

THE JOURNAL OF CLINICAL MEDICINE

MODERN MEDICINE

VOLUME 38 NUMBER 3
MARCH 2013



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References: 1. Richter JE, Peura D, Benjamin SB, Joelsson B, Whipple J. Efficacy of omeprazole for the treatment of symptomatic acid reflux disease without esophagitis. *Arch Intern Med* 2000;160:1810-1816; 2. Dekkers CPM, Beker JA, Thjodleifson B, Gabryelewicz A, Bell NE, Humphries TJ. Double-blind, placebo-controlled comparison of rabeprazole 20 mg vs omeprazole 20 mg in the treatment of erosive or ulcerative gastroesophageal reflux disease. *Aliment Pharmacol & Ther* 1999;13(1):49-57; 3. Klinkenberg EC, Nelis F, Dent J, Snel P, Mitchell B, et al. Long-term omeprazole treatment in resistant gastroesophageal reflux disease: efficacy, safety and influence on gastric mucosa. *Gastroenterology* 2000;118(4):661-669. [S4] Omez 10. Each capsule contains omeprazole 10 mg. Reg. No. 34/11.4.3/0299. [S4] Omez 20. Each capsule contains omeprazole 20 mg. Reg. No. 34/11.4.3/0300. [S4] Omez 40. Each capsule contains omeprazole 40 mg. Reg. No. 34/11.4.3/0301. Dr. Reddy's Laboratories (Pty) Ltd. Reg. No. 2002/014163/07. Tel: +27 11 324 2100 www.drreddys.co.za

Cardiology • 15

Post Myocardial Infarction

Diabetes • 24

Management of Foot Ulcers

Neurology • 29

Parkinson's Disease

Diabetes • 32

Cost-effectiveness
of Saxagliptin

Gerontology • 34

Falls in Older People

Also ...

On the Horizon
Quoth the Maven
Here & Now
RoundUp

Get Your CPD Points Inside!



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Lifelong Learning

CARDIOLOGY



Patients Post Myocardial Infarction: Tailored Management Improves Outcomes 15

PETER L THOMPSON, ANGUS G THOMPSON

Patients who have had a myocardial infarction need aspirin and statin therapy and careful evaluation to identify those who will benefit from revascularisation or implantable device therapy and appropriate additional pharmacological treatment.

DIABETES



Diabetes-related Foot Problems: Urgent Management of Ulcers 24

ANGELA EVANS, PAT phillips

Diabetes-related foot problems are largely preventable with appropriate medical assessment, patient education and on-going monitoring. However, many patients with diabetes present with foot ulcers that require emergency attention, as in the case described here.



PAGE 24

NEUROLOGY



Therapeutic Progress in Parkinson's Disease 29

ANDREW EVANS, SIMON SUNG

Pharmacological dopamine replacement is the most effective form of treatment for patients with early Parkinson's disease. However, it is only a symptomatic therapy. Future therapeutic strategies should therefore focus not only on ameliorating the symptoms of Parkinson's disease, but on neuroprotective or neurorescue therapies.



PAGE 34

DIABETES

Cost-effectiveness of saxagliptin in type 2 diabetes in South Africa 32

STAFF WRITERS

A cost-effectiveness analysis was undertaken to estimate the long-term economic and health impact of type 2 diabetes on South African patients.

GERONTOLOGY



Preventing Falls and Fall-Related Injury in Older People: How GPs can Help 34

JAQUELINE CT CLOSE

Falls and fall-related injury are common in older people, with some events having a direct impact on the person's ability to function and live independently. There is good evidence that falls and fall-related injury can be prevented, and GPs have a key role in screening, assessment and implementing effective intervention strategies.

Continued on page 2

MODERN MEDICINE

REGULAR FEATURES

ON THE HORIZON



... find out what the future will bring us 3

- Smart Capnography with CO2 Specific Laser-Based Technology
- New Release of Popular Doctors' App
- Increased Procedural Efficiency in Knee Implant Positioning
- Detachable Coil System for Treating Cerebral Aneurysms
- Preventing Recurrent Strokes in Patent Foramen Ovale Patients
- Embolisation Device Rebuilds Wide-necked Intracranial Aneurysms
- Portable Precise Point-of-Care Imaging
- Innovative Treatment for Pneumothorax and Pleural Effusions
- Oesophageal Doppler Monitoring (ODM) in Surgery Could Yield Big Savings

OPINIONS

Quoth the maven

9

- Senescence, Black Clouds and Getting Involved

HERE & NOW

... newly available in South Africa

10

- Sony Extends Medical Line-up with New Radiology Diagnostic Monitors
- Renal Denervation: a Groundbreaking Way to Manage Treatment-resistant Hypertension
- AbbVie: A New Biopharmaceutical Company

ROUNDUP

... for doctors on the run

41

- 90 Dubious Tests and Therapies to Avoid
- Very early ART Achieves HIV Cure in Mississippi Infant
- How Long Does a Cough Last? Patients' Expectations Are Unreasonable
- Play to Become a Surgeon: Wii Games Boost Performance
- New Blood at iNova
- No Difference in Extrapyrimal Effects Between First and Second Generation Antipsychotics... Except the Expense

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On the Horizon

Smart Capnography with CO₂ Specific Laser-Based Technology

Oridion Capnostream uses the laser-based technology of molecular correlation spectroscopy (MCS) to increase the accuracy and reliability of capnography monitoring. With lock and key precision, MCS creates an infrared emission that precisely matches the absorption spectrum of CO₂.

The emission combines with Smart capnography, a family of algorithms that reduces clinically insignificant alarms and provides clinical utility for improved patient safety, for Smart Breath Detection Algorithm (BDA), Smart Alarm Respiratory Analysis (SARA) and the Integrated Pulmonary Index (IPI).

The BDA proprietary filter and pattern recognition algorithms screen out low amplitude etCO₂ changes superimposed on the etCO₂ waveform to focus on actual breaths, while rejecting shallow, non-breath etCO₂ excursions. SARA alarm management technology recognises and reduces respiratory rate nuisance alarms, while accurately reflecting the patient's condition and preserving caregiver alarm vigilance. IPI uses etCO₂, respiratory rate, pulse rate and SpO₂ to provide an uncomplicated, inclusive assessment of a patient's ventilator and oxygenation status.

By following the trend of the IPI, doctors can quickly assess the inter-relations of a patient's respiratory parameters and gain an early indication of changes in a patient's respiratory status that may not be indicated by the values of the individual parameters.

The etCO₂ measurement technology is versatile for use in any hospital environment and for all patient types. The etCO₂ breath sampling lines include elements



for accurate sampling from oral and nasal breathers, in high humidity environments, and even with the smallest of breath samples from infants or neonates. The array of sampling lines are designed to meet every clinical need, including longer term monitoring, high humidity environments and upper airway management during endoscopy procedures.





New Release of Popular Doctors' App



Medscape has just released its 4.0 version, one of the leading mobile medical resources used by doctors, nurses, medical students and other healthcare professionals for clinical information.

The application, from WebMD, offers evidence-based disease reference and updated medical news and education resources, authored and reviewed by 7700 doctors and pharmacists. A major improvement is the redesigned, user-friendly iPad interface.

The app, which requires operating system iOS 5 or later, is compatible with iPhone, iPod Touch, iPad and Kindle Fire, and is optimised for iPhone 5. It can be downloaded and installed on an Apple device but is not yet available for Android platforms. Users must register on the Medscape account, but the process and app download are free.

While users can download reference material for access to it offline, the news and education content is available only online. Homepage news and the reference and education material are customised to the user's speciality.

The app holds a clinical reference database of more than 8000 drugs, 4000 diseases and conditions, thousands of clinical images and procedure videos, drug interaction checker tools (for up to 30 drugs at a time) and medical calculators that offer 129 formulas, scales, and classification in addition to 600+ drug monographs with integrated dosing calculators.

