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Spirometry still underused in primary care

Jenny Ng

The use of spirometry continues to be an underutilized diagnostic tool for chronic obstructive pulmonary disease (COPD), according to an expert.

“Current guidelines recommend the use of spirometry to confirm airflow obstruction and to establish an accurate diagnosis in those suspected with COPD,” said Dr. Min Joo of the Department of Medicine, University of Illinois, Chicago, Illinois, US. “However, only about one-third of newly diagnosed COPD patients have had a spirometry performed, and in practice providers continue to diagnose and manage COPD without the use of spirometry.

Joo was speaking during the recent annual meeting of the Asian Pacific Society of Respirology (APSR) held in Yokohama, Japan.

Why spirometry is underutilized in COPD is not exactly known, said Joo. However, one qualitative assessment found that many primary care physicians believe spirometry is unnecessary for the diagnosis of COPD. They may have poor recognition of the guidelines and workflow constraints, but also many physicians simply believe there is a lack of evidence. [COPD 2013;10:444-449]

To assess the use of spirometry in the primary care setting, Joo and colleagues retrospectively assessed the clinical diagnoses of COPD in 521 patients and compared these with their corresponding spirometry results. They found that in those clinically diagnosed with COPD, only about 50 percent actually had obstruction based on spirometry, while 25 percent of patients who were diagnosed with not having COPD were found to be obstructed. [J Gen Intern Med 2011;26:1272-1277]

Moreover, in COPD patients who were falsely diagnosed, there was a two-fold higher chance for all-cause hospitalizations and emergency department visits compared with accurately diagnosed patients. Falsely diagnosed patients were also significantly more likely to have had a chest radiograph, chest CT, cardiac catheterization and a cardiac-stress test.

The over-treatment of patients who don’t have COPD, with medications that can be harmful for other conditions is a cause for concern. Inaccurate diagnoses can also risk an under-diagnosis of other diseases that may cause similar symptoms, stressed Joo.

To improve the use of spirometry, she suggested there is a need to first address the underlying skepticism in primary care. What is needed is the evidence to change provider beliefs in the utility of spirometry in COPD, Joo said.
Hepatitis burden a key focus of this year’s APASL meeting

Chronic viral hepatitis is one of the major health problems globally. However, attention to date in the field of transmissible diseases has focused on HIV, malaria and tuberculosis. Viral hepatitis has not had the prominence or advocacy that accompanies these other conditions.

It is only in recent years that the WHO has acted on knowledge available to it for some time about the global impact of chronic viral hepatitis. The facts are straightforward – there are 500 million people in the world with chronic hepatitis B (HBV) or C (HCV), with the vast majority in the Asian Pacific region.

Most people with HBV are infected in childhood. In the scenario of childhood infection, most will develop chronic disease with the subsequent risk of cirrhosis, liver failure, liver cancer and death. Vaccination programs are effective for HBV, but there remains a large pool of people without access to this strategy and a similarly large proportion of already infected individuals in whom vaccination is too late. Treatment for HBV with existing antivirals is life-long, expensive and available through government funding programs only in a minority of countries.

Although slightly less frequent than HBV, there are still more than 100 million people living with HCV in the Asian Pacific region. In most instances in this region, HCV is transmitted by inadequate blood screening, improper sterilization of medical instruments, or from instruments used in certain social and cultural traditions. Education of health care professionals, better population health studies, targeted prevention programs and access to emerging therapies are some of the solutions available to us. The emerging treatments for HCV are extremely successful. Many studies now report cure rates of greater than 95 percent with a combination of antiviral agents used for 12 weeks only. However, it appears that these therapies will be extremely expensive and out of the reach of many governments – particularly poor countries where the prevalence of HCV is high. Strategies not dissimilar to those used for HIV to lower cost...
and improve access to therapies may be needed.

Both HBV and HCV increase the risk of liver cancer. Primary liver cancer is the fifth most common cancer in the world – due largely to the high prevalence of viral hepatitis. Often detected when advanced, treatment options are limited and many people die from this malignant disease. In the western world, liver cancer is growing at a faster rate than any other malignancy.

All of these matters will be discussed at the Asian Pacific Association for the Study of the Liver (APASL) Annual Scientific Meeting in Brisbane from 12 to 15 March 2014. Clinicians, scientists and policy makers from all around the globe will converge to consider the current state of play in the field of viral hepatitis and liver diseases. This period is a remarkable era in research discoveries in the field of viral hepatitis. The impact of new therapies on clinical practice, disease burden and patient outcomes will be discussed in some detail. The specific issues related to the problems in the Asian Pacific region will be addressed – a new era in viral hepatitis and liver disease has begun.

For more about APASL 2014 go to: www.apasl2014.com
Research a catalyst for improving global health

Rajesh Kumar

Can research improve global health? The *Lancet* Editor-in-Chief Dr. Richard Horton posed this question to a packed audience at a lecture hall at the National University of Singapore recently to ignite a debate on the wider role of research, and universities, in improving global health.

Referring to the Times Higher Education world university rankings, he said metrics such as teaching, research, citations, industry income and international outlook are currently used to rank world universities.

“But if you think about the larger social world of universities, there isn’t a metric called social impact, let alone their impact on global health. Our metrics are really very narrow.”

The role of universities is not just to produce excellent research that gets published in journals with a high impact factor and attracts maximum citations. Instead, research should be able to directly influence political decision making to improve health, said Horton.

Quoting from the well known British conservative Professor Kenneth Minogue’s The Concept of a University, Horton said some intellectuals, however, favored universities as ivory towers where reflection can take place, divorced from the priorities shaping our societies.

As societies have forgotten the reasons why they created universities in the first place, the universities themselves have slipped into an existential crisis, which could only be resolved by giving them a social purpose, he said.

The UK social medicine pioneer and a professor at the University of Cambridge during the 1940’s, Professor John Ryle, believed that a physician had “a responsibility in the matter of disease prevention and health promotion and in the advocacy of social and other measures to secure them.”

“Can we import that idea into the way we think about our universities and our research enterprise today [to give them that social purpose]?” Horton asked.

The *Lancet* is already attempting it. The journal has been publishing series on different global health topics that bring together experts on the subject, focus on the best available evidence and point the evidence in a very clear policy direction.

Horton mentioned the recent series on nutrition, which he said was not designed to get citations, but to influence a political dialogue. The journal tried to inject that series into a political discussion at the G-8 meeting earlier this year and succeeded in attracting attention of the decision makers. A series on HIV prevention was, similarly, prepared as a blueprint for the South African government to tackle the epidemic.

The *Lancet* is currently helping young health researchers in the Palestinian territory to present their research findings, report on health progress in their region and identify health priorities. All this is fed back into the territory’s health strategy.

“This is a relationship whereby research is directly helping to strengthen the system of health provision in a particular region,” he said. “Research is an indispensable catalyst for health and political change.”
Task force aims for hepatitis prevention and control

Dr. Maria Katrina Florcruz

The Hepatology Society of the Philippines (HSP) recently convened the National Viral Hepatitis Task Force (NVHTF), a multisectoral coalition whose goal is to develop and maintain a national strategy to control and prevent hepatitis B and C in the Philippines.

The public-private partnership was launched last November 20, 2013 along with other member organizations including the Department of Health, World Health Organization, Philippine Society for Microbiology and Infectious Diseases, Philippine College of Physicians, Philippine Health Insurance Corporation, Philippine Pediatric Society, Philippine Society of Gastroenterology, Yellow Warriors Society of the Philippines and the Department of Labor and Employment. International partners of NVHTF include the Coalition for the Eradication of Viral Hepatitis in Asia Pacific, Viral Hepatitis Foundation and the World Hepatitis Alliance.

In the Philippines, about 16.7 percent of adult Filipinos have chronic hepatitis B infection. On the other hand, 1 percent of Filipinos may be infected with hepatitis C.

“Hepatitis B and hepatitis C are among the most common causes of liver cancer,” said Dr. Diana Payawal, HSP president and executive council member of the Asian Pacific Association for the Study of the Liver. “In addition to the toll on their health, persons with hepatitis B or hepatitis C suffer stigma and discrimination,” she added.

The NVHTF created a strategic plan, composed of four axes, called “Prevention and Control of Hepatitis B and C in the Philippines: A Call to Action.” It will serve as the roadmap to eliminate and decrease the prevalence of such diseases in the country.

Axis 1 includes raising awareness through public education and by promoting partnerships with organizations. It also involves raising funds, mobilizing resources, organizing and implementing programs for worker protection, health education and confidentiality and non-discrimination.

Axis 2 emphasizes the need for evidence-based data which will guide in creating policies and inciting actions. National data from the Philippine Red Cross and National Statistics Office as well as surveillance systems, cost-benefit analysis and identification of the impact of viral hepatitis on people with the infection, may be used as reference.

Axis 3 of NVHTF emphasizes the importance of transmission prevention through timely vaccination coverage as well as reduction of risky behavior through occupational safety and health promotional campaigns, among others.

Axis 4 aims to give appropriate information, counseling and clinical management to infected individuals. It also stresses the importance of early diagnosis and screening, awareness of the consequences and behavioral changes to prevent transmission.

“With this roadmap, we hope to eradicate or significantly decrease the burden of viral hepatitis in the country... Working together, we feel we can truly make a difference in viral hepatitis control and prevention in the country,” said Dr. Janus Ong, HSP committee head on Health Policy.
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Novel treatment for pelvic carcinomatosis

Dr. Carol Tan

Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) is a novel treatment modality for patients with pelvic carcinomatosis, according to Dr. Cecilio Hipolito Jr., section head in Surgical Oncology, St. Luke’s Medical Center.

Peritoneal carcinomatosis is caused by spontaneous tumor shedding from large intra-abdominal tumors or from iatrogenic dissemination of cancer cells during surgical manipulation. Prognosis depends on the histology, size and distribution. Colorectal cancer has the most favorable prognosis, with a median survival of 7.9 months while pancreatic cancer has a median survival of 12.5 months for patients with stage one pelvic carcinomatosis. Gastric has the worst prognosis, with most patients dying within 3 or 4 months.

Current treatment modalities for pelvic carcinomatosis include intravenous (IV) chemotherapy, CRS with IV chemotherapy and CRS with HIPEC.

CRS entails the complete removal of gross tumors to eradicate resistant tumor clones, recruit dormant cancer cells into the active phase of the cell cycle, and relieve obstruction to improve the nutrition and immune system of the patient. This should be followed by an effective adjuvant therapy, such as HIPEC, to destroy residual microscopic tumor cells.

“The principle of HIPEC is the intraperitoneal administration of heated chemotherapy. It exposes residual tumor cells to high local drug concentrations delivered directly in the abdominal cavity right after cytoreductive surgery, minimizing systemic drug circulation and bone marrow toxicity,” explained the speaker.

In HIPEC, the amount of chemotherapy absorbed systemically is limited since the peritoneal membrane acts as a filtering barrier. The drug is then metabolized by the liver and kidneys, leading to faster clearance and less adverse side effects.

Hipolito elaborated that hyperthermia is synergistic with chemotherapy in killing tumor cells, since it increases the penetration and concentration of chemotherapy among cancer cells.

Hyperthermia also destroys tumor cells through induction of apoptosis and destruction of their architecture and vasculature.

“Patient selection is very important if you want to do cytoreductive surgery with HIPEC,” added the Hipolito.

HIPEC should only be done in patients with complete macroscopic cytoreduction, favorable tumor histology with inherent sensitivity to chemotherapy, no distant systemic metastasis, and excellent performance status.
Various studies have demonstrated the effectiveness of CRS with HIPEC.

In colorectal cancer, the median survival in CRS with HIPEC was 22 months, compared to 12 months with palliative IV chemotherapy.

In gastric cancer, the median survival was 11 months for CRS with HIPEC, compared to 6.5 months for CRS with IV chemotherapy.

In ovarian cancer, the median survival was 19 months on CRS with HIPEC, compared to 11 months for CRS with IV chemotherapy.

“Cytoreductive surgery with HIPEC, I would like to emphasize, is not a standard treatment at present and should only be offered to selected patients,” noted Hipolito.
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The medical oncologist as an internist

Dr. Mary Lauren Europa

Medical oncologists are a special breed of internists. “A good medical oncologist is one who applies the thoughtful approach to problem-solving learned [in internal medicine (IM) to patients with cancer],” says Dr. Priscilla Caguioa, current president of the Philippine College of Physicians and a proud medical oncologist. During her speech, she said that the internist is a primary care gatekeeper who addresses all medical problems, recognizes those beyond the realm of his practice, and refers to specialists as appropriate.

Similarly, a medical oncologist implements all aspects of IM in patient care, but acknowledges his limitations and asks for co-management, Caguioa added. He often works with multiple disciplines such as surgery, pathology, radiology, radiation oncology, nursing, neurology, psychology, gynecology and rehabilitation medicine. Other subspecialists usually refer patients to medical oncologists after initial evaluation and work-up, but their role in the multisystemic management continues.

Oncology is a broad and medically complex practice, Caguioa said. Different cancer types have different tissue tropisms. For instance, brain, lung, liver and bone metastases all manifest differently. Paraneoplastic syndromes, on the other hand, include endocrinologic, metabolic, hematologic, renal, hepatic, dermatologic, neurologic and immunologic manifestations. Oncologic emergencies also exist and various adverse effects of cancer treatment have to be constantly dealt with.

According to Caguioa, the medical oncologist as an internist is at the frontline of all these challenges. Furthermore, they are often entrusted with final management decisions, such as the timing of surgery and/or radiotherapy, the decision on whether to do conservative or aggressive action, or to take curative or palliative approaches. They also have the
sociocivic duty to educate the general public regarding cancer prevention and inform them on social, occupational, nutritional and sexual practices that contribute to its development.

