Thrombolysis benefits elderly stroke patients

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Thrombolysis benefits elderly stroke patients

Rajesh Kumar

All patients with stroke, regardless of age, should receive thrombolysis according to findings from two studies.

In one, the third International Stroke Trial (IST-3), researchers determined whether all patients with stroke, irrespective of age, benefited from treatment with the thrombolytic agent alteplase, a recombinant plasminogen activator (rt-PA), when given up to 6 hours following stroke onset. [Lancet 2012;379:2352-2363]

This multicenter, randomized, open treatment trial assessed 3,035 patients (1,515 receiving alteplase and 1,520 in a control group) at 156 hospitals in 12 countries; of these 53 percent were older than 80 years. At 6 months, 554 (37 percent) patients in the alteplase group met the primary end point (ie, were alive and independent) compared with 534 (35 percent) of those in the control group (OR 1·13, 95% CI 0·95-1·35, P=0·181). For every 1,000 patients treated within 6 hours, 14 more were alive and independent.

The effect of alteplase on disability was, thus, not statistically significant. But the odds of surviving with less disability were 27 percent greater for patients treated with alteplase. Among the patients (about 80 percent of them aged >80 years) treated within 3 hours, the benefit was much greater—for every 1,000 treated, 80 more were alive and able to look after themselves at 6 months.

In terms of tolerability, fatal or non-fatal symptomatic hemorrhage within 7 days occurred in 104 (7 percent) of patients in the alteplase group versus 16 (1 percent) in the control group. More deaths occurred within 7 days in the alteplase group (163 [11 percent]) than in the control group (107 [7 percent]).

However, between 7 days and 6 months, there were fewer deaths in the alteplase group than in the control group, so that, by 6 months, similar numbers of patients had died in the two groups in aggregate (408 [27 percent] in the alteplase group vs. 407 [27 percent] in the control group).

“The data add weight to the policy of treating patients as soon as possible, and justify extending treatment to patients older than 80 years of age,” said co-author Professor Peter Sandercock of the University of Edinburgh and Western General Hospital, Edinburgh, UK.

“[The findings] do not support any restriction of treatment on the basis of stroke severity or the presence of early ischemic change on the baseline brain scan.”

The second paper reported an analysis of pooled data from 12 trials, including the IST-3
trial results, involving a total of 7,012 patients. [Lancet 2012;379:2364-2372]

This meta-analysis showed that for every 1,000 patients allocated to intravenous alteplase up to 6 hours after stroke, 42 more patients were alive and independent, and 55 more had the better outcome of being alive with a favorable outcome at the end of follow-up. This benefit occurred despite an increase in the number of early symptomatic intracranial hemorrhages and early deaths associated with thrombolysis.

Among the 1,711 patients older than 80 years, the absolute benefits from alteplase were at least as large as for the younger patients, especially with early treatment (for those over 80 treated within 3 hours, 96 patients more per 1,000 treated were alive and independent).

Although net benefit from thrombolysis clearly declines with increasing delay to treatment, the data suggest that the benefit probably extends beyond 4.5 hours, possibly as late as 6 hours in some patients, although the time probably varies with key individual or combined patients’ characteristics, which were not possible to identify from this analysis, said the authors.

“If small gains in functional ability by 3 months translate into greater long-term survival free of disability, this is likely to reduce health-care costs and increase quality of life and cost effectiveness.”

The key message of IST-3 and the updated meta-analysis is that many eligible patients from subgroups excluded by the European license should now be given alteplase, said Drs Didier Leys and Charlotte Cordonnier of the department of neurology (stroke unit) at the Roger Salengro Hospital in Lille, France, while commenting on the study findings’ clinical relevance. [Lancet 2012; DOI:10.1016/S0140-6736(12)60822-8]

When asked about their relevance for Asia, Professor Sandercock explained that as life expectancy increases in Asia, the proportion of very elderly people in the population, and hence the number of older stroke patients, will continue to rise over the coming decades.

“The finding that thrombolysis benefits the very elderly as much as younger patients is, therefore, very important,” he said.

In many Asian countries where traffic delays in reaching hospital quickly are a big problem, he said that thrombolysis with an expensive drug like rt-PA within 3 hours is only relevant to the very small number of wealthier individuals who can afford to pay for the treatment.

“The population health benefits will come from making sure all acute stroke patients are cared for in well-organized stroke units, not by thrombolysing the few.”
Finding a cure for HIV: The need for science, collaboration and advocacy

Excerpts from a plenary lecture delivered by Professor Sharon R. Lewin, director of the Infectious Diseases Unit, Alfred Hospital, and professor, Department of Infectious Diseases, Monash University, in Melbourne, Australia, during the 15th International Congress on Infectious Diseases held recently in Bangkok, Thailand.

Combination antiretroviral therapy (cART) has led to major reductions in HIV-related mortality and morbidity, but still HIV cannot be cured. Current paradigms of treatment are not sufficient. With increasing numbers of infected people, emerging new toxicities secondary to cART and the need for life-long treatment, there is now a real urgency to find a cure for HIV.

Currently, there are multiple barriers to curing HIV. The most significant is the establishment of a latent or “silent” infection in resting CD4+ T-cells as the virus is able to integrate into the host cell genome, but does not proceed to active replication. Reactivation of latently infected resting CD4+ T-cells can then re-establish infection once cART is stopped.

Other significant barriers to cure include residual viral replication in patients receiving cART. In addition, HIV can be sequestered in long-lived cells such as macrophages and astrocytes in anatomical reservoirs, such as the brain, gastrointestinal tract and lymphoid tissue. Achieving either a functional cure (long-term control of HIV in the absence of cART) or a sterilizing cure (elimination of all HIV-infected cells) remains a major challenge.

Several studies have demonstrated that treatment intensification with additional antiretrovirals (ARVs) appears to have little impact on latent reservoirs. One potential approach to eliminate latently infected cells is to promote viral production in these cells. If this is done in a patient in cART, subsequent rounds of viral replication will be inhibited and the infected cell will die. Drugs such as histone deacetylase inhibitors and methylation inhibitors, cytokines such as IL-7, or other activating agents including prostratin and anti-PD-1 show promising results in reversing latency in vitro when used alone or in combination.

In addition, gene therapy has been shown to effectively reduce expression of the HIV co-receptor CCR5 in both animal models and ex vivo human studies. Clinical trials using these approaches are underway. Recent new initiatives to fund collaborative private-public partnerships, enhance community engagement and define a scientific road map for cure research are also likely to significantly accelerate advances in the elusive path to finding a cure.

However, there are also a number of scientific challenges in HIV cure. We certainly need better in vitro and animal models to
evaluate new strategies, especially if we are to consider combination approaches to activating latent HIV, with or without boosting immunity. There should be standardized, non-invasive assays to quantify viral reservoirs in vivo particularly when we move into multi-site clinical trials. There is also a need for more drug development to increase specificity for latently infected cells and/or enhanced tissue delivery and finally, better understanding of the immune system in controlling low-level viremia and latent infection.

This area of endeavor also raises a whole range of ethical considerations. What are the acceptable risks and toxicities of interventions in a population doing quite well on stable cART? The perspective on this issue is very different amongst clinicians, patients and regulatory bodies and we therefore need far more open discussions about these issues. What surrogate markers of viral persistence will ultimately justify treatment interruptions as a clinical endpoint in subsequent clinical trials? We are now very well aware of the risk of treatment interruption, so when will we know that it will be safe to test whether an intervention has worked by stopping ART? Expectations of study participants in early “proof of concept” studies are also very important. Patients who participate in these studies are exposed to potential risks and will not get any benefit themselves but are contributing to future research. Finally, any work on HIV cure should never get in the way of universal access to ART for all patients infected with HIV.

In the last few years, we have seen a real increase in funding for research towards HIV cure, including some various significant investments in grant funding from both the National Institute of Health and the American Foundation for AIDS Research. Advocacy also remains a key component in achieving a cure. The International AIDS Society is leading this with the development of a global scientific strategy for HIV cure which will be launched in Washington in July.

In conclusion, there are multiple barriers to curing HIV. This will not be easy. A combination approach will almost certainly be needed. But we do know that sterilizing and functional cure is possible and we need to find a way to achieve this in more patients. There are multiple strategies being tested with most being early proof of concept, small and non-randomized studies – including activating latency, gene therapy and vaccination with or without intensification. Results from several of these studies should be available in the coming year. Engagement of the community, regulatory bodies and pharmaceutical companies will be very critical to advance the field, given the many ethical issues concerned.

Finally, the very significant and additional challenge to whatever we do is that some day we should identify a strategy for cure. This must ultimately be cheap, scalable and widely available to patients who need it.
ACE inhibitors linked to bone loss in elderly Chinese women

Christina Lau

Continuous use of angiotensin-converting enzyme inhibitors (ACEIs) for more than 4 years is associated with increased bone loss in elderly Chinese women, according to a local study.

According to authors from the Chinese University of Hong Kong and the Affiliated Hospital to Nantong University, China, the results suggest that careful consideration should be given when prescribing ACEIs to hypertensive subjects with osteoporosis. [J Bone Miner Metab 2012, e-pub 29 June]

The 4-year study was initiated in view of contradictory findings on the effects of ACEIs on bone loss. To analyze their independent effects, the researchers followed 2,161 community-dwelling elderly Chinese (age ≥65 years) in Hong Kong every 2 years for 4 years. Current smokers, and those who took osteoporosis-related medications and angiotensin II type I receptor blockers at either time point were excluded.

Results showed that female users of ACEIs had significantly greater bone loss in both total hip and femoral neck compared with non-users. The annualized percentage bone loss in continuous ACEI users vs non-users was -0.329 in the total hip (p=0.023) and -0.594 in the femoral neck (p=0.004), after adjustment for confounders such as use of thiazide diuretics and beta-blockers.

Although intermittent use of ACEIs was not associated with significant bone loss in females, there was a trend of increased bone loss with increased use of the drugs.

In male subjects, however, unadjusted annualized percentage bone loss was not significantly different between ACEI users and non-users. Although a significant difference was seen in the femoral neck after adjustment for confounders, the authors noted that the p value was borderline, and no trend could be seen related to intermittent vs continuous use of the drugs.

