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Spirometry still underused in primary care

Jenny Ng

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

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

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

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

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

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

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

To improve the use of spirometry, she suggested there is a need to first address the underlying skepticism in primary care. What is needed is the evidence to change provider beliefs in the utility of spirometry in COPD, Joo said.
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References:
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Further information is available upon request.
Chronic viral hepatitis is one of the major health problems globally. However, attention to date in the field of transmissible diseases has focused on HIV, malaria and tuberculosis. Viral hepatitis has not had the prominence or advocacy that accompanies these other conditions.

It is only in recent years that the WHO has acted on knowledge available to it for some time about the global impact of chronic viral hepatitis. The facts are straightforward – there are 500 million people in the world with chronic hepatitis B (HBV) or C (HCV), with the vast majority in the Asian Pacific region. Most people with HBV are infected in childhood. In the scenario of childhood infection, most will develop chronic disease with the subsequent risk of cirrhosis, liver failure, liver cancer and death. Vaccination programs are effective for HBV, but there remains a large pool of people without access to this strategy and a similarly large proportion of already infected individuals in whom vaccination is too late. Treatment for HBV with existing antivirals is life-long, expensive and available through government funding programs only in a minority of countries.

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

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

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

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

Rajesh Kumar

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

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

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

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

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

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

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

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

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

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

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

“This is a relationship whereby research is directly helping to strengthen the system of health provision in a particular region,” he said. “Research is an indispensable catalyst for health and political change.”
TeleStroke system triples number of patients receiving thrombolysis

Jackey Suen

A locally developed TeleStroke system allows neurologists to perform off-site assessment, enabling more patients to receive thrombolytic therapy, according to investigators from the Prince of Wales Hospital (PWH) and the Hong Kong Polytechnic University (PolyU).

The most effective treatment of ischemic stroke is thrombolytic therapy within 3 hours of stroke onset, underscoring the importance of an effective 24-hour thrombolysis service. “However, no public hospitals in Hong Kong can provide such a service as there are fewer than 60 neurologists responsible for acute stroke care in the public sector,” reported Dr. Thomas Leung of the Department of Medicine & Therapeutics, Chinese University of Hong Kong, at a press conference.

To make 24-hour thrombolysis service possible in Hong Kong, Leung’s team developed a TeleStroke system in collaboration with the Department of Health Technology and Informatics at PolyU. The system has been in use in PWH since May 2012 to provide 24-hour thrombolysis service.

“The key feature of this TeleStroke system is a security-enhanced software,” explained Dr. Fuk-Hay Tang of PolyU. “Off-site neurologists can assess medical images of acute stroke patients with almost no delay through a software installed on their mobile electronic devices [eg, laptop, tablet].”

Combining this image distribution system with video conferencing for consultation, off-duty neurologists can evaluate and determine patients’ eligibility for thrombolytic therapy, which is then initiated by trained on-site stroke nurses.

Since the implementation of the system, three times more patients have received thrombolytic therapy at PWH. Of the 53 patients who received thrombolysis through TeleStroke, 19 had almost fully recovered after 3 months. The rates of recovery, disability, severe intracranial bleeding and death were all comparable to those treated by on-site neurologists at PWH (all p>0.1).

“We are planning to extend the TeleStroke network to Alice Ho Miu Ling Nethersole Hospital and North District Hospital within 2 years,” said Leung.
Experts recommend early antiretroviral therapy for HIV-associated TB

Christina Lau

Antiretroviral therapy (ART) should be initiated early in patients with HIV-associated tuberculosis (TB) and a low CD4 cell count, according to public health researchers in Hong Kong.

The optimal timing of ART initiation in patients with HIV-associated TB has been controversial, as its concurrent use with anti-TB drugs is associated with overlapping toxicities, immune reconstitution inflammatory syndrome (IRIS), and complex drug-drug interactions. [Am J Respir Crit Care Med 2001;164:7-12; J Infect Dis 2007;196(suppl 1):S63-S75; S Afr Med J 2007;97:412, 414-415; Clin Dev Immunol 2011;2011:103917]

While studies have examined the association between the timing of ART and treatment outcomes of HIV-associated TB, most of the subjects were from developing countries with a high prevalence of TB and HIV, especially Africa.

Data from countries with an intermediate TB burden, a low HIV prevalence and good health infrastructure are scanty, according to researchers from the Center for Health Protection. [Hong Kong Med J 2013;19:474-483]

They therefore retrospectively reviewed the data of 260 patients with HIV-associated TB, reported to Hong Kong’s territory-wide TB-HIV Registry between 1996 and 2009, to evaluate the optimal timing for initiating ART.

Patients in the study had very low baseline CD4 counts (median, 74/μL) and were ART-naïve.

Twelve percent of the patients received early ART, initiated within 2 months after the start of anti-TB treatment. These patients had a more favorable outcome, with 91 percent being cured of TB or having completed TB treatment without relapse at 24 months.

In patients with ART started later or not initiated during the course of anti-TB treatment, only 67 percent had a favorable outcome (p=0.007).

Although adverse effects of anti-TB drugs and IRIS were more common in patients receiving early ART (41 vs 26 percent [p=0.08] and 22 vs 4 percent [p<0.001], respectively), no IRIS-attributable deaths occurred.

The researchers therefore recommended early initiation of ART in patients with HIV-associated TB and a low CD4 count of <200/μL. “Drug co-toxicity and IRIS that may be increased by earlier initiation of ART does not undermine TB treatment outcomes to a significant extent,” they concluded.

In an accompanying editorial, Dr. SS Lee of the Stanley Ho Center for Emerging Infectious Diseases, Chinese University of Hong Kong pointed out that the very low baseline CD4 counts of patients in the study suggest-
ed that a majority of the HIV diagnoses were made no earlier than the respective TB diagnoses. [Hong Kong Med J 2013;19:472-473]

“However, this does not mean that late diagnosis is becoming more common,” he wrote.

In fact, the number of annually reported AIDS cases has plateaued since 2009 despite a continuing rise in new HIV infections. [www.aids.gov.hk] The slowing of disease progression is possible only through measures such as earlier HIV diagnosis, earlier screening, and expanded use of ART, he suggested.

HK to top Asia Pacific’s prediabetes prevalence?

Christina Lau

Hong Kong has the second highest prevalence of prediabetes in the Asia-Pacific region, according to the latest data from the International Diabetes Federation (IDF).

The data, presented recently at the IDF World Diabetes Congress 2013, showed that Hong Kong isn’t too far from leading the region in terms of the prevalence of impaired glucose tolerance (IGT).

In 2013, 13.3 percent of Hong Kong’s population had IGT. The region’s top was in Malaysia, with a prevalence of 15.2 percent. [IDF Diabetes Atlas, 6th edition: www.idf.org/diabetesatlas]

The prevalence of diabetes in Hong Kong was 7.5 percent, compared with 10.9 percent in Malaysia, 10.4 percent in Singapore, and 9.6 percent in China.

“The prevalence of IGT is very high in the Asia-Pacific region, compared with that of diabetes,” said Dr. RM Anjana of the Madras Diabetes Research Foundation & Dr. Mohan’s Diabetes Specialities Center in Chennai, India, who presented the data. [IDF 2013, abstract 0400]

“This suggests the epidemic of diabetes is perhaps still very young, with a high potential for individuals with IGT to progress to diabetes,” she cautioned.
Mind-body exercises beat running in preventing mood disorders

Christina Lau

Mind-body exercises such as yoga, tai chi and qi gong are more effective than aerobic exercises in reducing an individual's risk of mood disorders, a recent study has shown.

The benefit is greatest when mind-body exercises are combined with aerobic exercises, according to researchers from the Chinese University of Hong Kong (CUHK).

The researchers surveyed 2,744 local citizens aged 18-75 years to examine their exercise patterns in the last 12 months and its association with their risk of mood disorders.

Results showed that only half of the respondents exercised regularly (at least twice a week, each time for at least 30 minutes), while 6.4 percent did not exercise at all.

Respondents who did not exercise were 3.7 times more likely to have a high risk of mood disorders than those who exercised regularly (13.7 vs 3.7 percent). Among respondents who exercised regularly, those who had carried on for more than 1 year were significantly less likely to be at high risk of mood disorders (4.2 percent vs 7.1 percent for <1 year).

The type of exercise matters, with mind-body exercises being more effective than aerobic exercises, walking or stretching.

In those who performed mind-body exercises, only 4 percent were at high risk of mood disorders. In those who performed aerobic exercises or walking, 4.8 percent and 6.2 percent were at high risk, respectively.

The most effective strategy was to combine mind-body and aerobic exercises. Respondents who did so were 4.5 times less likely to be at high risk of mood disorders than those who did not exercise at all (3 vs 13.7 percent).

"Physicians who recommend exercise to patients with anxiety and depression should recognize that conventional advice such as walking for 30 minutes per day, while possibly good for physical illnesses, is inadequate for mood disorders," said Professor Sing Lee of CUHK’s Department of Psychiatry.

"Not everyone with mood disorders may need, tolerate, or have easy access to conventional treatment. Tailor-made exercise programs can be developed as a form of treatment for mood disorders based on comprehensive assessment of patients’ symptom profiles and physical status,” said principal investigator, Professor Linda Lam of CUHK’s Department of Psychiatry and Director of the Chen Wai Wai Vivien Foundation Therapeutic Physical Mental Exercise Center.

As such, the researchers plan to examine the effects of combined mind-body and aerobic exercises on individuals with anxiety and/or depressive disorders, in addition to an ongoing clinical trial on aerobic exercise for depression. Training activities will also be organized for GPs, while professionally selected exercise combinations and mindfulness practices are available at the Center for individuals with mood disorders. [http://cwwpmex.med.cuhk.edu.hk]
A call for increased recognition of osteoporosis in Hong Kong comes amidst warnings of a dramatic rise in the number of hip and spinal fractures.