One disadvantage noted by some user reviews is that some generic names for certain medications are not noted.

Increased Procedural Efficiency in Knee Implant Positioning



Trumatch pin guide or cutting guide solutions by Du Puy Orthopaedics, bring a new level to personalised total knee replacement surgery. They are based on the proven philosophy of mechanical alignment with customised patient instruments and a computer software system that is designed to improve knee implant positioning and procedure efficiency.

It is the first system to utilise CT scans of the whole leg in conjunction with computer software to guide the development and production of femoral and tibial cutting blocks that are individually prepared to match the actual bone surface of each patient. The instruments are individually shaped to fit securely to the bone and provide key surgical cuts based on the patient's mechanical alignment. The use of CT scans rather than MRIs results in improved bone imaging, reduced scanning time, and lower costs.

The solution is intended for use with the Sigma knee system. It includes fixed bearing and rotating platform options that allow for more natural movement with less wear to the implant than traditional knee replacements. The pin guide offers surgeons intra-operative flexibility if changes need to be made during the surgical procedure. It makes use of a smaller, lower profile jig for less invasive procedures. The integrated alignment guide improves ease of use. Metal guides for pin drilling are reusable and can be resterilised.

The system reduces OR time by up to 35 minutes. Procedures require less instrumentation and eliminate up to nine surgical steps compared to total knee replacements performed without this system.



More on...
YouTube
Keywords:
Trumatch
bearing



Detachable Coil System for Treating Cerebral Aneurysms

The **Orbit Galaxy detachable coil system** has been released by Codman Neurovascular for the endovascular treatment of cerebral aneurysms. The coil is manufactured to have a random flex pattern so as to fill an aneurysm's volume more thoroughly.

The coil system comes in a complete range of stretch resistant Frame, Fill and Xtrasoft finishing coils. The coils feature a unique, complex random loop design. The shape makes the coils extremely comfortable and enables them to achieve high packing densities, as they seek and fill open spaces in the aneurysm.

This treatment has been correlated with low patient retreatment rates. The use of complex, random loop coils result in significantly higher packing compared to helical and complex coils which have pre-determined shapes. The coils are deployed with the Enpower detachment system, a push-button thermo-mechanical detachment that streamlines the coiling procedure.

The random loops and breaks conform to the true aneurysm shape and seek to fill open spaces from the periphery to the centre. They are designed to deliver outstanding packing density and to minimise



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compartmentalisation.

The junction where the coil meets the delivery system is a soft polymer gripper, suitable for the delicate nature of aneurysms. The soft, distal delivery zone of the coil system minimises micro-catheter movement during deployment. This helps to maintain the optimal position within the aneurysm and enables the placement of more coils. The simple hydraulic release system has proven to be reliable. It features the optional Luer activated valve, a coil accessory that enables the removal of the syringe during coil placement for enhanced ease of use.

Preventing Recurrent Strokes in Patent Foramen Ovale Patients

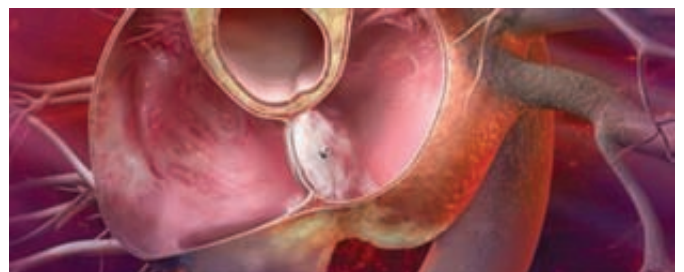
The **FDA has recently approved** the inclusion of the Gore Septal Occluder in the REDUCE study aimed at demonstrating Patent Foramen Ovale (PFO) closure with the device, plus anti-platelet medical management therapy to reduce the risk of recurrent stroke or imaging-confirmed transient ischaemic attack.

The occluder received the CE mark in June 2011 for the indication of PFO and atrial septal defect (ASD) closure.

The device, a permanently implanted prosthesis that uses a pre-assembled catheter delivery system via standard femoral venous access, successfully integrates innovative material and design to produce a treatment option intended to conform to the anatomy of the individual.

The device, a five-wire support frame covered with thin ePTFE patch-like material, bridges and eventually occludes the septal defect to stop blood shunting between the atria. The soft, strong and conformable membrane improves closure by providing an open microstructure that encourages cells to infiltrate and grow over the ePTFE membrane, ensuring successful closure of the defect.

In the heart, the membrane-covered wireframe forms two opposing discs, connected in the middle, that completely cover the hole.



In addition to simple ASDs, the non-self-centring design is beneficial in the treatment of defects with deficient anterior-superior rim or multiple fenestrations that can be covered by a single occluder. Implantation with more than one device has been undertaken on a patient with multiple ASDs and fenestrated septum.

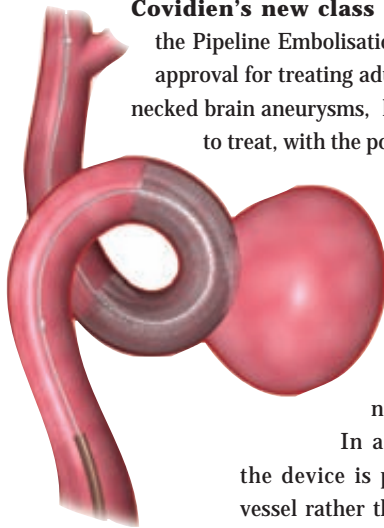
When deployed, the device has a flat profile with no bulky protrusions into the chamber. The nitinol support frame has a low nickel mass for minimal nickel exposure





On the
Horizon

Embolisation Device Rebuilds Wide-necked Intracranial Aneurysms



Covidien's new class of embolisation device, the Pipeline Embolisation Device, has received FDA approval for treating adults with large or giant wide-necked brain aneurysms, historically the most difficult to treat, with the poorest long-term prognosis.

The device redefines aneurysm therapy from traditional endovascular options to true parent artery remodelling by reconstructing the parent artery and restoring its natural flow.

In a flow-diversion technique, the device is placed in the parent blood vessel rather than in the aneurysm, where it restores original, natural blood circulation while

providing a permanent occlusion. The densely braided cylindrical mesh, implanted across the aneurysm neck, slows blood flow into the aneurysm, allowing the vessel to heal.

It is customisable in that multiple devices can be telescoped together, for longer constructs, and the entire device has uniform radiopacity.

The device has excellent vessel conformity even in tortuous anatomy, achieved through the optimised radial force and flexibility of 75% cobalt chromium / 25% platinum tungsten bimetallic design.



More on...
YouTube
Keywords:
Covidien
Pipeline

The curative remodelling of the device has a three to five times more surface coverage than other intracranial stents and a 30% - 35% surface coverage ratio to divert flow from the aneurysm. The design keeps perforators and side branch vessels patent. When flow into the aneurysm is eliminated, the construct becomes endothelialised, forming a permanent biological seal across the section of diseased parent artery.

Portable Precise Point-of-Care Imaging



More on...
YouTube
Keywords:
GE Logiq e

A cutting-edge ultrasound innovation, the Logiq e ultrasound, by GE, is a compact, portable, affordable system designed for use across a broad spectrum of medical disciplines. Its versatility, compact profile, precision tools and easy-to-use platform provides high-resolution image quality to help doctors make quick decisions with confidence. It is a fully capable system with the advanced technology of a larger unit, all in laptop size.

The device features a 20% improvement in contrast ratio compared to previous generations. It is capable of high-resolution soft tissue imaging. Its Power Doppler imaging sensitivity provides clear superficial and deep imaging so that different tissue types and normal to abnormal anatomy can be distinguished and compared. It is able to make use of panoramic imaging for better diagnosis.