According to the authors, the finding in female subjects was “quite unexpected, since previously we have reported a cross-sectional association between ACEI use and higher BMD [bone mineral density] in older Chinese men and women”. [Bone 2006;38:584-588]

Furthermore, other studies have shown that long-term use of ACEIs was associated with a decreased risk of fractures. [J Hypertens 2006;24:581-589; JAMA 2004;292:1326-1332] In female subjects with ACE DD genotype (associated with higher level of angiotensin II, a stimulator of osteoclastic resorption), ACEI treatment was associated with significantly increased BMD. [Am J Hypertens 2003;16:453-459]

“A possible reason may be that ACEIs act not only on the renin-angiotensin system that converts angiotensin I to angiotensin II, but also on the kinin-kallikrein system that stimulates...
HFMD alert following rising fatalities in Asia

Naomi Rodrig

The Center for Health Protection (CHP) has issued a notice to local doctors urging vigilance about febrile patients returning from Cambodia, following the ‘unknown’ outbreak that had killed over 50 children in that country before being declared a severe form of hand, foot and mouth disease (HFMD).

According to a CHP spokesman, the majority of the laboratory samples in Cambodia tested positive for Enterovirus 71 (EV71), which is one of the major causative agents of HFMD. “A small proportion of samples also tested positive for other pathogens, including Haemophilus influenzae type B and Streptococcus suis,” he added.

Investigations by Cambodian authorities and the WHO revealed that most of the children were <3 years old, and some of them suffered from chronic conditions and malnutrition. A number were given steroids, which may have worsened their condition.

Importantly, a more virulent strain of EV71 has been implicated in HFMD outbreaks in Southeast Asia over the past several years.

According to official statistics from the China Ministry of Health, at least 240 people, mostly children under 5, died from HFMD between January and May 2012, compared with 132 fatalities during the same period last year. In 2011, China recorded >1.6 million cases of HFMD, 509 of them fatal.

“EV71 is a statutory notifiable disease in Hong Kong. The infection is usually found among young children and most commonly presents with symptoms of HFMD. It may rarely cause more serious diseases such as viral aseptic meningitis, encephalitis, poliomyelitis-like paralysis and myocarditis,” the spokesman said.

HFMD is typically a self-limiting disease, presenting in young children as fever, oral lesions and rash on the hands, feet and buttocks. Most deaths in HFMD occur as a result of pulmonary edema or hemorrhage.

As of mid-July, the local activity of HFMD remained at a relatively high level, with about 7 institutional cases reported each week at schools and kindergartens. However, most children in Hong Kong recovered without sequelae, and only a few had laboratory-confirmed EV71 infection.

The usual peak season for HFMD and EV71 infection in Hong Kong is from May to July. In the past few years, a smaller
Organ donations on the rise

Naomi Rodrig

The Department of Health (DH) announced that the number of registered donors on the Centralized Organ Donation Register (CODR) has exceeded the 100,000 mark at the end of June, indicating increasing acceptance and support for organ donation in Hong Kong.

The CODR was established by the DH in November 2008 to facilitate voluntary registration for prospective donors to donate organs after death, and for their wishes to be reliably recorded. CODR’s promotion campaigns and educational materials play an important role, as people have refused to donate organs because of concerns that organ removal will affect the appearance of their body at the funeral. Others are worried that once they carry a signed organ donation card, they will not receive medical care if they are wounded in an accident. Since the establishment of the CODR, the registration number has continued to rise.

The CODR also enables the Hospital Authority’s transplant coordinators to respond quickly upon the death of a CODR-registered patient.

According to a DH survey conducted in September 2010, the major reasons for potential donors registering for organ donation were: “I want to help others/it is an act that should be done”; “emotionally touched by stories of successful organ donation reported in the media”; and “clicking into and making registration through the CODR website while web surfing”.

An analysis of CODR’s registration numbers revealed significant increases in registrations after certain events, such as the prominent media coverage about a man who donated part of his liver to save the life of a colleague. Earlier this year, extensive media reports followed the traffic accident death of a woman who saved the lives of six people by donating her organs. “Following each of these, the CODR saw dramatic increases in the number of registrations,” a DH spokesman said.

In addition, the DH assisted non-governmental organizations and student groups in launching street promotional activities for organ donation that contributed hundreds of new registrations to the CODR, instantly recording their wish to help others.

As of December 2011, there were nearly 1,800 patients on the waiting list for kidney transplantation, 500 awaiting cornea transplantation and 109 awaiting liver transplantation. In the past decade, live-donor liver transplantations have exceeded the numbers of deceased-donor procedures. As live-donor liver transplantation has become safer for donors and recipients alike, it offers another option for relatives or friends to help patients with liver failure.
Study suggests cause of implantation failure in IVF

Christina Lau

Scientists have discovered a molecular determinant of successful implantation that may explain why pregnancy does not occur in some women undergoing in vitro fertilization (IVF).

Using mouse endometrial epithelial cells, Professor Hsiao-Chang Chan of the School of Biomedical Sciences, Chinese University of Hong Kong and colleagues found that activation of the epithelial sodium channel (ENaC) plays a key role in embryo implantation. [Nat Med 2012, e-pub 24 June; DOI: 10.1038/nm.2771]

“We demonstrated that ENaC expressed on uterine epithelial cells can be activated by a serine protease, trypsin, released by an implanting embryo. This triggers a sequence of events that lead to enhanced production and release of prostaglandin E2, a key factor in implantation,” she reported. “In the animals, maximum activation of ENaC occurs at the time of implantation, as indicated by ENaC cleavage. Blocking or knocking down uterine ENaC resulted in implantation failure.”

Interestingly, they also found that uterine ENaC expression before IVF treatment was markedly lower in women with implantation failure than in those with successful pregnancy.

As ENaC expression is subject to regulation by ovarian hormones, the researchers hypothesized that its normal expression pattern may be altered during IVF with ovarian hyperstimulation, which may contribute to the low pregnancy rate achieved through the treatment. “Thus, defects in ENaC, either in expression or function, may be one of the underlying mechanisms for spontaneous miscarriage and implantation failure during IVF,” they noted.

“The problem with human reproduction is embryo abnormality. Miscarriages arise largely from abnormal embryos that are implanted. Unless it can be shown that trypsin pre-treatment significantly increases the rates of implantation and successful pregnancies, I believe implantation is mainly a function of the embryos rather than a function of the endometrium,” commented Dr. Clement Ho, Specialist in Reproductive Medicine in private practice in Hong Kong.

“If you look at the findings from another angle, it may be that only competent embryos release trypsin and implant,” he told Medical Tribune. “Also, it’s unclear how the authors studied uterine ENaC expression in women when their work was on mouse models.”

Furthermore, successful implantation hings on synchronization of embryo and endometrial maturity. “The implantation window falls on days 5 to 7 after ovulation. The transferred
Asia far behind in treatment of chronic pain

Christina Lau

Asia is far behind the West in treatment of moderate-to-severe pain, according to experts who spoke recently at a media workshop on chronic pain management in Hong Kong.

“The WHO has recommended since 1986 that opioid analgesics be used for treatment of moderate-to-severe pain, but more than 80 percent of patients worldwide remain inadequately treated,” said Dr. Steven Stanos of the Rehabilitation Institute of Chicago and Department of Physical Medicine & Rehabilitation, Northwestern University, USA. “Although global consumption of morphine increased after 1986, this was limited to a number of industrialized countries only.”

For example, opioids account for 40-50 percent of analgesic use in Australia, G5 Europe (France, Germany, Italy, UK, Spain), Canada and USA. In many Asian countries, however, they account for <10 percent of total analgesic use. [IMS data, 2007]

“Hong Kong and Singapore ranked 62nd and 63rd worldwide in daily doses of opioids used for medical and scientific purposes in 2010, while China ranked 99th,” said Dr. Alex Yeo, President of the World Institute of Pain (Southeast Asia Chapter) and Vice President of the Pain Association of Singapore.

According to Yeo, the under-use of opioid analgesics in Asia is due to an “opioidphobia” among physicians and patients, which actually harms more individuals by leaving their pain untreated.

“Some physicians still resist opioids because of fears of addiction, illegal diversion, side effects and social stigma,” he pointed out. “Other barriers to opioid use include faulty or difficult diagnosis of pain conditions; lack of expertise in pain management, in treatment of chronic pain in the context of suspected opioid addiction, and in treatment of medical and psychiatric conditions that develop with chronic pain; as well as difficulty in monitoring care of patients on opioid therapy.” [J Pain 2010;11:1442-1450]

Logistically, there is a lack of options for pain management and addiction referrals, limited information regarding diagnostic workup, as well as inadequate ancillary staff, time and insurance coverage for pain management services. [J Pain 2010;11:1442-1450]

“Monitored medical use of opioids does not lead to addiction,” stressed Yeo. “In this
regard, patients should be properly assessed for mental health and history of drug or alcohol addiction, and opioid treatment should be closely and collaboratively monitored by specialists in pain management through an integrated approach. Referral to a multidisciplinary pain management center is recommended.”

“In Hong Kong, chronic pain affects about 11 percent of the population but remains undertreated,” said Dr. Chi-Wai Cheung of the Department of Anesthesiology, University of Hong Kong, who is President of the Society of Anesthetists of Hong Kong and Vice President of the Hong Kong College of Anesthesiologists. “More resources should be dedicated towards increasing awareness, education and treatment, to enable early diagnosis and offer more treatment choices in the public healthcare system.”
The Asian Cancer Research Group (ACRG) in collaboration with the Shenzhen-based genomics company BGI recently published the results of a genome-wide study unveiling the mechanism of recurrent hepatitis B virus (HBV) integration in hepatocellular carcinoma (HCC) genomes. [Nature Genetics 2012. DOI: 10.1038/ng.2295]

HBV integration is thought to be one of the major causes underlying HCC development, as previous studies have shown that it may induce chromosomal instability, leading to carcinogenesis and tumor recurrence. “However, this is the first whole-genome sequencing study to systematically investigate the breakpoints of HBV DNA and the human genes which are affected by such integration in a large sample – 88 pairs of HCC tumor and non-tumor liver tissue obtained from 88 patients operated at Queen Mary Hospital [QMH],” said Professor Ronnie Poon, Chief of the Division of Hepatobiliary & Pancreatic Surgery at the University of Hong Kong (HKU), who was one of the study investigators. “The study was initiated by Dr. John Luk, a corresponding author of the paper, when he was working at HKU. He subsequently moved to the National University of Singapore where he recruited talents in bioinformatics analysis for the project.”