The new Asia Pacific regional audit conducted by the International Osteoporosis Foundation (IOF) found that more than 50 percent of all hip fractures worldwide will occur in Asia Pacific by 2050 as a result of an aging population, increased urban and sedentary lifestyles, increased vitamin D deficiency and low calcium intake, as well as a lack of prevention strategies.

Worldwide, one in three women and one in five men over the age of 50 will suffer a fracture due to osteoporosis, resulting in severe disability, loss of independence and productivity, and impoverishment.

In Hong Kong, about 4,500 hip fractures occur every year, resulting in hospital costs of USD 52 million annually, while 30 percent of women and 17 percent of men aged 70-79 years have had a vertebral fracture. [Hong Kong Med J 2013;19(Suppl 2):1-40]

“Osteoporosis has been a major public health problem in Hong Kong, but this disease has not received due attention from the policymakers as compared to other chronic diseases like diabetes, hypertension, cardiac or cerebrovascular diseases and dementia,” said Dr. Andrew Ho, President of the Osteoporosis Society of Hong Kong.

Currently, there are no fracture registries in Hong Kong and only 10 to 25 percent of hospitals have fracture liaison services in place. Moreover, the waiting time to receive a dual-energy X-ray absorptiometry (DEXA) may be up to 3 years in public hospitals, and a history of previous fracture is required for reimbursement.

Adding to this are the low levels of calcium intake and vitamin D deficiency. The average calcium intake is 400 mg/day in the Hong Kong population and 500 mg/day in Asians, while the WHO recommendation is 1,000-1,300 mg/day. Furthermore, an estimated 40 to 90 percent of Chinese children are deficient in vitamin D (<25 nmol/L).

“In Hong Kong, osteoporosis is not recognized as a medical specialty in itself, nor...
is it a recognized core component of medical training. This may be one reason why doctors underestimate the serious impact of osteoporosis and do not routinely prescribe anti-osteoporosis drugs, as well as calcium and vitamin D to those at high risk of fractures,” said Ho.

To address these needs, experts are recommending policymakers and physicians to support the development of more fracture liaison services, extend the treatment reimbursement criteria, provide adequate DEXA services, and devote more resources to educational initiatives.

**Experts discuss controversies in fracture prevention therapies for postmenopausal women**

The controversy continues regarding which therapies to use for fracture prevention in postmenopausal women.

At the meeting, experts discussed current evidence on the use of hormone replacement therapy, selective estrogen receptor modulators (SERMs) and calcium and vitamin D supplementation for improving bone density and reducing fracture risk in women with increased risk of osteoporosis.

Updates from the Global Consensus Statement on Menopausal Hormone Replacement Therapy (HRT) and 2013 International Menopause Society recommendations have outlined the efficacy of HRT in reducing vasomotor symptoms, preventing osteoporotic fractures, reducing all-cause mortality due to chronic heart disease and reducing vaginal atrophy. [Climacteric 2013;16:203-204; Climacteric 2013;16:316-317]

“What we should take from this is that HRT can be a good option. To improve benefits, HRT should be initiated before the age of 60 years or within 10 years of menopause, while using good progestogens and non-oral estradiols can reduce risks,” said Dr. Ling Xu from the Peking Union Medical College Hospital, China.

But for Professor Ego Seeman from the University of Melbourne, Australia, there is still no reason to initiate HRT only for fracture prevention due to the uncertainty in risks that were emphasized after publication of the 2002 landmark Women’s Health Initiative report. [JAMA 2002;288:321-333]

SERMs, however, have been developed to retain the beneficial effects of estrogens on the bone, while having anti-estrogenic activities on other tissues.
“One of the major differences between estrogens and early SERMs such as tamoxifen, and the newer SERMs such as raloxifene and bazedoxifene, is the specificity towards the uterus,” said Dr. Serge Ferrari of the Geneva University Hospital in Switzerland. “For example, tamoxifen favors uterine epithelium proliferations, thus increasing bleeding and cancer risk. New-generation SERMs, which are more antagonistic towards endometrial tissue, provide the best benefit-to-risk profile.”

While the benefits of HRT and SERMs are well established, the use of vitamin D and calcium supplements for reducing fracture risk is more controversial. “Although we continue to declare vitamin D and calcium deficiencies in the population, there are flaws in our definition of a deficiency, flaws in our study designs and flaws in the execution of trials,” explained Seeman.

“Studies on vitamin D and calcium supplementation have shown inconsistent results in terms of the efficacy in reducing the risk for hip fractures. What we need are more prudent trials showing clear evidence on the best dosage to take and the potential deleterious effects,” said Seeman.

Fracture liaison services necessary for secondary fracture prevention

Implementing fracture liaison services (FLS) may be the key to reducing the current gaps in secondary fracture prevention.

Currently, there is a global need for FLS that have not been met. One campaign looking to facilitate the implementation of FLS is titled Capture the Fracture.

“The key message with Capture the Fracture is that every single time a person presents with a fracture of the wrist, humerus or pelvis, there is an opportunity to identify this individual and to ensure that his or her future fracture risk can be assessed and that appropriate guideline-based care is delivered,” said Paul Mitchell of the University of Derby, UK.

The campaign looks to provide FLS through a coordinator-based system that ties together the key services of identification, investigation and intervention. Previous analysis has shown that more intensive FLS models
offering all three services have much greater success in terms of the proportion of patients receiving bone mineral density tests (79 percent vs 43 percent with a two-service model) and osteoporosis treatment (46 percent vs 23 percent with a two-service model). [Osteoporos Int 2013;24:393-406]

There is a demand for FLS amid knowledge of the gaps in care and the continually aging global population. “We know that people who have had one fracture will be at a two-fold increased risk for a second fracture. However, healthcare systems around the world are failing to identify these patients and prevent the second fracture,” said Mitchell.

In audits performed around the world, only about 20 percent of those suffering from a fragility fracture were shown to have been assessed for care. Hong Kong is one example where the expected rise in the number of elderly will be a significant burden if FLS cannot be provided.

The campaign thus aims for an improved global response in capturing fractures while setting best practice standards, facilitating change and creating awareness.
Important benefits for women who quit smoking early

Dawn Green

Smoking nearly triples the risk of pre-mature death in women and quiting nearly triples the risk of pre-mature death in women and quitting before age 30 avoided 97 percent of this added risk. Smoking before age 30 avoided 97 percent of excess mortality from cigarettes.

Multivitamins may protect against cancer

Rajesh Kumar

Researchers analyzed data from the Phy-

Million Women Study.

During the trial, 2,669 cases of cancer were detected, including 1,373 cases of pros-

tate cancer and 210 cases of colorectal can-

The multivitamin group had a similar re-

duction in total epithelial cell cancer, but not in other site specific cancers such as colorectal,

Non-smokers, smokers lost at least 10 years

life, women who smoked and stopped still

have “1 to 2 times the mortality rate of never-

smokers.” For those who continued to smoke

decade caused a modest but statisti-

cally significant 8 percent reduction in all

cancers among men in a large randomized,

double-blind, placebo control trial.

The men were randomized in 1997 to receive

male US physicians aged 50 years or older,

sicians' Health Study II involving 14, 641

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Drugs in the pipeline for MDR-TB

The promising data of four novel tuberculosis (TB) drugs provides hope to combat multidrug-resistant TB (MDR-TB), an expert suggests.

“MDR-TB, defined as TB resistant to at least isoniazid and rifampicin, affected 450,000 patients worldwide last year,” said Dr. Kwok-Chiu Chang of the Center for Health Protection, Department of Health. “It is associated with poor prognosis, and the current treatment success rate is 60 to 80 percent.”

Since WHO-recommended drugs for the treatment of difficult MDR-TB cases are associated with numerous side effects, new agents with better toxicity profiles are in clinical development. “There are four that are most promising, namely bedaquiline, delamanid, PA-824 and sutezolid,” he noted.

“Bedaquiline is a diarylquinoline that has no cross-resistance with existing TB drugs,” said Chang. The US FDA approved its use in 2012 as part of the combination therapy to treat adult MDR-TB when other effective regimens cannot be provided, after its effectiveness against TB was proven in two phase II studies of 440 patients. “However, it is associated with an increased incidence of QT prolongation that may lead to fatal arrhythmia,” Chang cautioned.

Delamanid, a metronidazole derivative, was shown in a phase IIB trial to increase the sputum conversion rate of MDR-TB from 29.6 percent to 45.4 percent, when added to an optimized background regimen. [N Engl J Med 2012;366:2151-2160] “Subject to selection bias, an observational study showed that the use of delamanid for ≥6 months significantly improved outcomes and reduced mortality, compared with ≤2 month’s administration,” he said. “However, the European Medicines Agency rejected the approval application of delamanid, as the evidence for its use in MDR-TB was inadequate.”

“PA-824 is another metronidazole derivative, which demonstrated very good efficacy against TB. As shown in a phase II trial, triple therapy with PA-824, pyrazinamide and moxifloxacin was more effective than doublet or single-agent therapy with newer drugs,” said Chang. [Lancet 2012;380:986-993] “Overall, it was safe and well tolerated.” [Antimicrob Agents Chemother 2009; 53:3720-3725]
“Sutezolid is a linezolid analog likely to have better activity and less toxicity than linezolid,” continued Chang. “A phase II trial assessing the efficacy of sutezolid in TB showed that it reduced the mycobacterial burden in sputum during 14 days of treatment. However, the control arm of standard four-drug therapy for TB showed a greater efficacy than sutezolid alone.” [Wallis R, et al, AIDS 2012, abstract THLBB02]

According to Chang, at least four clinical trials are ongoing to evaluate a combination of novel drugs with potential applications in MDR-TB treatment.

