Ustekinumab: a novel option for TNFi-refractory Crohn’s disease
CONTENTS

DECEMBER ISSUE

Cover Story
5 Ustekinumab a novel option for TNFi-refractory Crohn’s disease

Conference Coverage
6th Asia-Pacific Osteoporosis Meeting (IOF Regionals 2016), Singapore

7 Oestradiol depletion linked to bone structure decline
8 Long-term osteoporosis treatment should be for those with highest fracture risk
9 Denosumab benefit in osteoporosis persists for years
11 Fluoride salt, strontium ranelate beneficial in osteoporosis
   Maintenance statin therapy tied to grip strength decline
12 Smoking negatively affects hip BMD
   Vit D deficiency prevalent in some children
13 Anxiety disorder linked to osteoporosis
   Lumbar muscle volume loss tied to compression fractures

Conference Coverage
ASEAN Federation of Cardiology Congress (AFCC), Yangon, Myanmar
14 Trimetazidine may improve cardiac energetics, efficiency in SCAD
15 Combo therapy reduces CVD, mortality risks in hypertension
16 Early cardiac MRI helps detect worsening heart function
17 Short DTB time, less radiation for hybrid angiography unit PCI
   Collimation reduces radiation exposure
18 Individualized approach to reduce CV risk in diabetes
19 Strain imaging may be useful in detecting RV dysfunction

Newsbites
21 Bedtime media device use tied to poorer sleep in children and teens
22 Novel drug for chronic HBV gets FDA nod

ISSN 2410-7808

HOW TO CONTACT US
To subscribe: subscribe.sg@mimsdoctor.com
To contact the editor: editor.sg@mimsdoctor.com
To submit an article: contribute.sg@mimsdoctor.com
438A Alexandra Road, Alexandra Technopark
#04-01/02 Singapore 119967
Introducing the New

MIMS Community!

Join this exclusive social media platform for healthcare professionals

Connect with like-minded professionals from various healthcare-related industries, and engage in conversations from the latest medical news to career management, and even your everyday experiences on the job.

CONNECT @ https://community.mims.com
Oat fibre lowers LDL-C, other markers of CVD risk
Timing of eczema onset influences food allergy risk
SSRIs may increase risk of metabolic abnormalities
Longer duration of diabetes increases fracture risk in women
Efficacy of pertussis vaccine wanes over time

Clinical Insights
Q&A
Dr Helen Chen on postnatal depression
Managing acne in primary care

DEVICE
Skin patch safe, promising for treating peanut allergy
HIV test on USB stick: Is it ready for clinic use?

MIMS Community
Trending… nurses should be valued
Get the essential all-in-one clinical reference tool

Download MIMS app to receive critical prescribing information, medical news and CME articles on-the-go.

Latest news and updates in your specialty
- Up-to-date clinical news relates to your field of work
- Medical highlights on drugs and disease management trends
- Quick clinical insights through 5-minute expert opinion videos

Evidence-based clinical decision support
- At-a-glance disease management guidelines for quick referencing
- Find clinical calculators by specialty or index

Conferences
- Comprehensive calendar of upcoming medical conferences
- Retrieve detailed conference reports

Comprehensive drug prescribing information
- Search by disease, brand or generics
- Concise drug information for quick reference
- Full drug profiles for in-depth research
- One-tap access to local manufacturers and distributors information

Please scan the QR code for more information.
Ustekinumab
a novel option for TNFi-refractory Crohn’s disease
The monoclonal antibody ustekinumab induces clinical response and maintains remission in moderate-to-severe Crohn’s disease that is refractory to tumour necrosis factor inhibition (TNFi) or standard therapy, according to three pivotal studies, widening the treatment options for this chronic inflammatory condition.

“Patients with Crohn’s had limited treatment options previously, so this is a big advance,” said study author Professor William Sandborn from the University of California in San Diego, California, US. “[Ustekinumab] is also very convenient for patients – the maintenance dosing is only once every 8 weeks and patients can inject themselves.”

Ustekinumab is an interleukin-12/23 inhibitor approved for the treatment of plaque psoriasis and psoriatic arthritis, and recently Crohn’s disease, a complex disease of the ileum and the colon for which currently there is no cure. No one treatment works for every patient and the goals of therapy are to reduce inflammation to ease diarrhoea, rectal bleeding, abdominal pain and other symptoms, and bring about long-term remission.

In two induction trials of ustekinumab, patients receiving two single doses of intravenous ustekinumab (130 mg or approximately 6 mg/kg of body weight) had significantly higher response rates at week 6 vs those on placebo. In the maintenance trial, initial responders treated with subcutaneous ustekinumab (90 mg every 8 weeks or every 12 weeks) had greater benefit at 44 weeks vs those given placebo. [N Engl J Med 2016; 375:1946-1960; doi: 10.1056/NEJMoa1602773]

“Ustekinumab is effective, leading to a clinical remission [relief from abdominal pain and diarrhoea] in moderate-to-severe Crohn’s,” said Sandborn.

Clinical response was defined in both studies as a reduction from baseline of 100 points in the Crohn’s Disease Activity Index (CDAI) or a CDAI score of <150.

The phase III study, IM-UNITI, involving 397 responders in the induction trials showed that 53 percent of patients treated with subcutaneous maintenance injections of ustekinumab 90 mg every 8 weeks achieved remission at 44 weeks compared with 36 percent of those receiving a placebo (p=0.005).

In patients receiving ustekinumab every 12 weeks, 49 percent were in remission vs 36 percent in those receiving a placebo (p=0.04). Adverse events such as headache, nausea, arthralgia and infections were similar for placebo and ustekinumab maintenance therapy, which were consistent with safety trials of ustekinumab in psoriatic arthritis.

“The findings suggest that ustekinumab has a long duration of action, a likelihood that may become better understood in future trials,” said the researchers.

Experts said further investigation is clearly warranted to determine how long would remission last. The disease often recurs, frequently near the reconnected tissue, even after surgery.

“Patients with Crohn’s had limited treatment options previously, so this is a big advance” — Prof William Sandborn

“There was no increase in the rates of serious infection or cancer compared with placebo.”

Trials support ustekinumab’s approval

Studies have demonstrated ustekinumab’s efficacy in patients who had failed TNF antagonists or conventional therapies. In the UNITI-1 study of 741 Crohn’s disease patients (median disease duration, 10 years) with a history of TNF failure and treated with intravenous ustekinumab (130 mg or 6 mg/kg), the rates of response at week 6 were significantly higher with ustekinumab (34.3 and 33.7 percent) than with placebo (21.5 percent; p=0.003 for both).

In the UNITI-2 study of 628 patients (median disease duration, 6 years) who had been treated unsuccessfully with immuno-suppressives and corticosteroids but not TNF-blockers, or who had experienced unacceptable side effects, response rates were 51.7 and 55.5 percent for ustekinumab doses at week 6 vs 28.7 percent for placebo (p<0.001 for both).
Oestradiol depletion in premenopausal women with breast cancer linked to bone structure decline

PEARL TOH

Oestradiol depletion in premenopausal women with early breast cancer who were treated with ovarian suppression (OS) plus aromatase inhibition (AI) endocrine therapy was associated with severely deteriorated cortical and trabecular microstructure in their bones, according to preliminary data of an ongoing study.

"[The] severe and perhaps irreversible microstructural deterioration and the longevity of these women suggest there is a need to investigate the role of early intervention to preserve bone strength," said researchers from the Departments of Endocrinology and Medicine at Austin Hospital in Heidelberg, Victoria, Australia.

The case-control study enrolled 23 premenopausal cases (mean age 42.3 years) with breast cancer who were treated with OS+AI for a median duration 1.5 years, 42 healthy age-matched premenopausal women (mean age 44.4 years), and 35 healthy women who were 10 years post natural menopause (mean age 62.4 years).

Women who had been on tamoxifen therapy for >6 months or prior bone-related therapy were excluded from the study. [IOF 2016, abstract P174]

Microarchitecture and matrix mineral density (MMD) of distal radius and tibia were assessed using high-resolution peripheral quantitative computed tomography. OS+AI endocrine therapy for breast cancer led to more rapid oestradiol depletion than natural menopause, said the researchers.

Cases treated with OS+AI had higher cortical porosity in the distal radius in all measured outcomes of porosity including total cortex, compact cortex, outer and inner transitional zones, and lower MMD than premenopausal age-matched controls (p<0.001 for all).

Despite being almost two decades younger than women who were 10 years postmenopause, cases had similar cortical porosity in all measured outcomes mentioned above in the distal radius as postmenopausal controls.

MMD was also significantly lower in premenopausal cases than postmenopausal controls (p<0.001).

In addition, trabecular bone volume (BV/TV) in the distal radius was 1.47 percent lower in cases compared with premenopausal controls (p=0.008), and 0.67 percent lower compared with postmenopausal controls (p=0.07), which was due to fewer but not thinner trabeculae.

Similar results were also seen for measurements in the tibia, according to the researchers, although these were not included in the presentation.

Previous studies have shown that oestrogen deficiency can increase bone remodelling rate by increasing the lifespan of osteoclasts while decreasing that of osteoblasts. (Endocr Rev 2000;21:115-137) The rapid remodelling will reduce MMD and eventually lead to severe microstructural deterioration, according to the researchers.
Long-term osteoporosis treatment should be reserved for those with highest fracture risk

ROSHINI CLAIRE ANTHONY

Osteoporosis treatment should not be initiated unless the patient concerned has a sufficiently high risk of fracture, according to a presentation at the IOF Regionals 2016.

“Everything considered, optimal long-term management of osteoporosis is primarily dependent on an initial judicious selection of patients and of the most appropriate treatment for each patient,” said Professor Jean-Marc Kaufman from the Department of Endocrinology at Ghent University Hospital, Ghent, Belgium. [IOF Regionals 2016, abstract PL14]

Reassessment of risk after 3–5 years is recommended. If during the course of reassessment we find that the patient has a low fracture risk, this patient should probably not have been initiated on treatment to begin with, he said. The key questions that should be asked for an individualized approach are what the baseline fracture risk was, what treatment the patient is currently on and adherence to it, and what the reassessed present risk for new fracture is, said Kaufman. Studies have shown that efficacy of treatment – reduced fracture risk – is maintained with long-term therapy.