Its Follow-up Tool makes patient follow-up consistent and automatic. Live and historical images can be viewed side by side. The device can automatically recall all images, comments and body patterns from previous exams. B-Steer and CrossXBeam, exclusive GE algorithms, help maximise highlighted angular objects with a clearly visualised needle tip, with reduced blooming effects. This allows medications to be injected with accurate imaging of needle, anatomy and motion, even in colour and Power Doppler modes.

Tissue differentiation detects subtle changes in anatomy, minimal amounts of fluid and small structures. Inflammatory conditions or tumours can be monitored over time. The Easy3D option can scan specific areas and then reconstruct 3D volumetric images. The coronal plane or any combination of planes can be reviewed and constructed.



Innovative Treatment for Pneumothorax and Pleural Effusions

Medical Device Innovations, UK, has launched the ThoraQuik II device for the treatment of pneumothorax and pleural effusions, offering a quick release of pressure in trauma situations where tension pneumothorax pressure build-up can crush blood vessels carrying blood back to the heart, causing cardiac arrest.

The greater length of the device and the guarded needle offer significant advantages over the plastic cannulas commonly used to set up intravenous drips. In many cases, the cannulas may be too short to relieve the pressure build-up. While recommended treatment for suspected tension pneumothorax is immediate needle decompression; typical needle length, at 3cm to 6cm, may not always be long enough to reach the pleural space. Recommended minimum length is seven centimetres.

This ThoraQuik has a large bore 10cm needle ensuring success in reaching the pleural space and minimising the risk of catheter occlusion once the pleural space is penetrated. The catheter's internal diameter is 3.12mm-3.22mm.

Its one-way valve allows fluid and air to pass out of the catheter without risk of air entering the pleural cavity. The ergonomic hub and adhesive underside



secures the device to the patient to reduce the risk of catheter dislodgement. The large gauge, 10cm long cannula with three lateral eyes reaches the pleural space even in larger patients and minimises the risk of occlusion. A spring-loaded Veres needle gives added safety and reduces the trauma on insertion.

Oesophageal Doppler Monitoring (ODM) in Surgery Could Yield Big Savings

Use of Deltex Medical's (West Sussex, UK) CardioQ-ODM, which accurately measures changes in the rate of blood circulating around the body, could save the NHS £880 million a year in England alone, NICE guidance has shown.

ODM, which works by inserting an ultrasound probe into the oesophagus, an approach far less invasive than conventional blood monitoring devices, is suitable for major surgery including colorectal, genitor-urinary, general, vascular, urology and renal, orthopaedic and gynaecological surgery. The technology is highly sensitive and measures changes in flow immediately and accurately, enabling doctors to intervene quickly and safely.

Early detection of hypovolaemia, usually resulting from the combined effects of pre-operative fasting, the anaesthetic agent and the blood lost during the surgical procedure, enables the anaesthetist to intervene quickly by using a combination of specialised fluids and drugs before the condition becomes potentially life-threatening.

The technique of optimising a patient's haemodynamic status by giving the right fluid at the right time, known as Doppler Guided Fluid Management, is seen as the cornerstone of enhanced recovery as better quality, more cost effective care accelerates patient recovery.



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Quoth the Maven



Keith Bolton

Keith Bolton MBBCh, DCH (SA), FCP (Paeds)(SA), MSc Med (Bioethics & Health Law) is chief paediatrician at Rahima Moosa Mother & Child Hospital, Johannesburg and associate professor in the Department of Paediatrics & Child Health at University of the Witwatersrand. He has been an academic paediatrician in Johannesburg for about 30 years. He worked in private paediatric practice between 1989 - 1998.

Maven - A trusted expert who seeks to pass knowledge on to others.

What a depressing few weeks it has been for all South Africans who love this land. Murder, rape, mayhem, xenophobia and police brutality. Ominous black clouds have obscured the rainbow nation.

The scourge of rape has many medical connotations. Doctors are sometimes (thankfully rarely) the perpetrators of rape, but importantly we always have a major responsibility in the management of the victim and the documentation of the crime. As members of society, we also have a responsibility as role-leaders in protection of the vulnerable and the maintenance of morality.

I watched, on TV, all those vulnerable little girls, all potential victims, waving their hand-drawn posters and chanting mantras denouncing rape and I wished that the cameras had shown more of the potential perpetrators, that is the boys, with posters saying boldly; "I am a boy and my role is to protect girls and never abuse them". Rape is, of course, rooted in gender bias and discrimination and is usually about power and domination and less about sexuality. There are multiple settings where rape occurs, ranging from sexual coercion within an established intimate relationship to the seemingly inexplicable rape by a stranger of an 'arbitrary' infant in a community.

Convictions under 5%

The true prevalence of rape in SA is unknown because it is estimated that only one in 25 women who have been raped ever reported it to the police. Despite this underestimation, SA is recognised as the "Rape Hub" of the world. It would be naïve to believe that the perpetrators of this scourge are a few sexual psychopaths committing multiple attacks. Community-based surveys have shown that 28%-37% of SA men aged 18-49 years report having perpetrated a completed act of rape.¹ Where have we lost the plot? I think that we have failed as males because there are not enough good role models; caring, protective husbands and grandfathers and brothers and uncles.....

What should we do as doctors? We are neither very good at treating the victims nor at gathering evidence. Perpetrators of rape commit the crime with impunity. The local statistics regarding successful prosecution of rape are particularly unimpressive. Of the cases reported to the police, only about half result in an arrest, 10% come to trial and 3%-4% are found guilty and go to prison.² Health care workers need more training in collecting appropriate specimens utilising Sexual Assault Evidence Collection Kits (SAECKs), better attention to the administrative requirements of the courts and generally more commitment to get involved.³

Medicine for the ages

On a barely more cheerful note, the CPD articles this month can be categorised to reflect issues often associated with senescence. Before you are offended by terminology, remember we all get one day older every day and the alternative is usually worse. The case scenario of the diabetic foot reminds us that the progression of deterioration may demonstrate a very rapid and catastrophic outcome. The article on MI is encouraging in that if you survive an acute myocardial infarction there is much opportunity to individualise management so as to improve outcomes. There are some very exciting predictions regarding the management of Parkinson's disease. Current treatment is often associated with diurnal swings in symptoms and this may be very disturbing to the patient and their families. New advances may limit these swings.

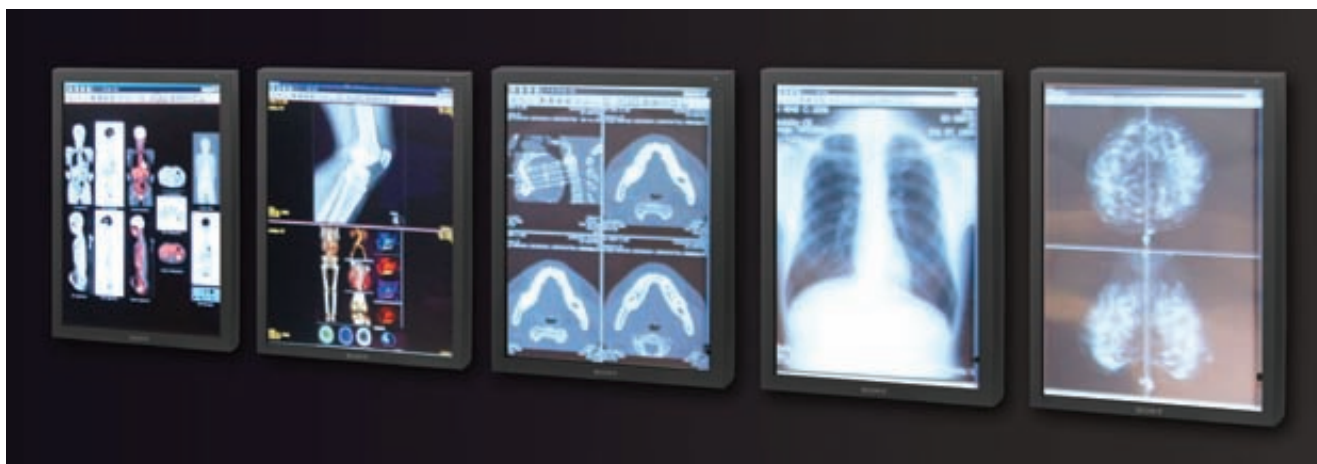
Enjoy this issue.