Can Chinese alternative therapy improve COPD?

Apart from medications and physical exercise, recent studies suggest that Chinese alternative therapies such as acupuncture, qi gong (QG) and tai chi (TC) may be beneficial for patients with chronic obstructive pulmonary disease (COPD).

“Acupuncture and transcutaneous electrical nerve stimulation over acupoints [Acu-TENS] are two major alternatives for the management of breathlessness in COPD,” said David Yu, Senior Physiotherapist at the Queen Elizabeth Hospital in Hong Kong. “Acupuncture can cause adverse effects due to its invasive nature. Therefore, non-invasive Acu-TENS is more commonly adopted by physiotherapists.”


“Acupuncture or Acu-TENS reduces shortness of breath possibly through up-regulation of sympathetic nervous system discharge, deactivation of the limbic region of the brain, increasing blood plasma endorphin level and decreasing respiratory muscle tone,” suggested Yu. “We look forward to larger clinical trials on acupuncture and Acu-TENS, and to investigating acupoints for different respiratory diseases.”

Meanwhile, Dr. Bobby Ng of the Department of Occupational Therapy, Kowloon Hospital, suggested the use of QG and TC for pulmonary rehabilitation (PR) in COPD patients. “Recently, we conducted a systematic review of 12 studies to investigate whether QG or TC produces better outcomes in COPD patients compared with conventional exercise,” he said.

Results showed that both FEV1/FVC (ratio
of forced expiratory volume in 1 second to forced vital capacity) and the 6-minute walk test scores significantly improved in patients performing QG or TC vs no exercise, but the effects were comparable to conventional exercise. “However, there is increasing concern about the role of low-grade systemic inflammation on the pathogenesis of COPD. Regular low-intensity exercise together with a meditative component, such as QG or TC, may suppress such inflammation,” noted Ng. [Eur J Cardio Prev Rehab 2009;16:430-437]

“This systematic review provided some evidence to support QG or TC as an alternative to conventional exercise in PR. They can be a good choice when patients are too frail to go outdoors, or when a formal PR program is not available,” concluded Ng.
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Doctors with dyslipidemia: Are they compliant with treatment?

Christina Lau

A recent survey showed that doctors with dyslipidemia may not be very compliant with lipid-lowering therapy although they often reinforce treatment compliance in their patients.

The CV Alliance, a multidisciplinary group of specialists in Hong Kong, interviewed 120 doctors (GPs, 58 percent; specialists, 42 percent) in the private sector to investigate the prevalence of dyslipidemia among doctors and their medication use.

“Results showed that 35 percent of respondents currently had dyslipidemia, which is higher than the population average,” said Dr. Chun-Kwan Chow, Convener of the Alliance.

However, 17 percent of doctors with dyslipidemia were not on medication to manage their lipid levels.

Among doctors who were on medication for dyslipidemia, 86 percent took their drugs daily, while 14 percent did so only when necessary.

Most of the respondents preferred a branded statin to manage their cholesterol levels.

When choosing statin therapy, they considered cholesterol-lowering efficacy (99 percent), safety and reliability (97 percent), minimal side effects (95 percent), strong medical evidence (93 percent) and reasonable price (93 percent) as the most important criteria. Advertisements and promotional activities were the least important.


The use of statins is expanded under the controversial guidelines. In addition to individuals with clinical ASCVD or primary elevations of LDL-cholesterol ≥4.9 mmol/L, those 40-75 years of age with LDL-cholesterol levels between 1.8 and 4.9 mmol/L are also candidates for statin therapy if they have diabetes or an estimated 10-year ASCVD risk of ≥7.5 percent as assessed by the new AHA/ACC risk calculator.

“More than 720,000 individuals in Hong Kong are estimated to be candidates for statin therapy under the new guidelines,” noted Leung.
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27th Hong Kong Society for Surgery of the Hand (HKSSH) Annual Congress
15/3-16/3
Info: Vincent Hau
E-mail: hkssh2014@gmail.com
www.hkssh.org

18th Annual Scientific Meeting
Hong Kong Society for Infectious Diseases
22/3
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33rd Annual General Meeting cum Scientific Meeting
Hong Kong Society of Gastroenterology
27/3
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Fax: (852) 2869 9533
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Annual Scientific Meeting 2014
Hong Kong Thoracic Society; American College of Chest Physicians
29/3-30/3
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11th Hong Kong International Orthopedic Forum
Department of Orthopedics & Traumatology, HKU
12/4-13/4
Tel: (852) 2255 4257
Fax: (852) 2817 4392
E-mail: ortho1@hkucc.hku.hk

4th Annual Scientific Meeting
Obstetrical and Gynecological Society of Hong Kong
24/5-25/5
Tel: (852) 2559 9973
Fax: (852) 2547 9528
E-mail: ogshk@icc.com.hk
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International Digestive Disease Forum
Institute of Digestive Disease, CUHK
7/6-8/6
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Annual Scientific Meeting 2014
Hong Kong Society of Dermatology and Venereology
21/6-22/6
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4th International Diagnostic Course Davos (IDKD) Intensive Course in Hong Kong
28/6-30/6
Info: Toby Chui
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Annual Scientific Meeting and Workshop 2014
Hong Kong Institute of Musculoskeletal Medicine
5/7-6/7
Info: MIMS (Hong Kong) Limited
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Hong Kong Events

MSKUS Workshop 2014
Hong Kong Institute of Musculoskeletal Medicine
1/8-3/8
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Hong Kong International Dental Expo and Symposium
Hong Kong Dental Association
22/8-24/8
Info: MIMS (Hong Kong) Limited
Tel: (852) 2155 8557 / 2116 4348
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9th Congress of the Asian-Pacific Society of Atherosclerosis and Vascular Diseases and 16th Diabetes and Cardiovascular Risk Factors – East Meets West Symposium
26/9-28/9
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Annual Scientific Meeting 2014
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1/11-3/11
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4th Congress of the World Association for Plastic Surgeons of Chinese Descent
Hong Kong Society of Plastic, Reconstructive and Aesthetic Surgeons
6/11-8/11
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Tel: (852) 2155 8557 / 2116 4348
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5th Asian Preventive Cardiology & Cardiac Rehabilitation Conference
Hong Kong College of Cardiology
6/11-9/11
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4th Five-Continent Congress
Hong Kong Dermatology and Laser Center
10/12-13/12
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Reducing salt intake improves heart, kidney health in CKD patients

Rajesh Kumar

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

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

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

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

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

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

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

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

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

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

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

Elvira Manzano

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

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

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

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

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

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

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

“Similar to our approach with patients who have coronary artery disease, risk factor and weight management should be considered standard for any patient with AF.”
Eating certain fruits reduces type 2 diabetes risk

Lianne Cowie

Although increased fruit consumption is recommended for the primary prevention of many chronic diseases, findings from epidemiological studies have been mixed. A recent prospective, longitudinal cohort study evaluating fruit consumption and the risk of type 2 diabetes found a significant reduction in risk following the consumption of blueberries, grapes and apples, but an increased risk following the consumption of fruit juice.

The study, followed-up by a self-report questionnaire, included 66,105 women from the Nurses’ Health Study (1984–2008), 85,104 women from the Nurses’ Health Study II (1991–2009), and 36,173 men from the Health Professionals Follow-up Study (1986–2008). All were free of major chronic diseases at baseline. [BMJ 2013;347:f5001]

During a follow-up period amounting to 3,464,641 person-years, 12,198 participants developed type 2 diabetes. After adjusting for personal, lifestyle, and dietary risk factors for diabetes, the pooled hazard ratio (HR) of type 2 diabetes for every three servings/week of whole fruit was 0.98 (95% CI 0.96–0.99). Analyses of the consumption of three servings/week of individual fruits gave adjusted pooled HRs for type 2 diabetes of 0.74 (95% CI 0.66–0.83) for blueberries; 0.88 (95% CI 0.83–0.93) for grapes and raisins; 0.89 (95% CI 0.79–1.01) for prunes; 0.93 (95% CI 0.90–0.96) for apples and pears; 0.95 (95% CI 0.91–0.99) for bananas; 0.97 (95% CI 0.92–1.02) for peaches, plums, and apricots; 0.99 (95% CI 0.95–1.03) for oranges; 1.03 (95% CI 0.96–1.10) for strawberries; and 1.10 (95% CI 1.02–1.18) for cantaloupe. The pooled HR for fruit juice consumption was 1.08 (95% CI 1.05–1.11).

The researchers, led by research fellow Isao Muraki from the Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts, US, suggested that the significant differences in risk seen with different types of fruit were probably linked to their different compositions.

“Our findings suggest that there is significant heterogeneity in the associations between individual fruits and risk of type 2 diabetes,” they wrote. “The differences in associations between individual fruits were not accounted for by variation in the glycemic index/glycemic load values of individual fruits. Overall these results support recommendations on increasing consumption of a variety of whole fruits, especially blueberries, grapes, and apples, as a measure for diabetes prevention.”
Energy drinks may affect cardiac function

Elvira Manzano

Consuming energy drinks with high amounts of taurine and caffeine can increase the contractility of the heart, according to a small study.

“We have shown that even small amounts of energy drinks have short-term impact on heart function,” said researcher Dr. Jonas Doerner of the cardiovascular imaging section, University of Bonn, Germany. Whether this alteration in heart function has any clinical benefit is not known.