One study showed that 7 years of continuous risedronate therapy led to improvement in bone mineral density (BMD), reductions in bone turnover, and no evidence of loss of anti-fracture efficacy. [Calcif Tissue Int 2004;75:462-468] Another study showed that 10 years of alendronate therapy led to an increase in BMD, which declined upon cessation of therapy. [N Engl J Med 2004;350:1189-1199] Results from the FREEDOM Extension study showed that treatment with denosumab for up to 8 years was associated with increased BMD, reduced bone turnover markers, a low incidence of fractures, and a consistent safety profile. [Osteoporosis Int 2015;26:2773-2783]

“Clearly, long-term treatment is efficacious ... [however], adherence to long-term treatment of osteoporosis is poor,” said Kaufman. Previously reported side effects of osteoporosis treatment include acute phase reactions, gastroesophageal irritation, impaired renal function, hypocalcaemia, osteonecrosis of the jaw (ONJ), and atypical femoral fracture (AFF), said Kaufman.

A previous study pointed to an association between long-term bisphosphonate therapy (in this study, alendronate) and ONJ and a potentially higher incidence risk in the Asian population. [J Clin Endocrinol Metab 2014;99:2729-2735] Another study noted an increased incidence of AFF with longer duration of bisphosphonate use. [J Bone Miner Res 2012;27:2544-2550]

“[ONJ and AFF] are associated with bisphosphonate use but they are rare occurrences and have limited impact on benefit-risk of osteoporosis treatment,” said Kaufman. “Concerns for risk of feared side effects like ONJ and [AFF] should only play a secondary role in decision making,” he said. Factors that predict a higher risk of fracture upon treatment discontinuation (alendronate) are age and a lower femoral neck BMD at time of discontinuation. [JAMA Intern Med 2014;174:1126-1134]

Studies have shown that discontinuing risedronate or denosumab treatment led to a decrease in BMD, while another study showed that patients who were on zoledronic acid for 6 years maintained the benefits for up to 3 years after discontinuing therapy. [J Clin Endocrinol Metab 2011;96:3367-3373; J Clin Endocrinol Metab 2011;96:972-980; J Bone Miner Res 2015;30:934-944]

“For drugs such as raloxifene, teriparatide, denosumab, or odanacatib, there is rapid offset of effect after stopping, and sustained fracture prevention requires either continued treatment or switching to another active treatment,” said Kaufman. “For at least some bisphosphonates, offset of effect is somewhat more protracted. Nevertheless, fracture incidence after stopping treatment does increase compared with continued treatment, in particular in patients with initially higher fracture risk,” he said. “Further management is mainly dependent on risk profile of the patient and the type of drug the patient is using.”
Continuous treatment of osteoporosis with denosumab provides long-term benefit

PEARL TOH

Denosumab continuously increases bone mineral density (BMD) at the spine and hip over 10 years, and long-term treatment is associated with reduced incidence of both vertebral and nonvertebral fractures, according to a presentation at the IOF Regionals 2016.

“The goal of [osteoporosis] therapy is to restore bone mass and bone quality in all aspects, whatever time that takes,” said Professor Serge Ferrari of Service of Bone Diseases at Geneva University Hospital in Geneva, Switzerland, suggesting a T-score target of -2 to -1.5 to minimize fracture risk in the long term.

Being highlighted was the FREEDOM extension trial, a multicentre open-label single-arm study which followed participants who had completed the initial 3 years of the FREEDOM trial for another 4 years. The extension study included 4,074 postmenopausal women with osteoporosis randomized to either subcutaneous denosumab 60 mg Q6M or placebo in the initial 3 years, who were continued (ie, long-term group) or crossed-over, respectively, to receive denosumab from years 4–7 during the extension period. [Osteoporos Int 2015;26:2763-2771]

Compared with the initial 3 years of denosumab treatment, nonvertebral fracture rate was 25 percent lower at year 4 in the long-term group (1.98 vs 1.48, rate ratio [RR], 0.75; p=0.127). Similarly, a significant reduction of 21 percent in fracture rate was observed in the cross-over group at year 4 of treatment (2.37 vs 1.2, RR, 0.79; p=0.0046).

Furthermore, the overall nonvertebral fracture rate was decreased by 21 percent during years 4–7 compared with the initial 3 years of denosumab treatment in the long-term group (1.98 vs 1.54, RR, 0.79; p=0.046).

Collectively, the study showed that treatment with denosumab beyond 3 years was associated with a further reduced risk of nonvertebral fracture which persisted throughout 7 years of continuous treatment, according to Ferrari.

Also, the extent of reduction in nonvertebral fracture risk achieved with denosumab appeared to be dependent on the femoral neck BMD achieved during the initial 3-year therapy, he added. “Fracture rate reduction in year 4 was most prominent in subjects with persistently low hip BMD.”

Discussing about the 10-year data with denosumab, Ferrari pointed out that denosumab persistently increased lumbar spine BMD and decreased new vertebral fracture incidence throughout the 10-year extension period of the FREEDOM study. [ASBMR** 2015, abstract 1157]

“Denosumab continuously increases BMD at the spine and hip over 10 years, resulting in a majority of subjects achieving a nonosteoporotic T-score”

“Denosumab continuously increases BMD at the spine and hip over 10 years, resulting in a majority of subjects achieving a nonosteoporotic T-score,” he said.

“As you treat longer, you need to balance the risk and benefit [of a therapy],” said Ferrari, noting that there was no cumulative risk of infections or other adverse events with denosumab treatment over 8 years as shown in the phase II study of the drug. [Osteoporos Int 2013;24:227-235]

*FREEDOM: Fracture REduction Evaluation of Denosumab in Osteoporosis every 6 Months
**ASBMR: American Society for Bone and Mineral Research
Where can I find SPECIFIC INFORMATION on this drug?

Look up more information in MIMS.com and MIMS Mobile
Fluoride salt, strontium ranelate up bone mechanical properties in osteoporosis

TRISTAN MANALAC

Strontium ranelate and fluoride salt, both established as strategies to reduce the risk of fractures in osteoporosis patients, improved the mechanical properties of the iliac crest samples of treated osteoporosis patients compared with untreated ones, according to a new study.

A total of 37 participants were recruited; eight were osteoporosis patients who had not received prior treatment, nine had received fluoride treatment, nine had received strontium ranelate, and 11 were healthy controls with no bone disease.

From each of the participants, iliac crest biopsies were collected for the downstream analyses. Instrumental neutron activation analysis was performed to measure the concentrations of both strontium and fluoride in the iliac crest samples.

The concentration of strontium in the samples correlated with the treatment period; strontium was mostly found in the newly formed bone. This was not the same for fluoride.

Bone samples from strontium- and fluoride-treated patients had lower cortical porosity compared with that from untreated patients. Healthy controls showed the lowest cortical porosity.

Treatments led to stronger backscatter signals compared to the untreated patients. Healthy controls showed the strongest backscatter signals.

Finally, strontium- and fluoride-treated iliac crests showed lower indentation distances compared with untreated bone samples. Similarly, those from healthy controls showed the shortest indentation distances.

Maintenance statin therapy tied to grip strength decline in elderly men

JAIRIA DELA CRUZ

Statin use in the maintenance setting may have a negative effect on muscle strength in elderly men, as evidenced by a decline in grip strength, according to the results of a Hong Kong cohort study.

After 2 years, grip strength decline was greater among male statin users than nonusers (mean change, −1.452 vs −0.756, respectively; p=0.035). This association was not observed in female subjects (mean change in grip strength, −1.555 among statin users vs −1.107 among nonusers; p=0.061).

From each of the participants, iliac crest biopsies were collected for the downstream analyses. Instrumental neutron activation analysis was performed to measure the concentrations of both strontium and fluoride in the iliac crest samples.

The analysis involved a cohort of 2,882 community dwellers in Hong Kong. Of 1,433 men and 1,449 women, 4 and 5 percent were continuous statin users and nonusers in both groups.

The analysis involved a cohort of 2,882 community dwellers in Hong Kong. Of 1,433 men and 1,449 women, 4 and 5 percent were continuous statin users and nonusers in both groups.

The issue of statin-associated muscle symptoms (SAMS) in the elderly has been largely neglected, Dr Liu-Ying Zhu from the Faculty of Medicine at the Chinese University of Hong Kong said.

Previous studies described an association between SAMS and reduced quality of life in geriatric patients. Factors such as low BMI, renal and hepatic function decline, comorbidities, and multiple medications all contributed to an increased risk of SAMS.

As SAMS has become increasingly common in the geriatric population, clinicians must exercise careful judgment when prescribing statins, especially for patients older than 80 years, Zhu said.
Smoking negatively affects total hip BMD

JAIRIA DELA CRUZ

Current smoking appears to promote a significant decrease in total hip bone mass density (BMD) in older men and women, according to a sub-study of the Taiwan Osteoporosis Survey.

On the other hand, lumbar spine BMD progressively declines with age, regardless of smoking status, but only in women.

The study population comprised 9,667 women and 2,529 men who were grouped according to age, (40 to 50 years, 51 to 60 years, 61 to 70 years, 71 to 80 years and 81 to 90 years). Total hip and lumbar spine BMD were measured and compared between the current-smoking and noncurrent-smoking participants. [IOF Regionals 2016, abstract 11]

Total hip BMD demonstrated a downward trend with increasing age. A significant decrease in total hip BMD was observed from the age of 61 years, and the decrease was greater among women and men who currently smoked than among their noncurrent smoking counterparts (61 to 70 years; p=0.01 in women and p=0.02 in men; 71 to 80 years; p<0.01 and p=0.02; 81 to 90 years; p=0.02 and p=0.13).

A similar trend for lumbar spine BMD was observed, but only in women. Current smoking women had slightly lower lumbar spine BMD compared with their noncurrent-smoking counterparts, with the difference not reaching statistical significance across all age groups.

The findings suggest that current smoking has a negative impact on total hip BMD, but not lumbar spine BMD, in both women and men in older age groups.

Vit D deficiency prevalent among children regardless of fracture history

STEPHEN PADILLA

Children with a history of bone fractures have significantly lower levels of vitamin D than those without such a history, according to a Saudi study.

Even without a history of fracture, vitamin D status correction is needed in the general Saudi paediatric population.

“Our data indicate an association between vitamin D status and bone fractures in Saudi children. Because fracture rates in children are increasing and bone health status in childhood may directly impact adult bone health, opportunities to intervene during childhood should be pursued,” researchers said.

“Given the high prevalence of vitamin D deficiency in Saudi children with and without fracture, a strong consideration should be given for routine vitamin D testing and correction in the Saudi paediatric population,” they added.

A cross-sectional study was conducted to assess the link between serum 25-hydroxyvitamin D levels and fractures in Saudi children. Included were 1,022 children without fracture history (476 boys [age 14.56 years; BMI 22.38] and 546 girls [age 13.57; BMI 22.24]) and 234 Saudi children with a history of fracture (148 boys [aged 14.25 years; BMI 22.66] and 86 girls [aged 13.76 years; BMI 21.33]. [J Endocrinol Invest 2016;39:1125-1130]

Researchers collected anthropometric and fasting serum biochemical data, and assessed serum 25-hydroxyvitamin D level using electrochemiluminescence.