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HERE & NOW

Sony Extends Medical Line-up with New Radiology Diagnostic Monitors



To demonstrate Sony's leadership in medical innovation, Sony Professional has introduced its first ever line of high-quality diagnostic displays, the LMD-DM Series. The range gives the discerning buyer five distinct options; three diagnostic displays being monochrome and the other two colour.

With their high-luminance and high-contrast capabilities, these superior monitors offer exceptional clarity allowing users to display and view medical images such as those obtained from MRI, X-ray and digital mammography.

With these new monitors, Sony is further expanding its footprint in radiology adding to its already long list of technology offerings including recording devices, printers, LCD displays and other essential equipment for medical applications.

Triple quality

The LMD-DM50 and LMD-DM30 will feature the company's Independent Sub-pixel Drive (ISD) technology that is capable of producing three times the resolution of monochrome LCDs. This technology triples the resolution of a screen by splitting each pixel into three independent 'sub-pixels'.

The technology's use of three independent sub-pixels in a single pixel enables a 5MP display to achieve a resolution up to 15MP. Correspondingly, the feature used with the 3MP display allows for a maximum of 9MP.

The unique ISD technology, which brings an even higher resolution output to the radiology market, ensures users are equipped for the future as imaging technology modalities continue to advance their systems with greater outputs.

"Now radiology users can experience and benefit from the breakthrough innovation in medical display technology that Sony has been successfully delivering to other areas of healthcare, including surgery," said Will Klopper, Sales and Marketing Manager for Sony Professional Products. "This development gives the market a full range of high quality radiology displays from Sony that help enhance visualisation."

Ideal for full field digital mammography

Available in both the 5MP and 3MP grayscale models, ISD creates reliable image quality for viewing high resolution diagnostic studies including CR and DR images, CT, MR and particularly full field digital mammography (FFDM) where detailed viewing of micro-calcifications is possible. The LMD-DM50 and LMD-DM30 can also be used in digital mammography PACS.

Colour versions

The three remaining diagnostic displays in the range, the LMD-DM30C, LMD-DM20C and LMD-DM20, can be used in displaying and viewing medical images such as MRI and CT. These displays are not designed for digital mammography. Those with 'C' suffixes are colour displays.

Range details

The five new radiology displays now available for purchase:

- 5MP Diagnostic Display for Full-Field Digital Mammography
- 3MP Color Display
- 3MP Grayscale Display
- 2MP Color Display
- 2MP Grayscale Display

Accurate colour, DICOM approved

All Sony displays are designed specifically for radiology review and are loaded with a high-luminance, high-contrast LCD panel that can simultaneously display 1024 shades of gray and deliver accurate colour reproduction. They deliver colour or grayscale results, can be used in portrait and landscape modes, and are fully DICOM GSDF Part 14 conformant.

SONY
make.believe



Redefining Clarity

Sony printing technology providing the most accurate image reproduction for a confident diagnosis



UP-DR80MD

- Medical grade colour video printer
- Dye sublimation technology
- A4 size
- Digital input



UP-25 and UP-D25

- Colour video printer for ultrasound and surgery
- Dye sublimation technology
- A6 size
- Analogue or digital option



UP-897MD and UP-D897

- Black and White video printer for ultrasound
- Thermal technology
- A6 size
- Analogue or digital option

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For patients with treatment-resistant hypertension,

THE PRESSURE

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What if you could give patients an average reduction of 32 mmHg without increasing pill burden?¹

How It Works

Renal denervation (RDN) is a groundbreaking way to manage treatment-resistant hypertension in conjunction with traditional drug therapy. Treatment-resistant hypertension is defined as a blood pressure of ≥ 140 mmHg despite the use of 3 or more medications.

- The nerves leading in and out of the kidney play a key role in sympathetic nervous system (SNS) hyperactivation, which in turn contributes to high blood pressure
- RDN uses a catheter that delivers low-power radio frequency energy to selectively ablate renal nerves within the SNS while leaving renal function unimpaired. This reduces the drive of the SNS, which thereby lowers blood pressure



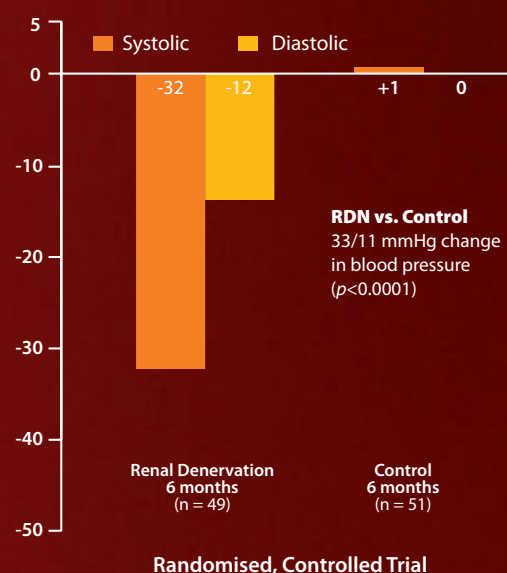
Demonstrated Safety

- Safety in the Symplicity HTN-2 trial was excellent¹
- No major adverse effects occurred
- No evidence of vascular injury/stenosis at treatment sites by imaging at 6 months
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- No evidence of aneurysmal dilation
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- In a randomised, controlled trial, the mean blood pressure of patients with treatment-resistant hypertension who were treated with the **Symplicity™ renal denervation system** was reduced to 146/84 mmHg from a baseline of 178/96 mmHg¹
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¹Symplicity HTN-2 Investigators. Renal sympathetic denervation in patients with treatment-resistant hypertension (The Symplicity HTN-2 Trial): a randomised controlled trial. *The Lancet*. 2010;376(9756):1903-1909.

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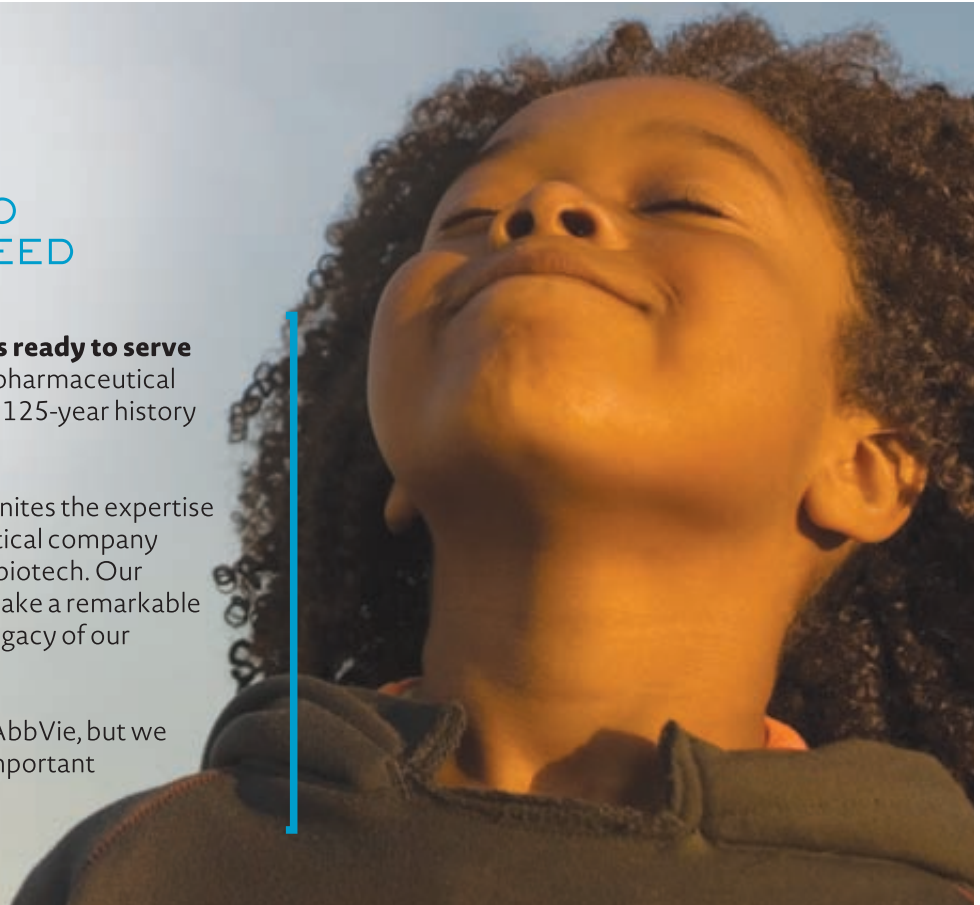
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CPD ARTICLE NUMBER ONE