In the study, healthy adults who downed the drinks had significant increase in peak strain and peak systolic strain (parameters for systolic left ventricular contractility) an hour later compared with baseline (p=0.001 for both). There were no effects on heart rate (HR), blood pressure (BP), or left ventricular ejection fraction (LVEF), but there were slight significant increases in left ventricular end diastolic volume and left ventricular stroke volume. [Radiological Society of North America 2013; Abstract SSC02-06]

“We don’t know exactly how, or if this greater contractility of the heart impacts daily activities, or athletic performance. We need additional studies to understand this mechanism and to determine how long the effect of the energy drink lasts,” said Doerner.

Most energy drinks contain taurine, an amino acid found in protein-rich foods such as meat and fish, and caffeine, a CNS and metabolic stimulant. The drinks used in the study had both taurine (400 mg/100 mL) and caffeine (32 mg/100 mL). Doerner said most of the effect appeared to be due to taurine, rather than caffeine.

The study involved 18 healthy individuals with a mean age of 27.5 years. Cardiac magnetic resonance imaging (CMR) was used to measure heart function before and 1 hour after taking the energy drink. Strain and LV function were recorded together with other vital parameters (BP and HR).

“We have shown that even small amounts of energy drinks alter heart function. Further studies have to evaluate the impact of long-term energy drink consumption and its effect on patients with heart disease to determine any potential risks or benefits,” Doerner said.

In the meantime, children and individuals with an irregular heart beat should avoid energy drinks until more studies are conducted, he added.

Commenting on the study, Dr. Reginald
Liew, consultant cardiologist at the Harley Street Clinic in Gleneagles Hospital and Mount Elizabeth Novena Hospital, Singapore, said the research is interesting as it scientifically shows that energy drinks, which are widely consumed and popular among the public, have short-term effects on the heart.

“It should be noted that the investigators reported effects on peak strain, which relate to the degree of cardiac contraction, but there were no overall effects on cardiac output or other cardiovascular parameters such as BP and HR. So the clinical significance or impact of this is unclear,” he said.

Other areas that deserve further attention are the longer term effects of regular energy drink intake on the heart, its interaction with other drinks such as alcohol, and the effects of these drinks on patients with other heart conditions, such as high BP or coronary artery disease. It is also unknown whether these energy drinks can worsen palpitations in patients with cardiac arrhythmias, Liew added.

“In the absence of further data, it would be sensible for patients with heart conditions or a history of arrhythmias to avoid high intake of such energy drinks.”
Short-term orlistat use not linked to raised colorectal cancer risk

Lianne Cowie

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

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

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

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

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

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

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

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

“The study is limited by the relatively short follow-up time, and we cannot exclude the possibility of adverse effects of long term orlistat use on risk of colorectal cancer.” They added: “Our study, based on a large, population based healthcare database, represents people actually taking orlistat in the real world, who tend to be different from the participants in clinical trials.”
Resveratrol may help to improve lipoprotein profile of overweight, obese patients

Rajesh Kumar

Taking high doses of the polyphenol compound resveratrol for 2 weeks reduced intestinal and hepatic lipoprotein particle production in a small group of overweight and obese people in a pilot study.

Overproduction of hepatic apolipoprotein B (apoB)-100 containing very-low-density lipoprotein (VLDL) particles and intestinal apoB-48 containing chylomicrons contributes to hypertriglyceridemia seen in conditions such as obesity and insulin resistance. [Arterioscler Thromb Vasc Biol 2013;33:2895-2901]

The study researchers sought to assess intestinal and hepatic lipoprotein turnover in humans following 2 weeks of treatment with the natural antioxidant resveratrol, also known as the red wine compound. They randomized eight overweight or obese individuals with mild hypertriglyceridemia to 1,000 mg resveratrol daily for week 1 followed by 2,000 mg daily for week 2 or placebo. The patients on placebo and resveratrol were then crossed over.

Resveratrol treatment reduced apoB-48 production rate by 22 percent (p=0.007), apoB-100 production rate by 27 percent (p=0.02) and fractional catabolic rate by 26 percent (p=0.04).

“It is the first study in any species to examine the effects of resveratrol on triglyceride rich lipoprotein (TRL) kinetics. Resveratrol reduced production of TRL by the liver (apoB-100 containing VLDL) and gut (apoB-48 containing chylomicrons),” said lead researcher Dr. Satya Dash, postdoctoral clinical fellow at the University of Toronto in Toronto, Canada.

However, because of a reduction in clearance, there was no net change in apoB-100 concentration. There was a trend towards reduced apoB-48 concentration in this small cohort of individuals, added Dash.

“A longer study in a larger cohort of hypertriglyceridemic individuals will be needed to see if resveratrol can reduce apoB-48 concentrations significantly. If it does, then resveratrol could also potentially affect cardiovascular risk as raised postprandial TRL concentrations are a risk factor for atherosclerosis,” said Dash.

An earlier study found oral resveratrol to be effective in improving glycemic control and suggested its potential role as adjuvant for the treatment and management of diabetes. [Nutr Res 2012; doi:10.1016/j.nutres.2012.06.003]

The prospective open-label study randomized 62 patients to either resveratrol (250 mg/day) or placebo, along with their oral hypoglycemic agents for a period of 3 months.

Supplementation with resveratrol significantly improved mean HbA1c, systolic blood pressure, total cholesterol, and total protein.
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New Singapore institute to focus on nutrition, early development research

Rajesh Kumar

The role of nutrition and early development in the onset and progression of obesity and diabetes among Asians will be the research focus for the newly established Singapore Centre for Nutritional Sciences, Metabolic Diseases, and Human Development (SiNMeD).

The S$148 million institute is a collaboration between the National University of Singapore (NUS) Yong Loo Lin School of Medicine and A*STAR’s Singapore Institute for Clinical Sciences (SICS).

Its key research programs are: early development, which will focus on mother and infant nutrition, growth and developmental epigenetics; nutritional sciences, which aim to develop strategies for optimal nutrition; and metabolic diseases, which will study obesity and insulin resistance in Asians.

The programs will build on existing collaborations that have attracted significant investments from major food and nutrition companies such as Nestlé, Abbott and Danone. They will expand on the success of the GUSTO (Growing Up in Singapore Towards healthy Outcomes) birth cohort study, as well as work by the EpiGen consortium – an alliance of leading epigenetics researchers from the UK and New Zealand.

GUSTO is one of the world’s most comprehensive birth cohort studies involving over 1,200 families, where women were recruited during pregnancy and followed until their infants were at least 3 years of age. Data was collected on a range of environmental exposures in parents and their offspring to evaluate the role of developmental factors in metabolic diseases.

“SiNMeD’s research will help us to understand how the food we eat can lead to epigenetic changes in our DNA, which will in turn, either protect or predispose us to diseases like obesity and diabetes. This opens up new approaches to prevent and treat these diseases,” said Dr. Benjamin Seet, executive director of A*STAR’s Biomedical Research Council.

“Our knowledge of how optimal nutrition and lifestyle can delay or prevent disease onset in Asians is sadly lacking. SiNMeD will pool the expertise of NUS and A*STAR to greatly improve our knowledge of this area, to the betterment of society,” added NUS Deputy President (Research and Technology) and Tan Chin Tuan Centennial Professor Barry Halliwell.

A S$25 million metabolic Translational and Clinical Research (TCR) Flagship program grant awarded by the National Research Foundation in 2008 brought clinical investigators from the National University Health System, KK Women’s and Children’s Hospital, Singapore General Hospital and Tan Tock Seng Hospital together with researchers from SICS and other A*STAR research institutes for the GUSTO study, now culminating in SiNMeD.
Help COPD patients relieve their shortness of breath and meet the demands of their day"
GSK to stop paying doctors to promote drugs

Rajesh Kumar

GlaxoSmithKline (GSK) will stop paying doctors for promoting its drugs and will launch a new way to compensate its sales force by ditching individual sales targets.

The move comes amidst a scandal in China where the local police is accusing the company’s top brass of funneling up to 3 billion yuan to travel agencies to facilitate bribes to doctors and officials to encourage prescription of its drugs.

In a media release, GSK said it intends to stop “direct payments to healthcare professionals for speaking engagements and for attendance at medical conferences” in all the countries it operates in.

Instead, the focus will shift to strengthening GSK’s own medical and scientific capability to engage with healthcare professionals and a greater use of multiple channels, including digital technologies, to provide appropriate product and disease area information to healthcare professionals.

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

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

Fees for services to healthcare professionals for GSK sponsored clinical research, advisory activities and market research will continue.

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

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

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

Incentives of the company’s sales professionals who work directly with prescribing healthcare professionals will no longer be tied to individual sales targets. From 2015, they will be evaluated and rewarded for their technical knowledge, quality of the service they deliver to support improved patient care, and the overall performance of GSK’s business.
Global prevalence of allergic diseases rising: Time for concerted action

Excerpted from a speech by Dr. Ruby Pawankar, president of the World Allergy Organization (WAO), at the 8th World Congress on Developmental Origins of Health and Disease (DOHAD) 2013 in Singapore from November 17-20.

The prevalence of allergic diseases worldwide is increasing dramatically in both developed and developing countries, including in Asia Pacific and South Asia. About 30 to 40 percent of the world’s population currently suffer from some forms of allergy such as asthma, drug and food allergy, anaphylaxis, rhinitis, eczema, urticaria, and angioedema.

The World Health Organization estimated that 300 million people worldwide have asthma. If trends continue, this could increase to 400 million by 2025. It is also estimated that 250,000 unavoidable deaths from asthma occur in the world each year. Another 400 million suffer from rhinitis. This increase is particularly problematic in children, who are bearing the greatest burden.