Despite these challenges, medical oncologists have enabled cancer survivors to thrive. A cancer survivor encapsulates the patient throughout the cancer trajectory, while cancer survivorship refers to a period between primary treatment and recurrence or end of life. This includes post-treatment surveillance, monitoring and the phase of permanent survival, where the focus is on long-term quality of life. During this time, a medical oncologist identifies the late effects of treatment, prevents potential late effects and recurrence, and promotes adjustment and healthy lifestyles.

“It is best that he who saw them through periods of illness and treatment, will see them through the times of better health,” concludes Caguioa, “because, after all, a medical oncologist is still an internist.”

Radiation modality offers precise tumor treatment

Dr. Carol Tan

Stereotactic radiosurgery is an effective and safe modality for delivering radiotherapy, according to Dr. Kathleen Baldivia, radiation oncologist with the Makati Medical Center.

“For any radiation modality ... the challenge is always how to enhance radiation dose delivery to the target and at the same time protect the nearby normal structures,” said Baldivia. She added that while a higher dose of radiation results to a greater chance of tumor control, adverse side effects also increase. Tumor size present another difficulty for radiation therapy because dealing with large lesions exposes more normal tissue to radiation while in smaller lesions, there are stricter dose constraints with little room for error.

Baldivia discussed a promising modality that can address these challenges. “Stereotactic radiosurgery is a special technique for delivering precisely-directed high dose radiation that conforms to a small specific target while delivering a minimal dose to surrounding tissues,” she explained.

Stereotactic radiosurgery is used to deliver high doses of radiation to intracranial targets while stereotactic radiotherapy is used for extracranial targets. Both methods are characterized by high precision and accuracy in the delivery of radiation, rapid radiation fall off around the periphery of the target, and high dose conformity. Due to these features, along with a marked reduction in the amount of normal tissue radiated, patients generally have improved tolerance for the therapy.

Technologies such as three-dimensional mapping techniques and immobilization devices are available to enhance the delivery of radiation in stereotactic radiosurgery and
radiotherapy. This technique determines the coordinates of the tumor in order to deliver radiation to the exact field. Immobilization devices ensure patients are positioned well during the entire treatment and that the target field is not missed. This is important for stereotactic radiotherapy, in which body frames are used to track tumor movement, since most internal organs are in constant motion.

Stereotactic radiosurgery can be used for treatment of primary brain tumors such as acoustic neuromas, metastatic brain lesions and arteriovenous malformations. It can also create small ablative lesions to treat trigeminal neuralgia and movement disorders such as epilepsy, Parkinson’s disease and tremors. Typically, radioresistant metastatic tumors of the spine may respond to stereotactic radiotherapy due to the high dose of radiation being delivered.

Stereotactic radiosurgery and radiotherapy have numerous clinical applications, making it a promising field to explore, concluded Baldivia.

Robotics improves secondary outcomes in rectal surgery

Dr. Yves Saint James Aquino

Robotics-assisted laparoscopic surgery offers advantages in short-term quality outcomes in minimally invasive procedures for total mesorectal excision, according to Dr. Robert Chang, colorectal surgeon with the Medical City in Pasig City.

The appearance of the surgical specimen makes a difference in the management of a particular disease, said Chang. Good specimen reflects positively on diagnosis, staging, treatment planning and strategy for stage-specific management. He explained that the ideal specimen includes a completely excised rectum and its mesentery, which means that the surgeon should remove the visceral mesorectal tissue down to the levators.

The importance of acquiring the ideal specimen motivated different trials to evaluate and compare conventional open surgical methods to laparoscopic and robot-assisted surgeries. Chang explained that various studies have shown that there is no difference between laparoscopic colon surgery and conventional surgery in primary, cancer-related outcomes on recurrence and survival. [N Engl J Med. 2004;350(20):2050-9] Studies, however, favor laparoscopy for secondary outcomes, including quality of life issues such as post-operative pain, wound complication, bowel function recovery and early ambulation. [Lancet Oncol. 2013;14(3):210-8]

“The speedy recovery or the less use of analgesics seems to favor a less stress response related to the immune system, and it’s not too far-fetched to extrapolate that this immune system response would lead to a better immune defense against cancer,” said Chang.

The rationale behind robotic surgery is to further enhance the surgical method.
present, robotics is usually needed for colon cancer and in some cases of rectal cancer. The small moving parts in robotics-assisted surgery can help improve precision in movements, magnify an operative view and minimize tremors to obtain an intact specimen.

"The small moving parts in robotics-assisted surgery can help improve precision in movement"

For these benefits, robotic surgery is usually indicated for cancers of the extra-peritoneal rectum or low rectal, patients with tight pelvis or those with high body mass index, explained Chang.

According to a consensus document on robotic surgery by the Society of American Gastrointestinal and Endoscopic Surgeons, the robotic procedure is comparable to laparoscopic surgery in terms of safety, short-term outcomes and oncologic outcomes. The difference as the consensus pointed out is that robotic surgery is superior in visualization, dexterity, pelvic nerve preservation and minimized blood loss compared with laparoscopic surgery.

Some concerns with robotic surgery include longer operating time and higher costs. Chang explained that future randomized trials might be able to provide cost-benefit analysis on robotic surgery.

“We have to emphasize that the most important objective of rectal cancer surgery is total mesorectal excision achieving an intact specimen with negative margins,” concluded Chang.

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Hepatotoxicity and hepatitis B reactivation in cancer treatment

Dr. Mary Lauren Europa

Due to the inherent hepatotoxic nature of cancer treatment, careful assessment of liver status is done prior to chemotherapy along with routine monitoring throughout its entire duration, according to Dr. Ian Homer Cua, gastroenterology consultant with St Luke’s Medical Center, Institute of Digestive and Liver Diseases. Hepatotoxicity may be direct or indirect, with the former resulting from drug-induced hepatocellular or cholestatic injury, and the latter via the potentiation of pre-existing liver disease.

Monitoring is done through enzymes that indicate liver injury, such as alanine aminotransferase (ALT), aspartate aminotransferase, alkaline phosphatase and gamma-glutamyl transferase, as well as enzymes that indicate its synthetic function, such as bilirubin, albumin and prothrombin time. These various serum biochemical markers are also used in severity classification and prognostication.

Chemotherapy-induced hepatotoxicity

According to Cua, risk factors for chemo-
therapy-induced hepatotoxicity include pre-existing liver disease, familial disposition, hepatic tumor or metastasis, age, gender, smoking, alcohol, drug interactions, obesity, metabolic syndrome and fatty liver. The clinical presentation may vary from having only asymptomatic increases in liver enzymes to having frank liver failure.

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HBV reactivation can range from a benign subclinical course, to severe or fulminant hepatitis, if recognition is delayed
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While there are no specific diagnostic criteria for chemotherapy-induced hepatotoxicity, a high index of suspicion, lack of prior illness, clues in the medical history and temporal profile, the appearance of signs, symptoms or laboratory abnormalities after drug administration, and improvement noted after discontinuation may lead a clinician to this diagnosis.

However, Cua noted that progressive hepatic tumor, viral hepatitis, concomitant medication toxicity, paraneoplastic syndromes, sepsis and hemolysis and fungal infection, among others, must be ruled out. Hepatotoxicity is common in methotrexate, asparaginase, carmustine, chlorambucil, cyclophosphamide, cytarabine, dacarbazine, doxorubicin, etoposide, gemcitabine, mitomycin C, streptozocin and busulfan.

Chemotherapy is stopped once the patient presents with clinical deterioration and/or progressive, increases in liver enzymes. Liver function tests are then monitored until improved. After which, a rechallenge with the drug may be attempted with dose modification of 20 percent decrements, until tolerated.

Dose modification strategies, however, are largely empiric, as there are no specific treatment and management guidelines at the moment for chemotherapy-induced hepatotoxicity, said Cua.

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...there are no specific treatment and management guidelines at the moment for chemotherapy-induced hepatotoxicity
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Hepatotrophics like silymarine and ursodeoxycholic acid, though promising, are not supported by enough evidence from larger clinical trials. On the other hand, the drug S-adenosylmethionine (SAM) or AdoMet, has been shown to improve methionine tolerance, prevent hepatic encephalopathy in cirrhosis, restore glutathione levels, increase plasma levels of tauroconjugated bile acids, decrease cytotoxic deoxycholic acid levels, normalize liver membrane fluidity, and regulate hepatocyte growth and survival. [Anticancer Res. 2003;23(6D):5173-9]

Chemotherapy-induced hepatitis B reactivation

Hepatitis B (HBV) reactivation is a common chemotherapy-induced liver injury and is a significant problem due to its high prevalence in the Philippines, said Cua. In patients with inactive HBV undergoing chemotherapy, the virus may become replicative and viral load increases, due to immunosuppression and loss of immune control.

Clinically, HBV reactivation can range from a benign subclinical course, to severe or fulminant hepatitis, if recognition is delayed. Risk factors for reactivation of hepatotoxicity include male gender, type of malignancy (eg, Non-Hodgkins Lymphoma and breast can-
cer), a high viral load and the use of certain chemotherapy agents (e.g., corticosteroids, antitumor antibiotics, plant alkaloids, alkylating agents, antimetabolites and monoclonal antibodies). Rituximab, in particular, causes typically late and severe HBV reactivation hepatoxicity, with dramatic enzyme elevations.

There is limited data on its management, but generally, antiviral therapy is employed in HBV-reactivation. “Effective treatment exists to prevent HBV reactivation but must be started early,” stressed Cua. It is best to implement pre-chemotherapy screening for all patients due to the hyperendemicity of the disease.

HBsAg and anti-HBc are common screening parameters, with follow-up HBV-DNA done if HBsAg is positive. If HBV-DNA is less than 2,000 IU/mL, any antiviral treatment, including lamivudine, can be started before chemotherapy, and continued until 6 months after the last chemotherapy cycle. On the other hand, if HBV-DNA is more than 2,000 IU/mL, or chemotherapy duration is anticipated to be 12 months or longer, entecavir or tenofovir is given. HBV-DNA and ALT are monitored every 3 months. [J Hepatol. 2009;50(2):227-42; Hepatology. 2009; 50: 661-62] The use of preemptive antiviral therapy reduces the risk of developing HBV reactivation hepatoxicity, added Cua.
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VTE and cancer considered as medical double jeopardy

Dr. Yves Saint James Aquino

Cancer that exists with thrombosis poses and important concern as it affects the prognosis of both conditions, said Dr. Celine Teves Aquino, section head in Cardiology, Department of Medicine, Cebu Velez General Hospital.

“The presence of cancer is going to cause a complication in the course of surgery. It is going to cause a delay in the course of treatment and it can compromise the quality of life altogether,” said Aquino.

Studies have shown that venous thromboembolism (VTE) is the second leading cause of death in cancer. Aquino pointed out that cancer itself increases VTE risk, recurrence and bleeding. Malignant neoplasm is the most commonly associated risk factor at 18 percent, along with other risk factors such as trauma (12 percent), congestive heart failure (10 percent) or neurological disease with extremity paresis (7 percent).

In the presence of predisposing factors, thrombosis develops when blood moves slowly at the periphery of the vein. Hypercoagulability may cause blood components to collect in one or both venous valve cusps, resulting in a clot that can grow big enough to cause blockage. The Virchow’s triad describes three categories of factors that contribute to thrombosis: stasis, endothelial injury and hypercoagulability.

“The thrombus can get big, and even propagate and get dislodged. And if it lodges through the circulation into the pulmonary circulation, it can ... cause the phenomenon of pulmonary embolism,” explained Aquino.

The vicious cycle in VTE and cancer

The relationship between cancer and VTE forms a vicious cycle, where one increases the risk of the other and vice versa. Aquino explained that the effect of cancer on increased risk of VTE might be rooted in various components: the circumstances of the cancer patient, the type of cancer and the type of chemotherapeutic agent used.

Usually in cancer treatment, the patient is immobilized, which allows for stasis. The patient is also exposed to inflammatory stimuli, to catheters or tissue destruction. These inflammatory events stimulate the inflammatory process that may cause thromboembolism.

The tumor itself contributes to VTE formation. The tumor has a compressive effect on surrounding tissue and blood vessels that may lead to stasis. Some types of cancer are also more thrombogenic than others as they
are considered to have more procoagulant activity, and this include hematologic tumors and tumors of the gastrointestinal tract.

Vascular endothelial growth factor is usually associated with thromboembolism, which is also regulated by the tissue factor. This implies a close relationship between thrombogenesis and the metastatic ability of the tumor. Recent studies have shown that the more thrombogenic the tumor, the more metastatic it is. This means that the control of thrombogenicity may also control metastatic ability of tumor. Studies reveal promising results of anticoagulants not only preventing thrombosis but also preventing tumor growth and metastasis. [Cancer. 2007;110:1149–1161.]

Chemotherapeutic treatment may also contribute to VTE formation. Thrombosis is more associated with agents causing irreversible damage. These agents cause cell loss through necrosis and apoptosis, which may manifest as cardiomyopathy, myocardial infarction or thrombosis. Treatments for endocrine cancers, such as cisplatin for example, cause endothelial toxicity and compromise the coagulation systems.

Preventing VTE in cancer

The first step in VTE prophylaxis is the estimation of both VTE risk and bleeding risk. When VTE risk is greater than the bleeding risk, physicians should initiate pharmacologic prophylaxis.

Major surgery is considered as the most important risk factor for VTE in cancer, said Aquino. Other independent predictors in the medically ill include intensive care admission, congestive heart failure, neoplasms, neurologic disease and thrombophlebitis. [Arch Int Med. 2001;160:809-15] The predictive model for VTE in cancer, which is offers a good correlation to VTE events, showing actual incidence closely related to predicted events (See table 1).