Patients Post Myocardial Infarction: Tailored Management Improves Outcomes

Patients who have had a myocardial infarction need aspirin and statin therapy and careful evaluation to identify those who will benefit from revascularisation or implantable device therapy and appropriate additional pharmacological treatment.

The management of the patient post myocardial infarction (MI) is a team effort between the hospital, cardiologist and GP to ensure that he or she receives the benefit of the substantial advances in treatment shown over the past 20 years to improve outcomes. The hospital has a responsibility to provide sufficient details on whether the patient had an ST elevation or non-ST elevation MI (STEMI or NSTEMI), the extent and location of myocardial damage, the procedures undertaken in hospital, his or her discharge medications and plans for follow-up investigations. The cardiologist needs to communicate the management plan clearly to the patient and GP. The GP needs to understand the rationale for treatment, ensure that the post-MI management plan is followed and ensure any treatment side effects are addressed appropriately. Fortunately, there is a large evidence base and detailed guidelines to help tailor post-coronary care management to the individual patient who has suffered a STEMI¹⁻³ or NSTEMI.⁴⁻⁶

About the authors

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Evaluation of the patient

In the evaluation of the patient post MI, three questions should be addressed:

- Is coronary angiography indicated and will this patient benefit from coronary revascularisation?
- What is the ideal pharmacological management and how long should it continue?
- Should this patient be considered for device therapy?

The following tests are available to help answer these questions, in addition to consideration of the detailed review of the in-hospital course and clinical assessment of the patient.

Coronary angiography

Coronary angiography is often performed in the early stages of hospital

treatment and the coronary anatomy guides decisions about post-MI management. If the patient has not had angiography and it is not readily available, non-invasive testing such as exercise testing/stress imaging can be used to stratify risk and decide on referral for angiography. Despite advances in the technique of coronary CT angiography, it still has significant limitations⁷ and coronary angiography by cardiac catheterisation remains the usual method of assessing coronary anatomy in the patient who has had a coronary event. Coronary CT angiography is not recommended for routine evaluation of the patient post MI at this time.⁸ Although coronary angiography is now performed in most patients who have had a STEMI or NSTEMI, when it is not available or contraindications exist alternative modalities such as stress imaging may be considered.

Exercise electrocardiography

Exercise electrocardiography remains a very useful investigation to detect

Key points

- A large evidence base and detailed guidelines are available to help tailor post-coronary care management to the individual patient.
- Definite indications for coronary revascularisation include patients who have had a myocardial infarction (MI) with on-going symptoms and the presence of a critical coronary stenosis, left main disease or triple vessel coronary artery disease with extensive ischaemia.
- Although all patients post MI should be given aspirin and statins, the choice and duration of other pharmaceutical therapy is determined by the patient's symptoms and presence of left ventricular dysfunction.
- Early implantation of an implantable cardioverter defibrillator does not benefit patients immediately post MI. However, device therapy is indicated in those who had an MI more than 40 days previously and whose ejection fraction is persistently below 35%.



Indications for revascularisation

Definite indications

- **Ongoing symptoms with a critical coronary stenosis**
The usual treatment is PCI. The choice of stent will depend on the clinical situation.
- **Ongoing symptoms with left main or triple vessel coronary artery disease**
CABG is the usual recommended approach; however, the role of multivessel PCI is being evaluated.¹⁴

Possible indications

- **Triple vessel disease and LV dysfunction**
CABG surgery is less effective when the LV dysfunction is due to extensive post-infarction scarring. Myocardial viability needs to be established with radionuclide myocardial perfusion scanning, MRI or PET scanning.
- **Asymptomatic with tight residual stenosis**
It is important to clarify the functional significance of a tight residual stenosis. If the stenosed vessel supplies an akinetic scar, there is little to be gained from percutaneous intervention.
- **Totally occluded infarct related artery**
PCI or CABG are usually considered only if the patient is symptomatic or has a large area of residual ischaemia. There is less enthusiasm for treating the asymptomatic patient since the 'open artery' hypothesis was tested in a randomised clinical trial and no benefit of late opening of the occluded artery was demonstrated.¹⁵

ABBREVIATIONS: CABG = coronary artery bypass grafting; LV = left ventricular; MRI = magnetic resonance imaging; PCI = percutaneous coronary intervention; PET = positron emission tomography.

myocardial ischaemia. It is of particular value for stable patients at low risk of further coronary events where ready access to coronary angiography or other imaging modalities is not available.

Echocardiography

Assessment of left ventricular (LV) function in the patient who has had a coronary event is best achieved with an echocardiogram. Serial echocardiographic assessment of LV function can assist not only in overall risk stratification⁹ but in making decisions regarding implantation of an implantable cardioverter defibrillator (ICD).

Stress imaging studies

Stress imaging studies with radionuclide myocardial perfusion scanning or stress echocardiography may be required to localise and assess the extent of myocardial ischaemia. The choice between the two modalities may depend on local experience and expertise.^{10,11}

Specialised investigations

Specialised investigations with cardiac magnetic resonance imaging or positron emission tomography scanning can assess cardiac viability with a high specificity and sensitivity. They may be needed in specialised situations to establish whether an extensive area of ischaemic myocardium will benefit from revascularisation.

Will this patient benefit from coronary revascularisation?

By the time patients who have had a myocardial infarction visit their GP for follow up, many will have already had revascularisation - percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) - in hospital. The trend for the patient at high risk of further coronary events managed in a tertiary hospital is to try to deliver early revascularisation on arrival or before hospital discharge. For patients at lower risk or those managed in a secondary or regional hospital who have not had revascularisation, the question of whether to refer for revascularisation is one of the most complex decisions. Surprisingly little evidence exists to guide decision-

making and it been the subject of much debate.^{12,13}

The definite and possible indications for revascularisation are listed in the box on this page.^{14,15}

What is the ideal pharmacological management and its duration?

Beta blockers

Guidelines recommend indefinite beta blocker treatment in all patients who have had STEMI¹⁶ but the role of beta blockers in the patient who has had STEMI and a successful coronary reperfusion with restoration of LV function to normal and no evidence of residual myocardial ischaemia remains doubtful.¹⁷ The recommendations for the patient who has suffered a small NSTEMI treated with PCI are based on even less strong evidence.

It would be acceptable practice to consider cessation of beta blockers several months after hospital discharge in a patient who has minimal residual coronary stenoses, no evidence of residual myocardial ischemia and no LV dysfunction, particularly if beta blockade has been associated with side effects. The recommendations for beta blocker treatment are shown in Table 1.