“Vitamin D levels were significantly lower in children with a history of fracture in both boys and girls than those without such a history,” researchers concluded.

Mean circulating 25-hydroxyvitamin (25OH) D level in children with a history of fracture was significantly lower in both boys (p<0.01) and girls (p<0.01) than those without. However, both groups had low mean 25(OH)D levels. Furthermore, age was positively associated with 25-hydroxyvitamin D in boys (p<0.05) and negatively in girls (p<0.05) with a history of fracture.

“One explanation for this observation may be conservative social and religious practices imposed on girls and the fact that advancing age in girls are more often covered compared to boys of similar age,” researchers said.

Boys were also more likely to have fracture than girls (148 vs 86). This might be due to higher outdoor activities such as sports in boys compared to girls and to physiological difference in this age group, according to researchers.
Anxiety disorder linked to osteoporosis

STEPHEN PADILLA

People with a history of anxiety disorder are more likely to have osteoporosis, a study in Taiwan has shown.

“The risk ratios [RRs] are highest for osteoporosis within 1 year of anxiety disorder diagnosis, but the risk remains statistically significant for more than 1 year,” researchers said.

Using data from the Longitudinal Health Insurance Database 2000 of Taiwan, a population-based retrospective cohort analysis was conducted to assess the association between anxiety disorder and the subsequent development of osteoporosis. Included were 7,098 patients from the anxiety disorder and no-anxiety groups who were matched according to age and sex between 2000 and 2013. Researchers calculated the incidence rate and RRs of subsequent new-onset osteoporosis for both cohorts. Cox proportional hazard models were used to assess the effect of anxiety disorder, and the Kaplan-Meier method was applied to estimate the cumulative osteoporosis incidence curves.

Patients in the anxiety cohort had a higher risk of osteoporosis than those in the comparison cohort. In addition, the incidence of newly diagnosed osteoporosis remained significantly increased within the stratified follow-up durations (0 to 1, 1 to 5, 5 to 10, ≥10 years).

Patients with anxiety disorder were 1.79 times more likely to develop osteoporosis than those without. There was also a significant increase in osteoporosis risk in patients with anxiety disorder who had comorbidities such as hypertension, diabetes mellitus and chronic liver disease.

Researchers suggested that clinicians should pay particular attention to osteoporotic comorbidities in patients with anxiety disorder.

Lumbar muscle volume loss tied to compression fractures

JAIRIA DELA CRUZ

Loss of paraspinal and psoas lean muscle volume at the low lumbar levels appears to be related to the risk of osteoporotic/osteopenic lumbar compression fractures among postmenopausal women, according to a study.

Sarcopenia is a geriatric syndrome characterized by progressive decline in muscle mass and function, and is a known contributor to increased risk of falls and fractures, a team of investigators from the Wan Fang Hospital-Taipei Medical University in Taipei, Taiwan said.

Decreased strength has been implicated in the loss of paraspinal muscle mass, but only one study has so far explored the relation between muscle composition and vertebral compression fractures, they added.

To address the dearth of evidence in this area, the investigators looked at 32 postmenopausal women — 18 of whom had compression fractures (mean age 80.1 years; mean BMI 23.2 kg/m²) while 14 were healthy (controls; mean age 53.3 years; mean BMI 24.5 kg/m²).

MRI images of the paraspinal muscles, multifidus and erector spinae, and psoas muscles at the lumbar disc levels were obtained. Lean muscle and fat volume of each muscle group was calculated individually, and the proportion of BMI-normalized muscle and fat volumes was compared between the fracture and control groups.

Women with compression fractures had significantly smaller mean sectional volume of lean muscle in the erector spinae muscle at L3/4, L4/5, L5/S1 levels compared with controls (p<0.05 for all). The results were similar for the mean sectional volume of multifidus muscle at L4/5 and L5/S1 levels (p<0.05 for all). On the other hand, the sectional volume of psoas muscles at all levels significantly differed between the fracture and control groups (p<0.05 for all).

“The proportion of lean muscle to total volume reflects the degree of fatty change and was also found to be significantly more prominent in the paraspinal muscles of [women with compression fractures] at the L5/S1 levels,” the investigators noted.
Trimetazidine may improve cardiac energetics and efficiency in SCAD

Elvira Manzano

Newer metabolic agents, including trimetazidine, represent ancillary forms of prophylactic antianginal therapy and may be useful in patients with stable coronary artery disease (SCAD) who are unsuitable for percutaneous or surgical revascularization, says a leading cardiologist at the recent AFCC 2016.

"On top of its antianginal properties, trimetazidine, administered at 35 mg twice daily, modulates myocardial metabolic efficiency and is recognized as a second-line agent in those whose angina persists despite use of standard antianginal therapy, and who are not suitable for invasive revascularization," said Prof Michel Komajda from the University Pierre et Marie Curie and the Pitie Salpetriere Hospital in Paris, France.

Trimetazidine reduces the mismatch between oxygen demand and delivery through a shift in cardiac metabolism in ischaemic conditions. "It shifts the cardiac cell metabolism from free fatty acid oxidation to glucose oxidation as a source of cardiac energy and therefore, improves cardiac efficiency," explained Komajda. "Potentiation of glucose oxidation optimizes cellular energy processes, maintaining proper energy metabolism during ischaemia."

Despite advances in pharmacotherapy and revascularization strategies, SCAD or stable ischaemic heart disease, remains associated with poor quality of life, poor outcomes, and disability, said Komajda.

"A significant proportion of patients revascularized by angioplasty still complain of angina pectoris, reflecting an impairment of coronary blood flow," he said. "One of three chronic stable angina outpatients remains symptomatic and at high risk of cardiovascular [CV] events."

"Angina occurs when myocardial oxygen demand exceeds oxygen supply. Trimetazidine, and other anti-ischaemic agents, is being used for second-line treatment and for the control of stable angina episodes."

Treatment options vary with the precise cause, and relevant to increased myocardial oxygen demand as against reduced supply. Current guidelines on SCAD by the European Society of Cardiology (ESC) recommend the use of ACE inhibitors, statins and aspirin, and medication relieving symptoms to prevent CV events, including acute coronary syndromes, in patients most of whom will experience angina as part of the disease's clinical manifestations. The pharmacological therapy is in addition to lifestyle changes and risk factor control. [Eur Heart J 2013;34:2949-3003]

"Angina occurs when myocardial oxygen demand exceeds oxygen supply. Trimetazidine, and other anti-ischaemic agents, is being used for second-line treatment and for the control of stable angina episodes," said Komajda.

Scan the QR code for full coverage of AFCC 2016
Combination therapy synergistically reduces CVD and mortality risks in hypertension

PEARL TOH

Antihypertensive combination therapy acts synergistically in reducing the risk of cardiovascular disease (CVD) and mortality, according to data presented at the AFCC 2016.

"Hypertension is the biggest reversible cause of death in the world today," said Professor Alistair Hall of the Heart Research Centre at Leeds General Infirmary in Leeds, UK, who stated that the ultimate goal of hypertension management is to protect against CVD and reduce mortality.

It was estimated that approximately 75 percent of patients with hypertension had uncontrolled blood pressure (BP), but only 32.5 percent of those being treated managed to keep their BP under control, based on a cross-sectional analysis of more than 142,000 adults. [JAMA 2013;310:959-968]

According to the latest guidelines from ESH/ESC*, monotherapy is only effective in reducing BP in a limited number of hypertensive patients, [Hypertens 2007;25:1105-1187] and that a combination of two or more drugs is required to achieve BP control in high-risk individuals with multiple comorbidities. [Eur Heart J 2013;34:2159-2219]

However, the effect on BP and CVD risk reduction varies with different combination of therapies. Citing data from the HOPE-3** trial, the combined therapy of hydrochlorothiazide plus the angiotensin receptor blocker (ARB) candesartan was not associated with a lower risk of major cardiovascular events among patients with intermediate risk without CVD compared with placebo, although the BP decreased by 6.0/3.0 mm Hg more in the treatment group, noted Hall. [N Engl J Med 2016;374:2009-2020]

"The once-daily dosing regimen could help improve patient compliance and thus, efficacy of treatment"

"The data on the use of ARBs in the HOPE-3 trial again emphasize the need to recognize the lack of important cardiovascular benefits with ARBs as compared with a placebo. These findings are in stark contrast to the benefits seen with ACE [angiotensin-converting-enzyme] inhibitors," wrote Hall and co-author in a separate correspondence. [N Engl J Med 2016;375:1190-1194]

"This is an important message for clinicians who are tasked with preparing guidelines."

Not only did the synergistic action of FDC with amlodipine and perindopril diminish their side effects, the once-daily dosing regimen could help improve patient compliance and thus, efficacy of treatment, said Hall.

*ESH/ESC: European Society of Hypertension/ European Society of Cardiology
**HOPE-3: Heart Outcomes Prevention Evaluation 3
Early cardiac MRI helps detect worsening heart function in at-risk patients

ROSHINI CLAIRE ANTHONY

Early cardiac magnetic resonance imaging (MRI) in patients with acute ST elevation myocardial infarction (STEMI) can predict worsening of left ventricular (LV) systolic function, LV remodelling and reverse remodelling, according to a study.

Participants in this prospective, observational study were patients aged 30—70 years (mean age 47.8 years) admitted to the Sarawak General Hospital Heart Centre between December 2012 and November 2014 who had been diagnosed with acute anterior or inferior STEMI. Participants must have achieved Thrombolysis in Myocardial Infarction (TIMI) 3 flow on a coronary angiogram (n=101) and undergone reperfusion with either percutaneous coronary intervention or thrombolysis.

MRI scans were carried out within 1 week of index admission and again between 3 and 6 months postadmission. Individuals unable to tolerate MRIs, those with end-stage renal failure (estimated glomerular filtration rate <45 mL/min/1.7m²), severe valvular disease, or a history of anaphylaxis to radiographic contrast were excluded from the study.

“The objective of my study was to see whether MRI was able to delineate factors that influence LV remodelling in successfully reperfused patients defined as TIMI 3 flow on coronary angiogram,” said Associate Professor Asri Said from the cardiology department at Sarawak General Hospital, Sarawak, Malaysia, who presented the findings.

Results of the study showed that age, sex, smoking, and presence of diabetes, hypertension, and dyslipidaemia did not influence LV remodelling; however, peak creatine kinase (p=0.018) and ejection fraction at admission (p=0.025) did predict LV remodelling at 6 months.

Infarct size was found to be larger in those with LV remodelling than those without (34.8 percent vs 24.8 percent; p=0.002); LV remodelling was 2.5 times more likely in the case of a larger infarct (≥35 percent). Forty-nine patients (48.5 percent) experienced reverse LV remodelling.