Due to the possibility of bleeding, prophylaxis is not given to every patient with VTE risk. The HAS-BLED scoring system, which was originally used for stroke patients, can be helpful in determining the bleeding risk in patients with or at risk of VTE (See table 2). As with the predictive model for VTE, in HAS-BLED, the higher the score, the greater the risk for bleeding.

<table>
<thead>
<tr>
<th>Table 1: Predictive model for VTE in cancer</th>
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<tr>
<td><strong>Patient Characteristics</strong></td>
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<td>Site of cancer</td>
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<td>· very high risk (stomach, pancreas)</td>
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<tr>
<td>· high risk (lungs, lymphoma, gynecologic, genito-urinary except prostate)</td>
</tr>
<tr>
<td>Platelet count &gt; 350,000/mm³</td>
</tr>
<tr>
<td>Glycated hemoglobin &lt; 10g/dL or using ESA</td>
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<tr>
<td>Leukocyte count &gt; 11,000/mm³</td>
</tr>
<tr>
<td>Body mass index &gt; 35</td>
</tr>
<tr>
<td>ESA = erythropoiesis-stimulating agent</td>
</tr>
<tr>
<td>Adapted from Cancer. 2005;104(12):2822-9.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2: HAS-BLED scoring for estimation of bleeding risk</th>
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</thead>
<tbody>
<tr>
<td><strong>Risk factor</strong></td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Abnormal liver/renal function (1 point each)</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>Bleeding</td>
</tr>
<tr>
<td>Labile INRs</td>
</tr>
<tr>
<td>Elderly (age &gt; 65 years)</td>
</tr>
<tr>
<td>Drug use (concomitant anti-inflammatory drugs, anti-platelet)</td>
</tr>
<tr>
<td>Alcohol use (&gt; 8 alcoholic drinks/week)</td>
</tr>
<tr>
<td>INR = international normalized ratios</td>
</tr>
<tr>
<td>Adapted from Chest. 2010;138:1093-1100.</td>
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</tbody>
</table>

In deciding for the pharmacologic prophylaxis for VTE in cancer, one should take into consideration the type and composition of the thrombus. Anti-platelets work in arterial thrombosis where the thrombi are predominantly composed of platelets; however, anti-platelets may not be as effective in venous thrombosis that involves mostly red blood cells and fibrin, with very little platelet content.

Anti-coagulants remain to be the effective option for VTE therapy. Drugs under this category have different sites of actions, with
varying degrees of effectiveness, side effects and duration. Warfarin is an example of anticoagulant with multiple sites of action, inhibiting the vitamin K-dependent clotting factors (II, VII, IX and X). Parenteral heparin in the form of unfractionated (UFH) or low molecular weight heparin (LMWH) indirectly inhibits of factor Xa, and partially inhibits factor II. Direct inhibitors of factor X are recent developments, including rivaroxaban, apixaban, edoxaban, betrixaban and eribaxaban.

Direct inhibitors of thrombin blocks factor IIa, preventing conversion of fibrinogen to fibrin. Some direct thrombin inhibitors also act on soluble fibrins to prevent propagation. Direct thrombin inhibitors include parenteral bivalent (eg, bivaluridin and hirudin), parenteral univalent (eg, argatroban) and oral univalent (eg, ximelagran and dabigatran) inhibitors.

Anti-thrombotic therapy

Aquino clarified that in conditions where there is already a thrombus formation, fibrinolytic agents, which act on the thrombus, have not been shown to provide survival advantage, and are only indicated in life- or limb-threatening venous thromboembolic events.

Use of anti-coagulants in anti-thrombotic therapy may involve overlapping use of warfarin and heparin. The overlapping dosage is the gold standard of management and is as follows: UFH given as a drip to maintain activated partial thromboplastin time of 2.5 times the normal or 5,000 U subcut every 8 to 12 hours; LMWH 100 to 150 ANTI-Xa U/KBW subcut every 12 hours; and warfarin given orally and overlapping with the heparin until international normalized ratio (INR) reaches > 2. [Chest. 2001;119:1765-1935.]

Rivaroxaban may be given with a dose of 15mg BID for 3 weeks then 20 mg daily for 3 months. The drug has been proven non-inferior to warfarin dosed to maintain INR of 2 to 3 and associated with less bleeding. [N Engl J Med. 2010; 363:2499-2510] Dabigatran given as 110 mg BID or two caps OD is also proven non-inferior to warfarin and associated with less bleeding, said Aquino.

Various guidelines such as European Society of Medical Oncology and the American Society of Clinical Oncology recommend VTE prophylaxis in all hospitalized cancer patients with no contraindications, particularly for those who are immobilized.

Based on international guidelines, for all cancer patients undergoing surgery, initial prophylaxis should be given for all surgeries lasting longer than 30 minutes. Prolonged treatment is continued post-operation for 28 to 35 days in patients who had major surgery and those considered at “high risk” for VTE and recurrence.

For ambulatory patients with cancer, routine prophylaxis is not recommended for patients with indwelling central venous catheters.

“Although theoretically, these (ambulatory cancer) patients should benefit, the evidence over the last 40 years does not indicate any survival advantage. It does indicate however a higher bleeding risk,” explained Aquino.

Treatment and prophylaxis of VTE in cancer should be done on an individual basis, taking into account the type of cancer or tumor, the patient’s overall health and the benefits over risks assessment. “In critical illness and cancer, the heparins are still the primary intervention,” said Aquino.
DOH delivers aid to typhoon victims

Dr. Maria Katrina Florcruz

Typhoon Yolanda affected more than 1,210 local health facilities leaving at least 200 health centers and 7 local government hospitals completely damaged. The Department of Health (DOH) further estimates that 1.4 billion pesos will be needed to rehabilitate the affected health facilities and to help prevent the spread of diseases.

According to DOH reports, more than 2,581,677 families were affected in 12,122 barangays located in 44 different provinces. By the second week of December, at least 30,168 injuries and 5,936 deaths, mostly due to drowning and trauma, have been documented.

A DOH Emergency Management Task Force headed by health secretary Dr. Enrique Ona and health undersecretary Dr. Janette Garin was created to oversee the response and recovery. More than 264 DOH medical teams, local health responders and foreign teams have also been deployed across typhoon-hit areas.

“These teams… encountered roads replete with debris and dead ends, severe congestion in ports and airports and had to compete for space in cargo planes with food supplies. Nonetheless they made it – but there are still many unreached areas and we will not stop until we get all our medical teams on the ground,” said Dr. Ted Herbosa, DOH undersecretary.

The DOH Quick Yolanda Response Team, first deployed to Tacloban City, conducted assessment of the community’s health, nutrition and water and sanitation needs.

More than 120,000 individuals in affected areas have been given medical consultations primarily on acute respiratory infection, acute watery diarrhea, open wounds and bruises, skin diseases and hypertension. Patients were also referred to hospitals in Metro Manila due wounds, fracture, gastroenteritis, leptosiprosis postexposure prophylaxis and pneumonia. Medical teams have been serving at the Villamor Airbase to give psychosocial services for typhoon Yolanda survivors arriving from Tacloban City.

In partnership with the World Health Organization, the DOH started the expanded program on immunization against measles and polio and supplementation with micronutrient, zinc syrup and vitamin A supplementation for children. Meanwhile, emergency delivery kits and iron supplementation for pregnant and post-partum mother have been prepared.

Typhoon victims were allocated provisions for hygiene kits, potable water, water testing and water treatment. Toilet and latrine units were installed and water containers were distributed. Fogging, dislodging activities and disinfection by spraying were also conducted. Teams also held information
drive on hygiene, handwashing, food handling, vector control and solid waste management.

At present, DOH officials continue to visit the affected areas while continuous coordination, mobilization, orientation and monitoring of medical teams are being undertaken. Drugs, medicines and medical supplies are being mobilized as well.

“Rest assured that the government is doing everything to bring back normalcy and that the present condition in all affected areas is only temporary,” Ona said.

Reference:
Effectiveness of rituximab across IPI groups

Improve outcomes have been observed in patients with diffuse large B-cell lymphoma (DLBCL) upon the inclusion of rituximab, a chimeric monoclonal antibody against CD20 protein, in the standard chemotherapy that includes doxorubicin, cyclophosphamide, vincristine and prednisone (CHOP).

With the use of rituximab, researchers saw the need to reevaluate the accuracy of the International Prognostic Index (IPI) used in aggressive lymphomas. A study in 2007 found that standard IPI remained predictive but only identified two risk groups, thus the recommendation for a revised IPI (R-IPI). A more recent study, however, found that the 2007 study had methodological problems, including small study population (n=365), a source of data coming from retrospective registries, and the absence of confidence interval data and independent validation set. The more recent study, which involved a total of 1,062 patients treated in prospective trials, concluded that the effects of rituximab overlapped with the standard treatment and there were no interactions between chemotherapy and antibody therapy, demonstrating that the standard IPI was still valid in the rituximab era. Meanwhile, these results have been repeatedly confirmed by other study groups.

Rituximab in young DLBCL patients

Young, low-risk patients. Rituximab improved outcomes in young, good-prognosis patients with an age-adjusted IPI of 0 or 1. Rituximab added to six cycles of CHOP-like chemotherapy given every 21 days improved long-term outcomes for this group with a 10% increase in overall survival compared to standard chemotherapy. Studies showed that the definition of prognostic subgroups allowed for a more refined therapeutic approach.

Young, high-risk patients. For young patients with poor prognosis DLBCL having an age-adjusted IPI of 2 or 3, rituximab has also improved standard treatment. Rituximab added to conventional therapy (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone or CHOEP) given every 14 days with or without radiotherapy provides the most encouraging results to date. There was no benefit in dose intensification of chemotherapy (Mega-CHOEP) with rituximab in patients with aggressive B-cell lymphoma. Mega-CHOEP was also found to have more toxic effects.

Rituximab in elderly DLBCL patients

Elderly patients comprise two-thirds of patients in some Western countries and may belong to various risk subgroups. The RICOVER-60 study, which involved 1,222 patients 61 to 80 years of age, compared the effectiveness of six or eight cycles of 2-week intervals using standard treatment (CHOPE-14) with or without eight cycles of rituximab (“Prephase” treatment mandatory). The study concluded that the two arms with rituximab had superior progression-free survival compared to the two arms without rituximab. Only the treatment with six cycles and not eight cycles of R-CHOPE had significantly better overall survival rate compared to standard treatment without rituximab (see Figure). Paradoxically, patients in 6xR-CHOPE-14+2R rituximab received more than 8xR-CHOPE-14, because there were less early treatment terminations. This demonstrates that by giving less than eight applications of rituximab, elderly DLBCL patients are put at risk.

Two-week cycle of standard treatment with rituximab (6-R-CHOPE-14 +2R) remains comparable to the 3-week cycle of standard treatment with rituximab (8-R-CHOPE-21) in terms of efficacy and acute toxicity, and either six cycles of R-CHOPE-14+2R or eight cycles of R-CHOPE-21 are recommended in the new European Society of Medical Oncology (ESMO) guidelines. However, due to shorter time under chemotherapy (10 versus 21 weeks), and less long-term cardiotoxicity R-CHOPE-14 may offer benefit especially for the elderly population.

Studies on the pharmacokinetics of rituximab showed that sex, age and weight determine drug clearance in DLBCL, with faster clearance seen in elderly males, young females and young males compared to elderly females. Meanwhile, recent studies show that (minimum) exposure time appears to be more important than peak and trough serum levels, and too short an exposure of rituximab appears to compromise its efficacy. Early densification of rituximab resulted in higher complete remission (CR)/unconfirmed complete remission (CRu) rates in the SMARTE-R-CHOPE-14 study compared to the RICOVER-60 trial. However, longer follow up is needed to determine whether the higher CR/CRu rate will eventually translate into better event-free survival, progression-free and overall survival rates.

Elderly patients (ie, >80 years of age) with DLBCL may benefit from mini-CHOPE or a dose adjustment (cyclophosphamide: 400 mg/m² on day 1 [D1]; doxorubicin: 25 mg/m² D1; vincristine: 1 mg total dose on D1 and prednisolone 40 mg/m² by oral route from D1 to D5) plus rituximab (375 mg/m² on D1) every 21 days for six cycles. The regimen may be used as a platform when introducing new first-line drugs in this population.

Key Messages

1. The International Prognostic Index used in aggressive lymphomas remains to be valid in the rituximab era.
2. The addition of rituximab in standard treatment of DLBCL has improved outcomes across risk subgroups.
3. ESMO recommends six cycles of R-CHOPE-14 plus two cycles of rituximab or eight cycles of R-CHOPE-21.

REFERENCES:

MIMS SPONSORED SYMPOSIUM HIGHLIGHTS

Professor Michael Pfreundschuh, MD
Professor of Medicine
Saarland University Medical School
Germany

Figure: RICOVER-60 overall survival rate

Adapted from ref. 5.
Two medical doctors share their personal accounts on how the community was mobilized and how volunteerism was inspired in order to provide medical relief to the survivors of typhoon Yolanda (Haiyan). Dr. Ceres Paulino of the Yolanda Medical Relief Team recounts how a call for mission helped catapult a movement involving hundreds of healthcare providers. Dr. Donna Capili of Bayanihan Para sa Mag-Ina tells the story of how the concerted effort of doctors, mothers, individuals as well as lactation and nutritional counsellors reached out to mothers and children affected by the typhoon.