Aspirin

Aspirin in a dose of 75mg to 325mg is recommended in all post-coronary management guidelines for patients who have had STEMI or NSTEMI. It is a low-cost and effective treatment, associated with a significant 25% reduction in major vascular events, or an absolute risk reduction of 35 vascular events per 1000 patients treated over two years.¹⁸ Observational studies suggest that bleeding complications are fewer with the lower dose but randomised allocation to low dose (100mg or less) versus standard dose (101mg to 325mg) showed no differences in bleeding.¹⁹ Enteric coated formulations may be associated with fewer adverse gastric effects than buffered aspirin, but the data remain unclear.²⁰

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TABLE 1

Drugs and other management in patients post MI

Patient category	Drug	Other management
Asymptomatic patient without LV dysfunction	<ul style="list-style-type: none">• Aspirin 100–150mg/day• Beta blockers (eg, metoprolol 25mg–50mg twice daily or atenolol 25mg–50mg/day)• Statin (atorvastatin 80mg/day or equivalent)	Consider referral for cardiac rehabilitation
Asymptomatic patient with LV dysfunction	<ul style="list-style-type: none">• Aspirin• Statin• Beta blockers of proven benefit in LV dysfunction (eg, bisoprolol, carvedilol, nebivolol or extended release metoprolol)• ACE inhibitor or angiotensin receptor blocker• Aldosterone antagonist (spironolactone or eplerenone)	If LV dysfunction is persistent and severe (LVEF<35%), consider referral for implantation of ICD
Symptomatic patient	<ul style="list-style-type: none">• As above• If angina: standard antianginal therapy• If dyspnoea: diuretics	Refer for detailed evaluation including coronary angiography and consideration of PCI and CABG

ABBREVIATIONS: ACE = angiotensin converting enzyme; CABG = coronary artery bypass grafting; ICD = implantable cardioverter defibrillator; LV = left ventricular; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention.

(DAPT) for the patient who has received PCI.^{21,22} The duration of DAPT depends on the complexity of the coronary anatomy and the type of PCI. The recommendations are summarised in Table 2. Patients need to be made aware that there is a risk of stent thrombosis if the DAPT is stopped for any reason (including elective surgery) during these recommended periods. When DAPT needs to be stopped during these periods, the issue should be discussed with the treating cardiologist.

The role of DAPT in patients who have recovered from conservative management of MI and have not received an intracoronary stent is moot. There is a risk of bleeding with long-term treatment²³ and, although 12 months of treatment may be justified, the benefit after six weeks is minimal.²⁴ In patients who have not received a stent, the long-term use of clopidogrel may be best limited to those who are at high risk of a thrombotic event and those who demonstrated a heavy thrombus burden at coronary angiography.

Prasugrel, a recently available alternative to clopidogrel, is more effective than

clopidogrel in reducing coronary events. However, the early phase of treatment is complicated by a higher bleeding rate, particularly in patients going to bypass surgery.²⁵ Its role in long-term treatment of patients after a coronary event remains to be established.^{26,27} but it may have a role in patients who have a history of stent thrombosis when taking aspirin and clopidogrel.

Statins

Statin therapy is an essential part of the post-MI regimen. It is associated with an average reduction in post-coronary events of 25% to 30%³⁰ and an absolute reduction for each 1.0mmol/L reduction in LDL cholesterol of 48 major vascular events per 1000 patients treated.³¹ The statin should be commenced in hospital and continued after discharge.³² The usual post-coronary statin used, based on the PROVE-IT trial (Pravastatin or Atorvastatin Evaluation and Infection Therapy trial), is 80mg of atorvastatin.³³

The target LDL cholesterol level for patients after a coronary event is less than 2.0mmol/L.³⁴ The safety of high dose atorvastatin has been confirmed.³⁵

It remains unclear whether a patient who achieves a reduction of LDL cholesterol to target levels with 80mg of atorvastatin should be changed to a lower dose of statin, but it may be reasonable to do this to limit side effects. A trial of high dose (80mg) of simvastatin was associated with a higher than acceptable incidence of myopathy.³⁶

Although rosuvastatin has been shown to be effective in high-risk cohorts, there is no specific trial to support its use in patients post infarction. Ezetimibe, either alone or in conjunction with statins, has the potential to lower LDL cholesterol levels³⁷ but, to date, there is no data to demonstrate any clinical benefit.

Other lipid modulations**Lowering triglycerides**

There is no clear-cut benefit for lowering triglyceride levels in patients post myocardial infarction. Trials of gemfibrozil³⁸ and bezafibrate³⁹ have not been sufficiently persuasive to establish fibrate therapy in the patient who has had a coronary event, and a large trial with fenofibrate did not achieve its primary end point in patients with type 2



TABLE 2

Duration of dual antiplatelet therapy (DAPT) Post-MI

Intervention or patient category	DAPT duration
Balloon angioplasty*	1–3 months
Bare metal stent*	12 months recommended, 1 month mandatory
Drug eluting stent	12 months [†]
Complex stenting or high risk complex coronary anatomy	Indefinite
Patient who has not had PCI	3–12 months (longer for patients at high risk of further events)

* Patients with planned surgery may have balloon angioplasty or bare metal stent to limit the duration of DAPT and allow early surgery.

[†] Newer drug-eluting stents may require shorter duration of DAPT, but this remains unclear.

Abbreviations: DAPT = dual antiplatelet therapy; MI = myocardial infarction; PCI = percutaneous coronary intervention.

diabetes at relatively high risk of further coronary events.⁴⁰

Raising HDL cholesterol

To date there is no effective HDL cholesterol raising drug available. A trial of torcetrapib demonstrated an increased mortality in patients at high cardiovascular risk.⁴¹ On-going trials with dalcetrapib may demonstrate a role for HDL cholesterol raising in the patient after a coronary event.⁴²

Omega-3 fatty acids

Fish oil-derived omega-3 fatty acids have been shown to moderately reduce total and sudden post-coronary deaths, but it is not clear if this is by a triglyceride lowering effect or other mechanisms.⁴³

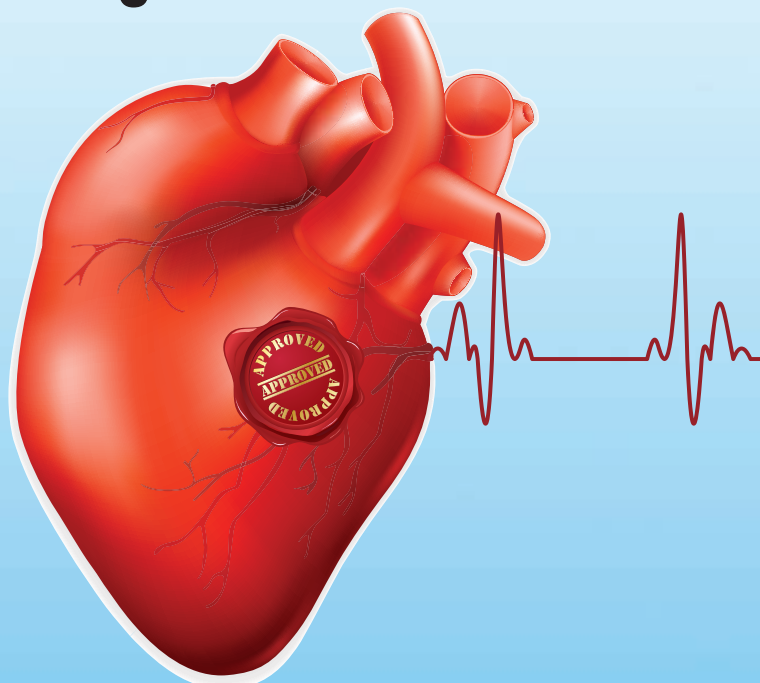
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PATIENTS POST MYOCARDIAL INFARCTION (cOntinued)



significant LV dysfunction.⁴⁴ However, their use in the absence of post-coronary LV dysfunction remains moot. Angiotensin receptor blockers as an alternative to ACE inhibitors have been trialled in patients who have had coronary events; however, the evidence base for this is not as extensive as it is for use of ACE inhibitors post infarction.⁴⁵

Aldosterone blockade

Spironolactone and eplerenone have shown clear-cut benefit in patients with cardiac failure and LV dysfunction.⁴⁶ Meticulous monitoring of renal function and potassium levels is required, particularly in patients taking concomitant ACE inhibitors.⁴⁷

Calcium channel blockers

Verapamil and diltiazem are contraindicated in patients who have had an MI and who have LV dysfunction.^{48,49} Amlodipine use has been shown to be safe in the presence of LV dysfunction.⁵⁰ The calcium channel blockers have not been shown to have a clear-cut benefit on prognosis and are not recommended for routine use for the patient post infarction.