In the study, which enrolled 81 HBV-positive and seven HBV-negative patients with HCC, HBV integration was observed more frequently in tumors than in normal tissues (86.4 vs 30.7 percent).

The researchers also identified a specific region of the viral genome that is most commonly cleaved during integration into the host genome. “Approximately 40 percent of HBV breakpoints within the HBV genome were located at a 1,800-bp region where the viral enhancer, X gene and core gene are located,” they wrote.

In addition to the previously reported human genes TERT and MLL4, they discovered three novel genes associated with recurrent HBV integration – CCNE1, SENP5 and ROCK1. All these genes are known to play an important role in cancer development and progression, and showed upregulated expression in tumor vs normal tissue.

Another observation was that the number of HBV integration events was positively correlated with tumor size, and serum levels of hepatitis B surface antigen (HBsAg) and alpha-fetoprotein.

The number of HBV integrations was also associated with patient survival. Patients with <3 detected HBV integrations survived longer than those with >3 integrations, suggesting that the number of integrations may be a prognostic indicator in HCC patients. “This is the first study that correlated HBV integration patterns
with clinical outcome in patients with HBV-related HCC,” emphasized Poon.

Notably, a higher frequency of HBV integration was observed in HCC patients who were in their twenties or thirties, which may explain the development of the tumors in younger individuals without chronic hepatitis or cirrhosis.

According to Poon, over 6 percent of the 3,500 primary HCC cases who presented to QMH between 2001 and 2010 were <40 years of age. “The median survival of these young patients is much poorer compared with older patients [8.3 vs 16.1 months], and this may be explained by the increased number of viral integrations as shown in this study,” he said.

Poon noted that current drugs which inhibit HBV replication cannot completely eradicate the virus nor prevent its re-integration into the human genome. “This study provides insight into future drug development to prevent hepatocarcinogenesis by HBV, although there is no drug being developed yet to disrupt HBV DNA integration into the human genome,” he said.

He stressed that such genome-wide cancer study is very demanding in terms of technology platforms and bioinformatics analysis, and would have been very difficult for a single academic institution to perform. ACRG is an independent, not-for-profit company established in 2010 by Eli Lilly, MSD and Pfizer to accelerate research on cancers that are common in Asia with a view to developing new therapies for these malignancies.

“Collaboration among institutes and with pharmaceutical companies is very important, and I appreciate such effort by pharmaceutical companies. HKU initiated the study, provided the samples, and performed some experiments and data analysis, especially the clinical correlation. ACRG not only provided funding support for the study, but its investigators were involved from the very early phase of study design. The mapping and sequencing analysis and several other experiments were performed by BGI. Their sequencing ability is obviously important to this study. This is really a collaborative effort and the credit should go to all parties and investigators involved,’’ said Poon.

HK boosting mental health services

Wey-Feng Ong

The spate of violent incidents involving persons with mental illness in recent years has resulted in tragedies for local communities and the Hong Kong society-at-large. These incidents have also brought to the forefront the dire lack of modern mental health services. “Only 1 percent of Hong Kong residents are currently receiving mental health treatment, whereas the prevalence of anxiety and depressive disorders are over 10 percent in most developed cities,” remarked Prof. Linda Lam, Chairperson of the Department of Psychiatry, Chinese University of Hong Kong, in a 2011 interview with BBC.
The status of psychiatry services in Hong Kong was again a subject of debate at a recent LEGCO meeting, where the provision of these services for residents of North Lantau New Town was queried by legislators. With the lack of an acute hospital, psychiatric patients in North Lantau are currently managed in primary care by the Tung Chung Health Centre and referred to specialist clinics or designated general outpatient clinical (GOPC) covered by the Integrated Mental Health Programme (IMHP) for follow up.

“Most patients living in the North Lantau New Town area who require additional psychiatric specialist support are followed-up at Kwai Chung Hospital under the Kowloon West Cluster. To further strengthen these services, HA will consider launching psychiatric specialist services in the planned North Lantau Hospital to provide residents with more comprehensive mental healthcare,” advised Food and Health Secretary, Dr. Wing-Man Ko, in reply to the queries.

This upgrade is part of a wider government scheme to address the growing needs. The Taskforce on Mental Health Service Plan was convened in 2009 to formulate the Hospital Authority (HA) Mental Health Service Plan, with the vision of providing “a person-centred service based on effective treatment and recovery of the individual”.

Following a review on the current and anticipated needs, the taskforce emphasized the need for high-quality care with the aim to restore patients to health, or to effectively manage their condition, while focusing on patient and carers’ needs in a timely manner.

Using an outcome-driven mental health service model, the taskforce proposed that psychiatric illnesses should be identified early and managed in the primary care setting whenever possible. They also recommend that treatment should be rendered in a relaxed and informal setting, and involve patients and their families.

Another recommendation is for ‘one-stop’ mental health services by multidisciplinary teams, so that psychiatric patients do not need to search for various service providers. For example, under the IMHP, stable patients are managed in the Common Mental Disorder Clinics by a multidisciplinary team consisting of psychiatrists, family medicine specialists, nurses and general practitioners in a community setting.

Community-based services should be further developed, with greater collaboration with disability-support and rehabilitation providers, as well as social services. Since October 2010, the HA has partnered with private organizations to progressively implement community-based mental health services by setting up one-stop psychiatric centres throughout Hong Kong.
Polypharmacy in psychiatry: Beware of pitfalls

In addition to often causing undesirable side effects, psychiatric medications have been associated with multiple drug-drug interactions. Hence, pharmacists play an important role in alerting both physicians and patients to potential pitfalls, and adjusting medications or drug dosing, experts argued.

“Pharmacokinetic interactions are usually related to CYP enzymes involved in drug metabolism and bioactivation, which affect changes in drug levels in the blood. For example, fluoxetine interacts with warfarin through the CYP 2C9 enzyme, and with antibiotics and antifungal agents such as clarithromycin or ketoconazole through CYP 3A4. There is also drug-drug interaction between omeprazole and fluoxetin, so patients on proton pump inhibitors should be warned,” said Professor Siu-Wa Tang, Director of the Institute of Brain Medicine (International), Hong Kong.

“To further complicate matters, CYP polymorphism is ethnicity based, with inter-racial differences in drug oxidation.”

Tang stressed that drug-drug interactions between antidepressant classes are also common, and may be complementary or antagonistic. For instance, both the serotonin-norepinephrine reuptake inhibitor (SNRI) venlafaxine and the selective serotonin reuptake inhibitor (SSRI) paroxetine have been shown to decrease clearance and increase the half-life of the tricyclic antidepressant (TCA) imipramine.

He noted, however, that polypharmacy is common in psychiatry because complete remission with a single antidepressant is achieved in only 50 to 60 percent of patients. “Doctors often resort to polypharmacy, which may have catastrophic consequences. A case in point is a combination of MAOIs [monoamine oxidase inhibitors] and SSRIs, which results in markedly elevated 5HT [5-hydroxytryptamine] concentrations in the synapse and can be disastrous,” he said.

Caution is also indicated when prescribing bupropion, indicated for major depressive disorder. The drug is associated with a dose-related risk of seizures, which may be further increased when coadministered with other agents that can reduce the seizure threshold, including antidepressants, CNS stimulants, acetylcholinesterase inhibitors, phenothiazines, and dopaminergic blocking agents such as neuroleptics and metoclopramide. “These agents are often individually epileptogenic and may have additive effects when combined,” stressed Tang.

Inappropriate use of psychotropic drugs in polypharmacy has been associated with an increased risk of falls among elderly inpatients, according to a Japanese study reported by
Professor Yukihiro Noda, Faculty of Pharmacy, Meijo University, Japan. “Among our elderly patients who were prescribed multiple drugs, the ratio of sedative-hypnotics or anxiolytics use in those with a documented fall was over 80 percent, suggesting that both drug types increased fall risk,” he reported, adding that the increase was mainly attributed to long-acting benzodiazepines.

“However, following an educational campaign on benzodiazepine prescribing delivered by our pharmacy staff, the incidence of falls decreased markedly,” he advised.

Professor William Kehoe, Chair of Pharmacy Practice, University of the Pacific, Stockton, USA, emphasized the importance of a multidisciplinary team for improving medication safety. “Our geropsychiatric team, which is managing mainly Alzheimer’s inpatients, includes psychiatrists, nurses, case managers and clinical pharmacists, all working together to assess the patient and their medications, ensuring appropriate use of antipsychotics for each individual patient,” he said.

Managing dermatologic toxicities of targeted cancer drugs

Cancer therapies targeting the epidermal growth factor receptor (EGFR) are notorious for their dermatologic side effects, which often need to be addressed in general practice, according to Dr. Alex Chan, a pharmacy specialist at the National University of Singapore.

“EGFR inhibition with the monoclonal antibodies cetuximab and panitumumab, or tyrosine kinase inhibitors [TKIs] such as gefitinib or erlotinib, is associated with abnormal chemokine expression and cell differentiation, stimulating the recruitment of inflammatory cells, which leads to cutaneous injury,” he explained. “This can manifest as pruritus or rash, hair loss, eyelash abnormalities, nail changes and hair loss, all of which might be quite painful and disturbing for patients.”

Chan noted that the severity of rash has been positively correlated with tumor response to cetuximab in clinical trials. “Furthermore, greater rash severity was also associated with longer median survival in patients receiving cetuximab, erlotinib or gefitinib. Therefore, it may be useful to inform patients that rash actually indicates response to their cancer therapy,” he suggested.

On initiation of EGFR-targeted therapy, patients should be advised to moisturize dry body areas, minimize exposure to sunlight, and shower with bath oil for trapping moisture. “If rash develops, suggest cold compresses to minimize itchiness, and avoidance of friction or pressure on the affected areas,” advised Chan.