Finding heroes amidst the storm

Dr. Ceres Paulino
Yolanda Medical Relief Team

During the first 48 hours after typhoon Yolanda (Haiyan) ravaged the Visayas region, communication lines were down and information on the storm surge’s impact came from limited television reports. By the third day, the rest of the nation started to grasp how much death and devastation the storm left in its wake.

Horror stories started to come in one by one. Entire communities have been wiped out. Thousands of people were dead while the survivors were desperate for food, water and medical attention.

It was a logistical nightmare. Transportation of relief was limited to a handful of airports in the area and, even at maximum traffic capacity, not enough goods can be flown in or evacuees flown out. Ships could carry more, but during the first few days after the storm, they were not enough to meet the overwhelming demand for supplies. Hundreds of relief trucks lined the highway going to Matnog ferry port, stretching to as far as 10 kilometers while eight ferry ships struggled to transport them round-the-clock.

The local government and police forces were severely incapacitated since they themselves were victims of the storm. Stories of looting and violence started to come in, which only made relief efforts more difficult. To make matters worse, the national government seemed to fail in coordinating and commanding an efficient response to a disaster of this magnitude.

The call for mission

Upon hearing these stories, a group of doctors and I wanted to do something to help. It all started with one post on social network last November 10, the third day after the storm.

I was able to get in contact with a private
company who offered to sponsor chartered planes to areas for medical relief missions. I made a short post on Facebook, asking my doctor friends if they would like to volunteer for the mission. The response was overwhelming.

Phone calls and text messages started to pour in and soon, it became an organized effort between me and other young doctors who collected donations and put up a website to call for volunteers and support. What initially started as a plan to go on a single mission trip to Tacloban City ended up being something more. Before we know it, we had a core group of organizers, a webpage with thousands of followers, dozens of volunteer doctors and two houses full of medical donations. This was how the Yolanda Medical Relief Team started.

**Flight for survival**

Our group’s objective was to bring essential medications for children and adults and to provide basic surgical care for the injured. We soon realized that there was no governing body that coordinated relief efforts that could at least direct us where to go. We realized that were basically on our own.

Trying to pinpoint a good location, compounded by the fact that communication was down in these areas, was our first problem while transportation was the second. At this point, the plane seat had become the most precious commodity and return flights were virtually impossible to secure because everyone wanted to get out of Tacloban City.

Amidst the chaos, the group learned to find its way by talking to anyone who might know anything and by following all leads. We talked to non-government and international organizations, local government units, doctors and even locals on the ground.

Security was another issue. We were prepared for worst case scenarios and to function as a self-sufficient group. However, when news of violence in Tacloban City came out, we had to hold out until we had security escorts.

By the first week of December, the Yolanda Medical Relief Team had gone to three medical mission trips to Visayas, reaching to seven different sites in Leyte, Aklan and Antique, including Tacloban City. Thus far, we have served more than 5,000 patients and given tetanus toxoid vaccination to at least 2,000 individuals. The team was also able to provide medicines to hospitals and health units that were devastated by the storm and have been cut off from supplies.

**The resilience and strength of heroes**

For each place that we visited, we have been greatly touched by the resilience of people in spite of all their losses. The people in these affected areas who have gone through so much are the real heroes in this story. We came to help them, but we were the ones humbled by their strength, their ability to see past their losses and their will to move on.

In San Jose, a coastal community in Ta-
In Cloban, the storm surge claimed thousands of lives. The team gave extra time for each patient in order to listen as they each shared their stories on escaping death and losing friends and families. More importantly, we heard stories of how they saved other people.

A woman shared how she held on to a coconut tree as the water and 300 kph winds pounded against her. She managed to reach out to three people and save them from the flood. We saw abrasions and bruises on her arms and face that give testimony to her heroism.

One man, with multiple deep lacerations on his legs and arms, told us how he and his family were washed into the sea. He had been floating around for 3 hours before he was finally washed ashore. Two of his family members are still missing and presumed dead.

Some children from the evacuation centers would tell us of their playmates who died in the storm. A lot of people that we saw, who were poor to begin with, have not received medical attention for years. Aside from providing medical aid, we felt how the presence of the team inspired these people and made them happy.

Rising in the aftermath

There is so much to be done in the aftermath of the storm. Looking at the big picture, our team is aware that in spite of our best efforts, we can only do so much.

During conversations with typhoon survivors, I tell them that as visitors, it may seem that what we can give as a group is only a few hours to share what we have and to listen to their stories. However, I also assured them that the main reason why we go there and give all effort to help is to let them know that they are not forgotten and that many people are thinking about them. I let them know that, the whole nation has been listening to the news, worrying about them and praying for them. Most of all, I tell them that we remember them and that they are not going through this alone. Every single survivor whom I have shared this with broke down in front of me and embraced me. This amount of support means something to them. And that alone makes it all worthwhile for our team.

For Christmas, our group organized a special mission to Guiuan, Eastern Samar which is one of the poorest regions in the Philippines and among the worst hit by the storm. We are also gearing up to help rebuild and rehabilitate one of the communities in this province.

Local and international interest in the relief efforts is slowly starting to wane and hopefully, these communities can be self-sufficient again soon.

To learn more about the Yolanda Medical Relief and for details on how to help, please visit the group’s page at www.facebook.com/YolandaMedical.
Bayanihan Para sa Mag-Ina was formed initially through the efforts of the non-government organization Kalusugan ng Mag-Ina, Inc (KMI) and the breastfeeding mothers support groups L.A.T.C.H., KAYA Women Empowerment Group and Breastfeeding Pinays. Bayanihan Para sa Mag-Ina aims to protect the vulnerable infants and young children through the principles of the internationally-recommended and DOH-adopted Infant and Young Child Feeding in Emergencies (IYCF-E) strategy.

Core to this strategy is the support for and continuation of breastfeeding as this is the only reliably secure, sustainable and safe feeding method for infants and young children especially in times when there is poor sanitation and hygiene and when there is hardly any water and fuel.

The catalyst for Bayanihan Para sa Mag-Ina’s formation was two-fold - the alert by breastfeeding mom and VAB volunteer Camille Favorito about the indiscriminate distribution of breast milk substitutes (BMS) at the Villamor Airbase (VAB) and the call for donor human breast milk from the Eastern Visayas Medical Center (EVMC) for its NICU admitted babies who all survived Yolanda.

Nanay Bayanihan – a Woman and Child Friendly space at VAB

In the days following Yolanda, images of crying and distraught children moved many to help ease the suffering. When survivors arrived in VAB, it was the chance to directly help fill the perceived gap in food supply and for the babies, it came in the form of donated BMS. This well-meaning act is potentially disastrous as it undermines the capability of the breastfeeding mother perhaps irreversibly so.

BMS compromises the safety of the child’s health, increasing risk of diarrhea and death due to its intrinsic contaminants, unhygienic practices in preparation and an increased risk of malnutrition due to the propensity for diluted mixing.

On November 15, the Bayanihan Para sa Mag-Ina group was witness to BMS being scooped into a row of bottles by the clothes-
sorting volunteers. There was no facility for handwashing, no ample labelling of what age group the BMS is for and no instruction on the proper reconstitution. Gravest of all, it was handed out freely, without questions asked about the need for BMS. May, a 20 year old from Tacloban and mother to a one-month old baby girl was a recipient of this prepared feeding bottle mix along with mineral water. If anyone had bothered to ask, she was exclusively breastfeeding.

In no time at all, Nanay Bayanihan was set up at VAB to provide a caring and comforting space for pregnant women, mothers and their children aged 0 to 2 years old. The space started as a tent underneath a tree. Women and children take refuge and lie down on woven mats placed atop cardboards, with pillows strewn for their use. Lactation and nutritional counselling was provided by volunteer KMI doctors together with the breastfeeding mothers as well as the LGU based IYCF-trained and breastfeeding peer counsellors fielded by the DOH-NCR and the National Nutrition Council. Soon after, support came from Arugaan, the Philippine Pediatric Society and private individuals.

Donations of hygiene packs, clothes and toys poured in. Unbelievably, a flux of donated BMS and feeding accessories came. We explained to donors these are turned over to the DOH-NCR for safekeeping along with the education why random donations of BMS is highly unnecessary in the present circumstances. Unnecessary because mothers who arrived from Leyte and Samar were breastfeeding. Eighty-four percent of mothers with babies 0 to 6 months old were breastfeeding while seventy-nine percent of babies over 6 months to age 1 year were also breastfed.
What mothers needed at that time was affirmation and support on their ability to continue breastfeeding and the provision for their basic needs. For mothers who use BMS, they were helped to start relactation with wet nursing or cup feeding with donor breast milk available as needed. To the select few for whom BMS, as last resort, is indicated after an individualized assessment, BMS must be generic, prepared by health workers with the government ensuring clean water, fuel and cups along with sustaining it until the infant no longer required it.

The Cold Chain Project

To address alternative options for giving breastmilk, there was wet nursing and use of donated breast milk. Generous donations of breast milk were largely due to the efforts of breastfeeding mother groups in the country especially in times of disasters. Donor milk was pasteurized in Human Milk Banks such as the Philippine General Hospital, Fabella Hospital and Philippine Children’s Medical Center.

Bayanihan Para sa Mag-Ina did an assessment of need for donor human milk and when confirmed, apart from providing cold transport, cold storage at the destination site is ensured through provision of freezers and generator sets with allotment for fuel. A fundraiser resulted in a freezer and generator set delivery to the EVMC with the cargo delivered by volunteer individuals or group efforts such as the Jaycees International Makati and the Bangko Sentral ng Pilipinas. This has benefited close to a dozen babies in the hospital.

Breastfeeding missions

Intricately tied with assessing the need for a cold chain link is the conduct of breastfeeding missions wherein pregnant women and mothers with their babies are gathered in evacuation sites. Lactation and nutritional education and counselling services are provided in the Nanay Bayanihan tent at the VAB. Networking with local health and nutrition staff is made to render technical guidance or support, as needed. Not surprisingly, recent missions to Busuanga, Northern Palawan and Bogo City and Daanbantayan in Northern Cebu have shown that exclusive breastfeeding rates are high among those aged 0 to 6 months.

More work still to be done

Preparations for disaster readiness and response must include the process in delivering the standard in nutrition for the infants and young children. Bayanihan Para sa Mag-Ina is currently involved in the country’s Nutritional Cluster as support to the DOH, in writing up the operational IYCF-E guidelines intend-
ed for the first responders and embedding into management of evacuation sites and affected communities. Linkages with other government agencies are necessary to ensure that procedure is known and will be followed by all, for the sake of the children.

Breastfeeding is best for babies and it is the responsibility of physicians to be knowledgeable about supporting breastfeeding and ensure that it is successful for the Filipino mothers and children. Fostering a culture of breastfeeding and appropriate complementary feeding in normal times is key to averting the potential secondary disaster brought upon by misguided perceived needs for BMS and its use in times of emergencies.

To find out more about Bayanihan Para sa Mag-Ina and its projects, visit www.facebook.com/bayanihanIFE.
PSEM raises concern on stem cell therapy for diabetes treatment

In a press conference held last October 22, 2013, the Philippine Society of Endocrinology and Metabolism (PSEM), a subspecialty organization under the Philippine College of Physicians, presented its position paper on the use of stem cell therapy in the treatment of diabetes.

“There is as yet, no conclusive evidence that stem cell therapy is effective and safe for diabetes and as such, it cannot be made available to individuals with diabetes as a standard treatment like the usual drug prescription,” said Dr. Cecilia Jimeno, PSEM president.

The PSEM expressed its concern over patients who might easily be led to use the stem cell because of the hope for cure.

“The promise of stem cell therapy must be backed by science-and evidence-based medicine, before it can be part of the standard health care. Any clinical use of stem cell products outside of the FDA-approved indications is illegal,” added Jimeno.

Typhoon victims receive special PhilHealth privileges

The Philippine Health Insurance Corporation (PhilHealth) issued an advisory which grants special privileges to all individuals and health care providers who were affected by typhoon Yolanda.

Some of the privileges mentioned in the advisory include exemption from the 45-day benefit limit and single period of confinement for admissions directly or indirectly related to the fortuitous event, reimbursement for both referring and receiving health care institutions, and payment of valid claims due for submission that are destroyed by the typhoon. There will also be an extension on the period to file claims after discharge, deadline for submission of the required or mandatory health care institution reports and of the accreditation validity, and/or deadline for submission of application for accreditation of health care providers.

For more information, PhilHealth may be reached through any of the Regional and Local Health Insurance Offices.
MARKET WATCH

Japanese ambassador confers award to RIT/JATA

The Research Institute of Tuberculosis/Japan Anti-Tuberculosis Association (RIT/JATA) received a certificate of commendation from Japanese Ambassador Toshinao Urabe.

Tuberculosis affects about 140,000 persons in the Philippines and approximately 30,000 lose their lives to this disease each year. In the past, TB has claimed lives in Japan such that in 1939, JATA was established through a special decree from Her Majesty the Empress in order to fight the disease.

In 1992, JATA was started in Cebu City where the Cebu Regional Tuberculosis Reference Laboratory was established. The program expanded to the rest of Region 7, Manila and Quezon City. The RIT/JATA Philippines (RJPI) was eventually established with focus on raising TB awareness in urban poor communities. At present, RJPI has trained doctors, nurses and volunteers on TB treatment. At the same, it has also helped the Philippine Tuberculosis Control Program of the Global Fund in developing TB training modules.

Health groups push for graphic health warnings

In a recent forum attended by NewVois Association of the Philippines (NVAP), a group of throat cancer survivors, HealthJustice project manager Atty. Diana Triviño revealed that text-only warnings on the lower front side of cigarettes packages have not been effective in convincing the public to stop smoking.