“From the MRI, we noted that patients with reverse remodelling were patients with smaller infarct size,” said Said. There were 15 major adverse cardiovascular events (MACE) including four deaths, five new heart failures, one new myocardial infarction (MI), and one unplanned revascularization.

“We identified that a larger infarct size is a predictor for MACE ... [and] the lower the ejection fraction, the more likely [the incidence of] MACE,” said Said.

According to Said, acute MI has a variable impact on outcome and long-term survival of patients, with an 18—24 percent risk of developing heart failure after 30 days and up to 33 percent at 5 years.

“We must have a way to differentiate which patients require specialized care, who are the high-risk patients,” he said, commenting that this study represents a small step towards the evaluation of patient-tailored therapy based on risk stratification using early cardiac MRI.

“This study suggests that early [cardiac magnetic resonance imaging] is feasible in acute STEMI patients. In our cohort, the patients with larger infarct size and [microvascular obstruction (MVO)] present experienced significant LV remodelling and poorer LV systolic function even after achieving TIMI 3 flow on angiogram,” said Said, who mentioned that a study using a bigger sample size over a longer follow-up period and incorporating analysis of early and late MVO and oedema is in the works.
Short DTB time, less radiation for hybrid angiography unit PCI

Primary percutaneous coronary intervention (PCI) can be safely performed in a hybrid angiography unit without compromising door-to-balloon (DTB) time and with less radiation, according to a Singapore study.

Mean fluoroscopy time was remarkably similar between the hybrid angiography unit and the conventional angiography unit (17.66 vs 20.06 mins) as was X-ray time (p=0.43). The DTB time was 55 mins in the hybrid unit vs 52 mins in the conventional angiography unit. However, there was a significant difference in the X-ray skin dose between the two groups at 486.76 and 705.71 mGy, respectively. [AFCC 2016, abstract P17]

This means less radiation exposure to the patient, wrote researchers Neil Wilkinson and Paul JL Ong from the Department of Cardiology, Tan Tock Seng Hospital, Singapore, which could be due to a slight difference in the field of view between the two angiographic systems (16cm2 for hybrid vs 15cm2 for conventional). They sought to investigate if there is any dose difference between emergency interventional procedures performed in a hybrid vs a conventional angiography unit (21 cases each). Acquisition protocol for both systems were similarly calibrated. Fluoroscopy and DTB time were compared, as well as X-ray skin dose.

Interventional cardiologists move with precision to save patient lives. Emergency PCI should be carried out in the shortest DTB time. The American College of Cardiology and the American Heart Association (ACC/AHA) guidelines recommend a door-to-balloon interval of no more than 90 minutes in patients with ST segment elevation myocardial infarction (STEMI) requiring primary PCI.

Collimation reduces radiation exposure

Using collimation to the required visual fluoroscopy field significantly reduced exposure to radiation, which may have important implications for the risk of potential radiation hazards in both patients and operators, according to a study.

Fluoroscopy remains a cornerstone imaging technique in electrophysiology (EP) practice. To assess the impact of collimation to the required field size on clinically significant parameter of radiation exposure, researchers conducted a hospital-based comparative study in the Cardiac Catheterization Laboratory of Cardiology Department at Yangon General Hospital.

The study involved 72 EP procedures performed by a team of cardiologist, a nurse, an X-ray technician, and an EP technician. Of these, 35 procedures were performed with collimation and 37 without. [AFCC 2016, abstract MP3]

An Optically Stimulated Luminescence Dosimeter was used to measure radiation doses. Radiation dose per minute of fluoroscopy time was determined between each study group.

There were significant reductions in radiation exposure in the collimation group. The greatest reduction was seen in the cardiologist (0.0796 mSv per procedure or 57 percent reduction). The X-ray technician, EP technician, and nurse had estimated radiation dose per minute of 0.0065 (46 percent), 0.0071 (34 percent), and 0.0072 (37 percent), respectively.
Individualized approach to reduce CV risk in diabetes patients

PEARL TOH

Glucose control must remain at the core of type 2 diabetes (T2D) management but requires an individualized approach to help reduce cardiovascular (CV) events, according to data presented at the AFCC 2016.

Glycaemic control should still be the focus of T2D management in order to avoid acute complications such as dehydration, osmolarity, and infections that could arise with severe chronic hyperglycaemia, and to optimize the prevention of micro- and/or macrovascular complications, said Professor Jean Mbanya from the University of Yaoundé in Yaoundé, Cameroon.

While the incidence of macrovascular events and associated complications had been shown to be reduced with controlled glucose levels in T2D, protective benefits on macrovascular events remained uncertain, especially on coronary heart disease events, said Mbanya.

It was likely that long-term perspective and selection of patients were required to reveal the benefits, he suggested.

"It takes time to observe a significant benefit of glucose control on microvascular complications," Mbanya said, referring to the UKPDS* which found that the risk for microvascular disease, including retinopathy and nephropathy, was significantly reduced in T2D patients who received intensive glucose therapy (eg, sulfonylurea or insulin) compared with those receiving conventional dietary intervention, and this benefit persisted for 10 years after the trial (p=0.001). [N Engl J Med 2008;359:1577-1589]

The study also demonstrated significantly reduced risks for myocardial infarction (15 percent; p=0.01) and death from any cause (13 percent; p=0.007) at 10 years follow-up. This was in contrast with the results from the ACCORD** and VADT*** studies, which found either increased or no change in death risk with intensive glucose therapy. [N Engl J Med 2008;358:2545-2559; N Engl J Med 2009;360:129-139; Lancet 2010;376:419-430]

"A more modest benefit [on macrovascular events] is likely to be present, but probably emerges only after many years of improved control," said Mbanya.

Additionally, Mbanya noted that these cohorts had a long duration of T2D (10 years), in contrast with the newly diagnosed patients included in the UKPDS.

Drawing from lessons learnt from these studies, several factors to be considered when personalizing glucose targets include diabetes duration, history of glucose control (ie, risk of hypoglycaemia), pre-existing CVD, comorbidities, frailty, life expectancy for performing intensive glucose control for more than 5 years, and patient’s preference. [Diabetes Care 2016;39:S187-S195]

"[There is] no one size fits all when managing diabetes," said Mbanya, calling for clinicians to individualize patient care in terms of setting glucose target and treatment intensification strategy.

"Overly aggressive control in older patients with more advanced disease may not have significant benefits and may indeed present some risk," he cautioned, citing recommendations stated in the ADA# and EASD## latest position paper. [Diabetologia 2015;58:429-442]

While the incidence of micr

*UKPDS: UK Prospective Diabetes Study
**ACCORD: Action to Control Cardiovascular Risk in Diabetes
***VADT: Veteran’s Affairs Diabetes Trial
#ADA: American Diabetes Association
##EASD: European Association for the Study of Diabetes
Strain imaging potentially useful in detecting right ventricular dysfunction

ROSHINI CLAIRE ANTHONY

Strain imaging is an alternative, noninvasive method suitable for detecting right ventricular (RV) dysfunction in repaired Tetralogy of Fallot (TOF) patients, though not a replacement for cardiac magnetic resonance imaging (MRI), according to a study.

“RV function has been shown to be a major determinant of clinical outcome in congenital heart disease patients,” said Dr Lorielyn Mandigma from the Golden Gate General Hospital in Batangas, Philippines, who presented the findings.

However, according to Mandigma, measurement of RV function is not always easy to perform, and MRI remains the gold standard and reference method to evaluate volume and ventricular function.

To determine the accuracy and cut-off values of RV strain imaging parameters that would detect RV dysfunction, Mandigma and colleagues conducted a prospective, cross-sectional study involving 22 patients (mean age 16.7 years) from the Philippine Heart Centre between August 2015 and January 2016. Patients underwent cardiac MRI and two-dimensional strain imaging on the same day.

Results of the study showed that cut-off values of -16.25 percent for the RV free wall (RVFW) mid-segment strain and -20.66 percent of the global longitudinal strain enabled detection of RV dysfunction, defined in this study as cardiac MRI-derived RVEF <50 percent.

The cut-off values for RV dysfunction detection were both sensitive at 83.33 percent and specific at 100 percent, said Mandigma. The findings also validated the correlation between the global and regional RV strain (the extent of regional shortening and thickening) and strain rate (rate at which deformation takes place) with cardiac MRI-derived RVEF, she said.

Nonetheless, Mandigma cautioned that RV strain imaging is not yet a surrogate for cardiac MRI in determining RVEF, but the utilization of RV strain imaging can complement the current echocardiographic assessment of repaired TOF patients as well as accurately predict the presence of RV dysfunction.

“Accurate assessment of RV function might be important for the optimal timing of RV outflow revalvulation, especially because [RV ejection fraction (RVEF)] is now being used as one of the criteria influencing the timing of pulmonary valve replacement.”
MIMS Mobile
your all-in-one clinical reference tool

Drugs
Search the MIMS database of concise and full prescribing information

News & CME
Stay up-to-date with the latest medical news & CME updates

Special Reports
Medical congress highlights and updates on drugs, diseases and clinical management trends

Calculators
Instant access to clinical calculator and scoring tools

Disease Resources
At-a-glance disease management guidelines for quick referencing on-the-go

Multimedia
Gain quick clinical insights through 5-minute expert opinion videos

Download MIMS from the app store today!

Join over a million MIMS members who have incorporated MIMS into their daily workflow. Connect with MIMS today.
Use of bedtime media device tied to poorer sleep in children and teens

PEARL TOH

Use of screen-based mobile devices near bedtime, or even the mere presence of them, was associated with poorer sleep health and excessive daytime sleepiness in children aged 6–19 years, revealed a meta-analysis of recent studies.

"Portable mobile and media devices have become a ubiquitous part of children's lives," noted researchers.

"The use of mobile media devices at bedtime provides socially and physiologically stimulating material at a time when the transition to sleep requires the brain to wind down," said Drs Charles Czeisler and Theresa Shanahan from Harvard Medical School in Boston, Massachusetts, US, in a separate editorial. [JAMA Pediatr 2016;doi:10.1001/jamapediatrics.2016.2986]

Among the 125,198 children and adolescents (mean age, 14.5 years) from 20 cross-sectional studies included in the meta-analysis, those who used portable media devices at bedtime were more than twice as likely to have inadequate sleep, defined as <9 and <10 hours of daily sleep for children and adolescents, respectively, than those who did not use these devices (odds ratio [OR], 2.17; p<0.001). [JAMA Pediatr 2016;doi:10.1001/jamapediatrics.2016.2341]

They were also more likely to have poor sleep quality, which referred to frequent difficulty in initiating or maintaining sleep or having a nonrefreshing sleep (OR, 1.46; p=0.003), and excessive daytime sleepiness (OR, 2.72; p=0.007).