For more severe cases, pharmacotherapy is indicated, and should be tailored to the type of lesion, such as emollients to alleviate dryness or topical antiseptics to dry pustules. “Topical or oral antimicrobials are indicated to treat severe erythroderma associated with secondary infections, while corticosteroids have anti-inflammatory effects,” he said. “Antihistamines may be also used to provide relief for pruritus.”

Chan stressed that treatments of skin toxicities
should be easy to administer and provide rapid results, to ensure patient compliance. However, most of them also have adverse effects, such as photosensitization or gastrointestinal upset with antibiotics, or skin atrophy with chronic use of steroids. “Many reports advise against the use of retinoids, as they have overlapping adverse reactions with EGFR inhibitors and may interfere with their anti-tumor activity,” he noted.

“Current research is focusing on topical vitamin K3, which has demonstrated efficacy in preventing erlotinib- and cetuximab-induced skin toxicities in animal studies,” added Chan.

In general, he advised that physicians consult clinical practice guidelines for the prevention and treatment of EGFR inhibitor-associated dermatologic toxicities. Published last year by the Multinational Association of Supportive Care in Cancer (MASCC) Skin Toxicity Group, the guidelines provide detailed recommendations for managing skin as well as other dermatological toxicities, including grading of evidence for the various treatment options. [Support Care Cancer 2011;19:1079-1095]

When dermatologic toxicities become intolerable despite treatment, dose modification of the EGFR inhibitor, treatment holiday or treatment discontinuation might be prescribed by the attending oncology specialist.

End-of-life care decisions: Is it time in Hong Kong?

Naomi Rodrig

A recent survey among terminal cancer patients indicated that it was feasible to discuss advance directives on end-of-life care with Chinese patients with advanced malignancy, and over 60 percent of them had signed such documents. [Hong Kong Med J 2012;18:178-185]

Advance directives, or living wills regarding end-of-life care decisions, are common in Western countries, but the concept is less acceptable in Asia. Living wills empower patients, while sparing doctors and relatives from making difficult decisions on the patient’s behalf, particularly withholding life-sustaining treatment.

Investigators from the Department of Clinical Oncology in Tuen Mun hospital collected data from 191 eligible Chinese patients. All patients were hospitalized in palliative care, having failed all available therapeutic options for their malignancy. Mentally incompetent patients were excluded. Overall, 120 patients (63 percent) had signed an advance directive form – a document declaring the patient’s understanding of their disease status, aims of future treatment preferred and refusal of futile treatment or resuscitation. Patients’ understanding and acceptance of poor prognosis was the most significant factor for signing a living will. Any family objection was also an important factor, although it did not reach statistical significance.

These data are in contrast to government policies. “It is not the appropriate time to implement advance directives of terminal care at this stage through any form of legislation,” said former Secretary for Food and Health, Dr. York Chow in June. However, he suggested more public education is needed, “with a view to introducing the concept.... in a gradual and progressive manner.”
Mainland websites selling cancer ‘biosimilars’

Christina Lau

A local concern group is warning patients of the dangers of buying cancer ‘biosimilars’ from mainland websites, which charge a fraction of the prices of branded originals and offer express delivery to Hong Kong.

Among many mainland websites that sell drugs without a prescription, one was found to sell ‘biosimilar’ versions of erlotinib and gefitinib. These products are said to be Indian-made “generics” that are identical to the branded originals – except that they are 66-86 percent cheaper.

“Because of the huge price difference, some patients in Hong Kong have started online discussions about the purchase of these ‘biosimilars’. Some have even made the purchase, and one forum participant told others about how the condition of a family member got worse after taking the drug,” said Dr. Fernando Cheung of the Lung Cancer Treatment Concern Group.

“The sources, quality, safety and efficacy of these ‘biosimilars’ are questionable,” said Cheung. “These products can cause harm to patients with advanced lung cancer, who are in a frail condition. In addition, it is illegal to import these products as they are not registered with relevant local authorities.”

Although erlotinib and gefitinib are approved for first-line treatment of advanced lung cancer in Hong Kong, they are listed as self-financed items in the Hospital Authority’s Drug Formulary. The patents of erlotinib and gefitinib are yet to expire. “The drugs are not covered by the government’s safety net,” said Cheung. “Patients in need can only get financial assistance from the Community Care Fund for use of gefitinib with effect from August. Those unable to afford targeted therapy will have to resort to chemotherapy, which comes with more side effects and a lower efficacy.”

According to Concern Group member Dr. Patricia Poon of the Radiotherapy and Oncology Center, Hong Kong Baptist Hospital, erlotinib and gefitinib were shown to prolong progression-free survival of advanced lung cancer patients by 9.1 and 3.2 months, respectively, vs chemotherapy (median, 13.7 and 9.5 months, respectively).

“The Lung Cancer Treatment Concern Group therefore urges the government to include both targeted therapies in its safety net as soon as possible,” said Cheung.

Addressing the recent Oncology Forum of Hong Kong, Professor Vivian Lee, School of Pharmacy, Chinese University of Hong Kong, warned that ‘biosimilars’ of targeted cancer therapies – which are produced using complex biotechnological processes – can never be identical to the original products.

“Unlike generics of small-molecule drugs, which have the same properties and activity as the branded products, the pro-
duction of complex antibodies or proteins involves many steps, and even a small deviation at any step will result in a different molecule, with different therapeutic properties or side effect profile,” she explained. “In some cases, use of ‘biosimilars’ has caused serious adverse reactions, so extreme caution is necessary.”

As many targeted cancer agents are due to lose patent protection in the near future, regulatory authorities worldwide are preparing to address the problem by issuing strict requirements for approval of ‘biosimilars’. “All new biomolecules, including ‘biosimilars’ of cancer drugs, will be considered as new drugs; as such, they will be required to undergo testing in phase III clinical trials,” advised Lee.

Epidemic of drug-resistant TB in China

Naomi Rodrig

The incidence of multidrug-resistant (MDR) tuberculosis (TB) in mainland China is reaching epidemic proportions, according to a recent report from the Chinese Center for Disease Control and Prevention. [N Engl J Med 2012;366:2161-2170]

The study estimated the proportion of TB cases in China that were resistant to antibiotics by means of cluster-randomized sampling of TB cases in the public healthcare system and testing for resistance. First-line anti-TB drugs tested included isoniazid, rifampin, ethambutol and streptomycin; second-line drugs were ofloxacin and kanamycin. The investigators then used published estimates of TB incidence in China to calculate the incidence of MDR TB.

Among 3,037 patients with new cases of TB and 892 with previously treated TB, approximately 1 in 4 had disease that was resistant to isoniazid, rifampin, or both, and 1 in 10 had MDR TB. Overall, 5.7 percent of new cases and 25.6 percent of previously treated patients had MDR TB, defined as resistance to at least isoniazid and rifampin.

Furthermore, some 8 percent of the patients had extensively drug-resistant (XDR) TB, defined as resistance to at least isoniazid, rifampin, ofloxacin and kanamycin.

In 2007, there were 110,000 incident cases of MDR TB and 8,200 incident cases of XDR TB, the majority of them resulting from primary transmission.

According to the authors, previous TB treatment at public hospitals was the most important risk factor for MDR TB. Patients with multiple previous treatments who had received their last treatment in a TB hospital had a 13.3-fold increased risk of MDR TB.

“Among 226 previously treated patients
with MDR TB, 43.8 percent had not completed their last treatment,” they wrote. “Among those who had completed treatment, TB developed again in most of the patients after their treatment in the public health system.”

“China has a serious epidemic of drug-resistant TB. MDR TB is linked to inadequate treatment in both the public health system and the hospital system, especially TB hospitals,” the authors concluded.

SHS linked to COPD, stroke

Naomi Rodrig

A prospective, long-term study conducted in Xian, China demonstrated that people exposed to second-hand smoke (SHS) are at increased risk of death from stroke and chronic obstructive pulmonary disease (COPD) as well as from lung cancer and heart disease. [Chest 2012. DOI:10.1378/chest11-2884]

The study followed up 910 subjects (439 men) over 17 years, examining the relationship between SHS and tobacco-related deaths. At baseline, 44.2 percent of them were exposed to SHS at home, 52.9 percent in the workplace, and 67.1 percent at home or work.

During the study period, 249 subjects died. Compared with controls, people who were exposed to SHS had increased mortality due to coronary heart disease (relative risk [RR], 2.15), ischemic stroke (RR, 2.88), lung cancer (RR, 2.00), COPD (RR, 2.3) and all causes (RR, 1.72). The study also demonstrated significant dose-response relationships between cumulative SHS exposure and increased risk of cause-specific and total mortality.

The authors noted that the evidence linking SHS to COPD and ischemic stroke is scarce. While the current study is not sufficient to establish a causal relationship, it provides new evidence to support the role of SHS in COPD- and stroke-related deaths.
The use of HPV testing as a first-line screening tool for cervical cancer will be investigated in Hong Kong, as recent studies suggest that local women have a positive attitude towards the test that accurately identifies infection with high-risk types of the virus.

“We are recruiting Chinese women aged 30 to 60 years to participate in our study on the use of HPV testing as a first-line cervical cancer screening tool. Participants will receive a free HPV test together with Pap smear at designated clinics of the Family Planning Association of Hong Kong [FPA],” said Professor Hextan Ngan of the Department of Obstetrics and Gynecology, University of Hong Kong (HKU). [http://www.obsgyn.hku.hk; tel: 2255 4265]

“In Hong Kong, HPV testing is currently used as a second-line test for those with atypical squamous cells of undetermined significance [ASC-US] on cytology. The test may have a role in first-line cervical screening,” she continued.

“ASC-US account for 60-80 percent of all abnormality in cervical cytology,” said Professor Annie Cheung of HKU’s Department of Pathology. “We found that 56 percent of local women with ASC-US are positive for high-risk HPV. The sensitivity and negative predictive value of the HPV DNA test approached 100 percent.”

According to Cheung, women with ASC-US who are positive for high-risk HPV have a 20 times increased risk of detecting high grade squamous intraepithelial lesions or more advanced malignancy at follow-up, compared with women with ASC-US who are negative for high-risk HPV. “As such, those with ASC-US and high-risk HPV should be referred for colposcopy directly without waiting for repeat smears,” stressed Cheung.