Instead, health groups advocate the use of graphic health warnings to inform the public about the harmful effects of smoking.

“Interestingly, the Philippines was part of the key facilitators of Framework Convention on Tobacco Control Article 11 on graphic health warning requirement. Other countries are wondering why we have yet to have a law on this,” added Dr. Ulysses Dorotheo, project director at the Southeast Asia Tobacco Control Alliance (SEATCA).

The Philippines has an estimated 17.3 million adult smokers, the second highest tobacco consumers in the Southeast Asian region just next to Indonesia.
Asian conference aims for asbestos-free world

The 6th International Conference on the Asian Asbestos Initiative was recently held with the goal of raising awareness on the health hazards of asbestos. The event was organized by the Department of Health (DOH) along with the World Health Organization (WHO), International Labor Organization and the University of Occupational and Environmental Health-Japan.

According to WHO, all kinds of asbestos may cause asbestosis, mesothelioma and cancer of the lungs, ovaries and larynx and that there is no safe threshold level of asbestos exposure.

In 2012, the Lung Center of the Philippines reported 44 unregistered cases of mesothelioma with no verifiable history of asbestos exposure. However, the lack of public awareness may have led to an underestimation of asbestos-related diseases.

According to DOH secretary Enrique Ona, the most effective way to prevent diseases due to asbestos is to eliminate the use of asbestos in the future and to properly manage asbestos currently in place.

Globe HealthCloud revolutionizes healthcare delivery

During the Digital Life Congress and Expo, Globe Business officially launched the new ICT-health application called Globe HealthCloud which aims to enable real-time, secure and convenient health information access within the healthcare ecosystem.

“Globe HealthCloud harnesses the convergence of healthcare and information and communications technology. We envision Globe HealthCloud to be a catalyst of the growing acceptance of the two sectors toward health informatics – the synergy of the two aforementioned discipline,” said Francisco Claravall, Globe vice-president for IT-enabled Services Product Group.

Dealing with acne: Why the need to adapt or change?

Maria Juliet E Macarayo, MD
Member, Acne Board of the Philippines
Secretary, Philippine Dermatological Society

Acne is a condition that tends to relapse or persist for a long time. Since it can negatively affect patients’ quality of life (QoL),1-3 it must be treated appropriately. Management also entails the consideration of several factors, and treatment should not only be confined to adolescents because this condition also affects patients from other age brackets.

Acne vulgaris was the top skin disease in the Philippines in 2011 to 2012, as seen in the 11 institutions accredited by the PDS.4 Onset is commonly in adolescence, but the condition persists in 42.5% and 50.9% of adult men and women, respectively.5

Sebum production, alteration in the keratinization, Propionibacterium acnes colonization of the follicles and inflammatory events are known to affect the progression of acne lesions.6 Apart from the effect of androgenic stimulation, genetic and external factors in acne formation, P. acnes contribute to the development of acne by stimulating toll-like receptors (TLRs) present on the membranes of inflammatory cells. This evidence could also contribute to the pathophysiology of acne by acting as a neuroendocrine-inflammatory organ coordinating and executing a local response to stress and normal functions.7

Acne in younger age groups should be abated

Pre-adolescent acne (ie, acne in patients 7 to 11 years of age) is increasing in prevalence and may also be associated with earlier onset of puberty.8,9,10 This is critical because early-onset acne is believed to be associated with worse future disease severity.9 Prepubertal acne is classified as mild, moderate or severe, depending on the inflammatory lesions and comedones present and degree of scarring involved.11

Early aggressive therapy is warranted in cases of early-onset acne to limit the duration of active acne and to reduce the likelihood of physical and emotional scarring. Maintenance therapy is also necessary to attain optimal outcomes and minimize the risk of relapse.12 Major therapeutic goals in management include: resolution of existing lesions, prevention of scarring and the suppression of the development of new lesions.13,14

Different anti-acne therapies may be given to address the various factors involved in its development. Topical retinoids, for instance, work by normalizing desquamation and BP is recommended, whereas the combination of antibiotics should be avoided.12 Three months of treatment is usually sufficient to assess whether acne management is appropriate.

Several investigations using adapalene/BP combination have shown its efficacy in patients with antibiotic resistance (Figure 1).12 The adapalene/BP gel also provided significant advantages versus vehicle even in patients with severe acne, by preventing relapse and continuously improving disease symptoms for 6 months.13

Figure 1. Reduction in bacterial counts after adapalene/BP gel combination treatment

The adapalene/BP 0.1%/0.5% gel combination is the first acne treatment approved for patients younger than 12 years of age, with excellent tolerability (Figure 2). Several clinical trials have also shown that even in the adolescent age group of 12 to 17 years, the combination was effective, well-tolerated, and statistically superior to adapalene monotherapy, BP monotherapy and vehicle gel.14,15

Figure 2. Mean scores of tolerability signs for acne vulgaris in patients <12 years of age treated with adapalene/BP gel vs vehicle gel

SUMMARY

Acne vulgaris is a condition that needs serious attention because of its potentially negative effects on patients’ QoL. Antibiotic resistance is a significant concern in current acne treatment and may result in poor therapeutic response and treatment failures. Efforts must be made to minimize the development of antibiotic-resistant acne, as well as to preserve the therapeutic value of antibiotics. For instance, monotherapy with topical antibiotics should be avoided and combination treatments should be encouraged. As an anti-resistance strategy, BP is an effective anti-acne agent that may be used in combination with other agents, such as in the fixed-dose combination of adapalene/BP. This combination has proven efficacy and safety even in the presence of antibiotic-resistant acne and is a logical choice in adult and pre-adolescent patients.
Reducing salt intake improves heart, kidney health in CKD patients

Rajesh Kumar

Patients with chronic kidney disease (CKD) who reduce their salt intake can improve their heart and kidney health, according to a small randomized, placebo-controlled trial.

The LowSALT CKD crossover study compared the effects of high (180 to 200 mmol/day) and low (60 to 80 mmol/day) sodium intake on ambulatory blood pressure (BP), 24-hour protein and albumin excretion, fluid status, renin and aldosterone levels, and arterial stiffness in 20 adult patients with hypertensive stage 3-4 CKD. [JASN 2013; doi:10.1681/ASN.2013030285]

Overall, reducing salt intake by roughly one tablespoon per day resulted in statistically significant and clinically important reductions in BP (mean reduction of systolic/diastolic BP, 10/4 mmHg; 95% CI 5-15 /1-6 mmHg), extracellular fluid volume, albuminuria, and proteinuria. The magnitude of change was more pronounced than for that reported in patients without CKD, suggesting that patients with CKD are particularly salt-sensitive.

“The BP reduction (of 10/4 mm Hg) is comparable to that achieved with antihypertensive drugs and is larger than that usually seen in studies of people with normal kidney function,” said researcher Dr. Katrina Campbell, senior research fellow at the Nutrition & Dietetics Department, Princess Alexandra Hospital in Brisbane, Queensland, Australia.

“If maintained long-term, this could reduce risk of stroke by up to 40 percent and coronary heart disease by 20 percent in people with CKD.”

Co-researcher Ms. Emma McMahon, a Ph.D. candidate at the same university, was particularly impressed with the 50 percent reduction in protein excretion in the urine.

“If maintained long-term, this could reduce risk of progression to end-stage kidney disease by 30 percent,” she said.

The current guideline recommends salt reduction, but patients are often unable to strictly adhere to it. The findings suggest
that salt restriction is an inexpensive, low-risk and effective intervention for reducing cardiovascular risk and risk of worsening kidney function in people with CKD.

“If these findings are transferable to the larger CKD population and shown to be sustainable long-term, this could translate to markedly reduced risk of cardiovascular events and progression to end-stage kidney disease, and it could generate considerable health-care savings,” said Campbell.

In an accompanying editorial, Drs. Cheryl Anderson and Joachim Ix of the University of California San Diego School of Medicine in San Diego, California, US, commended the researchers for providing important clinical trial data in support of current clinical practice consensus guidelines, noting that “this study makes us cautiously optimistic.”

Larger studies with longer follow-up specifically designed and carried out in CKD populations are needed to help inform recommendations to both individual patients and policymakers, they added.
Weight loss reduces AF burden in obese patients with AF

Elvira Manzano

Weight loss, combined with intensive management of cardiometabolic risk factors, resulted in fewer episodes of atrial fibrillation (AF) and lower symptom burden in obese patients with AF compared with risk factor management alone, according to a study in Australia.

After a mean follow-up of 15 months, patients on intensive intervention had a significantly greater reduction in AF symptom burden scores compared with controls (11.8 points vs 2.6 points; p=0.001), symptom severity scores (8.4 vs 1.7 points; p=0.001), and number of episodes (2.5 vs no change; p=0.01). Moreover, cumulative duration of AF decreased by 692 minutes in the intervention group but increased by 419 minutes in the control group (p=0.002). Weight loss was also greater in the intervention group (14.3 kg vs 3.6 kg; p=0.001). [JAMA 2013;310:2050-2060]

“Weight loss combined with risk factor management also proved beneficial for cardiac remodeling,” said study author Dr. Prashanthan Sanders, director, Centre for Heart Rhythm Disorders, University of Adelaide, Australia. The new findings are important given that no studies have shown that risk factor management was beneficial in AF. “Hence, therapy directed at weight and risk factors should be a normal part of AF management,” he added.

The study involved 150 adult patients with paroxysmal or persistent AF, a BMI >27 kg/m², and waist circumference of >90 cm for women and >100 cm for men. All patients received intensive risk factor management, including medications to control blood pressure, cholesterol and blood sugar, as required. Sleep apnea, alcohol and tobacco use were also managed. Thereafter, patients were randomized to weight loss intervention consisting of a strict diet and exercise, behavioral modification and personal clinic visits every 3 months or general lifestyle advice on nutrition and exercise.

The primary outcome was AF symptom burden (measured through the Atrial Fibrillation Severity Scale). Score ranges from 3 to 30, with higher scores indicating greater AF burden. AF events, atrial size and interventricular septal thickness were tracked at baseline and at 12 months using Holter and ECG monitors, respectively.

Results showed reductions in the interventricular septal thickness of 1.1 mm for the intervention group and 0.6mm for the control group (p=0.02). For the left atrial area, reductions were 3.5cm² and 1.9 cm², respectively (p=0.02).

Sanders said it is impossible to separate obesity from other risk factors. When a person loses weight, his diabetes also improves and sleep apnea and hypertension also seem to go away. The study thus pointed to one of treating weight and risk factors, he added.

“Similar to our approach with patients who have coronary artery disease, risk factor and weight management should be considered standard for any patient with AF.”
Short-term orlistat use not linked to raised colorectal cancer risk

Lianne Cowie

Preclinical studies have suggested that the use of the anti-obesity drug orlistat significantly increases the number of aberrant colonic crypt foci, and may thus increase the risk of colon cancer. However, the suggestion remains controversial. Now, a population-based study from the UK has found no evidence of an increased risk of colorectal cancer after short-term use of orlistat.

Orlistat is currently the top selling drug in the global market of anti-obesity drugs, with worldwide sales of US$663 million in 2011, said the study researchers. “Given such extensive use of orlistat, the lack of data from population based studies on its effects on the risk of colorectal cancer is a major concern.”

The retrospective, matched-cohort study evaluated the risk of colorectal cancer after orlistat initiation by analyzing data from September 1998 to December 2008 from the UK Clinical Practice Research Datalink.

A total of 33,625 adults aged ≥18 years who began to take orlistat were each matched with up to five non-initiators (160,347) by age, sex, body mass index (BMI), and calendar time. The median age of the 193,972 individuals evaluated was 47 years; 77 percent were women and approximately 90 percent were obese (BMI ≥30).

Compared with non-initiators, orlistat initiators were more likely to have a history of diabetes or hypertension and to receive prescriptions for anti-diabetes drugs, statins, and aspirin. [BMJ 2013;347:f5039]

An intention-to-treat analysis identified 57 colorectal cancer events among orlistat initiators compared with 246 among non-initiators (median follow-up 2.96 and 2.86 years, respectively).

The incidence rate of colorectal cancer per 100,000 person years was 53 (95% CI 41–69) and 50 (95% CI 44–57), respectively. The adjusted hazard ratio of 1.1 (95% CI 0.84–1.47) indicated that orlistat initiation was not associated with a greater risk of colorectal cancer. This finding did not differ in the as-treated analysis or in patients aged ≥50 years, the morbidly obese, and those with a history of diabetes.

“Our study provides no evidence of an increased risk of colorectal cancer after starting orlistat treatment in UK adults,” concluded the researchers.

“The study is limited by the relatively short follow-up time, and we cannot exclude the possibility of adverse effects of long term orlistat use on risk of colorectal cancer.” They added: “Our study, based on a large, population based healthcare database, represents people actually taking orlistat in the real world, who tend to be different from the participants in clinical trials.”
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High intake of plant-derived omega-3 polyunsaturated fatty acid (alpha-linolenic acid, ALA) during childhood and adolescence by individuals who were underweight at birth may provide lasting benefits equivalent to years of statin or antihypertensive treatment in older adults predisposed to vascular disease.

“Dietary or supplemental intake of ALA may at least partially prevent the well-established association of impaired fetal growth with atherosclerotic vascular disease and raised blood pressure (BP),” said Dr. Michael Skilton, senior research fellow at the Boden Institute of Obesity, Nutrition, Exercise and Eating Disorders at the University of Sydney in Australia.

Impaired fetal growth is known to increase arterial wall thickening, which in turn is a cardiovascular risk factor predictive of heart attack or stroke. Measuring arterial intima-media thickness (IMT) can be a good proxy for ascertaining later cardiovascular disease, Skilton said.