If current trends continue, up to 400 million people could be suffering from asthma by 2025.

Globally, some 220 to 250 million people may suffer from food allergies, significantly affecting the quality of life of sufferers, mainly children. Fatal food-induced anaphylaxis, not only from peanuts, but also milk, egg, shell fish, tree nuts and lentils, varies across different regions. There are other places, for example Singapore, where bird’s nest is an important source of allergy. Awareness about this is crucial because when people move from one place to another, they could develop new types of allergies.

We must be prepared to meet patients’ needs by enhancing the diagnostic process, including the traceability of responsible foods and the availability of food substitutes. We
also have to do more in assisting hospitalized patients and preventing mortality.

Large areas in the world, particularly many countries in Asia, also lack legislation on stricter food labeling. As diagnostic and therapeutic strategies are not well known everywhere, evidence-based guidelines are necessary for clinicians, patients, governments and industry to deal with the challenge of food allergy. Such guidelines, for example the WAO recommendation on the Diagnosis and Rationale Against Cow’s Milk Allergy (DRACMA), are available and ready to be implemented.

Epidemiologic studies are also necessary, particularly in less developed areas of the world.

The continuing increase in the complexity and severity of allergic disorders in children and young adults will increase the burden even more when they reach adulthood. This would result in decreased quality of life and increased morbidity and mortality and, ultimately, increased socio-economic costs and economic burden to countries.

Allergy not only causes long-term immune dysfunction, but also has underlying inflammation, which forms the baseline for many non-communicable diseases. Other factors may also come into play such as gene-environment interactions.

Because of the huge extent of allergy prevalence, allergy should be regarded as a major public health problem. Unfortunately, so little effort is made to provide care for patients who suffer from allergies that they often seek alternative and complementary therapeutic remedies. For physicians, they shouldn’t just rely on medications to suppress the symptoms but should identify the allergens causing the symptoms but disease to prevent symptoms and disease progression.

Looking ahead, the future direction is not just endorsing allergy – that is why it is very important to include allergy in the NCD agenda. It is to endorse health, strengthen tolerance, adopt a new attitude to allergy, avoid allergens only if mandatory, recognize and treat severe allergies early, improve air quality, and reduce risk factors.

Finally, the Declaration of the WAO recommends the following: to conduct more epidemiological studies to establish the true burden of allergic diseases and asthma, initiate more allergens and environmental control measures, enhance the level of research and clinical practice available across different countries, provide undergraduate and postgraduate education and training and recognize the specialty of allergy, and increase public awareness of allergic diseases and their prevention to decrease the burden of allergic diseases in future years. A concerted effort of multiple stakeholders is essential to address this issue.
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Early development affects fat deposits in newborns

Rajesh Kumar

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

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

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

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

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

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

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

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

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

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

*GUSTO: Growing Up in Singapore Towards healthy Outcomes

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

Elvira Manzano

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

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

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

A poor diet in infancy can lead to chronic disease later in life.

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

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

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

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

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

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

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

Elvira Manzano

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

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

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

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

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

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

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

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

“These findings support the need for interventions targeting maternal depression early in pregnancy,” Reynolds concluded.
High intake of plant-derived omega-3 polyunsaturated fatty acid (alpha-linolenic acid, ALA) during childhood and adolescence by individuals who were underweight at birth may provide lasting benefits equivalent to years of statin or antihypertensive treatment in older adults predisposed to vascular disease.

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

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

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

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

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

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

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

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

The difference between the highest and lowest ALA intake tertiles equates to about
30-50 percent increase in dietary ALA, which in small children is equivalent to about one to two walnuts per day, which Skilton noted was a small dietary change.

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

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

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**Current diabetes tests for pregnant women inadequate**

**Radha Chitale**

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

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

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

These inconsistencies are reflected in practice, Venkataraman said.

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

However, both South Asians and Caucasians had similar postnatal fasting plasma glucose rates, though postnatal 2-hour plasma glucose rates were higher in South Asians.

Postnatal oral glucose tolerance tests were normal in 86 percent of the population. The most common abnormality in all the tests was 2-hour glucose abnormality, of 7 percent. Diabetes prevalence was 1.7 percent.

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

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

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

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

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**Metabolic phenotype influenced by ethnicity, environment**

Radha Chitale

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

“Ethnicity is not simply your genes, it’s also your environment and practices,” said Dr. Yap-Seng Chong, senior consultant in the Department of Obstetrics and Gynaecology at Singapore’s National University Hospital.

“Genetics accounts for only about 10 percent of a person’s susceptibility to type 2 diabetes... [Metabolic] data are scarce for many ethnic groups and only a few qualitative studies have focused on these communities.”

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

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

“Increased birth weight did not correlate to GDM across ethnicities

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

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

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

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

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

“Possibly the driver of insulin sensitivity is actually the fat in Malays and Chinese and maybe muscle in Indians,” Chong said. “Understanding the ‘Asian Phenotype’… [shows that] one size does not necessarily fit all.”
Treatment Updates on Diabetes and Lipid Disorders

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

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

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

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

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

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Challenges ongoing in tuberculosis research

Jenny Ng

One of the biggest challenges in achieving targets for tuberculosis (TB) is the need for improving diagnostics and development of new drug regimens.

“There is a lot of effort going into developing new preclinical approaches to identify optimized drug combinations for MDR TB, but these trials can take decades to finish,” said Dr. Charles Yu, head of the APSR Tuberculosis Assembly. “To speed up TB vaccine discovery and clinical testing, we need to identify TB surrogate end-point biomarkers and to consider new approaches in how we conduct clinical trials.”

One innovative paradigm developed by the TB Alliance is leading the way. By testing a pipeline of TB drugs in various combinations, they are able to identify new drug candidates and combination regimens in a period of years rather than decades and reduce the time to market by 75 percent. [TB Alliance, http://www.tballiance.org/pipeline/innovation-detail.php?id=11]

But while new drugs and optimized trial designs are underway, there is an emerging bottleneck in the number of vaccines that can be tested due to limitations in clinical site capacity worldwide.

“There is an extreme lack of balance between the areas in which we need to do research and the places that can provide them. Where we have the highest rates of TB is where we have the greatest shortage in resources – this is especially true of Africa as well as in Asia,” stressed Yu.

Limitations in diagnostic capacity are another challenge that is preventing an effective response to TB. Innovative approaches that are more sensitive and specific than microscopy, more user-friendly and safer than culture examinations, and more reliable than X-ray examinations are needed, advised Toru Mori of the Research Institute of TB, Japan.

Direct-detection methods with PCR technologies such as GeneXpert and loop-mediated isothermal amplification (LAMP) are leading the way in the development of new diagnostics. “LAMP has a 45 percent sensitivity and 99 percent specificity, and could increase the case finding rate by 40 percent compared to a smear testing,” said Mori.

Interferon gamma release assay (IGRA) is another tool that is beginning to replace the traditional method of TB skin testing. However, they are still in the process of evolving, with trials looking at improvements in the use of skin testing with specific antigens, use of other specific antigens, and use of the Quantiferon Microtube assay or the enzyme-linked immunospot assay (ELISpot)-based IGRA.
Immunotherapy benefits patients with asthma

Jenny Ng

New therapeutics for the management of asthma can minimize symptoms while inducing a stronger immune response.

A number of researches focusing on immunotherapies in preventing asthma exacerbation have shown a direct correlation between virus infection and T cell responses in asthmatics.

“Virus infection plays a key role in the severity of asthma exacerbations,” said Professor Sebastian Johnston of the Imperial College London, England. “By targeting the pathways involved in this immune response, we prevent and reduce the frequency of exacerbations.”

Johnston and colleagues looked at the immune responses in healthy and asthmatic patients who were clinically infected with rhinovirus and found that the type-2 helper T cell (Th2) cytokine responses after infection were significantly increased in both mild and moderately asthmatic patients.

“We saw a very clear correlation between the induction of the Th2 cytokines, interleukin [IL]-4, IL-5 and IL-13, and the severity of cold and lower airway symptoms,” said Johnston. “Moreover, Th2 cytokines can lead to the suppression of interferon and antiviral immunity.”

Other mediators involved in Th2 responses, such as bronchial epithelial cell derived IL-33, also increased after viral infection in both healthy and asthmatic persons. Researchers found that the levels of IL-33 derived from both nasal and bronchial secretions were related to an increase in lower respiratory symptom severity as well as virus load and IL-5.

The findings provide greater insight into the interaction between virus infection and allergies. Typically, a viral infection would be expected to suppress Th2 responses; however, in asthmatic patients viral infection actually induces the Th2 response.

Targeting these Th2 responses has been a focus in the discovery of new preventative therapies. Therapies that can block IL-4, IL-5 and IL-13 in clinical trials have shown to be effective in reducing exacerbation frequency, possibly through the restoration of antiviral immunity.

Even more attractive may be blocking of IL-33, suggested Johnston. Blocking IL-33 would essentially block the induction of IL-4, IL-5 and IL-13 all at once, although this has yet to be tested in clinical trials.

“An attractive intervention strategy for me is a broad spectrum antiviral that could block any virus infection,” said Johnston. “In development now is an inhaled interferon-β therapy, which in early clinical trials has shown to be effective in improving exacerbation frequency, symptoms and lung function in moderate and severe asthmatics.”
Endovascular revascularization or stenting followed by a supervised exercise regimen may decrease claudication pain and increase walking distance in patients with peripheral artery disease (PAD), the ERASE* trial shows.