In another recent study, the HKU researchers found that local Chinese women are positive about HPV testing. “In the study, 292 women who attended the FPA Wan Chai clinic were asked to complete self-administered questionnaires before and after reading an educational message about HPV and HPV testing. The proportion of women willing to be tested for HPV was 93 and 97 percent, respectively,” reported Ngan. [Psychooncology 2010;19:1329-1339]

To prevent cervical cancer, the experts agreed that vaccination is important. “It is important not only to vaccinate girls. Clearly, boys should be vaccinated as well,” said Professor Harald zur Hausen, recipient of the 2008 Nobel Prize in Physiology or Medicine for his discovery of HPV as the causative agent of cervical cancer. “If you can only vaccinate boys, you can probably prevent more
cervical cancers than only vaccinating girls.”

At present, a new nanovalent HPV vaccine is being tested in a clinical trial. “We have participated in the trial, but the interim data aren’t available yet,” Ngan told Medical Tribune. “I’m not sure if the manufacturer has made public what HPV types the nanovalent vaccine protects against.”

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**Hong Kong Events**

**50th Anniversary Multidisciplinary Conference – The Evolution and Revolution of Child Health in Hong Kong: Past, Present and the Future**
Hong Kong Pediatric Society; American Academy of Pediatrics; Hong Kong Pediatric Nurses Association
17/8-19/8
Tel: (852) 2871 8897
Fax: (852) 2871 8898
E-mail: HKPS@hkam.org.hk
www.medicine.org.hk/hkps

**5th International Infection Control Conference**
Hong Kong Infection Control Nurses’ Association; HKU; Hong Kong College of Radiologists
24/8-26/8
Info: MV Destination Management Ltd.
Tel: (852) 2735 8118
Fax: (852) 2735 8282
E-mail: hkcna@mvdmc.com
www.mvdmc.com/hkcna/index.html

**1st Endoscopy Nurse Skills Workshop – Management of Non-variceal Upper GI Bleeding**
Hong Kong Society of Digestive Endoscopy; CUHK Jockey Club Minimally Invasive Surgical Skills Center; The Nethersole School of Nursing, CUHK
25/8
Tel: (852) 2632 2644
Fax: (852) 2632 4708
E-mail: info@hkmisc.org.hk
www.hksde.org

**International Association of Gerontology and Geriatrics (IAGG) Master Class on Aging**
International Association of Gerontology and Geriatrics (IAGG); Research Center of Heart, Brain, Hormone & Healthy Aging, HKU; Hong Kong Geriatrics Society
29/8-30/8
E-mail: hbha@hku.hk
www.med.hku.hk/hbha/iaggmca2012/index.html

**2012 FDI Annual World Dental Congress**
FDI World Dental Federation
29/8-1/9
Tel: (852) 2528 5327
Fax: (852) 2529 0755
E-mail: congress@fdiwoldental.org
www.fdiworldental.org

**AADO 20th Anniversary – 2012 International Symposium: Advance in Orthopedic Trauma cum Mini-symposium**
1/9-3/9
Tel: (852) 2532 3482 / 2632 1653
Fax: (852) 2647 7432
E-mail: secretariat@aado.org / olc@ort.cuhk.edu.hk
www.aado.org/index.htm

**HK College of Community Medicine Annual Scientific Meeting 2012 – Occupational Health for All: From Prevention to Rehabilitation**
15/9
Tel: (852) 2871 8844 / 2871 8745
Fax: (852) 2580 7071
E-mail: yandy_hkccm@hkam.org.hk / hkccm@hkam.org.hk
www.hkccm.org.hk/index.php

**Hong Kong Pain Society Annual Scientific Meeting 2012 – New Light on Pain**
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Fax: (852) 2547 9528
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Breakthrough with BRILINTA™: Save More Lives Beyond Clopidogrel*

Marking the first in a new chemical class of oral antiplatelets (OAP) different from thienopyridines¹, BRILINTA™ is shown to reduce CV mortality and morbidity of ACS patients beyond clopidogrel therapy.¹,²

- 16% Reduction in CV death, MI or stroke
- 21% Reduction in CV death
- 16% Reduction in MI

Such results were achieved without any significant increase in fatal or total major bleeding compared to standard therapy.² The PLATO trial, carried out with more than 18,000 patients, was designed to reflect clinical practice.

The broad patient applicability of BRILINTA™ has demonstrated not only coverage of patients with UA, STEMI and NSTEMI, but can be applied to patients intended for invasive or non-invasive treatment strategies.² BRILINTA™ is already included in international guidelines even prior to our availability in Hong Kong and even recommended ahead of clopidogrel therapy.³,⁴

Starting BRILINTA™ can bring benefits to your patients in as early as 30 days.² The same dosage regimen* applies for all appropriate ACS patients: 180 mg loading dose, followed by 90 mg bid for up to 12 months. Unless contraindicated, acetylsalicylic acid (ASA) daily maintenance dose of 75-150mg should be prescribed in conjunction with BRILINTA™.⁵

*Result from PLATO study – BRILINTA™ reduced CV deaths vs clopidogrel without increasing overall major or fatal bleeding, but with increase in non-CABG major & minor bleeding.

ACS – Unstable angina (UA), non ST elevation myocardial infarction (NSTEMI) or ST elevation myocardial infarction (STEMI) who are to be managed medically and those who are to be managed with percutaneous coronary intervention (PCI) (with or without stent) and/or coronary artery bypass graft (CABG).

“ BRILINTA™ to be used in combination with low-dose acetylsalicylic acid (ASA).⁵

BRILINTA™ and 倍林達 are trade marks of the AstraZeneca group of companies.

References:

Correction
In Medical Tribune June 2012, page 11, “Dual therapy stent may cut duration of antiplatelet therapy”, the reference in paragraph 12 was mistakenly quoted as “the REMEDEE OCT study.” It should read “the EGO-COMBO study.”

Editor
Patients with a fever lasting more than 2 weeks where there is no sign of localized infection should be treated with the common antimicrobial agent doxycycline, according to an expert.

“Empirical treatment with doxycycline is the most cost-effective strategy for the management of patients with acute undifferentiated fever in Asia,” said Professor Yupin Suputtamongkol, from the Faculty of Medicine, Siriraj Hospital, Mahidol University in Bangkok, Thailand. “This sub-group of patients has a very good prognosis and clinical response is dramatic with appropriate antimicrobial therapy.”

For severe cases, a combination treatment with either ceftriaxone or penicillin G is recommended, she added.

The diagnosis of acute undifferentiated febrile illness has been a challenge for physicians in Southeast Asia. “Acute undifferentiated fever is very common in this region but its specific etiology is often unknown, making accurate diagnosis and effective treatment difficult,” Suputtamongkol said.

The majority of patients present with non-specific symptoms such as fever, headache, chills, nausea, muscle ache and vomiting that mimic clinical manifestations of secondary sepsis caused by different circulating pathogens. “Physicians should be aware that malaria, dengue infection, rickettsial infections, and leptospirosis are major causes of acute undifferentiated fever in Asia. Travelers to endemic areas are also at risk.”

Currently, there is no single rapid test that would differentiate one disease from the other. Even when dengue fever and leptospirosis are suspected, available rapid serologic tests cannot reliably detect IgM antibodies until at least the sixth day of clinical illness. Rapid serologic testing was able to identify only half of the cases of leptospirosis in Thailand during an outbreak between 1999 and 2003.

“It’s not practical to request for a serial diagnostic test for dengue, leptospirosis or scrub typhus because most of the time it’s only about 50 percent accurate. We need a test that can detect these three infectious diseases in one go,” Suputtamongkol said.

“We came up with clinical practice guidelines in the management of acute febrile illness after conducting a series of clinical trials on patients in various hospitals in Thailand during an outbreak of leptospirosis in 1999. The guideline has four components - investigations, severity assessment, empirical therapy and follow-up,” she said.

“This is diagnosis by exclusion. Exclude malaria and dengue first. Then consider rickettsial infection or leptospirosis. If scrub typhus is the cause of fever, the patient will improve in 48 hours following doxycycline therapy. If there’s no clinical response and the patient remains febrile, then the cycle of strategy has to be repeated.”

Patients with severe leptospirosis could die of lung hemorrhage. As for scrub typhus, the important cause of death is acute respiratory disease syndrome so respiratory support is also very important, Suputtamongkol added.

“Early diagnosis of the cause of acute fever is important to guide appropriate antimicrobial therapy. Empirical treatment is necessary because rapid, sensitive and affordable diagnostic tests for scrub typhus, leptospirosis and murine typhus are not available,” she concluded.
Hepatitis B e antigen (HBeAg) seroconversion is an inadequate end-point in hepatitis B management because it does not indicate or guarantee long-term remission and virus inactivity, according to a leading hepatologist.

“While hepatitis B surface antigen (HBsAg) seroconversion comes as a near ‘cure’ for chronic hepatitis B (CHB), it is only achievable in 10 percent of patients with all current therapies,” said Dr. Ching-Lung Lai, chair professor of hepatology and medicine, and chief of the Gastroenterology and Hepatology Division, Department of Medicine, University of Hong Kong. “It is also genotype-dependent, and rarely achieved in patients with genotypes B and C, which are the common genotypes in Asia.”

In a study in Hong Kong, 60 percent of 85 HBeAg-positive patients had HBeAg seroconversion following pegylated interferon therapy at year 5, however only 11 percent had undetectable HBV DNA (≤400 copies/mL). About 2.4 percent of patients achieved HBsAg seroclearance at 2.6 and 84 months post-treatment. [Hepatology 2010; 51:1945-1953]

“HBeAg seroconversion to anti-HBe is thus only a half-way process in the natural history of CHB in patients who acquire the disease during early childhood,” said Lai.

In another study, more than 60 percent of patients had no significant decline in HBsAg levels following 2 years of treatment with entecavir, a mononucleos(t)ide analogue agent. Early decline in HBsAg levels at weeks 12 and 24 was not associated with HBV DNA suppression or HBeAg seroconversion. [Am J Gastroenterol 2011;106:1766-1773]

“HBeAg seroconversion in patients with chronic hepatitis B is only meaningful when accompanied with permanently low and undetectable HBV DNA,” said Lai. “This is very important if we are to reduce the risk of the disease developing into cirrhosis and hepatocarcinoma.”