The lifestyle intervention STRIP* study randomized 1062 children aged 6 months to individualized dietary and lifestyle counseling to reduce known environmental risk factors for atherosclerosis or typical information given in well baby doctor visits and school healthcare.

Data on complete birth weight, gestational age and at least one blood pressure measure was available for 1,009 children, of which 115 (11 percent) were small for gestational age (SGA, birth weight ≤10th percentile for gestational age and gender). The children were followed up every 6-12 months until age 19, when aortic IMT was assessed by ultrasound (n=413).

In SGA-born children and adolescents, increased ALA intake was inversely related to BP. For each 100 percent increase in dietary ALA, systolic BP fell 2.1 mm Hg (p=0.001), diastolic BP fell 1.2 mm Hg (p=0.01) and pulse pressure fell 1.4 mm Hg (p=0.01). This relationship was conserved in subjects with normal birth weight.

“The omega-3 fatty acids are having an effect on BP irrespective of birth weight – it’s an effect across the board,” Skilton said.

Average long-term ALA intake was similarly inversely associated with aortic IMT at age 19 in SGA children, with a 0.30 mm Hg reduction per 100 percent higher dietary ALA intake (p=0.008). However there was no such association among children of normal birth weight.

In fact, the researchers never reported an association between ALA intake and IMT in normal birth weight children. However, split into tertiles, SGA children with the lowest ALA intake had the highest aortic IMT, those with an average intake had IMTs similar to the normal birth weight group, while those with the highest intake had the lowest IMT (p for interaction = 0.005).

The difference between the highest and lowest ALA intake tertiles equates to about

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DOHaD 2013: 8th World Congress on Development Origins of Health and Disease, November 17-20, Singapore

More omega-3 in childhood as good as years of statin and antihypertension meds

Radha Chitale
30-50 percent increase in dietary ALA, which in small children is equivalent to about one to two walnuts per day, which Skilton noted was a small dietary change.

However, the resulting 0.08-0.14 mm decrease in aortic IMT and 0.03-0.05 mm decrease in carotid IMT is “equivalent to the projected benefits of about 3-5 years of statin treatment in hypercholesterolemic adults, or about 5-8 years of antihypertensive treatment in adults with hypertension,” Skilton said.

* STRIP: Special Turku Atherosclerosis Risk Factor Intervention Project for Children

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**Current diabetes tests for pregnant women inadequate**

**Radha Chitale**

Current tests for identifying women, during pregnancy or postnatally, who may be at risk for developing type-2 diabetes leave many women overlooked and untreated.

Identifying such women can help implement lifestyle changes to delay progression to diabetes, said Dr. H. Venkataraman of the University of Warwick in the UK, “therefore postnatal screening is a unique window of opportunity in these women, not only to prevent progression to type 2 diabetes but also to prepare them for the next pregnancy.”

However, different advisory groups such as the American Congress of Obstetricians and Gynecologists and the International Workshop on Gestational Diabetes Mellitus fail to show a consensus for how to identify women at risk – whether to use fasting plasma glucose (FPG) or oral glucose tolerance tests (OGTT), and when.

These inconsistencies are reflected in practice, Venkataraman said.

To determine if fasting plasma glucose is enough to screen for diabetes, and what the threshold should be, Venkataraman and her team conducted retrospective study of 1289 women in the UK with gestational diabetes prevalence of 9.7 percent. About half of this group returned for postnatal screening and 13 percent had abnormal results, predominantly in Caucasian women (64 percent) but also among South Asians (27 percent). The South Asians tended to be younger, had higher body mass index and lower offspring birth weight.

However, both South Asians and Caucasians had similar postnatal fasting plasma glucose rates, though postnatal 2-hour plasma glucose rates were higher in South Asians. Postnatal oral glucose tolerance tests were normal in 86 percent of the population. The most common abnormality in all the tests was 2-hour glucose abnormality, of 7 percent. Diabetes prevalence was 1.7 percent.

If the postnatal fasting plasma glucose cutoff were 6 mmol/L, Venkataraman said they would have missed 53 percent of all glucose
abnormalities and two cases of diabetes. If the fasting plasma glucose cutoff were lowered to 5.6 mmol/L, they would still miss 30 percent of abnormalities and one case of diabetes.

A two-step glucose testing approach using FPG at two different time intervals at a cutoff of 6 results in 93 percent fewer OGTTs, Venkataraman said, which was good, but such a regimen would miss about 1/5th of the diabetes cases and 86 percent of patients with impaired glucose tolerance. Dropping the cutoff to 5.6 similarly would miss 10 percent of diabetics and 57 percent of those with impaired glucose tolerance.

“Therefore, fasting plasma glucose is not a good test at current cutoff levels,” she said. “FPG alone is not the answer in... a mixed ethnic population. Using FPG postnatally misses more South Asians than Caucasians.”

Future directions include tailored tests to look at antenatal blood glucose before deciding postnatal test and possibly a combined HbA1c and FPG testing regimen, Venkataraman said.

Metabolic phenotype influenced by ethnicity, environment

Radha Chitale

Understanding differences in metabolic phenotype among Singapore’s different ethnic groups can help tailor guidelines and therapies and help implement effective prevention and early intervention strategies for a range of chronic diseases.

“Ethnicity is not simply your genes, it’s also your environment and practices,” said Dr. Yap-Seng Chong, senior consultant in the Department of Obstetrics and Gynaecology at Singapore’s National University Hospital. “Genetics accounts for only about 10 percent of a person’s susceptibility to type 2 diabetes... [Metabolic] data are scarce for many ethnic groups and only a few qualitative studies have focused on these communities.”

Chong used data from GUSTO (Growing up in Singapore Towards Healthy Outcomes), the large birth cohort study on the effects of maternal and infant diet and lifestyle on growth, to examine variations in maternal and child body mass index (BMI) and diabetes, both indicators for other chronic diseases later in life.

Singapore’s population is about 75 percent Chinese, 13 percent Malay, 9 percent Indian and 3 percent other, which the GUSTO cohort roughly reflects.

“Increased birth weight did not correlate to GDM across ethnicities”

Diet analysis showed that Indians eat less protein and more carbohydrates and fiber compared with Chinese or Malays. Chinese people eat more food from outside the home while Indians consume the least, in addition
to eating less meat.

After testing for gestational diabetes mellitus (GDM), the prevalence in the whole cohort was 18.9 percent. Chinese and Indian women had significantly higher GDM prevalence (21 and 22.3 percent, respectively) compared with Malays (12.1 percent), but the risk factors varied among the three groups.

A previous history of GDM was associated with increased GDM risk among both Chinese and Malay mothers and Malays also had increased GDM risk with obesity. However, neither of these risk factors were associated with significant GDM risk in Indians.

However, increased birth weight did not correlate to GDM across ethnicities. Despite similar GDM figures between Malay and Indian women, Malay babies had between 4-5 times the risk of being in the 90th percentile for birth weight when born to mothers with GDM while Indians were more than 5 times as likely to be in similar percentiles.

Insulin sensitivity was strongly associated with ethnicity as well, with Indians already exhibiting low insulin sensitivity even at modest BMIs of 18, and it decreased further as they put on weight. Overweight Chinese and Malay subjects had similar insulin sensitivity to Indians, but were responsive to weight loss, and improved their sensitivity at lower BMIs.

“Possibly the driver of insulin sensitivity is actually the fat in Malays and Chinese and maybe muscle in Indians,” Chong said. “Understanding the ‘Asian Phenotype’... [shows that] one size does not necessarily fit all.”
Early development affects fat deposits in newborns

Rajesh Kumar

A study involving whole body MRI scans of newborn infants found that those from certain ethnicities, relatively higher birth weight and born to mothers with gestational diabetes had higher reserves of deep subcutaneous fat, even when their mean birth weight was well below clinical macrosomia.

Deep subcutaneous fat is metabolically as important as visceral fat, which is linked to obesity and metabolic diseases. The findings suggest that circumstances during the time of conception, at the time of birth and in early infancy can affect the early development biology of the fetus.

The researchers in Singapore’s first birth cohort study GUSTO* performed the scans on 334 healthy new born infants of Chinese, Indian and Malay ethnicities (>34 weeks gestational age and >2 kilogram birth weight) within 7 to 10 days after delivery. Of these, 22 infants came back for a repeat MRI in 6 weeks and 31 came back at 6 months.

Adipose tissue was categorized as superficial subcutaneous (ssc) fat, deep subcutaneous (dsc) fat and internal fat.

When compared with the Chinese infants, the infants of Indian and Malay ethnicities had higher dsc adiposity at one week of age. Indian infants had 8 percent more ssc and 22 percent more dsc fat compared to the Chinese infants, despite their lower birth weight. No significant difference was found in internal fat deposits.

Also, maternal gestational diabetes was associated with greater subcutaneous fat deposits in offspring at 1 week. In different birth tertile groups, the same association was seen in the highest tertile group only, even though the mean birth weight in this group was 3.6 kilograms, which is well below the clinical definition of macrosomia.

The researchers also noticed a disproportionate abdominal adipose tissue gain relative to the infants’ overall weight gain in the first 6 weeks of life, compared to subsequent growth in this group.

During early development, the fetus receives early cues from the mother about the predicted environment that he or she is going to encounter after birth and makes the modifications to improve its immediate chance of survival. The phenomenon has earlier been described as predictive adaptive response.

GUSTO Research Associate Dr. Mya Thway Tint of the department of obstetrics and gynecology at the National University of Singapore (NUS) said these adaptations can cause long term variability in phenotype.

If faced with under nutrition in-utero, the fetus prioritizes liver blood flow leading to synthesis of fatty acids and subsequent fat deposition. And in circumstances of nutrient excess or excess blood glucose due to maternal obesity or insulin resistance, the excess glucose and other nutrients transferred through the placenta are stored by the fetus as fat. This propensity to store fat leads to increased adipose tissue deposition.
“An understanding of these differences will facilitate development of specifically targeted and more efficacious interventions from early life,” said Mya. The study is ongoing.

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**Early-life diet may influence risk of chronic disease in adulthood**

Elvira Manzano

Early life nutrition has long-term effects and influences the risk of chronic disease in adulthood, a new study shows.

“There is a cause for concern about the later health consequences of diet composition during early life. It appears that the latter part of the first 2 years of life provides opportunities for dietary intervention to prevent adult cardiometabolic diseases [CMDs],” said researcher Dr. Nanette Lee from the Office of Population Studies Foundation, Inc., University of San Carlos in Cebu City, Philippines.

The study examined the effects of protein and fat intake from complementary foods at 6, 12, 18, and 24 months on young adults’ body mass index (BMI), waist circumference (WC), body fat (BF), blood pressure (BP), fasting glucose (FG) and lipid profiles -- total cholesterol (TC), low and high density lipoprotein cholesterol (LDL, HDL) and triglycerides (TG). Researchers used data from 1,613 individuals from the Cebu Longitudinal Health and Nutrition Survey who were born between 1983 and 1984. Diet data in the first 2 years of life were collected prospectively from the mother using a 24-hour recall. Exclusively breastfed infants were excluded from the analysis.

Overall, fat and protein intake from weaning foods was associated with lipid levels at a mean age of 21 years. Fat intake at 18 months was associated with high total and LDL cholesterol levels, while protein intake at 12 months was associated with low HDL cholesterol levels. Similarly, fat and protein...
intake in early childhood was associated with obesity measures in adulthood, for example, protein intake at 18 months was associated with being overweight as was fat intake at 18 and 24 months. Moreover, fat intake at 24 months was significantly associated with adult WC and percent body fat. There were no significant early diet effects on TG, BP and FG. The effects were similar for both genders.

The analysis sample included only singleton births. Outcome variables were measured in 2005 when subjects were between age 20 and 22 years.

“The prevalence of cardiometabolic risk factors in our sample was already relatively high,” Lee said. “Females were more likely to have high total and LDL cholesterol and higher WC while males were more likely to have low HDL cholesterol, high TG levels, high BP and were overweight.”

Dairy (formula milk and other milks) was an important source of protein across all time points, although its contribution was reduced as children got older. Infant cereal was the top source of protein at 6 months, while fish and bakery products beginning 12 months and onwards. Milk and coconut oil (used for cooking) were the main sources of fat at 6 months. The use of coconut oil increased as children got older.

Previous studies have shown that a higher animal intake, especially for the source of dairy and protein, at 12 months was positively associated with body fatness at 7 years. [Am J Clin Nutr 2007;86:1765-1772] However, there was paucity of relevant studies from developing countries like the Philippines.

The current findings are particularly important in developing and transitioning countries like the Philippines where CMDs are among the leading causes of morbidity and mortality. Although clear policies on breastfeeding, as well as the timing of complementary feeding, are in place in the country at this time, the quality of the weaning diet still has to be emphasized to mothers, Lee added.

“Interventions to reduce the risk of chronic disease in future generations should include dietary change in early life.”
Maternal depression affects child’s outcomes, health later in life

Elvira Manzano

Maternial depression during pregnancy and after birth influences a child’s outcomes, with potential adverse and long-term effects on health later in life.

“Depression in pregnancy can increase the chances of having a premature or low birth weight baby, with altered set-point of hypothalamic-pituitary-adrenal (HPA) axis that can result in long-term neuropsychiatric sequelae,” said Professor Rebecca Reynolds, Honorary Consultant Physician from the University of Edinburgh, UK.

Similarly, severe stress and anxiety in pregnancy can cause affective and behavioral problems such as mood swings, increased fearfulness, sleep problems and lower cognitive performance in infants, Reynolds said. Depression was also linked to attention deficit hyperactivity disorder (ADHD) and schizophrenia in children and adults, respectively.