“This [approach] should be considered as an initial treatment,” said researcher Dr. Farzin Fakhry from the Erasmus University in Rotterdam, Netherlands. “Although guidelines recommend supervised exercise as initial therapy in patients with intermittent claudication, our results suggest a combined therapy might be the best option.”

The ERASE trial included 212 patients (mean age 66 years) from 10 centers in the Netherlands with PAD and intermittent claudication randomized to endovascular therapy plus supervised exercise, or supervised exercise alone. The primary endpoint was maximum walking distance at 12 months. Two-thirds of the patients were men, about 60 percent had diabetes and >90 percent were smokers. [Abstract 19577]

At 1 year, patients in the combined treatment group experienced greater improvements in maximum walking distance (+282 meters; p=0.001) compared with baseline. Similarly, they were able to walk without pain for a quarter mile farther (+408 meters; p<0.001) than patients in the exercise-only group. Patient-reported quality of life as assessed by the VascuQol questionnaire was also significantly better in the combined treatment group (p<0.001). There was also greater improvement with physical functioning (p=0.002).

Discussant Dr. Mary McGrae McDermott from the Northwestern University Feinberg School of Medicine in Chicago, Illinois, US, said there are a few caveats with the findings. First, exercise takes time and patient commitment and the improvements are more gradual whereas the beneficial effects of revascularization tend to wane with time. “So whether this significant benefit might further diminish after 12-month follow-up remains to be seen,” she said.

Another point she raised was that current guidelines recommend exercise therapy three times a week, followed by angioplasty. By comparison, this study had two to three sessions a week for the first 3 months, one session a week for months 4 to 6, and then down to one session each month for months 7 to 12, which “is not an ideal test of this therapy,” McDermott said.

*ERASE: Endovascular Revascularization And Supervised Exercise

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

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

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

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

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

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

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

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

The findings further confirm the important roles pharmacists play in a multidisciplinary team to optimize patients’ treatment outcomes, Chan concluded.
The material is for the reference and use by healthcare professionals.

**INTEGRATED SAFETY INFORMATION:**

**Contraindications:** Hypersensitivity to the active substance or to any of the excipients of the captured product Warnings and Precautions:

- It is not recommended in severe active central nervous system lupus, severe active lupus nephritis, HV, a history of or current, hepatitis B or C, hypogammaglobulinaemia (IgG <400 mg/dl) or IgA deficiency (IgA <10 mg/dl), a history of major organ transplant or hematopoietic stem (cell) marrow transplant or renal transplant. Caution should be exercised if Belimumab is co-administered with other B cell targeted therapy or cyclophosphamide.

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- Live vaccines should not be given for 30 days before, or concurrently, with Benlysta. Caution should be exercised when considering belimumab therapy for patients with a history of malignancy or when considering continuing treatment in patients who develop malignancy. The following adverse events have been reported with a frequency of ≥ 1/100:

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Please refer to the full prescribing information for further information and prior to administration.

**ABBREVIATED PRESCRIBING INFORMATION:**

Belimumab™ (Belimumab) powder for concentrate for solution for infusion (120mg, 400mg) Belimumab is a human IgG1 monoclonal antibody specific for soluble human B Lymphocyte stimulator protein (BAFF), also referred to as BAFF and TNFSF13B.

**INDICATION:** As add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g., positive anti-dsDNA and low complement) despite standard therapy. DOSAGE: Treatment should be initiated and supervised by a qualified physician experienced in the diagnosis and treatment of SLE. BENLYSTA™ infusions should be administered by a qualified healthcare professional trained to give infusion therapy. Administration of BENLYSTA™ may result in severe or life-threatening hypersensitivity reactions and infusion reactions. Following the use of BENLYSTA™, patient each time BENLYSTA™ is administered. The mechanism of action of BENLYSTA™ could increase the potential risk of infections, including opportunistic infections and may interfere with the response to immunizations. Exercise caution when considering

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

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

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

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

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

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

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

Trade-off when bivalirudin used for PCI: EUROMAX trial

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

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

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


Long-term statin therapy may protect against dementia

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

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

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

Belimumab: Novel biologic DMARD for the treatment of systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease, the underlying cause of which is not fully known. Recently, biologic disease-modifying anti-rheumatic drugs (DMARDs) have started to be considered for the treatment of SLE due to their improved tolerability profiles compared with conventional therapies. This report profiles belimumab, a novel biologic DMARD, which has been approved for use in the treatment of certain patients with SLE.

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

Introduction
Systemic lupus erythematosus (SLE) is a chronic autoimmune disease. The underlying cause is yet to be fully elucidated. It appears clinically as a heterogeneous disorder, with disease activity ranging from indolent to fulminant and a variable course of symptom flares and remission. [PubMed Health. Systemic lupus erythematosus. http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001471/] The classic presentation consists of fever, joint pain and rash, typically in women of childbearing age. Fatigue is also an almost universal symptom. Other manifestations include arthritis (although rarely erosive or deforming), malar rash, photosensitivity, renal disease, neuropsychiatric disorders, pleuritis, gastrointestinal symptoms, pericarditis, stroke, anemia and thrombocytopenia. [Ther Clin Risk Manag 2012;8:33-43; BMJ Open 2013;3:e002852] SLE can be both debilitating and life-threatening, hence can significantly impair quality of life. Because it can compromise major organs including brain, heart, lungs and kidneys, SLE is associated with one of the highest rates of mortality among autoimmune diseases. [Pharmacy Therapeutics 2012;37:212-26]

Symptom control and suppression of disease activity are the goals of treatment for SLE. The European League Against Rheumatism (EULAR) recommends that glucocorticoids and antimalarial agents be used in patients with SLE and no major organ involvement. [Ann Rheum Dis 2008;67:195-205] Non-steroi-
Drug Profile

January 2014

Anti-inflammatory drugs should only be used short term and in those patients with a low risk of complications due to these agents. In those who do not respond to steroids at long-term maintenance doses or those experiencing a disease flare, immunosuppressive agents may be considered. [Ann Rheum Dis 2010;69:1269-1274] It should be noted however, that many of the drugs used to treat lupus are ‘off-label’, that is, without regulatory approval for an SLE indication.

More recently, biologic disease-modifying anti-rheumatic drugs (DMARDs) have started to be considered for SLE. There is a strong rationale for their development given the side effect profile of current therapies (which includes weight gain, hypertension, increased susceptibility to infection and osteoporosis for corticosteroids and increased infection risk, malignancy and infertility for immunosuppressants). Some patients with refractory disease require prolonged high-dose corticosteroids and/or long-term immunosuppression to maintain remission. In an attempt to avoid this unfavorable risk–benefit profile, several biologic DMARDs have been explored for the treatment of SLE. The existing DMARDs that inhibit tumor necrosis factor (TNF) were not viable options since these drugs are known to induce SLE. One DMARD that has been explored is rituximab – a monoclonal antibody that reacts with the CD20 antigen expressed on B lymphocytes. This drug has been shown to be effective for rheumatoid arthritis, however results have been mixed in SLE. While some small uncontrolled trials and case series suggested that rituximab may be effective and steroid-sparing in severe, refractory SLE, an exploratory phase II/III study found no difference between rituximab and placebo. [Lupus 2009;18:767-76, Arthritis Rheum 2010;62:222-233] In contrast, the clinical trial program for belimumab – an IgG1 monoclonal antibody that inhibits the activity of the soluble cytokine BLyS (B lymphocyte stimulator) – has demonstrated efficacy and resulted in the first regulatory approval of a biologic DMARD for SLE.

Belimumab

Pharmacology and pharmacokinetics

The pathogenesis of SLE involves a complex interplay of activation and dysregulation of the innate and adaptive immune responses. B lymphocytes play a central role in the disease, primarily by producing autoantibodies but also by producing cytokines and presenting antigens to T cells. One of the key players in the process is BLys, also known as B cell activating factor (BAFF). BLyS is a member of the TNF family of cytokines and plays a crucial role in B cell selection, maturation and survival. [Ther Adv Chronic Dis 2012;3:11-23] Belimumab binds to soluble BLys, thereby inhibiting the survival and differentiation of B cells. [Ann Rheum Dis 2008;67:195-205] Phase I dose-ranging studies of belimumab showed that it has a terminal half-life of 19-20 days, a small volume of distribution and slow clearance rate. [BMJ Open 2013; 3: e002852]

Clinical efficacy

The feasibility and safety of belimumab therapy for SLE was demonstrated by a 12-week, phase I, double-blind, randomized, placebo-controlled study (n=70) which showed no difference in the rate of adverse events and reductions in peripheral B cell levels (although this study was not designed to test efficacy). [Arthritis Res Ther 2008;10:R109] Belimumab was then tested in a larger cohort of patients with SLE (n=449) in a 52-week,
phase II, double-blind, randomized, placebo-controlled study on a background of standard care – that is, a stable regimen of steroids, antimalarials, or other immunosuppressants for 60 days prior to the first belimumab infusion. This investigation failed to show any significant improvement in the primary endpoints of disease activity at week 24 and time to first SLE flare over 52 weeks. [Arthritis Rheum 2009;61:1168-1178] However in a post-hoc analysis of the subgroup of patients with serologically active disease at study entry (n=321) did show a significant improvement in several secondary endpoints with belimumab. [Arthritis Rheum 2009;60(Suppl. 10):1149]

Investigation of belimumab for SLE then moved into phase III, with two multicenter, randomized, double-blind trials; Belimumab In Subjects with Systemic lupus erythematosus (BLISS-52 and BLISS-76). Patients enrolled had relatively high disease activity (SELENA–SLEDAI score ≥6) and were seropositive with anti-nuclear antibodies (ANAs) and/or antibodies to double-stranded DNA (dsDNA) detected at two independent time points. Treatment consisted of belimumab 1 mg/kg or 10 mg/kg for 52 weeks or placebo for 76 weeks. In the BLISS-52 study at 52 weeks (n=865), active treatment at 10 mg/kg was associated with disease activity reduction in a significantly greater proportion of patients compared with placebo (58 percent vs 44 percent, respectively; p<0.001). Belimumab was also associated with a significant improvement in physician’s global assessment scores at week 24 relative to placebo (−7.07 vs −14.3, p≤0.05). [Lancet 2011;377:721-731] Similarly, in the BLISS-76 study (n=819), the proportion of patients with significantly reduced disease activity was also greater with belimumab 10 mg/kg compared with placebo at 52 weeks (43 percent vs 34 percent, p=0.021). [Arthritis Rheum 2010;62(Suppl. 10):1454] A combined analysis of data from the BLISS-52 and BLISS-76 trials concluded that the evidence suggests belimumab is clinically effective for SLE, however differences in the trial populations limit the generalizability of these results. [Pharmacy Therapeutics 2012;37:212-226]

Adverse effects

The most commonly reported AEs in clinical trials with 10 mg/kg of belimumab were nausea, diarrhea, pyrexia, nasopharyngitis, bronchitis, insomnia, extremity pain, depression, migraine and pharyngitis. Serious infections (most commonly upper respiratory infections) occurred in 6 percent of patients receiving belimumab compared with 5.2 percent of those in the placebo arm.