Sustained virologic suppression is critical to CHB therapy. “Five-year treatment with tenofovir and entecavir has resulted in a continuing HBV DNA suppression of up to <3-400 copies/mL in more than 90 percent of patients. This is associated with histologic improvement, including reversal of severe fibrosis.”

Entecavir and tenofovir are potent, safe and associated with little or no resistance, Lai added.
Personal Perspectives

“The talk on HIV today, which tackled new areas we need to look into in terms of development and cure for HIV, was so revealing. Another interesting lecture was on global biosurveillance. But coming from Nigeria, we have so many limitations. They are going too high when we haven’t even reached where they are now. We are lagging behind [and] we need their support. Africa is famous for malaria, TB and intestinal helminths. If they could help research in our country, then that would be great.”

– Dr. Chinenye Afonne, field epidemiologist, Department of Epidemiology and Medical Statistics, College of Medicine, University of Ibadan, Ibadan, Nigeria

“All the lectures I’ve been to have been great. It’s good to have an Asian perspective. There’s a lot of data on emerging infections and a lot of epidemiology that we don’t necessarily get to hear about unless we come to conferences like this.”

– Dr. Sanchia Warren, Royal Hobart Hospital, Hobart, Tasmania, Australia

“One of the ICID highlights to me was looking at all the new diagnostic tools that are available for infectious diseases. It’s very interesting to think about diagnostic testing in the clinic and being able to give patients the results immediately. That is one of the major strides that we are making. By using point-of-care diagnostics, we could treat millions of people who mostly live in low-resource settings.”

– Dr. Ruanne Barnabas, post-doctoral research fellow, Fred Hutchinson Cancer Research Center, Seattle, Washington, US.
Three major observational studies examining the use of long-acting insulin have found no increased risk of a wide range of cancers in patients using glargine, contradicting previous suggestions of a glargine-cancer link.

Researchers in the US and Europe independently compared the use of insulin glargine for diabetes patients with other long-acting insulins and found no basis for the previous suggestion made by a series of studies published in 2009.

One study group from Kaiser Permanente examined data for 115,000 patients with diabetes who were taking either insulin glargine or neutral protamine Hagedorn (NPH) insulin. They compared cancer risk in new insulin users as well as patients who had switched from NPH to glargine. There was a median duration of 1.2 years for glargine use and 1.4 years for NPH. This study found a “suggestion” of an association between insulin glargine use and a modest increase in breast cancer risk, but only among new insulin users (HR 1.6, 95% CI 1.0 to 2.8). However, in patients who had been on insulin for a longer period of time and had switched from NPH to glargine, there was no increased risk.

“We think this may be a chance finding,” said principal investigator Dr. Laurel Habel, research scientist at the Kaiser Permanente Northern California division of research in Oakland, California, US, adding there was no biological reason why the cancer risk would be seen only in new users.

The group found no association with prostate, colorectal cancer or all cancers combined in new users or in prior users.

“The preponderance of the evidence suggests that there is no increased risk of cancer associated with relatively short-term use of insulin,” said Dr. John Buse, director of the diabetes center at the University of North Carolina School of Medicine in Chapel Hill, North Carolina, US.

The second group of researchers at the University of North Carolina used a large automated healthcare database to identify 43,306 patients initiating glargine and 9,147 initiating NPH, all of whom were free of cancer when they initiated insulin use. The mean duration of treatment was 1.2 years for the glargine group and 1.1 years for those taking NPH. Follow-up was discontinued when a patient experienced a change in their insulin treatment.

“We found no evidence of an increased risk for cancer and we specifically found no increased risk for breast cancer in the small group that stayed on these drugs for more than 24 months,” said principal investigator Dr. Til Stürmer, professor of epidemiology and director of the center of excellence in pharmacoepidemiology and public health at the University of North Carolina Gillings school of global public health.

“Our study adds to the important evidence about long-term outcomes of these antidiabetic treatments,” said Stürmer.

The Northern European Study of Insulin
and Cancer, is the largest of the three studies comprising 447,821 diabetic patients using insulin, over 1.5 million person-years of observation and 17,500 new cases of cancer in the cohorts. The average follow-up time is longer at 3.1 years for those on glargine and 3.5 years for other insulins.

This study looked at the risk for all cancers, as well as individually for breast, lung, pancreas, colorectal and prostate cancers.

“There was no difference in risk between glargine and other insulins found in any of the pre-defined primary and secondary hypotheses of this study,” said principal investigator Dr. Peter Boyle, President of the International Prevention Research Institute in Lyon, France.

Linagliptin effective in combination with insulin, metformin

Rajesh Kumar

The DPP-4 inhibitor linagliptin (Trajenta®, Boehringer Ingelheim) has been shown to be effective when combined with other antidiabetic therapies in achieving clinically meaningful blood glucose control in adults with type 2 diabetes.

In a randomized phase III clinical trial involving 1,261 adult patients with type 2 diabetes, linagliptin 5mg once daily was significantly more effective at lowering blood glucose levels compared with placebo when used as an add-on therapy to basal insulin alone or in combination with metformin and/or pioglitazone.

It demonstrated a placebo-adjusted reduction in HbA1c of 0.65 percent ($P$≤0.0001) from a baseline HbA1c of 8.3 percent at 24 weeks, without weight gain or additional risk of hypoglycaemia.

“Once patients are on insulin, there is not much you can do to make their diabetes control better, [therefore a] 0.65 percent reduction in HbA1c is a very good reduction in insulin treated patients,” said Dr. Mark Cooper, director of the Danielle Alberti Memorial Centre for Diabetes Complications and head of the diabetes division at the Baker IDI Heart and Diabetes Institute in Melbourne, Australia.

“Linagliptin, which we have always considered better to use in earlier stage of diabetes, can actually be used in any stage – early, middle or late,” said Cooper.

Patients were eligible for the study if they had inadequate glycemic control with a stable dose of basal insulin (ie, insulin glargine, insulin detemir or NPH insulin) with or without metformin and/or pioglitazone.

There was a similar overall frequency of adverse events (linagliptin 71.8 percent, placebo 72.5 percent) and hypoglycemia (linagliptin 25.7 percent, placebo 27.3 percent) in each group. In addition, body weight did not significantly change from the baseline in the linagliptin and placebo groups (-0.17 kg and +0.13 kg, respectively; $P$=0.07).

A post-hoc analysis from a second phase III trial found that on a background of metformin randomized to add linagliptin or glimepiride, a greater proportion of patients taking linagliptin achieved the target of HbA1c <7 percent without weight gain and/or hypoglycemia than those taking glimepiride after 104 weeks (54 percent vs.
23 percent). The overall reduction in HbA1c was similar in both groups.

In patients who were at high risk of declining renal function, yet another post-hoc analysis showed that linagliptin achieved significant reduction in urinary albumin-to-creatinine ratio (UACR) of 33 percent from baseline ($P≤0.05$), in addition to a 0.71 reduction in HbA1c.

The analysis included pooled data from four 24-week trials involving a total of 227 patients at high risk of declining renal function who were on stable treatment with angiotensin-converting enzyme inhibitors (ACEs) or angiotensin receptor blockers (ARBs).

“This analysis is important because approximately 65 percent of patients living with type 2 diabetes are at risk of declining renal function, which can limit treatment options,” said Professor Per Henrik Groop of the division of nephrology at Helsinki University Central Hospital in Helsinki, Finland.

“Patients treated with linagliptin showed improvements in blood glucose levels and reduction of albumin in the urine, a sign for renal dysfunction. We will continue to further investigate this area as we recognize the importance of considering declining renal function when treating type 2 diabetes patients.”
Promising new antidiabetic drug

Rajesh Kumar

The investigational antidiabetic drug empagliflozin, a sodium glucose co-transporter-2 (SGLT-2) inhibitor, has demonstrated promising results in a phase II trial.

SGLT-2 inhibitors, which lower high blood glucose independently of insulin by blocking glucose re-uptake in the kidneys and thereby excreting excess glucose via the urine, lower HbA1c and weight, irrespective of beta cell function or insulin resistance.

In the trial, 659 adults with type 2 diabetes who had participated in earlier 12-week phase II-b trials of the drug, were then randomized to receive open-label treatment with either 10 mg or 25 mg of empagliflozin (as monotherapy or add-on to metformin), metformin alone, or sitagliptin plus metformin for an additional 78 weeks.

At week 90, patients assigned to empagliflozin 10 mg alone achieved a 0.34 percent reduction in Hb1Ac from baseline and a weight loss of 2.24 kg. Monotherapy with the 25mg dose led to a HbA1c reduction of -0.47 percent, along with weight loss of 2.61 kg, versus metformin alone (-0.56 percent and 1.28 kg, respectively).

When used as an add-on to metformin, significant decreases from baseline in mean HbA1c levels and weight loss were observed with empagliflozin 10 mg (-0.34 percent; -3.14 kg) and 25 mg (-0.63 percent; 4.03 kg), versus sitagliptin (-0.40 percent, 0.41 kg).

The Boehringer Ingelheim/Eli Lilly-sponsored study showed the drug in both 10 mg or 25 mg doses was generally well tolerated.

More than 90 percent of the adverse events (AEs) reported in the trial were mild or moderate in severity. Between 0.9 percent and 3.6 percent of patients on empagliflozin reported hypoglycemic vents, versus 7.1 percent on metformin monotherapy and 5.4 percent on sitagliptin.

AEs related to urinary tract infections were reported in 3.8 to 12.7 percent of patients on empagliflozin, 3.6 percent of patients on metformin monotherapy, and 12.5 percent of patients on sitagliptin. AEs related to genital infections were reported in 3.0 percent to 5.5 percent of patients on empagliflozin, 1.8 percent of patients on metformin monotherapy, and none of the patients on sitagliptin.

Empagliflozin is now in phase III clinical development, with more than 14,500 patients planned to be enrolled.

“Type 2 diabetes is characterized by three main factors: persistent hyperglycemia, impaired insulin secretion and increased insulin resistance,” said Dr. Hans-Juergen Woerle, vice-president of the medicine therapeutic area (metabolism) at Boehringer Ingelheim, Ingelheim am Rhein, Germany.