Children whose mothers experienced prenatal depressive symptoms were at increased risk of having depression themselves at age 18. They were 1.28 times more likely to have depression for each standard deviation increase in maternal depression score during pregnancy (p=0.003). Moreover, postnatal depression was a risk factor for mothers with low education, with offspring 1.26 times more likely to have depression for each standard deviation increase in postnatal depression score (p=0.01). For more educated mothers, there was little association between postnatal depression and offspring depression (p=0.42). [JAMA Psychiatry 2013; doi:10.1001/jamapsychiatry.2013.2163]

“This suggests that treating maternal depression antenatally could prevent child depression during adulthood,” said Reynolds. “We don’t know the underlying mechanisms yet but glucocorticoids, neurotransmitters and diet may play an important role.”

Previous studies have shown that increased maternal anxiety was associated with increased fetal exposure to maternal cortisol, the primary stress hormone. Normal levels of cortisol have neutral effects on the brain but excessive amounts can cause alterations in the hippocampus (responsible for memory) and amygdala (responsible for mood and emotions).

Sustained exposure to glucocorticoids may lead to fetal growth restriction, impairment in neurological development, insulin resistance, hypertension, and altered HPA responsiveness in later life, Reynolds said.

Findings from Reynolds’ own study, now under review, showed that maternal depression is linked to serotonin transfer, increased placental sensitivity to glucocorticoids and 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD-2) and the glucocorticoid receptor (NR3C1), two placental genes implicated in the transfer of maternal glucocorticoids to the developing baby.

“These findings support the need for interventions targeting maternal depression early in pregnancy,” Reynolds concluded.
Treatment Updates on Diabetes and Lipid Disorders

Find out what these experts have to say about upcoming treatments for diabetes and lipid disorders and the risks related to obesity

Dr John Foreyt
Lifestyle approaches to manage weight loss in obese patients through exercise and dietary modifications

Professor Christophe de Block
Risks associated with obesity and the benefits of early prevention

Professor Brian Tomlinson
Future therapies to treat familial hypercholesterolemia and difficulties in measuring the prevalence of this disease in Asia

Dr David Sullivan
Effective therapies for dyslipidemia when statins are insufficient and future treatments in development

Professor Jonathan Shaw
The importance of glucose control associated with cardiovascular risk and the safety of DPP4-I and GLP-1 treatments

Professor Helena Gylling
The effective use of plant sterols and stanols in lowering LDL-cholesterol and how these products can be used to treat dyslipidemia

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Type 2 Diabetes (T2DM) is an increasingly epidemic in Asia. A substantial proportion of T2DM patients have complications or comorbidities, which makes the selection of drug therapy more challenging. Effective and well-tolerated treatment options are needed for T2DM patients aged 65 years or older and those with pre-existing hepatobiliary diseases. New data on the role of linagliptin in managing T2DM in such populations were presented at the 2013 International Conference on Diabetes and Metabolism and 5th Asian Association for the Study of Diabetes (AASD) Annual Scientific meeting.

Introduction
With the largest number of diabetes and pre-diabetes patients in the world, Asia is at the epicentre of the current global diabetes epidemic. Studies indicate that pathophysiology of T2DM differs somewhat in Asian compared to Caucasian populations. Asians develop diabetes at a younger age and at a lower BMI levels and may be more predisposed to β-cell dysfunction. Asian patients with T2DM have a higher risk of developing renal complications than Caucasians and, with regard to cardiovascular complications, a predisposition for developing strokes.

The high prevalence of comorbidities such as renal impairment and hepatobiliary disease in Asian patients with T2DM makes the selection of drug therapy more challenging. Fortunately, various new therapies have been added to the treatment armamentarium for T2DM, notably DPP-4 inhibitors. DPP-4 inhibitors prevent the breakdown of endogenously produced incretins, such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), which stimulate insulin secretion, inhibit glucagon secretion, and suppress appetite in a physiological manner. To date, five DPP-4 inhibitors are licensed globally for T2DM, namely sitagliptin, vildagliptin, saxagliptin, alogliptin (not currently available in Southeast Asia), and linagliptin. Linagliptin is a 2nd generation DPP-4 inhibitor that directly binds to the active site of the target enzyme, providing inhibition for 24 hours. Linagliptin is unique among other DPP-4 inhibitors in that it is excreted unchanged via bile and gut. Linagliptin has a safety profile similar to placebo and no dose adjustments are required in patients with renal or hepatic impairment.

In addition, recent evidence has confirmed the efficacy and safety of linagliptin in adults with T2DM and liver disease, as well as in Asian people aged 65 years or older with T2DM.1-11

Efficacy and tolerability in patients with T2DM and previous/current hepatobiliary disease
Given that the major elimination of linagliptin via the enterohepatic system, it is particularly important to further characterise the efficacy and safety of linagliptin in T2DM patients with liver and biliary complications.

A pooled analysis of 17 double-blind placebo controlled randomised clinical trials investigated the efficacy and tolerability of linagliptin in people with T2DM and self-reported previous/current liver and biliary disease. The analysis included 614 patients with hepatobiliary disorders (linagliptin: n=412, placebo: n=202) and 6244 patients without hepatobiliary disorders (linagliptin: n=4120, placebo: n=2124). The populations evaluated were well matched in terms of baseline demographic characteristics and had similar rates of renal impairment.

Hepatic steatosis was the most frequently reported pre-existing hepatobiliary disorder, affecting 55.2% of patients in the study population. Gallbladder pathology was also common, as 22.7%, 10.1% and 2.9% of patients had cholelithiasis, cholecystitis and gallbladder polyps, respectively. Linagliptin demonstrated a statistically significant placebo-adjusted reduction in HbA1c of 0.52 and 0.62 percent in patients with- and without hepatobiliary disorders, respectively, from baseline to 24 weeks (Figure 1). Linagliptin also reduced mean adjusted fasting plasma glucose (FPG) in both groups regardless of hepatobiliary status. On the other hand, placebo was associated with increases in FPG in both groups. Linagliptin was well-tolerated in patients with or without hepatobiliary disease. The overall incidence of adverse events (AEs) compared with placebo was similar for hepatobiliary (65.1% vs 68.0%) and non-hepatobiliary patients (56.7% vs 62.0%). Rates of serious AEs versus placebo were also similar between the hepatobiliary (7.9% vs. 9.9%) and the non-hepatobiliary group (4.7% vs. 6.6%). Fewer patients in the linagliptin group experienced drug related AEs than placebo (12% vs 15.3% hepatobiliary; 11.6% vs. 13.6% non-hepatobiliary).12

Based on this analysis, linagliptin is an efficacious and well-tolerated treatment option for patients with T2DM and hepatobiliary disease.

Efficacy and safety in Asian elderly patients with T2DM
A second pooled analysis investigated the efficacy and safety of linagliptin (as monotherapy or in combination with common anti-hyperglycaemic drugs) in Asian people aged 65 years or older with or without uncontrolled T2DM.

Linagliptin demonstrated a statistically significant reduction in HbA1c of 0.90%, compared to a 0.08% reduction with placebo, resulting in a treatment difference of 0.82% after 24 weeks (Figure 2).12 Overall incidence of adverse events (AEs) or serious adverse events (SAEs) with linagliptin was similar to placebo (AE 53.6% vs 61.9% and SAE 4.5% vs. 6.9%, respectively).12 Drug-related AEs were lower in the linagliptin arm than with placebo (12.6% vs. 17.5%, respectively); as was the occurrence of investigator-defined hypoglycaemia (9.5% vs. 18.1%, respectively).12

The incidence of symptomatic hypoglycaemia events was similar to placebo (1.1% vs 1.5%) when patients were not on insulin or sulphonylurea background therapy.12

Efficacy and Safety in Asian patients with uncontrolled T2DM
A subgroup analysis investigated the safety and efficacy of linagliptin in Asian patients with T2DM for up to 2 years. Asian patients from four 24-week clinical trials and a 78-week open label extension were analysed. Patients initially randomised to linagliptin and continued on linagliptin therapy were treated for a total of 102 weeks (Group A: n=646), while patients initially randomised to placebo and switched to linagliptin were treated for 78 weeks (Group B: n=246).

Results showed that glycaemic control was sustained for up to 2 years with linagliptin as monotherapy or in combination with other oral antidiabetes drugs, with a mean reduction in HbA1c of 0.7% in both groups.11 Long term therapy with linagliptin was well tolerated, with no new clinically relevant safety signals emerging. The occurrence of hypoglycaemia was similar for Group A and Group B (18.9% vs 21.2%, respectively).11 More than 90% of patients experiencing hypoglycaemia received background sulphonylurea therapy.12

References
10. Study 1123 (Hypoglycaemia and Resolution of Hyponatraemia in Patients with Type 2 Diabetes Mellitus) T2DM. Boehringer Ingelheim International GmbH. Germany, 2010.
11. Study 1123 (Hypoglycaemia and Resolution of Hyponatraemia in Patients with Type 2 Diabetes Mellitus) T2DM. Boehringer Ingelheim International GmbH. Germany, 2010.
Pharmacist-led intervention improves CV medication adherence in patients with ACS

Elvira Manzano

A pharmacist-led intervention after acute coronary syndrome (ACS) improved patient adherence to cardiovascular medicines, but this did not translate to immediate clinical outcomes.

The multicenter trial of 253 adult patients (mean age 64) with acute myocardial infarction (MI) or unstable angina showed that after 1 year of intervention, patients were more likely to be adherent to essential cardiovascular medications compared with those who received usual care (89.3 percent vs 73.9 percent; p=0.003). [JAMA Intern Med 2013; doi:10.1001/jamainternmed.2013.12944]

However, better adherence did not translate to statistically significant differences in blood pressure (59 percent vs 49 percent; p=0.23), low density lipoprotein cholesterol (LDL-C) levels (72 percent vs 83 percent; p=0.140) or rates of clinical outcomes between the intervention and control groups. Mortality (9 percent vs 7.6 percent; p=0.86), MI (6.6 percent vs 4.2 percent; p=0.60) and revascularization rates (11.5 percent vs 17.6 percent; p=0.24) were comparable between the two groups.

“These medications are important for patients after they’ve been hospitalized for ACS ... In terms of the clinical outcomes, I think part of the reason for not seeing a difference is the relatively short duration of follow-up,” said researcher Dr. Michael Ho of the Denver Veteran Affairs Medical Center in Colorado, US.

Patients were randomized before discharge to an intervention (consisting of pharmacist-led medicines reconciliation and tailoring, patient education and regular messaging to remind them to take medicines and refill their prescriptions), or to usual care. The primary outcome was the proportion of patients who were adherent to cardioprotective medications (clopidogrel, statins, beta-blockers and angiotensin converting enzyme inhibitors or angiotensin receptor blockers) in the year following discharge, with adherence based on a mean proportion of days covered greater than 0.80 (calculated from pharmacy refill data). Each intervention patient received at least 4 extra hours of pharmacist time.

“The pharmacist input is important in terms of having someone available to address patient-specific questions and/or problems,” said Ho. “Because non-adherence can be related to a variety of reasons and the reasons can change over time, it is important to have someone available and with knowledge of the medications to address potential reasons for non-adherence.”

Moving forward, Ho said a follow-up trial is needed to determine if differences in outcomes would become apparent in the longer term.

Commenting on the study, Associate Professor Alexandre Chan of the Department of Pharmacy, National University of Singapore (NUS), said the study is interesting as it did not only evaluate clinical outcomes, but ad-
herence rates and cost-savings as well. He added that the components included in the intervention program were, however, not unique.

The findings further confirm the important roles pharmacists play in a multidisciplinary team to optimize patients’ treatment outcomes, Chan concluded.
GSK will stop paying doctors for promoting its drugs and will launch a new way to compensate its sales force by ditching individual sales targets. The move comes amidst a scandal in China where the local police is accusing the company’s top brass of funneling up to 3 billion yuan to travel agencies to facilitate bribes to doctors and officials to encourage prescription of its drugs.

In a media release, GSK said it intends to stop “direct payments to healthcare professionals for speaking engagements and for attendance at medical conferences” in all the countries it operates in. Instead, the focus will shift to strengthening GSK’s own medical and scientific capability to engage with healthcare professionals and a greater use of multiple channels, including digital technologies, to provide appropriate product and disease area information to healthcare professionals.

The company will however support “fair, balanced and objective” medical education for healthcare professionals through provision of unsolicited, independent educational grants.

“The measures are designed to bring greater clarity and confidence that whenever we talk to a doctor, nurse or other prescriber, it is patients’ interests that always come first. We recognize that we have an important role to play in providing doctors with information about our medicines, but this must be done clearly, transparently and without any perception of conflict of interest,” said GSK Chief Executive Sir Andrew Witty.

Fees for services to healthcare professionals for GSK sponsored clinical research, advisory activities and market research will continue. “These activities are essential in providing GSK with insights on specific diseases; identification of symptoms and diagnosis; application of clinical trial data or medication dosage and administration; and how to effectively and appropriately communicate the benefits and risks of its medicines to help meet patient needs,” said the media release.

“The company will also continue to invest in community programs to strengthen healthcare infrastructure, particularly in least developed countries.”

GSK already discloses the payments it makes to healthcare professionals in countries including Australia, France, Japan, the UK and the US, as per local guidelines, and plans to work towards transparency in other countries as well. The company said it intends to work through the practical details of these changes with healthcare professionals, medical organizations and patient interest groups to define how they can be implemented effectively and in line with local laws and regulations. This consultation begins this year for the changes to be in place across GSK’s global business by early 2016.
Exercise programs prevent fall-related injuries in elderly

Falls are common among the elderly and resulting injuries frequently require medical attention. A recent meta-analysis found exercise intervention programs to be effective in preventing fall-related injuries.