Antiarrhythmic drugs

Antiarrhythmic drugs have not been shown to improve prognosis for the patient post MI and their use in this setting is not recommended.⁵¹

Nitrate therapy

Nitrates are indicated for the patient with symptomatic angina but do not have a role in the management of the patient post infarction who does not have angina.⁵²

Diuretics and digoxin

Diuretics are useful for the symptomatic relief of cardiac failure but they have not been convincingly shown to improve prognosis.⁵³ It is important to review a patient's need for ongoing diuretic therapy at the time of hospital discharge. Digoxin does not have any clear-cut role in the patient post infarction, except in those who require it in addition, or as an alternative, to beta blockers for rate control of atrial fibrillation.⁵⁴

Coumadins and oral antithrombins

Coumadins do not have a clear-cut role in preventing recurrence in the patient post MI. If a patient has had a large infarction, he or she may benefit from a period of warfarin anticoagulation to prevent stroke.⁵⁵ This is particularly the case in the presence of severe LV dysfunction and/or large apicoanterior infarct and definitely if there is intra-cardiac thrombus demonstrated on echocardiography.⁵⁶ New oral antithrombins such as rivaroxaban have been tested in patients who have had coronary events and shown to reduce recurrences but at an increased risk

Continued on page 31

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Diabetes-Related Foot Problems: Urgent Management of Ulcers

Diabetes-related foot problems are largely preventable with appropriate medical assessment, patient education and on-going monitoring. However, many patients with diabetes present with foot ulcers that require emergency attention, as in the case described here.

Diabetes-related foot problems are responsible for significant morbidity, mortality and healthcare costs. They are second only to cardiovascular disease as a cost of diabetes to the health-care system (mostly because of hospital costs associated with foot ulcers).¹ Amputations often lead to loss of independence and quality of life, further amputation and premature mortality. However, the number of lower extremity amputations might be halved with appropriate medical assessment, patient education and on-going monitoring. All too often, foot problems lead to disasters in people with diabetes, as illustrated by Anna's case, described in a condensed form below:

- Monday: Anna went shopping for new shoes.
- Tuesday: Anna went on a guided tour of the Botanical Gardens wearing her new shoes; she noticed a blister on her right little toe that night.
- Wednesday: She noted right foot redness and discharge at the lesion site

and found a 'new' sore on the sole of the same foot.

- Thursday/Friday morning: The swelling and redness had worsened and fever developed so Anna visited her GP, who referred her to hospital.
- Friday afternoon: She had a right below-knee amputation.

This article reviews the assessment of Anna's right foot that should have occurred on her presentation on Friday morning, the precautions that might have avoided the original problem and the action that should have been taken on Tuesday to prevent further damage to her foot. Each of these components of professional care and self-care is crucial in avoiding preventable amputations.

Assessment of the 'diabetic foot'

Anna's right foot was red and swollen and the ulcer was discharging yellow pus. Initial assessment guides the overall plan of management.

Circulation

Is the blood supply to Anna's feet adequate?² If not, a vascular surgeon should be involved as soon as possible. Without a sufficient blood supply to the affected area, it will be difficult to control the infection and heal the ulcer. Anna's pulses should be checked. If a pulse cannot be felt in her swollen foot, a Doppler ultrasound should be arranged to check

that the ankle brachial systolic pressure ratio is less than 0.9. It is not possible to rely on the fact that the foot and lower leg are red: the redness is not the pink of a healthy circulation but the red of inflammation that still occurs even if the circulation is inadequate. However, an ischaemic and infected leg will usually blanch when the person is supine, the leg is lifted towards the vertical position and the leg and foot are massaged towards the heart.

Infection

Clearly, Anna's foot is infected and she will need antibiotics. How deep is the infection and is it in the deep fascial planes or in the bone? Will she need surgery to debride the ulcer, drain collections in the deeper tissue or remove necrotic debris? An ultrasound, or even better an MRI, will define this, but if deep tissue involvement is suspected then a surgical assessment is needed, preferably by someone with experience in dealing with infected feet in people with diabetes.

Pressure

Is the ulcer likely to be under pressure during its treatment? Any pressure will effectively reduce circulation and slow, stop or reverse the healing process. If pressure is likely, measures should be taken to relieve the pressure and to monitor that this pressure relief is effective. Advice from a podiatrist may be useful.

Initial management

The priorities are to debride affected tissue, start antibiotics and use the appropriate dressing.

About the authors



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TABLE 1

Ulcer dressings⁵

Ulcer type	Dressing principle	Dressing type*	
		For shallow ulcer	For deep ulcer
Clean, (granulating or epithelialising)	Maintain moist environment Infrequent changes (eg, every three to four days)	Impregnated dressing† Polyurethane film	Hydrogels
Light to moderate exudate (not infected)	Absorb exudate Infrequent changes (eg, every four days)	Hydrocolloids	
Heavy exudates (and/or infected)	Absorb and remove exudate	Alginates	Polyurethane foams

* Use occlusive dressings unless the ulcer is deep, infected or has a heavy exudate.

† Impregnated with, for example, biostats and/or odour-absorbers (charcoal).

Debridement

Debridement includes cleaning the ulcer and draining any collections of pus (by surgical intervention, if necessary). Anna's foot blister and ulcer were both painless, so considerable debridement and exploration of the ulcer and its edges could probably be done without anaesthetic. Debridement may be performed by an experienced GP as long as ulcers and peripheral perfusion are normal.

Antibiotics

Anna has diabetes and is likely to have a mixed infection. Consider performing culture and sensitivity testing of a wound sample (swabbed from the wound fluid base), and of a blood sample if there are signs of systemic infection, and then start the antibiotic immediately. The antibiotic schedule can be changed later on the basis of the microbiology. Usually two or more bacteria are involved and antibiotic therapy should cover all the likely organisms.⁴

Dressing

Anna has a discharging ulcer. If saline gauze dressings are used, then they will need to be changed frequently to absorb and remove the debris. Alternatively, an absorptive dressing could be used. This would not require changing so frequently (Table 1).⁵

It is important that the dressing used does not adhere to the surface or edges

of the ulcer. If it does adhere, changing the dressing will not only remove the 'rubbish' but damage healthy and healing tissue. In the authors' experience, frequent dressing with saline gauze dressings (eg, four-hourly initially) is simple and effective as long as the nursing staff appreciate the importance of frequent dressing changes and that the dressing must not adhere to the ulcer. If frequent dressing changes are not practical, there are many effective absorbent dressings available, some of which have added antiseptic agents such as silver,



Figure. Foot ulcer in a woman with diabetes (not the patient in the case).

chlorhexidine and iodine. It should be remembered, however, that the ideal dressing and perfect dressing technique will not heal the ulcer if it is not debrided adequately and/or is under pressure. A favourite aphorism of one of the authors is: 'It doesn't matter what dressings you put on an ulcer to heal it, it's what you remove that matters: debris and pressure.'

If the blood supply is adequate, the wound is clean, any infection is controlled, the dressing technique is satisfactory and there is no pressure on the area, then the wound should heal, with the surface area decreasing by about 30% each week. Monitoring is easy in this era of photography using cell phones, but the old technology of making a tracing of the edges of the wound can still be useful. If the wound is not healing, check that all the above conditions are being met and particularly whether the presence of pressure or a poor dressing technique is slowing progress.