"Delays in sleep initiation can set off a reinforcing physiological cascade to further delay sleep onset and restrict sleep duration on subsequent nights," said Czeisler and Shanahan.

In addition, when mobile devices were present in the bedroom (even without use) at night for at least three times per week, there was increased likelihood of having inadequate sleep (OR, 1.79; p<0.001), poorer sleep quality (OR, 1.53; p=0.009), and excessive daytime sleepiness (OR, 2.27; p<0.001) among the children and adolescents compared with those not exposed to such devices.

"Interventions should be developed and evaluated to reduce media device access and use at bedtime," said the researchers. "We support age-specific guidance for media device access and use and parent-led initiatives to reduce device access and use in collaboration with teachers and healthcare professionals."

Technologies that restrict service between prespecified hours of the day or allow only a maximum duration of media use daily, or software programs that reduce light intensity emitted from screens of media devices can help reinforce consistent bedtimes, according to Czeisler and Shanahan.

"Increasing awareness of guidance and technology that assist parents, educators, healthcare professionals, and policy makers in balancing the benefits and reducing the risks of mobile media in children is important for this and future generations," they added.

Due to the self-reported data and nonrandomized studies included in the analysis, substantial heterogeneity was present and thus, the findings should be interpreted with caution, according to the researchers.
The US Food and Drug Administration (FDA) has approved tenofovir alafenamide (TAF), a nucleoside analog reverse transcriptase inhibitor, as a single agent for the treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease.

The approval represents an important development for people living with chronic hepatitis B, said Professor Calvin Pan, an investigator in the TAF trials from the New York University Langone Medical Center, New York, US.

TAF’s approval was based on a 48-week data from two parallel phase III studies (108 and 110), which showed that TAF had similar efficacy profile to, and at a dose less than one-tenth that of, Gilead Sciences’ other anti-hep B drug, tenofovir disoproxil fumarate (TDF), in treatment-naïve and treatment-experienced adults with chronic HBV infection.

The approved dosing for TAF was 25 mg once daily, much lower than TDF’s dosing of 300 mg. This means less adverse effects on the kidney and bone due to lower plasma levels of the drug while exerting similar antiviral efficacy as the older TDF.

TAF’s label will carry a boxed warning citing risks of lactic acidosis/severe hepatomegaly with steatosis and post-treatment severe acute exacerbation of hepatitis B. The new HBV treatment is not recommended for patients with HBV/HIV-1 coinfection.

Studies 108 and 110 included 1,298 patients, with 425 in the e-antigen (HBeAg)-negative study and 873 in the e-antigen (HBeAg)-positive study, randomized in a 2:1 fashion to receive TAF or TDF for 96 weeks, to be followed by a 48-week open-label extension in which all participants were given TAF.

The primary endpoint was efficacy at 48 weeks, defined as the proportion of patients whose HBV DNA was below 20 IU/mL of blood. Secondary endpoints included bone and renal safety parameters.

In the HBeAg-negative study, 94 percent of those on TAF and 93 percent of those on TDF reached the endpoint whereas in the HBeAg-positive study, 64 percent and 67 percent, respectively, reached the endpoint. Both studies met the primary endpoint of noninferiority to TDF at 48 weeks of treatment. [International Liver Congress 2016, abstracts GS06 and GS12]

An integrated analysis of both studies found improvements in bone and renal safety parameters in patients treated with TAF vs TDF.

“The approved dosing for TAF was 25 mg once daily, much lower than TDF’s dosing of 300 mg. This means less adverse effects on the kidney and bone due to lower plasma levels of the drug while exerting similar antiviral efficacy as the older TDF”
Oat fibre lowers LDL-C, other markers of CVD risk

PEARL TOH

Eating oats not only lowers low density lipoprotein cholesterol (LDL-C) levels, but also reduces levels of non-high density lipoprotein cholesterol (non-HDL-C) and apolipoprotein B (apoB), markers known to be more closely associated with cardiovascular disease (CVD) risk than LDL-C, according to a new meta-analysis.

“The appreciation of these markers for CVD risk is especially important in adults with metabolic syndrome and/or diabetes as LDL-C is not typically elevated in this population,” said the researchers.

Participants taking a median dose of 3.5 g/day of the oat fibre β-glucan for a median duration of 6 weeks had significantly reduced levels of LDL-C by 4.2 percent (-0.19 mmol/L; p<0.00001), non-HDL-C by 4.8 percent (-0.20 mmol/L; p<0.00001), and apoB by 2.3 percent (-0.03 mmol/L; p<0.0001) compared with those on a control diet. [Br J Nutr 2016;116:1369-1382]

Meta-regression analysis showed that the higher the baseline LDL-C, the greater the effects of oat β-glucan on LDL-C reduction (p=0.004), although this association was not observed with non-HDL-C and apoB.

Also, reduction in LDL-C levels in trials that administered ≥3.0 g/day of oat β-glucan was almost double that of studies that administered <3.0 g/day (p=0.051), suggesting that the greater the intake of oat β-glucan, the lower the LDL-C levels.

“These results further support the health claims set by Health Canada and US FDA that cholesterol lowering can be achieved with a minimum of 3 g/day of oat β-glucan,” the researchers said. “Inclusion of oat-containing foods may be a strategy for achieving targets in CVD reduction.”

The meta-analysis included 58 randomized clinical trials (38 with parallel design and 20 with crossover design) lasting for at least 3 weeks (median duration of 6 weeks) and involving a total of 3,974 participants aged 10–67 years who were generally middle-aged (median age 50.6 years).

Due to the large number of trials included, there was considerable unexplained heterogeneity in the meta-analysis, which the authors said was inevitable.

“Timing of eczema onset influences food allergy risk

JAIRIA DELA CRUZ

The risk of developing food allergy at the age of 3 years is high among infants whose eczema occurred within the first 4 months of life, according to the results of T-CHILD* study.

“Our findings may contribute to a better understanding of the timing of eczema onset as a potentially modifiable risk factor and to defining those who may need to be on guard for food allergy,” said researchers from the National Center for Child Health and Development in Tokyo, Japan.

Of the 1,330 children included in the analysis, 27.9 percent developed eczema in the first year of life. Eczema was associated with parental history of allergic diseases (p<0.01), pet ownership (p=0.03), and annual household income (p<0.01). [J Dermatol Sci 2016;84:144–148]

Food allergy symptoms occurred at some point within the response period in 7.5 percent of 1,311 children with follow-up data at 1 year of age and in 7.5 percent of 1,136 of those with follow-up data at 3 years of age.

Eczema during the first year of life was associated with a nearly fourfold risk of developing food allergy at 3 years (adjusted odds ratio [aOR], 3.90; p<0.001).

*T-CHILD: Tokyo Children’s Health, Illness and Development
Connecting You to the Latest Medical Advancements for Better Decision-Making

MIMS Disease Resource Centres
All the Information You Need to Better Treat Your Patients

- Search for disease-specific drug information
- Read about recent conferences and views from key opinion leaders
- Find out what leading experts have to say on disease-focused topics
- Enhance clinical practice from treatment guidelines and journals
- Stay updated with relevant medical news and resources

Visit MIMS Disease Resource Centre
www.mims.com

MIMS DRC Filler - 206x276mm
SSRIs may increase risk of metabolic abnormalities in patients with schizophrenia or bipolar disorder

ROSHINI CLAIRE ANTHONY

Individuals with schizophrenia or bipolar disorder who are on selective serotonin reuptake inhibitors (SSRIs) may have an increased risk for metabolic abnormalities, a study from Norway shows.

After adjusting for all potential confounders, each defined daily dose (DDD) of an SSRI per day was associated with a 3.94 mg/dL elevation in total cholesterol levels (95 percent confidence interval [CI], 0.35–7.50 mg/dL; p=0.032). [J Clin Psychopharmacol 2016;doi:10.1097/JCP.0000000000000582]

Compared with individuals not using SSRIs (serum concentration=0), a serum SSRI concentration in the middle of the reference interval was associated with a 14.56 mg/dL elevation in total cholesterol levels (95 percent CI, 5.27–23.85 mg/dL; p=0.002).

Both SSRI serum concentration and dose were associated with elevations in low-density lipoprotein (LDL) cholesterol (8.50 mg/dL, 95 percent CI, 0.22–16.77 mg/dL; p=0.044 and 3.52 mg/dL, 95 percent CI, 0.31–6.69 mg/dL; p=0.031, respectively), while only SSRI serum concentration was associated with an elevation in triglyceride levels (46.49 mg/dL, 95 percent CI, 26.53–66.46 mg/dL; p<0.001).

SSRI serum concentrations and dose did not appear to affect high-density lipoprotein (HDL) cholesterol, glucose, or blood pressure levels, or waist circumference or body mass index. SSRI serum concentration was associated with the occurrence of metabolic syndrome (adjusted odds ratio [aOR], 2.10, 95 percent CI, 1.21–3.62; p=0.008), but not SSRI dose (aOR, 1.16, 95 percent CI, 0.49–1.41; p=0.150).

Previous studies have demonstrated an increased risk for cardiovascular disease in individuals with schizophrenia and metabolic disease in individuals with bipolar disorder, though the mechanisms behind these risks have not been determined. [Front Psychiatry 2014;5:137; J Clin Psychiatry 2014;75:46-61]

“[Patients with schizophrenia or bipolar disorder], due to their underlying disease, have an increased risk of metabolic disturbances, potentially making them even more susceptible for such adverse reactions caused by SSRIs," they said, though they cautioned against drawing any firm conclusions as causality was not established in this study.

Study participants were 1,301 individuals aged 18–65 years diagnosed with schizophrenia or bipolar disorder who were enrolled in the ongoing Thematically Organized Psychosis (TOP) study, 280 (21.5 percent) of whom were treated with SSRIs. The SSRIs used by the participants were escitalopram (n=154), citalopram (n=51), sertraline (n=40), fluoxetine (n=25), paroxetine (n=8), escitalopram and citalopram (n=1), and escitalopram and sertraline (n=1).

The researchers believed that analysing the impact of both SSRI serum concentration and dose on metabolic outcomes is one of the strengths of the study.
Type 2 diabetes (T2D) is significantly associated with an increased risk of hip fracture, and women with T2D for a decade have more than 30 percent increased risk of major osteoporotic fracture (MOF) and more than 90 percent increased risk of hip fracture than those without diabetes, according to a recent study.

The results showed that the use of conventional fracture risk assessment tools (FRAX) failed to capture these elevated risks as they relate to duration of disease.

"In a large study we found it was long duration of diabetes that was more important than the diagnosis itself in predicting fracture risk, and that FRAX underestimates risk in women with diabetes," researchers said.