The meta-analysis included 17 randomized controlled trials involving a total of 4,305 community dwelling older (>60 years) adults. The participants had been randomized to undergo a fall prevention exercise intervention (n=2,195) or to act as controls (n=2,110). The mean age of the participants was 76.7 years and 77 percent were women. The exercise interventions included group and/or home exercise, individualized exercises, Tai Chi, programs with gait, balance and functional training components, and strength/resistance training.

Exercise was found to have a significant effect on four categories of falls. The pooled rate ratio for all injurious falls was 0.63 (95% CI 0.51–0.77, 10 studies, I²=50%, p=0.04) and that for severe injurious falls resulting in fractures, head injury, soft tissue injury requiring suturing or any other injury requiring hospital admission was 0.70 (95% CI 0.53–0.92, 8 trials, I²=20%, p=0.027). The pooled rate ratios for falls resulting in medical care and falls resulting in fractures were 0.57 (95% CI 0.36–0.90, 7 trials, I²=46%, p=0.09) and 0.39 (95% CI 0.22–0.66, 6 trials, I²=0, p=0.96), respectively.

A recent study modeled the effects of a proposed 20 percent tax on sugar-sweetened drinks on rates of obesity and overweight in the UK.

Census data on obesity and overweight rates were combined with data extracted from the Living Costs and Food Survey 2010, the National Diet and Nutrition Survey 2008 to 2010, the Health Survey for England 2010, and the Scottish Health Survey 2010 to estimate average expenditure on sugar-sweetened drinks among the total population as well as drink consumption by income (low, middle and high income) and age (16-29, 30-49, and >50 years).

The 20 percent tax was estimated to reduce the number of obese adults (body mass index [BMI] ≥30) in the UK by 1.3 percent (95% CI 0.8-1.7 percent), the equivalent of 180,000 (110,000-247,000) individuals, and to reduce the number of overweight adults (BMI ≥25) by 0.9 percent (0.6-1.1 percent) or 285,000 (201,000-364,000) individuals. Predicted reductions among the low, middle, and high income groups were 1.3 percent (0.3-2 percent), 0.9% (0.1-1.6 percent) and 2.1 percent (1.3-2.9 percent). The effect on obesity was found to decrease with age.

In an accompanying editorial, Assistant Professor Jason Block from the Obesity Prevention Program at Harvard Medical School in Boston, Massachusetts, US, noted that although such a tax could work it may not be feasible since existing taxes in Europe and the US are typically less than 10 percent. He suggested that further studies are required to provide real-world evidence of the effects of such taxes.

Trade-off when bivalirudin used for PCI: EUROMAX trial

A large international trial has compared the effects of bivalirudin and heparin on rates of bleeding and death in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention (PCI).

The European Ambulance Acute Coronary Syndrome Angiography (EUROMAX) trial enrolled a total of 2,218 patients from 65 sites in nine European countries. Patients were randomized to receive bivalirudin (bolus 0.75 mg/kg bodyweight followed by a 1.75 mg/kg/h infusion continued for at least 4h after PCI at a dose of 0.25 mg/kg/h, n=1,102) or unfractionated (100 IU/kg without a glycoprotein inhibitor, 60 IU/kg with one), or low-molecular-weight heparin (enoxaparin intravenous bolus 0.5 mg/kg, n=1,116) along with optional glycoprotein IIb/IIIa inhibitors. Study drugs were administered in an ambulance or non-PCI hospital and the patients were transported urgently to a PCI hospital where treatment was continued.

An intention-to-treat analysis of 2,198 patients showed that at 30 days, the risk for the composite of death or major bleeding not associated with coronary artery bypass grafting (CABG) was significantly reduced among patients who received bivalirudin compared with controls (relative risk [RR] 0.60, 95% CI 0.43–0.82, p=0.001). The risks for the composite of death, reinfarction, or non-CABG major bleeding (RR 0.72, 95% CI 0.54–0.96, p=0.02) and of major bleeding alone (RR 0.43, 95% CI 0.28–0.66, p<0.001) were also reduced in the bivalirudin group. However, the risk of acute stent thrombosis was higher among bivalirudin recipients (RR 6.11, 95% CI 1.37–27.24, p=0.007). No significant differences between bivalirudin and placebo recipients were observed in terms of death (2.9 percent vs 3.1 percent) and reinfarction (1.7 percent vs. 0.9 percent) rates.


Long-term statin therapy may protect against dementia

The short-term cognitive effects of statin therapy remain controversial with concerns of a possible association with memory loss and confusion. However, the findings of a recent systematic review suggest that not only do statins have no negative effect on short-term cognitive function, but they may protect against the long-term incidence of dementia in adults with no history of cognitive dysfunction.

Researchers conducted reviewed only randomized controlled trials and prospective cohort studies of statin therapy identified as high quality by a formal risk of bias assessment.

No consistent effect of statin therapy was detected with respect to short-term cognitive end points; the mean change from baseline in Digit Symbol Substitution Testing scores, a validated measure of cognitive function, was not significantly different between statin and placebo recipients (1.65, 95% CI -0.03-3.32; 296 total exposures in three trials). The eight long-term studies included 23,443 patients with a mean exposure duration of 3 to 24.9 years. Three of the studies found no association between statin use and incident dementia, but five found a reduction. When the results were pooled a 29 percent reduction in incident dementia was detected among statin recipients (hazard ratio 0.71, 95% CI 0.61–0.82). The absolute risk reduction was determined to be 2 percent (95% CI 1-3 percent) with a number needed to treat of 50 (95% CI 33-100).

JANUARY

16th Congress of the European Society for Sexual Medicine
29/1/2014 to 1/2/2014
Location: Istanbul, Turkey
Info: ESSM Secretariat
Tel: (39) 25 6601 625
Fax: (39) 27 0048 577
Email: admin@essm.org
Website: www.essm-congress.org/congress

2nd International Conference on Nutrition and Growth
30/1/2014 to 1/2/2014
Location: Barcelona, Spain
Info: Kenes International
Tel: (41) 22 908 0488
Fax: (41) 22 906 9140
Email: nutrition-growth@kenes.com
Website: ng.kenes.com

FEBRUARY

10th Asian Pacific Congress of Hypertension (APCH)
12/2/2014 to 15/2/2014
Location: Cebu, Philippines
Info: APCH Secretariat
Tel: (66) 2 748 7881
Fax: (66) 2 748 7880
E-Mail: apch2014@kenes.com
Website: www.apch2014.org

3rd Global Congress for Consensus in Pediatrics & Child Health (CIP)
13/2/2014 to 16/2/2014
Location: Bangkok, Thailand
Info: Paragon Group
Tel: (41) 22 533 0948
Fax: (41) 22 580 2953
E-Mail: cip@cipediatrics.org
Website: www.cipediatrics.org

19th World Congress on Controversies in Obstetrics, Gynecology & Infertility (COGI)
20/2/2014 to 23/2/2014
Location: Macau, China
Info: COGI Secretariat
Tel: (972) 73 706 6950
Fax: (972) 3 725 6266
Email: cogi@congressmed.com
Website: www.congressmed.com/cogimacau

UPCOMING

5th Congress of Asia Pacific Pediatric Cardiac Society (APPCS)
Location: New Delhi, India
Info: APPCS Secretariat
Tel: (91) 11 2658 8116
Fax: (91) 11 2658 8663
E-Mail: appcs2014@gmail.com
Website: www.appcs2014.org

Asian Pacific Association for the Study of the Liver (APASL) 2014
12/3/2014 to 15/3/2014
Location: Brisbane, Australia
Info: Gastroenterological Society of Australia
Tel: (61) 3 9001 0279
Fax: (61) 3 9802 8533
E-Mail: apasi2014@gesa.org.au
Website: www.apasl2014.com

Royal College of Gynaecologists (RCOG) World Congress 2014
28/3/2013 to 30/3/2013
Location: Hyderabad, India
Info: Royal College of Obstetricians and Gynaecologists
Tel: (44) 0 20 77726200
Website: http://www.rcog.org.uk/rcog2014

American College of Cardiology (ACC) Annual Scientific Sessions 2014
29/3/2013 to 31/3/2013
Location: Washington DC, US
Info: ACC Resource Center
Tel: (202) 375-6000, ext. 5603; (202) 375-6000, ext. 5603
E-Mail: accregistration@jspargo.com
Website: http://accscientificsession.cardiosource.org/ACC.aspx
16th Asia Pacific League of Associations Against Rheumatism (APLAR)
31/3/2013 to 5/4/2013
Location: Cebu, Philippines
Info: APLAR Conference Committee
Tel: (65) 6292 0723
Fax: (65) 6292 4721
E-Mail: info@aplar.org
Website: www.aplar.org/About/Pages/AboutAPLAR.aspx

WCO-IOF-ESCEO World Congress of Osteoporosis
Location: Seville, Spain
Info: Yolande Piette Communication
Tel: (32) 4 254 12 25
Fax: (32) 4 125 12 90
Email: info@piettecommunication.com
Website: www.wco-iof-esceo.org

21st Regional Conference of Dermatology (RCD) 2014
9/4/2013 to 12/4/2013
Location: Danang, Vietnam
Info: Congress Administration
Tel: (603) 4023 4700
Fax: (603) 4023 8100
Email: secretariat@asianderm.org
Website: http://asianderm.org/21rcd/index.htm

20th ASEAN Federation of Cardiology Congress 2014
12/6/2014 to 15/6/2014
Location: Kuala Lumpur, Malaysia
Info: AFCC Secretariat
Tel: (60) 3 7955 6608
Fax: (60) 3 7956 6608
Website: www.nham-conference.com/?event=3&cmd=home

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TIMOR LESTE: A PATH LESS TRODDEN

Rajesh Kumar

The small beach facing the deep blue Banda sea in Baucau, north eastern part of Timor Leste, is arguably one of the most unspoilt beaches in Asia.

Its vernacular name, Imia-Mata Bundura, literally means powdery white sand beach and it delivers on what it promises. Then some. Crystal clear waters, thriving coral beds kissing the shoreline, awe inspiring views and star-saturated night skies. Above all, no throng of tourists. For now, at least.

For intrepid travelers always on the lookout for a path less trodden, Timor Leste may well be the next big fix. As the country returns to peace after decades of violence and destruction and slowly builds its economy, the government is hoping its unspoilt beaches like Imia-Mata Bundura, natural beauty, abundant marine life and great diving and hiking spots would attract enough visitors to kick start its tourism sector.

Located between Indonesia and Australia, Timor Leste is part of the Coral Triangle (including tropical marine waters of Indonesia, Malaysia, Papua New Guinea, Philippines and Solomon Islands) that contains hundreds of species of reef building corals.

The sheer diversity of marine life in the region has earned it the nickname “Amazon of the seas.” For this very reason, Atauro and Jaco islands are fast becoming popular with die hard divers looking for exotic locales.

“Just four days ago, we had three adult blue whales coming through the lagoon. Nowhere else in the world can you see them this close to the shore,” said Mr. Kevin Austin, chief executive of Sustainable Marine Industry Development Facility that runs Baucau Beaches, a tourism project to help the impoverished local community with high unemployment.

“Most of the time, we spot green turtles, sharks, reef sharks, and occasionally manta rays,” Austin told me and other visiting media persons.

That aside, the World War II era Japanese bomb shelters in Venilale, Lekirika Mana stalactites/stalagmites cave system high in the eastern
tropical forests and remnants of the centuries of Portuguese colonial rule add just a dash of history to what, for us, was quite an adventurous voyage into the unspoilt unknowns.

We were told that Lekirika Mana cave was used as a shelter by rebel forces hiding from the Indonesian military during the latter’s brutal occupation of Timor Leste soon after the Portuguese left in 1975. The occupation continued until the country’s self determination in 1999, followed by UN administration until December 2012.

In the capital city Dili, the Jesus Statue (Cristorae) located atop Cape Fatucama on the eastern tip, Cathedral of Immaculate Conception and the Presidential Palace seemed popular with domestic and international visitors alike.

About 8 kilometers west of Dili lie Tasi-tolu Wetlands, a protected area comprising three salt lakes, an esplanade, and a beach. The area was designated Tasitolu Peace Park in 2002 due of its cultural and historical significance. Tasitolu is notorious as the site where Indonesian soldiers allegedly killed and dumped many young rebels during the country’s bloody independence struggle.

Nearby is Pope John Paul II monument that commemorates the pontiff’s visit to the country in 1989, during the Indonesian occupation. The catholic country of 1.2 million proud, friendly people comprises the eastern half of the island of Timor the nearby islands of Atauro and Jaco, and Oecusse, an exclave on the northwestern side of the island within Indonesian West Timor. The two halves were occupied by the Dutch and the Portuguese respectively, the Dutch half now with Indonesia.

Timor Leste has embarked on a slow and painful path to progress, thanks to money from its oil and natural gas bounty. But it is proving to be a long and arduous journey.

In its efforts to attract tourists, Timor Leste will not emulate Bali with its night clubs, neon signs and unchecked urban sprawl. Instead, the focus will be on sustainable eco-tourism with particular regard for the fragile environment, the country’s tourism minister said. One can only hope so.
“Didn’t I tell you not to eat?”

“What do you mean I don’t have any friends? My dentist just sent me a birthday card!”

Okay, but just this once!”

“No wonder you can’t read the fine print. That’s precisely the side effect of this medicine. Difficulty reading the fine print!”

“But doctor, you told us to wear masks during flu season!”

“Why is it taking so long to change one electric fuse?!”

“Usually I don’t advise giving this medication for such a condition … but in your case, I’m terribly curious!”
Save the date!

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