Dosing

The recommended dosage regimen for belimumab is 10 mg/kg at 2-week intervals for the first three doses and at 4-week intervals thereafter. It is administered as an intravenous infusion over a period of 1 hour. Consideration should be given to coadministration of premedication for prophylaxis against infusion reactions and hypersensitivity reactions. [Belimumab Prescribing Information]
Industry Update brings you updates on disease management and advances in pharmacotherapy based on reports from symposia, conferences and interviews, as well as latest clinical data. This month’s updates are made possible through unrestricted educational grants from Novartis, Mundipharma, Pfizer, Eli Lilly, GSK and Takeda.

Novel dual bronchodilator therapy for COPD
Meeting Highlights

Novel dual bronchodilator therapy for COPD

The mainstay of therapy for chronic obstructive pulmonary disease (COPD) includes long-acting β2-agonists (LABAs), long-acting muscarinic antagonists (LAMAs) and inhaled corticosteroids (ICSs).

At the recent Autumn Respiratory Seminar 2013 organized by the Hong Kong Thoracic Society and American College of Chest Physicians (Hong Kong and Macau Chapter), Professor Wisia Wedzicha of the University College London Medical School, UK, discussed the role of combination therapy in COPD management, focusing on the novel LABA/LAMA combination of indacaterol (Onbrez®, Novartis) and glycopyrronium.

New direction: Dual bronchodilation

The current Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline recommends LABA/ICS combination therapy or LAMA alone as the first choice for group C (high risk, fewer symptoms) and D (high risk, more symptoms) COPD patients. [Global Strategy for the Diagnosis, Management, and Prevention of COPD, GOLD 2013: http://www.goldcopd.org/]

“Targeting one bronchodilatory pathway alone may not maximize bronchodilation,” noted Widzicha. “Combining different classes of bronchodilators may provide bronchodilation beyond that achievable with monotherapy.” [Eur Respir J 2008;31:742-750]

The INTRUST [Indacaterol Plus Tiotropium Versus Tiotropium Alone in Patients With Chronic Obstructive Pulmonary Disease] studies 1 and 2 were designed identically to access the efficacy of indacaterol plus tiotropium vs tiotropium alone. At study end (12 weeks), both the trough inspiratory capacity and forced expiratory volume in 1 second (FEV₁) were higher in the combination group than the monotherapy group. [Thorax 2012;67:781-788]

“Therefore, LABA/LAMA combination therapy is a reasonable alternative for COPD patients in GOLD groups B [low risk, more symptoms], C and D,” she said.

Shifting away from LABA/ICS

The efficacy of LAMA alone is equivalent to that of ICS plus LABA on exacerbation prevention in COPD. For example, the LAMA tiotropium is associated with comparable exacerbation rates vs the LABA/ICS combination of salmeterol plus fluticasone. [Am J Respir Crit Care Med 2008;177:19-26]

“Importantly, the GOLD 2013 guideline advocates a greater focus on symptom relief, which may improve patient outcomes,” said Wedzicha. “Anti-inflammatory therapy generally has only a small effect on FEV₁, as shown in a previous study of LABA/LAMA vs LABA/ICS.”
In contrast, LABA/LAMA provides more optimal bronchodilation and symptom relief, which benefits pulmonary rehabilitation. The paradigm may shift from LABA/ICS to the novel LABA/LAMA combination,” she continued.

**Dual bronchodilation: LABA/LAMA**

“Apart from bronchodilation, both indacaterol and glycopyrronium alone were shown to reduce COPD exacerbations,” said Wedzicha.

“A pooled analysis of the INHANCE [Indacaterol vs Tiotropium to Help Achieve New COPD Treatment Excellence], INVOLVE [Indacaterol: Value in COPD: Longer Term Validation of Efficacy and Safety] and INLIGHT-2 [Indacaterol Efficacy Evaluation Using 150 µg Doses with COPD Patients] trials showed that indacaterol 150 µg and 300 µg significantly prolonged the time to first moderate-to-severe exacerbation vs placebo over 26 weeks [hazard ratio, 0.74 and 0.73, respectively],” she highlighted.

The efficacy of glycopyrronium in reducing exacerbations was demonstrated in the GLOW2 study (Glycopyrronium Bromide in COPD Airways Clinical Study 2). “In this study, 1,066 patients were randomized to receive glycopyrronium 50 µg, placebo or tiotropium 18 µg for 52 weeks,” said Wedzicha. “At study end, glycopyrronium significantly reduced the time to first moderate-to-severe exacerbation by 34 percent vs placebo. The effect was comparable to that of tiotropium.” [Eur Respir J 2012;40:1106-1114]

**Benefits of a selective LAMA**

“As shown in the COPENHAGEN and ECLIPSE [Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints] studies, patients in GOLD ‘low risk’ group B had worse survival rates than those in the ‘high risk’ group C,” noted Wedzicha. “This is partly due to the higher incidence of cardiac disease, particularly heart failure, in group B.” [Eur Respir J 2013;42:636-646; Am J Respir Crit Care Med 2012;186:975-981]

The high incidence of cardiac events prompted an investigation of the mechanisms of action of the bronchodilators used. “LAMA blocks the muscarinic acetylcholine receptor M3 to inhibit acetylcholine-induced bronchoconstriction of airway smooth muscle. The non-selective LAMAs also block the M2 receptor, which may lead to adverse cardiac and urinary effects. Therefore, highly M3-selective blockers such as glycopyrronium and tiotropium should be used in COPD treatment,” she pointed out. [Drugs 2002;62:1204-1205; Pharmacol Rev 1998;50:279-290; Life Sci 1999;64:419-428]

**Indacaterol/glycopyrronium: The IGNITE program**

“The novel indacaterol/glycopyrronium combination has been evaluated in the IGNITE [Indacaterol and Glycopyrronium Bromide Clinical Studies] program, which consists of eight clinical trials completed in more than 5,700 COPD patients,” said Wedzicha.

**SHINE: Improved FEV1 and dyspnea**

The SHINE study compared the efficacy of indacaterol/glycopyrronium with indacaterol, glycopyrronium, open-label tiotropium or placebo in 2,144 patients with moderate-to-severe COPD. “The mean trough FEV₁ at study end [week 26] was significantly better in all active treatment arms than placebo. Notably, the
indacaterol/glycopyrronium arm had the best mean trough FEV₁. This benefit was sustained throughout the study,” emphasized Wedzicha. (Figure 1) “In addition, the indacaterol/glycopyrronium combination significantly improved dyspnea vs placebo and tiotropium, but this effect was comparable to that of indacaterol or glycopyrronium monotherapy.” [Eur J Respir 2013;42:1484-1494]

**SPARK: Reduced exacerbations**

The 64-week SPARK [COPD Exacerbation with The Dual Bronchodilator QVA149 Compared with Glycopyrronium and Tiotropium] study evaluated the effect of indacaterol/glycopyrronium, glycopyrronium or tiotropium on exacerbations in 2,224 patients with severe or very severe COPD. “The dual bronchodilator arm significantly reduced moderate or severe exacerbations by 12 percent vs the glycopyrronium arm [p=0.038], but this effect did not reach statistical significance vs the tiotropium arm,” reported Wedzicha.

“The rate of total annualized exacerbations [mild, moderate and severe] was significantly reduced by 15 percent with the dual regimen compared with glycopyrronium and by 14 percent compared with tiotropium,” she noted. [Lancet Respir Med 2013;1:199-209; Novartis data on file (qva149a2304—study-report-body, pages 99 and 102)] “The trough FEV₁ was consistently and significantly higher in the indacaterol/glycopyrronium arm throughout the 64 weeks.”