Women aged ≥40 years with 10 or more years of prior healthcare coverage undergoing hip dual-energy X-ray absorptiometry measurements (1996 to 2013) were identified using a clinical dual-energy X-ray absorptiometry registry linked with the Manitoba administrative databases. Researchers analysed each incident MOF and incident hip fractures over 7 years.

A total of 8,840 women with and 49,098 without diabetes were included in the study (31.4 percent >10 y duration; 20.1 percent 5 to 10 y; 23.7 percent <5 y; 24.8 percent new onset). [J Clin Endocrinol Metab 2016;doi:10.1210/jc.2016-2569]

"[W]e confirmed that type 2 diabetes is a FRAX-independent risk factor for MOF and hip fractures and demonstrated that the duration of diabetes is important in terms of understanding and quantifying this increased risk," researchers said.

FRAX-adjusted analyses showed that only duration longer than 10 years was associated with an increased risk of MOF (hazard ratio [HR], 1.47; 95 percent CI, 1.3 to 1.66), and this was similar in the fully adjusted models (HR, 1.34; 1.17 to 1.54). On the contrary, there was an increased risk of hip fracture for all durations in a dose-dependent fashion (eg, FRAX-adjusted HR, 2.1; 1.71 to 2.59 for duration >10 y vs HR, 1.32; 1.03 to 1.69 for new onset).

"Indeed, at least 10 years of a diagnosis with diabetes needed to be present before women were at a significantly increased risk of MOF, whereas the risk of hip fracture was increased even before the diagnosis of diabetes," according to researchers.

The MOF risk (calibration ratio, 1.24; 1.08 to 1.39) and hip fracture risk (1.93; 1.5 to 2.35) were significantly underestimated by FRAX in those with a diabetes duration longer than 10 years.

The study has several limitations, such as the failure to distinguish type 1 from T2D, diagnoses of diabetes based on administrative data, absence of any measures of glycemic control or measures of bone strength or quality as influenced by glycemic control, and the lack of detailed information on smoking; physical activity; falls not requiring hospitalization or mediators of falling such as hypoglycaemia; or measures of diabetic complications such as neuropathy, myopathy, retinopathy, or nephropathy; or chronic kidney disease.

"Lastly, our findings may lack generalisability because the population was drawn from one province in Canada and the subjects were predominantly white, and we examined only women," researchers noted.
Efficacy of pertussis vaccine wanes over time

ROSHINI CLAIRE ANTHONY

While initially effective, the efficacy of the pertussis vaccine declines over time, particularly in recipients of the acellular vaccine, according to a Canadian study.

Vaccine effectiveness for individuals with up-to-date vaccination status was 80 percent (95 percent confidence interval [CI], 71-86 percent; p<0.05) at 15-364 days postvaccination compared with unvaccinated subjects. The effectiveness increased slightly at 1-3 years (84 percent, 95 percent CI, 77-89 percent; p<0.05), but decreased by 4-7 years postvaccination (62 percent, 95 percent CI, 42-75 percent; p<0.05). Eight or more years after vaccination, vaccine efficacy was 41 percent (95 percent CI, 0-66 percent; nonsignificant).

These findings were similar in partially vaccinated individuals (75, 68, and 56 percent at 15-364 days, 1-3 years, and 4-7 years postvaccination, respectively; p<0.05 and 36 percent ≥8 years postvaccination; nonsignificant) compared with unvaccinated individuals.

Recipients of only the acellular form of the vaccine were particularly affected by the reduction in efficacy with a 27 percent increased risk of testing positive for pertussis with each passing year postvaccination among those with up-to-date vaccination status (adjusted odds ratio [adjOR], 1.27, 95 percent CI, 1.20-1.34). They also had a higher risk of pertussis compared with individuals who received at least three priming doses of the whole-cell vaccine (adjOR, 2.15, 95 percent CI, 1.30-3.57).

“Our results showed that receiving one or more doses of whole-cell vaccine as an infant provided significant protection from pertussis more than a decade later,” said the study authors.

To assess the efficacy and duration of immunity provided by the pertussis vaccine, researchers used data from 5,867 residents of Ontario, Canada born between April 1992 and January 2013, 486 of whom tested positive for pertussis. Of these, 193 individuals (39.7 percent) had up-to-date vaccination against pertussis, 134 (27.6 percent) were partially vaccinated, and 159 (32.7 percent) were unvaccinated. Of the control group (n=5,381), 62.9, 22.5, and 14.6 percent were up to date, partially, and unvaccinated, respectively.

According to the authors, the results of this study point to the need to reevaluate strategies for pertussis vaccination as individuals aged ≤18 years in Ontario have only received the acellular vaccine.

“Our finding that the low-effective whole-cell vaccine is still better for priming than the currently used acellular vaccine nearly 2 decades after the change in practice has profound implications for understanding the effectiveness of the pertussis vaccine,” they said.

“Vaccination in pregnancy is recommended in the US and the UK, and is likely an effective strategy to reduce disease in infants. Consideration should also be given to introducing whole-cell vaccine for infant priming given the observational data showing significant long-term protective effects.”

“Vaccination in pregnancy is recommended in the US and the UK, and is likely an effective strategy to reduce disease in infants. Consideration should also be given to introducing whole-cell vaccine for infant priming given the observational data showing significant long-term protective effects.”
Access Drug Information At Point Of Prescription

MIMS Mobile provides the most comprehensive and up-to-date local drug information at your finger tips!

Built for both iOS and Android platforms, MIMS Mobile provides essential drug information like Drug Indications, Dosage, Adverse Drug Reactions, Mechanism of Actions and many more!

Download MIMS from the app store today!

Join over a million MIMS members who have incorporated MIMS into their daily workflow. Connect with MIMS today.

www.mims.com  MIMS mobile/tablet app  facebook.com/mimscom
Hypertension more prevalent in Chinese children

STEPHEN PADILLA

The prevalence of hypertension in Chinese children, adjusting for height, grew by 0.19 percent per year on average over the past two decades, which is much less than that reported in previous researches, according to a recent study. This trend is consistent with the obesity trend and appears regardless of sex and area.

Researchers re-evaluated the secular trends of blood pressure and hypertension prevalence in Chinese children and adolescents by adjusting for growing body sizes. They obtained data from the China Health and Nutrition Survey (1991 to 2011), which included 7,358 boys and 6,881 girls aged 8 to 17 years. [J Hypertens 2016:34:2337-2343]

National references were used to standardize body size measurements and blood pressure into z-scores to allow comparisons among different age groups and survey years. National and international age-specific and height-specific references were used to define prehypertension and hypertension rates.

Systolic and diastolic blood pressures increased 0.07 and 0.09 SD per survey year, respectively. Body mass index, waist circumference and height increased 0.14, 0.11 and 0.29 SD, respectively.

The general obesity prevalence rose to 8.1 from 1.5 percent (p≤0.0001 for trends), with an average annual increase (AAI) of 0.36 and 0.42 percent for urban and rural boys, respectively, and of 0.33 and 0.22 percent for urban and rural girls, respectively.

The hypertension prevalence rose to 10.7 from 6.9 percent (p≤0.0001 for trends), with an average AAI of 0.19 percent. The overall AAI in hypertension was threefold higher among boys (0.29 percent) than among girls (0.09 percent), explaining the sex difference in the rural population.

Researchers noted that even after applying the international criteria, the area and sex differences in AAI remained.

Comorbidities influence antiplatelet therapy adherence

ROSHINI CLAIRE ANTHONY

Comorbidities such as diabetes, hypercholesterolaemia, and hypertension, and a recent incidence of myocardial infarction (MI) may influence a patient’s adherence to antiplatelet therapy, a recent study shows.

Individuals with hypertension (hazard ratio [HR], 0.69, 95 percent confidence interval [CI], 0.52–0.93), diabetes (HR, 0.52, 95 percent CI, 0.37–0.72), and hypercholesterolaemia (HR, 0.45, 95 percent CI, 0.33–0.60) who were taking aspirin had a lower risk of antiplatelet discontinuation following an MI.

In contrast, individuals with diabetes (HR, 1.74, 95 percent CI, 1.11–2.73) and hypercholesterolaemia (HR, 1.43, 95 percent CI, 1.12–1.83) who were taking clopidogrel had a higher risk of antiplatelet discontinuation (all p<0.05). [Br J Clin Pharmacol 2016;doi:10.1111/bcp.13139]

Individuals who had an MI more recently were less likely to discontinue any antiplatelet therapy (HR, 0.38, 95 percent CI, 0.19–0.77 for MI occurring in 2008–2010 and HR, 0.69, 95 percent CI, 0.61–0.79 for MI occurring in 2003–2007 compared with MI occurring in 2002 or earlier; p<0.05).

Individuals who were taking vitamin K antagonists were at a higher risk of stopping any antiplatelet therapy (HR, 18.97, 95 percent CI, 16.91–21.28).

“As the concomitant use of an antiplatelet drug and an oral anticoagulant is associated with bleeding, this combination should be avoided. However, there are indications, such as for those with atrial fibrillation undergoing coronary stenting, in whom the combination is indicated,” said researchers.

In this retrospective study from the Netherlands, subjects were 4,690 patients (aged ≥18 years) from the Utrecht
Cardiovascular Pharmacogenetics cohort who had been hospitalized for their first MI between 1986 and 2010 and followed up for up to 10 years (median 5.6 years) after being discharged from hospital.

Information on drug therapy was obtained from the Pharmaco-Morbidity Record Linkage System database. Individuals prescribed antiplatelets were divided into three groups, ie, persistent users (gap between prescriptions ≤90 days), nonpersistent users (>90-day gap with no refills), and restarters (new prescription filled after >90-day gap).

The number of persistent users of antiplatelet drugs reduced from the 1-year follow-up to the 10-year follow-up (84 percent vs 32.8 percent). However, many of the patients who stopped taking antiplatelets later resumed therapy, with 89.3 percent of patients on antiplatelets at 10 years post-MI.

For individuals on aspirin, persistence was 77.3 percent at 1 year versus 27.5 percent at 10 years (overall use of aspirin at 10 years was 77.1 percent after accounting for restarters), while clopidogrel persistence was 39 percent at 1 year (26 percent overall users at 6 years after including restarters). Dual antiplatelet therapy persistence was 31.5 percent at 1 year with many nonpersistent users switching to single therapy.

“In spite of the restart, it is important to be aware that the gap between discontinuation and restart is a critical period for the occurrence of recurrent [cardiovascular] events,” said researchers.

“A discontinuation of antiplatelet drugs early after [coronary heart disease] and [percutaneous coronary intervention] might lead to a recurrent [acute coronary syndrome (ACS)] event. The present study showed that in 30 percent of the patients who discontinued antiplatelet drugs within 6 months after the first MI, a recurrent ACS occurred within 6 months after the discontinuation date,” they said.

