shampoos (eg, selenium sulfide shampoo, ketoconazole shampoo) or oral anti-fungals (eg, itraconazole, ketoconazole). Advice on personal hygiene is important to prevent recurrence.

A complete list of references can be obtained upon request from the editor.

**Online Resources:**

- American Academy of Dermatology
  www.aad.org
- British Association of Dermatologists
  www.bad.org.uk/doctors/guidelines
- NHS National Electronic Library for Health
  http://rms.nelh.nhs.uk/guidelinesfinder
- Centers for Disease Control
  www.cdc.gov/ncidod/hip/Aresist/mrsa.htm
- Infectious Diseases Society of America
  www.idsociety.org
"We've got ourselves another rejection!"

"One hundred bucks? Well Merv, you get what you pay for!"

"Are those pills working, Larry?"

"I tried to donate blood today. Didn't realise you had to give your own!"

"What are you? Some kind of a health fanatic?"

"The doctor no longer sees patients in his office. You must go to www.whatsupdoc.com!"

"Sorry I'm late for the appointment. The last time I saw Dr. Titzhok he told me to slow down!"
At the corner of Armenian Street and Lebuh Pantai, I met Mr. Lee Deng Poay. He was just sitting in his rickshaw, waiting for customers. It was late afternoon, the light was golden and the raging mid-day heat had already given way to a more pleasant evening warmth. Ideal conditions for a little ride.

“I’m Poay. I’m born here in George Town. Would you like to see my favorite places?” he asked. “Yes, of course!” I replied keenly.

Our first stop, the Khoo Kongsi, wasn’t far away. A kongsi is a Chinese clan house, partly temple and partly meeting hall. The Khoo Kongsi is the impressive clan house of the Khoo fam-
ily, an influential Chinese Clan from Penang Island with an extensive lineage that can be traced back 650 years. The building is a work of art. The impressive roof, artistically decorated with colorful dragons and other symbols of Chinese mythology, is the first thing to draw one’s attention.

In the area round Armenian Street, the culmination of cultures and heritage unique to Penang and George Town is very apparent. Passing the famous Kapitan Kelling Mosque with its huge domes and the golden minaret, the Indian Sri-Mahamariamman Temple, which is the starting point for the dramatic Thaipusam Hindu festival, ancient Chinese temples and Christian churches such as St. George’s, the oldest Anglican church in Malaysia, one can sense the charm and history of what is a cosmopolitan city.

We left behind busy market streets, atmospheric shophouses and the omnipresent British colonial architecture, such as the Cityhall or the 18-meter high Clock Tower built in honor of Queen Victoria.

On to the Little India market and it was clear that Poay was an expert at dodging traffic. However, he mainly stuck to the quiet side-streets. One of these took us to the UNESCO world heritage listed area called Chew Jetty or Seh Chew Keo, located near the island’s ferry terminals. This area, the largest
of the eight waterfront settlements or clan jetties in George Town, was created in the mid-19th century. Each of the clan jetties has a small shrine to pay homage to the sea deities, explained Poay.

In George Town there are currently about 100 rickshaw-or trishaw-drivers. Thirty years ago there were around 1,000, said Poay. With the expansion of the local public transport system, the number has markedly fallen over the years. However, that trend is now reversing due to the growing influx and demand of tourists coming to Penang. Poay himself left a job as a parking attendant 3 years ago to become a rickshaw driver.

“Look at this house,” Poay said. I looked up and saw a huge painting of a rickshaw driver, relaxed lying in his rickshaw, waiting for customers. It reminded me of Poay when I first met him, an hour ago.

“It’s called ‘The Awaiting Trishaw Paddler and measures around 15 by 15 meters,” he said. One of many mural paintings lining the streets of the town, this one was done by the Lithuanian artist, photographer and filmmaker Ernest Zacharias—indeed, a fitting tribute to the friendly and knowledgable rickshaw drivers of George Town.
JULY

9th Asian Dermatological Congress
10/7/2013 to 13/7/2013
Location: Hong Kong
Info: ADC 2013 Secretariat
Tel: (852) 3151 8900
Email: adcc2013@swiretravel.com
Website: www.adc2013.org

Asian Pacific Digestive Week
21/9/2013 to 24/9/2013
Location: Shanghai, China
Info: APDWF Secretariat
Tel: (65) 6346 4402
Email: congress_international@gastro2013.org
Website: www.gastro2013.org

21st World Congress of Neurology
21/9/2013 to 26/9/2013
Location: Vienna, Austria
Info: Kenes International
Email: wcn@kenes.com
Website: www2.kenes.com/wcn/Pages/Home.aspx

AUGUST

9th Singapore International Congress of Obstetrics & Gynaecology
22/8/2013 to 24/8/2013
Location: Singapore
Info: Scientific secretariat, MIMS
Tel: (65) 6290 7400
Email: secretariat.sicog@mims.com
Website: www.sicog2013.com

Asia-Pacific League of Associations for Rheumatology Symposium
29/8/2013 to 1/9/2013
Location: Bali, Indonesia
Info: Kenes Asia
Tel: (65) 6292 4710
Email: aplarsymposium@kenes.com
Website: www2.kenes.com/aplar/Pages/home.aspx

49th Annual Meeting of the European Association for the Study of Diabetes
23/9/2013 to 27/9/2013
Location: Barcelona, Spain
Info: EASD Secretariat
Email: registration@easd.org
Website: www.easd.org

13th Asian Federation of Sports Medicine Congress
25/9/2013 to 28/9/2013
Location: Kuala Lumpur, Malaysia
Info: AFSM Organizers
Email: 13afsm@gmail.com
Website: www.13afsm.com

SEPTEMBER

European Respiratory Society Annual Congress
7/9/2013 to 11/9/2013
Location: Barcelona, Spain
Info: ERS 2013 c/o K.I.T. Group
Email: ers2013registration@kit-group.org
Website: www.erscongress2013.org

Primary Care Forum 2013 and the 4th Singapore Health & Biomedical Congress 2013
27/09/2013 to 28/09/2013
Location: Singapore
Tel: (65) 6496 6684 / (65) 6496 6682
Email: secretariat@pca.sg
Website: www.pca.sg/events

European Cancer Congress 2013 (ECCO-ESMO-ESTRO)
27/9/2013 to 1/10/2013
Location: Amsterdam, Netherlands
Info: ECCO Secretariat
Tel: (32) 2 775 02 01
Fax: (32) 2 775 02 00
Email: ecco@ecco-org.eu
Website: eccamsterdam2013.ecco-org.eu/

UPCOMING

Taiwan Digestive Disease Week 2013
4/10/2013 to 6/10/2013
Location: Taipei, Taiwan
Info: Congress Secretariat
Email: service@tddw.org
Website: www.tddw.org

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

9th International Symposium on Respiratory Diseases
8/11/2013 to 10/11/2013
Location: Shanghai, China
Info: MIMS, China
Email: secretariat@isrd.org
Website: www.isrd.org/