“SGLT-2 inhibitors such as empagliflozin represent an innovative, insulin-independent mode of action. To date, clinical data have demonstrated that these drugs have the potential to improve persistent hyperglycemia irrespective of the two other factors.”
Ethical clinical decisions must consider both mother and fetus

Radha Chitale

The rights of both mother and fetus must be considered when managing pregnancy because unilateral clinical decisions breach clinical ethical standards, said Dr. Frank Chervenak, Weill Cornell Medical College, New York, New York, US.

Perinatal ethics span a wide variety of situations, including abortion, stem cell research, mental health and pregnancy, and caesarean delivery.

Clinicians’ professional responsibility to the mother and fetus can seem conflicted, requiring unacceptable compromises.

However, considering the rights of only the mother or the fetus (at all gestational ages) is simplistic and, Chervenak said, will result in conceptual and clinical failure.

Instead of this kind of counterproductive reductionism, the professional responsibility model of obstetric ethics should gird clinical decisions, he added, and be comprised of medical science and compassionate clinical care for both the pregnant and fetal patients. [Am J Obstet Gynecol 2011;205:315.e1-5]

“Incorporating the psychological and social dimensions is required to have a clinically adequate model to guide obstetric care and avoid clinical tunnel vision,” Chervenak said.

The professional responsibility model also hinges on high quality informed consent of the pregnant patient to encourage autonomy.

According to the American College of Obstetricians and Gynecologists, “screening and invasive diagnostic testing for aneuploidy should be available to all women who present for prenatal care before 20 weeks of gestation regardless of maternal age.” [Obstet Gynecol 2007;109:217-227]

In a study to evaluate how pregnant women use risk assessment information for trisomy 21, 30,564 consecutive, singleton pregnancies were assessed based on maternal age, fetal nuchal translucency thickness and maternal proteins during the first trimester. [Am J Obstet Gynecol 2005;193:322-326]

Patients were counselled about estimated risk and informed that invasive testing, which has miscarriage risks of about 1 percent, were necessary to determine whether the fetus had chromosomal abnormalities.

Women were informed of the possibility of a 1 in 300 risk of fetal trisomy 21 but that the choice of whether or not to test was theirs. Median maternal age was 34 years.

The rate of invasive testing increased exponentially with increasing estimated risk ($P<0.0001$). Estimated risk for trisomy 21 was at least 1 in 300 in 8.4 percent of patients, of which 77.6 percent had invasive testing. Among the 91.6 percent of women whose estimated risk for trisomy 21 was less than 1 in 300, 4.6 percent had invasive testing.

“These empiric data compliment the arguments of normative ethics to create evidence-based ethical standards for informed consent regarding invasive testing,” the researchers said.
Chervenak noted that women were able to use sophisticated risk assessment data to make informed, rational decisions about invasive fetal testing. Given that high quality informed consent on behalf of the mother and fetus requires adequate time, he suggested that clinicians who cannot meet this ethical standard should refer patients to centers that can.
Regulators affirm dabigatran efficacy, safety

Yen Yen Yip

The superiority of the direct thrombin inhibitor dabigatran (Pradaxa®, Boehringer Ingelheim) over warfarin in preventing ischemic and hemorrhagic strokes has now been affirmed by the US Food and Drug Administration.

This latest update, reflected in the prescribing information of dabigatran 150 mg twice daily, was based on results from the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial, which established that dabigatran 150 mg reduced the risk of stroke and systemic embolism by 35 percent compared with well-controlled warfarin.

In the study, investigators also showed that dabigatran 110 mg twice daily was as effective as warfarin in preventing stroke. [N Engl J Med 2009;361:1139-1151]

RE-LY was a prospective, randomized, open-label trial with blinded end point evaluation, conducted in more than 18,000 patients with non-valvular atrial fibrillation (NVAF).

Dabigatran also received a nod from a European regulatory agency for its safety profile. Concerns had previously been raised about bleeding events associated with use of the drug.

The European Medicines Agency (EMA) recently acknowledged that the frequency of reported fatal bleedings with dabigatran was significantly lower than levels reported in clinical trials.

The EMA arrived at this conclusion following a review of available data from clinical trials and post-marketing surveillance reports on the risk of serious or fatal bleeding with dabigatran.

“The latest available data are consistent with the known risk of bleeding and that the risk profile of dabigatran is unchanged,” the EMA stated.

The EMA Committee for Medicinal Products for Human Use (CHMP) pointed out dabigatran’s importance as an alternative to other blood-thinning agents. However, given that the risk of bleeding is a common complication of all anticoagulants, CHMP has also recommended more specific guidance on patient management, when dabigatran should not be used, and how dabigatran’s anticoagulant effect can be reversed if bleeding occurs.
New guidelines to manage osteoporosis in men

Radha Chitale

ew guidelines from the US-based Endocrine Society outline a clinical approach for managing osteoporosis, which results in lost bone density, bone weakness and increased risk of fracture, in men. [J Clin Endocrinol Metab 2012;97:1802-1822]

Osteoporosis is most often associated with women but the disorder causes significant morbidity and mortality in men.

“One in five [men] will experience an osteoporosis-related fracture in their lifetime,” said authoring task force chair Dr. Nelson Watts, Mercy Health Osteoporosis and Bone Health Services in Cincinnati, Ohio, US. “Mortality after fracture is [two to three times] higher in men than in women. Of the 10 million Americans with osteoporosis, 2 million are men. Of the 2 million fractures due to osteoporosis that occur each year, 600,000 are in men.”

“Testing was recommended in high-risk men when they are age 70 or older or when they are between ages 50-69 and have risk factors for osteoporosis including low body weight or a history of smoking.

A history of adult bone fractures, particularly after age 50, is a strong indicator of osteoporosis risk.

The task force said clinicians should recommend reducing alcohol intake and smoking, increase weight-bearing exercises, and get sufficient calcium and vitamin D in order to promote good bone health.

“In contrast to the large fracture-end point trials of osteoporosis therapies in women, studies in men have generally been small, with change in bone mineral density as the primary end point,” the authors said.

However, trials have shown positive effects of drug therapies on bone mineral density and markers for bone remodelling, so “we conclude that available therapies are likely to be effective in men and that it is appropriate to recommend pharmacological therapy in men with increased fracture risk.”

Men over 50 who have had spine or hip fractures, who have low bone mineral density or any other clinical or lifestyle risk factors are recommended for pharmacological treatment with any approved osteoporosis drugs, including alendronate, risedronate and teripatatide.

Zolendronic acid is recommended for men with recent hip fractures.

Use of a risk assessment tool that calculates the 10-year risk of fracture, like the FRAX questionnaire, to help plan therapy can also be helpful as it may identify more men in need of treatment than bone density tests alone.

“Acknowledging the shortcomings of the available data, we recognize the need to be sufficiently inclusive to identify both an adequate number of the men at risk and to incorporate multivariable risk models,” the researchers said.
Modest drinking may prevent bone loss in women

Radha Chitale

A few drinks per day may prevent bone loss among postmenopausal women.

New research showed a drop in markers for bone turnover – the process of bone breakdown and reformation – after 2 weeks of abstaining from alcohol followed by a quick rise again to pre-abstinence levels after consumption resumption.

“After less than 24 hours to see such a measurable effect was really unexpected,” said study author Dr. Urszula Iwaniec, associate professor in the College of Public Health and Human Sciences at Oregon State University, Coquille, Oregon, US.

Although alcohol abuse is associated with reduced bone mineral density, moderate alcohol consumption, about 28 grams per day, has been linked previously to increased bone mineral density, though the effect of confounding variables has not been teased out.

Forty healthy postmenopausal women, mean age 56.3, who consumed between 18-20 grams of alcohol per day were included in the study. [Menopause 2012 Jul 9. Epub ahead of print]

Immunoassays for the bone formation marker serum osteocalcin and the bone resorption marker C-terminal telopeptide (CTx) were done at baseline, after 14 days of abstaining from alcohol, and again 12-14 hours following alcohol resumption.

Serum levels for both markers increased during the abstinent period compared to baseline after assessment at 14 days (osteocalcin 4.1 ± 1.6 percent, P=0.01; CTx 5.8 ± 2.6 percent, P=0.02), indicating increased turnover.

After the women were allowed to drink alcohol normally, serum levels for both osteocalcin and CTx fell immediately, within 12-14 hours, upon testing the next day to levels similar to baseline (osteocalcin 3.4 ± 1.4 percent, P=0.01 and 3.5 ± 2.1 percent, P=0.05).

The study was not ethnically diverse and therefore not generalizable and the type of drink was not controlled for, the researchers noted.

In addition, the process of bone remodelling, whereby reabsorbed bone cavities are filled with new bone, takes about 4 months, and the study results may have underestimated the effects of alcohol due to residual effects of long-term alcohol use.

“Nevertheless, the small but significant increases in osteocalcin and CTx after short-term abstinence provide substantial evidence that moderate alcohol consumption decreases bone turnover,” they said.

Eighty percent of patients with osteoporosis are postmenopausal women and while pharmacological interventions are available, they are costly and have side effects.