Researchers did not account for the reasons behind antiplatelet discontinuation, which they said was an area for future research. They also did not identify if treatment discontinuation was initiated by the patient or physician.

“Patients need to understand the reasons and rationale behind a doctor recommending a treatment”

According to Assistant Professor Ho Kay Woon, a senior consultant at the Department of Cardiology, National Heart Centre Singapore (NHCS) who was not affiliated with the study, patients with the above comorbidities will more likely need other medications for their treatment. Thus, there is likely to be longer chronic disease follow-up with their family practitioner and hence, a greater likelihood of persistence with antiplatelet agents.

Assistant Professor Chin Chee Tang, a senior consultant at the same institution, agrees. “Patients with these comorbidities are likely to have more severe ischaemic heart disease, perhaps had more MIs or a greater degree of cardiac dysfunction after their MI. These comorbidities are also risk factors for other cardiovascular diseases such as strokes or peripheral arterial disease. As these patients have experienced more complications of these diseases than a similar patient without these comorbidities, they may be motivated to be more compliant with medications like antiplatelets so as to reduce the chance of recurrent events,” he said.

“Because these patients may also be seeing physicians more frequently for management of these comorbidities, the degree of compliance may be greater as they are frequently being asked about medication adherence,” said Chin.

According to Ho, antiplatelet nonpersistence is a problem in Singapore. “Noncompliance to medication or follow-up are common even amongst patients with prior MI,” he said.

“Medication adherence and compliance can be improved by patient education and reinforcement. Patients need to understand the reasons and rationale behind a doctor recommending a treatment. Similarly, the physician must be sensitive and aware of possible reservations that the patient may have, specifically, the patient should be made aware of possible side effects that they may encounter and so not be alarmed if they do occur,” said Chin.
Pearl Toh spoke with Dr Helen Chen, head and senior consultant of the Department of Psychological Medicine at KK Women’s and Children’s Hospital (KKH) in Singapore on factors affecting postnatal depression (PND) and how clinicians can help their patients cope with this condition.

What is the prevalence of PND among mothers in Singapore?

The prevalence of PND in Singapore is about 7 percent, when considering both milder forms as well as more severe forms of depression.

How is PND usually diagnosed?

Diagnosis is generally done by clinical assessment by trained professionals, or using structured interview tools. Screening tools, such as the Edinburgh Postnatal Depression Scale, can also help identify those that are likely cases. As there can be false positives or false negatives from the screening, an assessment is typically recommended if the woman is symptomatic.

What are the symptoms to look out for that should alert the doctor that the patient might be having PND?

Some common signs and symptoms of PND include:

- Low mood
- Crying
- Irritability
- Appetite changes
- Loss of energy
- Poor concentration or forgetfulness
- Excessive self-blame or guilt
- Feelings of hopelessness
- Sleep disturbance unrelated to baby’s needs
- Thoughts of harm to self or baby, or suicide

In PND, there is usually a combination of these symptoms lasting for 2 weeks or longer, with significant impact on the mother's functioning – for example, she is unable to tend to the needs of her baby, or handle her daily activities.

Your recent study showed that women who experienced persistent childbirth pain after delivery had an increased risk of PND. [World Congress of Anaesthesiologists 2016, abstract PR 196] What are the major factors that might contribute to PND besides persistent childbirth pain?

Various factors can contribute to PND – usually, it is an interplay of factors for each woman. Major risk factors of PND include history of depression, and positive family history of PND (the risk of PND is increased twofold if her mother or sister had PND).

Other factors would be concurrent stress factors such as marital problems, work-related stress, issues with in-laws or available support. Early motherhood is not easy, especially with sleep deprivation, and challenges of breastfeeding, so exhaustion can set in and contribute to PND.

Women who experienced poor maternal care during childhood will
also be at risk – because the difficult emotional memories that have been repressed can surface at this time of transition, and present as an internal stress, wherein they doubt themselves, or feel too broken to be good enough mothers.

Difficult or traumatic labour experience can also contribute to post-traumatic stress symptoms and PND. This is not an uncommon reason for women to delay or avoid a subsequent pregnancy.

Personality types that predispose women to PND include especially those who have anankastic traits – ie, being rigid or perfectionist.

Women and their families often think that postnatal emotional changes might be due to hormonal change alone, so they prefer to wait for things to settle. But if it is so, then we should expect to see 100 percent of women getting depressed, because everyone experiences hormonal changes with delivery. Rather, it is because women are more vulnerable at this time when their bodies are going through tremendous physical changes so that any added stress can tip them into depression.

**In Singapore, what are the current support system/programmes available for mothers to cope with or to reduce persistent childbirth pain physically and psychologically?**

Prompt and adequate pain control is most effective in ensuring mothers do not experience persistent childbirth pain. The experience of pain is also often influenced by the psychological state of the mother, as our research has clearly shown, so holistic care that incorporates emotional support addressing the individual needs is important.

At KKH, we have been running the PND Intervention Programme since 2008 – this programme provides free emotional health screening for postnatal women and identifies early those who need psychological support. Depending on the nature or severity of their emotional distress, women are then offered supportive counselling, support group intervention, psychiatric intervention, or psychological therapy. Our postnatal patients are screened for severity of pain, and patients with persistent pain will be referred to a specialist for further assessment.

**What advice would you give doctors or mothers facing PND?**

Early intervention is crucial, as PND can impact on the capacity of mothers to care well for their infants. Evidence has shown that mothers who are depressed tend to be less attuned to the needs of their infants, and are less able to stimulate their infants, and this therefore affects their emotional and cognitive development.

Mothers often fear getting help because they think medications are harmful, especially if they are breastfeeding, or they fear others thinking they are mad or of unsound mind.

To reassure my patients, I often share that PND is a medical condition that is caused by brain neurotransmitter imbalance due to various stress factors as mentioned above, just like diabetes is caused by insulin imbalance. Also, medication can be chosen for mothers to safely nurse their babies – indeed, mothers who are depressed tend to stop breastfeeding prematurely, and stress can actually hamper their milk production and milk let-down. Importantly, our mainstay of intervention is supportive counselling and therapy, whilst medication is only necessary for those with at least moderately severe depression.

For doctors, I think it is common for them to fear asking how mothers are feeling, lest she says she is depressed and suicidal but refuses to accept a referral to get help. So I usually advise that it is alright if the mother refuses – the burden is not on the doctor who asked to ensure, just as it is with any screening procedure. Nonetheless, the doctor can and should give advice to a mother who is depressed to get help – and perhaps some days later, she might decide to call the helpline.

It is also helpful not to say to a mother “you are depressed, you need to see a psychiatrist”, as this typically invites a defensive response. Instead, say “I wonder if you would like some help – you might be suffering from depression.”
Acne is a chronic inflammatory skin disorder that results in skin blemishes. Primary care doctors are likely the first point of contact for those with acne. Radha Chitale spoke with Dr Tan Lixian Chris, an associate consultant in the Division of Dermatology at National University Hospital, Singapore, about how GPs can best diagnose and treat patients with acne.

Managing acne in primary care

Acne is a chronic inflammatory disorder of the pilosebaceous unit. It often starts with excess sebum production and abnormal shedding of skin cells. Bacteria that feed on the sebum then proliferate and lead to inflammation.

Adolescents are most at risk of developing acne. In a community-based cross-sectional study of 1,045 adolescents in Singapore aged 13-19 years, 88 percent of those surveyed identified themselves as having acne. [Br J Dermatol 2007;157:547-551]

This is comparable to international data where up to 90 percent of adolescents have some form of acne.

GPs are often the first point of contact in disease management and health promotion for the majority of our population. They have built trusting patient-doctor relationships within the community that they serve. Hence, they have the access and confidence to identify and initiate early acne treatment measures in patients who visited them even for a different ailment initially.

Diagnosing acne

Acne requires a clinical diagnosis and the spectrum of acne lesions ranges from noninflammatory open or closed comedones (blackheads and whiteheads) to inflammatory lesions, which may be papules, pustules, cysts or nodules. The presence of excoriations, post inflammatory hyperpigmentation, and scars should also be noted. Lesions can also occur on the neck, chest, upper back, and upper arms, in addition to the face which is the most common. Internationally accepted guidelines published by the Global Alliance for Acne can be a useful guide for GPs in managing their patients. The American and European academies of dermatology have also published similar guidelines.

In 2015, a group of dermatologists from Southeast Asia jointly developed a set of treatment guidelines to aid physicians in managing acne in Southeast Asian patients. [J Dermatol 2015;42:945-953]

There are several different types of acne:

- **Cosmetic Acne:** This describes an association between the use of cosmetic products and acne, a phenomenon attributed to follicular plugging induced by certain agents. Patients present with insidious, slow development of the small bumps of skin called comedones (whiteheads and blackheads) and, eventually, inflammatory lesions. In addition, follicular irritation related to the application of cosmetics may result in the rapid appearance of small inflammatory papules.

- **Acne excoriée:** A scarring acne condition often, but not always, seen in young women. Relatively mild acne comedones or inflammatory papules are chronically and obsessively picked and excoriated, leading to erosions and scarring. An underlying psychiatric disorder can be associated, and treatment may involve antidepressants and psychotherapy.

- **Post Adolescent Acne:** Acne occurring in individuals in adulthood, typically after the age of 25. This type of acne affects females more often than males. Clinical signs and symptoms are similar to conventional adolescent acne. However, a minority of patients may also present with hirsutism, seborrhea and coarse skin, suggesting an underlying hyperandrogenic state.

- **Acne fulminans:** The presence of fever and joint pain with an acute eruption of large inflammatory nodules.
and friable plaques with haemorrhagic crusts. This rare condition affects adolescent males primarily. Lesions usually involve the trunk, but may be present elsewhere.

- Acne conglobata: Acne conglobata is a severe form of nodular acne that is most commonly seen in young males. Lesions are most prominent on the back, chest, and buttocks, but can also appear in other sites. Large draining lesions, sinus tracts, and severe scarring may occur. Systemic symptoms are absent.

GPs should be aware of and distinguish between other conditions that may have similar clinical features to acne. This is because these patients may not respond well to conventional acne therapies. These conditions include rosacea, perioral dermatitis, and pityrosporum folliculitis. A detailed clinical history and thorough physical examination of the skin will help, as will keeping up with current medical knowledge.

**Treating acne**

After making the diagnosis and identifying the relevant aggravating factors (eg cosmetic products, habitual excoriations, etc), GPs should determine the severity of the acne and treat accordingly. Therapy choice may also be influenced by age of the patient, comorbid medical conditions, site of involvement, and patient preference.