Besides, patients receiving the combination therapy had better health status (assessed by the St. George’s Respiratory Questionnaire [SGRQ] total score) and less frequent use of daily rescue medication than those receiving either indacaterol or glycopyrronium alone. [Lancet Respir Med 2013;1:199-209]

**ILLUMINATE: Superior efficacy vs LABA/ICS**

The ILLUMINATE [Efficacy and Safety of Once-daily QVA149 Compared with Once-daily Salmeterol-Fluticasone in Patients with COPD] study is a head-to-head comparison of the indacaterol/glycopyrronium and salmeterol/fluticasone (LABA/ICS) combinations in 523 patients with moderate-to-severe COPD. “Patients receiving indacaterol/glycopyrronium had significantly fewer events of dyspnea at both weeks 12 and 26,” said Wedzicha. (Figure 2) “The FEV₁ AUC0-12h [area under the curve from 0 to 12 hours post dose] at week 26, and pre-dose trough FEV₁ at weeks 12 and 26 were significantly higher in patients receiving indacaterol/glycopyrronium.” The SGRQ total scores were slightly lower in patients on indacaterol/glycopyrronium, but did not reach statistical significance. [Lancet Respir Med 2013;1:51-60]

“This study highlighted the potential of LABA/LAMA therapy to replace and provide superior efficacy to LABA/ICS in GOLD group B patients,” pointed out Wedzicha.

**Patient-reported dyspnea and safety profile**

Indacaterol/glycopyrronium was shown in the BLAZE [The Effect of QVA149 on Dyspnea in Patients with COPD] study to significantly improve patient-reported dyspnea, vs tiotropium or placebo. [Eur Respir J 2013, doi: 10.1183/09031936.00124013]

“In addition, data from the SPARK and SHINE studies confirmed the good safety profile of the indacaterol/glycopyrronium combination,” said
Wedzicha. “In SPARK, serious adverse events associated with indacaterol/glycopyrronium, glycopyrronium or tiotropium were comparable. In SHINE, no serious cardio- and cerebrovascular events were seen with the combination regimen.” [Lancet Respir Med 2013;1:199-209; Eur J Respir 2013;42:1484-1494]

**Conclusion**

The GOLD 2013 guideline advocates a greater focus on symptom relief in COPD management. Dual bronchodilation with LABA/LAMA provides better symptom control than the currently recommended LABA/ICS combination, suggesting a shift towards the use of dual bronchodilator therapy.

Indacaterol/glycopyrronium is a novel LABA/LAMA combination therapy that is shown in the IGNITE program to be efficacious with a good safety profile, indicating a potential to replace ICS/LABA in GOLD group B patients.

“Symptomatic patients and patients not well controlled with other medications should switch to LABA/LAMA for greater reduction of exacerbations and better outcomes,” suggested Wedzicha.

The opinions expressed in this publication do not represent those of the Hong Kong Thoracic Society or the American College of Chest Physicians (Hong Kong and Macau Chapter). Any liability or obligation for loss or damage howsoever arising is hereby disclaimed.
### JANUARY

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

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

### FEBRUARY

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

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

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

### UPCOMING

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

**Asian Pacific Association for the Study of the Liver (APASL) 2014**  
**12/3/2014 to 15/3/2014**  
Location: Brisbane, Australia  
Info: Gastroenterological Society of Australia  
Tel: (61) 3 9001 0279  
Fax: (61) 3 9802 8533  
E-Mail: apasli2014@gesa.org.au  
Website: www.apasli2014.com

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

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

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

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

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

Uncover the secrets of Brooklyn’s trendiest neighbourhood. By Weitin Bang

Williamsburg, New York, is having a hip moment. Once known for being the dusty epicentre of manufacturing jobs in New York, these days it is engaged in an inexorable march towards all things trendy and cool. Indeed, Williamsburg is quickly overtaking Greenwich Village as the artistic rod of New York, attracting a myriad of creative types – think aspiring street artists, budding songwriters, students, film producers and writers – no doubt drawn by the comparatively low rent, abundance of airy disused factory lofts and a certain air of je ne sais quoi. The result: A distinctive neighbourhood filled with life, culture, innovation and an endless list of must-sees and dos.

For alternative art ...

**THE SKETCHBOOK PROJECT**

Known for its burgeoning art scene, Williamsburg is the place to hit if you’re in search of up-and-coming artists. Enter The Sketchbook Project, a global, crowd-sourced project featuring the sketchbooks of professional and amateur artists alike. Anyone can participate in this travelling exhibition – just order a sketchbook, fill up the pages and choose which tour you’d like your book to go on. There is also an option to turn one’s work into a digitised version to be housed in the online library. For those less artistically inclined or who simply wish to browse through these inspirational pieces instead, the permanent collection at the Brooklyn Art Library houses nearly 30,000 sketchbooks, making it a must-see pit stop for art lovers.

Located at 103A North 3rd St or visit www.sketchbookproject.com for more information.

Eat at ...

**CRIF DOGS**

Coney island isn’t the only place to go for hotdogs. Both Manhattan’s Lower East Side and
Williamsburg are home to Crif Dog, a 12-year-old establishment that serves up some of the best weiners in town. And don’t just take my word for it – celebrity chef Anthony Bourdain is a fan too. Despite the location – it’s a skip away from Bedford Ave subway station – the basement unit can be hard to spot. Still, you’d be able to distinguish it by the long snaking queue that starts to form outside its doors come sunset. Don’t let the crowd or dimly-lit space put you off: The tasty hotdogs and wide assortment of flavours and toppings available will make everything good again.

Located at 555 Driggs Ave

**MOMOFUKU MILK BAR**

Part of restauranteur David Chang’s famed Momofuku Restaurant Group, Momofuku Milk Bar is its bakery/dessert arm headed by Christina Tosi, 2012 James Beard Rising Star Chef of the Year. Decor-wise, the simply clad interior, with a single neon “Milk” sign adorning its windows, isn’t much to look at, but frankly, who cares? The emphasis is all on the sweet treats on offer. While the cereal milk soft serve and compost cookies are mouthwatering fare that deserve a mention, it’s the crack pie (the name has since earn a trademark) you want to make a beeline for. Boasting a buttery-oaty outershell and gooey insides, it is possibly as addictive as its name sake. I dare you to stop at just one slice.

Located at 382 Metropolitan Ave

**BROOKLYN BREWERY**

No trip to Brooklyn is considered complete until you visit this 25-year-old institution. Known for its wide selection of alcoholic beverages such as Brooklyn Lager, and seasonal craft beers like Brooklyn Chocolate Stout, Summer Ale and Oktoberfest, the famed brewery is a beer enthusiast’s paradise. Music and social events as well as tours and tastings are also held regularly, so go thirsty.

79 North 11th Street in Williamsburg, Brooklyn, 11249 between Berry Street and Wythe Avenue.

**SUMMERSCREEN**

The brainchild of Noemie Lafrance of Sens Productions, Alex Kane of Jelly NYC, and brothers Scott and Daniel Stedman of The L Magazine, Summerscreen is part movie screening and part music gig rolled into one. Since its inception in 2006 where 3,000 people flocked to see Spike
Lee’s seminal work Do The Right Thing, the festival has been transformed into one of the most popular summer events, drawing locals and tourists alike. Held every Wednesday over six weeks (July to mid August), Summerscreen not only airs crowd pleasers like Neverending Story and Speed but also introduces a slew of up-and-coming indie rock bands to the mostly 20 to 40-something crowd, so there is no lack of topics should you wish to strike up a conversation with the folks on the next mat.

Located at McCarren Park at the corner of Bedford Ave and North 12th Street

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Most under-rated attraction ...

**EAST RIVER FERRY**

Compared to being stuck underground in the musty old L train, hopping on the East River Ferry is by far a more civilised and scenic way to get to Brooklyn. Part of New York Mayor Michael Bloomsberg’s three-year pilot project to improve the commuting facilities of New York’s waterways, the new East River Ferry is a year-round service that takes you between 34th Street in midtown Manhattan, Long Island City in Queens, Greenpoint, North Williamsburg, South Williamsburg and the Financial District. Translation: You’d get to enjoy sights including the iconic Empire State Building, Chrysler Building, Brooklyn Bridge and more. For a leisurely tour around Williamsburg, disembark at Greenpoint and explore the neighbourhood on wheels. Citibikes are available for rental anytime of the day. Ferry fares range from US$3 – US$5.50 per ride from 7am to 8pm on weekdays and 9am to 7pm on weekends.

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For a piece of randomness ...

**CITY RELIQUARY MUSEUM**

Blink and you might miss this nondescript hole-in-the-wall attraction – indeed, at first glance, I thought I had entered a gypsy-esque antique shop! But upon closer inspection, I quickly realised this not-for-profit community museum really is a gem. It houses a random and eclectic selection of local artifacts that would never quite make it into high-brow institutions like the MET or Guggenheim. From baseball cards and water bottles to booths dedicated to burlesque and even bits of screws collected from the original subway excavation, this charming curation of curiosities is a neat way to experience the less-known side of Williamsburg.

Located at 370 Metropolitan Ave

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Recharge at ...

To say New Yorkers are obsessed with yoga is an understatement – there are over 300 studios in the city that never sleeps, according to online magazine YogaCity NYC. Do what locals do and head to Kula Yoga Project, a shala located conveniently at Bedford Ave Station. This is where frazzled urbanites seek refuge from the madding crowd. The sanctuary offers an average of eight vinyasa flow classes each day during the week, perfect for rejuvenating tired minds and bodies. Bridie Woodward, 30, account manager, says: “This is quite simply one of the most beautiful spaces to practise yoga in Williamsburg, and it also has a sauna and serves great salads and fresh juices.”

85 North 3rd Street Brooklyn
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“Didn’t I tell you not to eat?”

“Okay, but just this once!”

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

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

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

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

“Usually I don’t advise giving this medication for such a condition ... but in your case, I’m terribly curious!”
10th International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) Outreach Course, Singapore

in conjunction with
5th Scientific Congress of the College of Obstetricians & Gynaecologists, Singapore (COGS)

4-6th May 2014
Raffles City Convention Centre, Singapore

SAVE THE DATE!

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CUHK: The Chinese University of Hong Kong  
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