“It is therefore important to identify modifiable lifestyle factors that influence the risk of osteoporosis,” said the researchers, but added that abstinence for longer than the 14-day trial would be required to determine the total effects of alcohol on bone turnover.
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Corporate Director, Clinical Informatics Research & Development, Partners HealthCare System, Harvard Medical School, Brigham & Women’s Hospital

Closing Keynote by Dr Charles SAWYER
MD, FACP
Associate Chief Health Information Officer Geisinger Health System

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August

60th Annual Scientific Meeting of the Cardiac Society of Australia & New Zealand
16/8/2012 to 19/8/2012
Location: Brisbane, Australia
Info: The Conference Company
Tel: (64) 9-360 1240
Fax: (64) 9-360 1242
Email: csanz@icc.co.nz
Website: www.csanz2012.com/

11th Asian Congress of Urology of The Urological Association of Asia
22/8/2012 to 26/8/2012
Location: Pattaya, Thailand
Info: 11th ACU Local Organiser
Tel: (662) 287 3942 to 3
Fax: (662) 677 5868
Email: secretariat@11thacu2012.org
Website: http://www.11thacu2012.org/

European Society of Cardiology Congress 2012
25/8/2012 to 29/8/2012
Location: Munich, Germany
Info: European Society of Cardiology
Tel: (33) 4 9294 7600
Fax: (33) 4 9294 7601
E-Mail: ascoregistration@jspargo.com
Website: www.escardio.org/congresses/esc-2012

September

European Respiratory Society Annual Congress
1/9/2012 to 5/9/2012
Location: Vienna, Austria
Info: European Respiratory Society
Tel: (41) 21 213 01 01
Fax: (41) 21 213 01 00
E-Mail: ers2012groups@kit-group.org
Website: www.erscongress2012.org/

14th Congress of the International Society for Peritoneal Dialysis
9/9/2012 to 12/9/2012
Location: Kuala Lumpur, Malaysia
Info: International Society for Peritoneal Dialysis
Tel: (603) 2162 0566
Fax: (603) 2161 6560
E-Mail: ispd2012@console.com.my
Website: www.ispd2012.org.my

Hospital Management Asia 2012
13/9/2012 to 14/9/2012
Location: Hanoi, Vietnam
Info: Ms. Sheila Pepito
Tel: (632) 846 8339
Email: sheilapepito@exedraevents.com
Website: hospitalmanagementasia.com

London College of Clinical Hypnosis (LCCH-Asia) Certificate in Clinical Hypnosis
22/9/2012 to 23/9/2012
Location: University of Malaya, Kuala Lumpur, Malaysia
Info: LCCH Secretariat
Tel: (60) 3-7960 6439 / 7960 6449
Email: info@hypnosis-malaysia.com
Website: www.hypnosis-malaysia.com

15th Biennial Meeting of the European Society for Immunodeficiencies (ESID 2012)
3/10/2012 to 6/10/2012
Location: Florence, Italy
Info: Secretariat Office of GW-ICC & APHC (Shanghai Office)
Tel: (86) 21-6157 3888 Extn: 3861/62/64/65
Fax: (86) 21-6157 3899
Email: secretariat@heartcongress.org
Website: www.heartcongress.org

23rd Great Wall International Congress of Cardiology (GW-ICC) – Asia Pacific Heart Congress (APHC) 2012
11/10/2012 to 14/10/2012
Location: Beijing, China
Info: Secretariat Office of GW-ICC & APHC (Shanghai Office)
Tel: (86) 21-6157 3888 Extn: 3861/62/64/65
Fax: (86) 21-6157 3899
Email: secretariat@heartcongress.org
Website: www.heartcongress.org

42nd Annual Meeting of the International Continence Society
15/10/2012 to 19/10/2012
Location: Beijing, China
Tel: (41) 22 908 0488
Fax: (41) 22 906 9140
Email: ics@kenes.com
Website: www.kenes.com/ics
8th International Symposium on Respiratory Diseases & ATS in China Forum 2012
9/11/2012 to 11/11/2012
Location: Shanghai, China
Info: UBM Medica Shanghai Ltd.
Tel: (86) 21-6157 3888 Extn: 3861/62/64/65
Fax: (86) 21-6157 3899
Email: secretariat@isrd.org
Website: www.isrd.org

National Diagnostic Imaging Symposium
2/12/2012 to 6/12/2012
Location: Orlando, Florida, US
Info: World Class CME
Tel: (980) 819 5095
Email: office@worldclasswscme.com

Asian Pacific Digestive Week 2012
5/12/2012 to 8/12/2012
Location: Bangkok, Thailand
Tel: (66) 2 748 7881 ext. 111
Fax: (66) 2 748 7880
E-mail: secretariat@apdw2012.org
Website: www.apdw2012.org

World Allergy Organization International Scientific Conference (WISC 2012)
6/12/2012 to 9/12/2012
Location: Hyderabad, India
Info: World Allergy Organization
Tel: (1) 414 276 1791
Fax: (1) 414 276 3349
E-mail: WISC@worldallergy.org
Website: www.worldallergy.org
Shanghai set for regional respiratory forum

Elvira Manzano

The 8th International Symposium on Respiratory Diseases (ISRD) and American Thoracic Society (ATS) in China Forum to be held in Shanghai from 9-11 this November is expected to attract delegates and leaders in pulmonary and respiratory medicine from all over the world.

The 4-day conference at the Shanghai International Convention Center will consist of plenary and state-of-the-art lectures, oral presentations and satellite symposia, including a session on translational respiratory medicine. Some of the main highlights in the scientific program include latest trends in the diagnosis and management of COPD and lung cancer, as well as updates on sleep medicine and mechanical ventilation.

Conference president Professor Chunxue Bai, chairman of the Shanghai Respiratory Research Institute (SRRI), which is hosting the event, and chairman of the Respiratory Department of Zhongshan Hospital and Fudan University, Shanghai, China, said 2012 marks a significant milestone for the ISRD, with its inaugural joint scientific sessions with the ATS.

"[The] ATS in China Forum reinforces our ‘east meets west’ approach where renowned speakers from the US, Europe, Asia Pacific and China will share their insights, knowledge and experiences in respiratory research and clinical practice for better disease management outcome."

Bai expects around 1,500 delegates, 80 percent of which are from China, to attend the conference. He said the event will provide a forum for clinical and scientific researchers with complementary experience and expertise to debate and foster collaboration towards prevention and management of respiratory diseases and its complications.

“It is our hope that, with the support and contribution from delegates, speakers and industrial companies, ISRD will grow to become an international academic brand attracting more respiratoryologists as well as clinical and translational researchers,” Bai said.
Beijing ready for regional cardiology congress

The 23rd Great Wall International Congress of Cardiology (GW-ICC) Asia Pacific Heart Congress (APHC) 2012 in Beijing, China from 11-14 October will showcase the latest research and clinical advances in cardiology in the Asia Pacific.

This year’s congress will be held in over 30 venues, with around 13,000 delegates anticipated to participate in 400 academic exchanges, thematic sessions, training presentations and exhibitions.

Congress president Professor Dayi Hu, chief of the Cardiology Division, Peking University’s People’s Hospital, Beijing, China, said participants can also look forward to keynote lectures, post-graduate courses, workshops and 17 joint symposia with leading international societies including the American College of Cardiology (ACC), European Society of Cardiology (ESC) and World Heart Federation.

Discussions will focus on opportunities and challenges in cardiovascular care in the US and China, advances in the management of heart failure and acute coronary syndromes, cardiac and stroke rehabilitation care, updates in cardiovascular imaging, cardiac catheterization and revascularization, new approaches to AF ablation and latest recommendations in pharmacotherapy, among other topics. Both English and Chinese sessions will be provided.

“We hope this congress will be an exciting and productive gathering of cardiologists from all over the world and provide [them] an opportunity to share knowledge, experience and views on current cardiology topics,” said Hu.

Over the years, the GW-ICC APHC has brought together leading cardiologists and researchers to discuss developments in cardiovascular research and practice. The congress has been attracting participation from a number of international academic organizations annually.

This year’s theme is “Emphasis on Rehabilitation and Secondary Prevention, from hospital back to home.”

The GW-ICC and APHC is organized by the GWICC congress committee together with 23 leading international academic societies.
“As far as I can see, it could be anything!”

“Lucy, I think we should get a divorce!”

“Don’t worry, it takes time to get used to progressive lenses!”

“The patient in the next bed is highly contagious. Please Harry, don’t go near him!”

“So, your wife had a doctor’s appointment and you couldn’t find a babysitter?”

“Darn it Dr. Flask, you shouldn’t have touched that thing!”

“Should I take this medicine orally or in written form?”
The sun glistens on the Amstel River, forming a seemingly endless pathway of diamonds, an illusion interrupted only by small boats. The boats, largely ferrying tourists on the edge of their seats attempting to get the best views of the narrow, gabled houses leaning into one another, weave in and out of the canal network, skillfully avoiding docked houseboats. Occasionally, a ‘party boat’ breaks the monotony with a boisterous crowd on board lost in their heady fog of loud music and alcohol.

Amsterdam, touted as ‘the Venice of the North,’ blends history, art and culture seamlessly with hedonism. From the various tourist attractions, parks and pleins (squares) to the bars, clubs and the red-light district which come alive at sundown, this city has something to offer everyone.

With over 60 museums, 50 theaters and 140 art galleries, Amsterdam is a mecca for culture vultures. The aptly named Museumplein alone boasts three very popular Dutch museum institutions, the Rembrandt-heavy Rijksmuseum (Dutch National Museum), which houses an impressive collection of paintings from the Dutch Golden Age, the Van Gogh museum, and the modern art Stedelijk museum.
The Anne Frank Museum, drawing almost a million visitors annually, is a moving experience. The restored cramped, dark secret annexe where two Jewish families hid from persecution by the Nazis, provides a bleak contrast to the optimistic journal entries of Anne.

Various markets selling a hodgepodge of items guarantee you will score a bargain or two. The Albert Cuyp street market sells everything from fruits to clothes, cosmetics and spices. A personal favorite is the Bloemenmarkt, the floating flower market on the Singel canal. Roses, peonies and tulips in full bloom spill from the stalls onto the pavement in an explosion of colors.

Options are a plenty for getting from one place to another in Amsterdam. Arm yourself with a map and you will find that most places are within walking distance through the charming, distinctly European cobbled streets. The city is also serviced by frequent trams, convenient after a long day of sightseeing.

A more favorable option is hiring a bicycle. The number of bicycles in Amsterdam is said to outnumber the population, and this is very apparent with the multi-story bicycle parking lot in the heart of the city, visible as soon as you step out of Amsterdam Central Station.

Stepping out of the flurry of activity in the capital, a visit to the Netherlands is not complete without visiting the Dutch countryside. The immediate scenery change sees breathtaking views of vast farmland dotted by lazily grazing cows. Head to the picturesque village of Zaanse Schans and gape in awe at the six remaining windmills that line the River Zaan. A cheese-making factory close by lets you sample Dutch cheese and take home an assortment of cheeses, chocolates and Delftware (blue pottery).

A ferry ride away, the postcard-worthy fishing villages of Volendam and Marken make for perfect spots to bask in the sun by the waterfront and devour fresh seafood or indulge in an assortment of desserts sold by the harbor front.

The sights and sounds are sure to reel you in and leave you feeling like you’ve left a piece of your heart in the Netherlands.