Mild acne is typically treated with topical therapies alone. These include benzoyl peroxide (BP), salicylic acid, antibiotics, combination antibiotics with BP, retinoids, retinoid with BP and aze- laic acid. Recommended first line topical therapies for mild acne include retinoids alone or combination therapies such as retinoid with BP, antibiotic with BP, or all three combined.

Topical retinoids are vitamin A derivatives. They are comedolytic, resolve the precursor microcomedone lesion, and are anti-inflammatory. Retinoids are ideal for comedonal acne and, when used in combination with other agents, for all acne variants.

BP is an antibacterial agent that kills acne-causing bacteria through the release of free oxygen radicals and is also mildly comedolytic. No resistance to this agent has been reported, and the addition of BP to regimens of antibiotic therapy enhances results and may reduce resistance development. BP with retinoid combination is a convenient once-a-day application that has shown high efficacy and tolerability in treating mild and sometimes even moderate acne.

Moderate and severe acne would usually require the addition of systemic therapies to topical therapies. Evidence supports the efficacy of systemic antibiotics like tetracycline, doxycycline, minocycline, trimethoprim/sulfamethoxazole (TMP/SMX), erythromycin and azithromycin. Combination oral contraceptive pills (COCs), anti-androgens like spironolactone and oral isotretinoin are also used.

Importantly for GPs to note, topical or systemic antibiotics should not be used as monotherapy to prevent risks of Propionibacterium acneus antibiotic resistance. They should be used judiciously in combination with non-antibiotic preparations such as BP and retinoids. In the case of systemic antibiotics, concurrent use of topical BP and retinoids help limit the duration of systemic antibiotic use to the shortest possible duration, typically 3 months.

GPs should be mindful of drug allergies and tolerability to acne medications. For example, topical retinoids may cause irritation in people with eczema and generally sensitive skin. However, this can be prevented by measures such as addition of a regular moisturizer, using a more gentle facial cleanser, and reducing the frequency of application. Care should also be taken to assess the risk-benefits when prescribing COCs and strict contraception measures must be taken in women of child-bearing age treated with oral isotretinoin.

Although there are studies that show efficacy in complementary treatments such as chemical peels and light therapy, there is limited evidence to routinely recommend these therapies to all patients.

There is also emerging but limited evidence that diet plays a role in the pathogenesis of acne.

GPs should refer patients to a specialist if they are unsure of the diagnosis, if patients have poor or no response to therapy, if complications such as allergies or contact dermatitis arise from therapy, if the acne is severe with systemic manifestations of significant scarring and abscess formation, and if the acne is associated with hyperandrogenism (eg, hirsutism).

**Conclusion**

The highest incidence of acne occurs in adolescents, a group that is highly conscious of their physical appearance. Hence, acne poses significant stress to their self-esteem and can lead to social withdrawal and isolation. Even adults can have conspicuous acne, which makes patients self-conscious and depressed in severe cases. Diagnosing and treating acne as early and as accurately as possible can help minimize severe progression and permanent scarring.

**Online resources**

American Academy of Dermatology - www.aad.org
European Dermatology Forum - www.euroderm.org
European Academy of Dermatology and Venerology www.eadv.org
Asian Academy of Dermatology and Venerology www.asianderm.org
Skin patch safe, promising for treating peanut allergy

PEARL TOH

Delvery of peanut protein through the skin by means of a wearable skin patch, an approach known as epicutaneous immunotherapy, is safe and shows promise for treating peanut allergy, especially in young children, according to interim results of an ongoing study. “Despite active avoidance, the risk of an adverse reaction from exposure is ongoing,” said researchers, who noted that peanut allergy presents the most common life-threatening food allergy. “An effective treatment for peanut allergy would be highly desirable.”

The multicentre, double-blind, phase II trial randomized 74 individuals (aged 4–20 years, median 8.2 years) with peanut allergy to placebo (n=25), 100 µg (VP100; n=24) or 250 µg (VP250; n=25) peanut immunotherapy delivered through a skin patch known as Viaskin Peanut. The participants were assessed for treatment success, which referred to success in a 5,044 mg protein oral food challenge or achievement of ≥10-fold increase in success fully consumed dose (SCD) of protein at week 52 compared with baseline. [J Allergy Clin Immunol 2016;doi:10.1016/j.jaci.2016.08.017] Compared with placebo (12 percent), there were more participants in the VP100 group (46 percent; p=0.005) and VP250 group (48 percent; p=0.003) who had achieved treatment success at week 52.

Treatment success was significantly higher among younger children (aged ≤11 years) compared with those older than 11 years (61 percent; p=0.0003 for VP250 and 59 percent; p=0.0006 for VP100 versus 6 percent for placebo). SCD also changed significantly from 0 mg of protein in the placebo to 43 mg and 130 mg in the VP100 (p=0.014) and VP250 (p=0.003) groups, respectively. Significant increases were observed in both peanut-specific IgG4 levels and IgG4/IgE ratios (p<0.0001 for both) between treatment and placebo groups. There were also trends toward reduced peanut specific T2 cytokines (p=0.059 for interleukin [IL]-4 and p=0.04 for IL-13) and basophil activation.

“The trends seen in both basophil and T-cell responses suggest that exposure to peanut through intact skin might modulate T2 responses and basophil reactivity,” researchers said. Compliance with treatment was high (97.1 percent of doses), suggesting that the patch was convenient and well tolerated.

Although patch-site reactions occurred more frequently in the treatment groups (79.8 percent of VP100 and 79.7 percent of VP250 doses) compared with placebo (14.3 percent; p=0.003), most were mild (≤grade 2). Reactions extending past the patch area occurred in 8.9 percent of VP100 and 16.2 percent of VP250 doses compared with 1.5 percent of placebo dose, while nonpatch-site reactions were uncommon (0.2 and 0.1 percent of VP100 and VP250 doses vs 0.2 percent of placebo dose).

“Additional time on therapy is needed to determine whether the modest clinical changes noted will be enhanced after a longer duration of therapy and will provide clinically meaningful protection from anaphylaxis,” said researchers, who were awaiting further results at 130 weeks of the study.
Scientists in the UK have developed a USB stick that can accurately test for viraemia in less than 30 minutes among individuals with suspected human immunodeficiency virus (HIV). A drop of blood placed onto the USB stick is all they need to produce results.

Current HIV tests in the market take at least 3 days and involve sending of blood samples to the laboratory for analysis. In poor-resourced settings with high HIV burden, access to those tests is even limited.

“Our HIV specific pH-LAMP assay, coupled with novel CMOS technology, shows great potential as a route to a point-of-care diagnostic suitable for use in clinical settings without access to a laboratory infrastructure,” said study author Dr Graham Cooke from the Department of Medicine at Imperial College London, UK.

The test can also detect viraemia in HIV-infected individuals receiving antiviral treatment as well as identify multiple pathogens.

Regular monitoring of viral load is crucial to the success of any HIV treatment, so is detection of treatment failure. Current methods often require costly and complex equipment that can take days to produce a result, said Cooke. “We have taken the job done by this equipment, which is the size of a large photocopier, and shrunk it down to a USB chip.”

The RT pH-LAMP is based on a novel CMOS chip platform and uses a drop of blood to detect HIV. Heaters and thermal sensors are imbedded in the chip to detect HIV-1 viral load without the need for additional power supply, labels, or fluorescence detection.

Screening of 991 clinical samples – 164 on the chip – yielded a sensitivity of 95 percent (in vitro) and 88.8 percent (on chip) at >1000 copies/reaction across a broad spectrum of HIV-1 viral clades. Median time to detection was 20.8 minutes in samples with >1000 copies RNA. [Scientific Reports; doi:10.1038/srep36000]

Viral load is the earliest marker of HIV infection and a high viral load is related to seroconversion symptoms. According to the World Health Organization (WHO), detection of viral loads >1000 copies/mL is enough to establish sufficient sensitivity. [Antivir Ther 2008; 13;1-13]

The authors said the 95 percent detection rate for the LAMP reaction at >1000 copies/reaction is “encouraging.” However, more studies are warranted before the test can be used in the clinic. “Further development is required, including an evaluation of specificity across a wide range of clinical isolates.”

The device was created by Cooke’s team at the Imperial College London and the privately-held US firm DNA Electronics, with funding from The National Institute for Health Research Imperial Biomedical Research Centre.
<table>
<thead>
<tr>
<th>Month</th>
<th>Dates</th>
<th>Location</th>
<th>Tel.</th>
<th>Email</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>DECEMBER</td>
<td>03-06</td>
<td>58th American Society of Hematology Annual Meeting &amp; Exposition</td>
<td>+202 776 0544</td>
<td>[email protected]/Contact-Us</td>
<td><a href="http://www.esmo.org/Conferences/ESMO-Asia-2016-Congress">hematology.org/Conferences/ESMO-Asia-2016-Congress</a></td>
</tr>
<tr>
<td>DECEMBER</td>
<td>16-19</td>
<td>European Society for Medical Oncology (ESMO) Asia 2016 Congress</td>
<td>+81-3-6380-0102</td>
<td><a href="mailto:info@apasl2016.org">info@apasl2016.org</a></td>
<td><a href="http://www.apasl2016.org/conf_contact.html">http://www.apasl2016.org/conf_contact.html</a></td>
</tr>
<tr>
<td>MARCH</td>
<td>02-04</td>
<td>4th International Conference on Nutrition and Growth</td>
<td>+41 315 280 432 ext. 50</td>
<td><a href="mailto:customerservice@hematology.org">customerservice@hematology.org</a></td>
<td><a href="http://www.hematology.org/Highlights/Asia/3544.aspx">http://www.hematology.org/Highlights/Asia/3544.aspx</a></td>
</tr>
</tbody>
</table>
“Just a nurse”: A nurse speaks up against her profession being devalued
A Queensland nurse’s impassioned Facebook post hitting back at people belittling her profession has gone viral. Our very own community of doctors, nurses and pharmacists chime in on the discussion and share how nurses should be valued.

Too Busy for exercise
“No time to exercise” is one of the most common statements when doctors stress the need for regular exercise. Doctors have a responsibility to do a better job of pointing out the necessity of physical activity to prevent medical complications. How do you stress the need for exercise to a patient who claims to be busy?

What is the strangest thing you have heard a patient say?
Many patients come into the clinic or hospital with some bizarre misconceptions about their health. What is the strangest thing you’ve heard your patients say?

The challenges of treating transgender patients
Transgender is basically an umbrella term that is used for individuals with gender identification different from the gender given them during birth. They face several challenges as far as health care is concerned due to their specific unique needs.

Was there one patient that made your years of education all worth it?
Share with us your most memorable experience with a patient and how this particular patient has brightened your outlook on career and life!

Want to take part in the MIMS Community discussions regarding medical news and healthcare?
Join our growing community of healthcare professionals to share your learnings and network with your peers.

www.mims.com