Assessment and response to the ABCS of foot risk in diabetes

Assessment

Anna has at least two of the risk factors for diabetes-related foot problems, known as the ABCS of foot care, namely Anaesthesia (loss of sensation) and Care (inadequate care, reflecting inadequate

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TABLE 2

The ABCS of foot risk in diabetes: The foot risk traffic lights*

Foot factor assessment	Foot risk traffic lights		
	Red lights – ‘Danger’	Amber lights – ‘Caution’	Green lights – ‘Healthy’
Anaesthesia <ul style="list-style-type: none">• Pinprick, light touch (eg, 10g monofilament)• Reflexes	No stimuli felt No reflexes	Reduced stimuli Reduced reflexes	All stimuli felt Normal reflexes
Blood supply <ul style="list-style-type: none">• Pulse palpation	No pulses	Reduced pulses	Normal pulses
Care <ul style="list-style-type: none">• Questioning• Observation	– Skin breakdown	Foot care, footwear could be better Threatened skin breakdown	Appropriate foot care, footwear Normal skin
Structure <ul style="list-style-type: none">• Observation	Weight-bearing ulcer	Callus or corn	No skin lesions

* The ABCS of foot risk stratification include:

- Low risk – people with no risk factors and no previous history of ulcer/amputation
- Intermediate risk – people with one risk factor (neuropathy, peripheral artery disease or foot deformity) and no previous history of ulcer/amputation
- High risk – people with two or more risk factors (neuropathy, peripheral artery disease or foot deformity) and/or a previous history of ulcer/amputation.

education and self-care).⁶ She may well have one or both of the other two risk factors, Blood supply (inadequate blood supply, which may have impaired her capacity to heal the foot damage and ward off infection) and Structure (abnormal foot structure, which can predispose her to the excess shoe pressure that caused the damage). The foot risk ABCS are traffic lights indicating foot risk (Table 2).^{6,7} Red and amber lights indicate risk, and the presence of one or more should trigger action to reduce this risk.

Response

The required response to a person's foot risk 'traffic lights' is guided by:

- The particular risk(s) and level of risk.
- The complexity of foot care needs and the need for special care.
- The capacity to provide the necessary self-care.

The more amber or red lights, the more the need for special care and the more immediate the need for this care. Sometimes the risk of ulceration/ amputation can be eliminated by appropri-

ate self-care, appropriate footwear and regular general practice assessment and ongoing education. Patients at intermediate or high risk (amber or red traffic lights) will benefit from specialist assessment and intervention, eg, vascular reconstruction, orthotics, special footwear.

Anna's neuropathy was a red light and could have triggered a foot care programme in which she checked her feet daily, becoming more aware that her shoes should protect her feet, not damage them.^{8,9} She would have been given her 'foot report' and an action plan.^{6,10-13} Anna might then not have worn the stiff new shoes for a prolonged period, would have detected all the damage early and promptly sought appropriate help, and not have lost her leg.

Summary

- Diabetes-related foot problems cause significant morbidity, mortality and healthcare costs. Fifty percent of lower extremity amputations may be preventable.
- Foot problems are a diabetic urgency requiring initial assessment of cir-

ulation, infection and likely wound pressure. Initial treatment includes thorough wound debridement, a local or general anaesthetic if necessary, antibiotic therapy for any infection, and appropriate dressing and dressing technique.

- If blood supply is adequate, the wound is clean, any infection is controlled, the dressing and dressing technique are appropriate and there is no pressure, then the wound surface area should decrease by 30% each week. If the wound is not healing, review the assessment and management of the wound and ensure these conditions are being met.
- A diabetes-related foot problem should prompt the assessment of the ABCS of foot risk (Anaesthesia, Blood supply, Care and Structure). Any indications that a foot is less than healthy should prompt intensification of the patient's individualized care program, with on-going monitoring of foot health. Patients should be provided with their own foot report and action plans to guide reaction to any future problems.

References are available on request.



Therapeutic Progress in Parkinson's Disease

Pharmacological dopamine replacement is the most effective form of treatment for patients with early Parkinson's disease. However, it is only a symptomatic therapy. Future therapeutic strategies should therefore focus not only on ameliorating the symptoms of Parkinson's disease, but on neuroprotective or neurorescue therapies.

Symptomatic therapies for Parkinson's disease remain the most effective means for control of Parkinson's motor symptoms. However, there are several limitations associated with their use. After taking their Parkinson's disease medication for a while, patients usually notice that after each medication dose their symptoms go away for hours at a time (ON times) and then return (OFF times). Symptoms also return during the 'wearing-off' period, when Parkinson's treatments become less effective. The challenge of currently available symptomatic therapies is to maintain optimal ON time and reduce OFF time without causing disabling medication-induced abnormal involuntary movements (dyskinesias). This article discusses the limitations of current treatments for Parkinson's motor symptoms and future therapeutic strategies.

Current treatment strategies

The dopamine precursor levodopa is the most effective drug available for treating the motor symptoms of Parkinson's

disease. However, chronic use of the drug is limited by several factors, including:

- 'Wearing-off' (the re-emergence of motor fluctuations before the next scheduled dose or a shortened response to each dose).
- Dyskinesias (levodopa-induced abnormal involuntary movements).
- A potential to exacerbate some non-motor symptoms of hypotension.
- Failure to prevent the progression of Parkinson motor symptoms.

Other treatment options include dopamine agonists, which activate dopamine receptors, and monoamine oxidase B inhibitors, which increase dopamine levels by blocking its metabolism. Such agents can result in the continuous stimulation of brain dopamine receptors to prevent or diminish the emergence of 'wearing-off' and dyskinesias, but are not as effective as levodopa at improving the symptoms of Parkinson's disease.

Levodopa Extending the half-life of levodopa

Medium to long-term therapy with levodopa can result in an individual's response to this drug becoming unstable due to a combination of deteriorating peripheral levodopa pharmacokinetics and progressive degeneration of the substantia nigra. The emergence of motor fluctuations associated with levodopa is

aggravated by:

- The short plasma half-life of levodopa.
- The primary absorption of levodopa in the duodenum after oral administration.
- Interference in absorption of levodopa by the presence of food in the stomach.

Levodopa administered orally alone is rapidly decarboxylated to dopamine in peripheral tissues such that only a small amount of each dose reaches the central nervous system, and the high peripheral levels of dopamine contribute to its side effects, eg, nausea. The major route of peripheral metabolism of levodopa is via the dopa-decarboxylase pathway, with a smaller proportion through the catechol-O-methyltransferase (COMT) pathway. When levodopa is administered with a peripheral dopa-decarboxylase inhibitor (DDCI; carbidopa or benserazide), the peripheral formation of dopamine is blocked, extending the half-life of levodopa and allowing more to reach the central nervous system.

The addition of a COMT inhibitor to the levodopa/DDCI combination can further extend the peripheral half-life of levodopa and increase brain bio-availability. Adding the COMT inhibitor at the onset of the 'wearing-off' symptoms,

Future therapeutic approaches

Pharmacological approaches

- Novel longer-acting dopaminergic drugs
- Antidyskinetic therapies

Restorative approaches

- Neuroprotective strategies
- Neural growth factors
- Cellular replacement

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TABLE

The Parkinson's disease drug pipeline

Compound	Mechanism of action	Comments
Rotigotine	A nonergolinic dopamine receptor agonist formulated as a transdermal delivery system designed for once-daily application.	Safe and effective in early Parkinson's disease. ⁵ In patients with Parkinson's disease and early-morning motor dysfunction, significantly benefits control of motor function and nocturnal sleep disturbances. ⁶
Rasagiline	A novel, highly potent irreversible monoamine oxidase B inhibitor, anti-Parkinsonian drug.	Effective as monotherapy or adjunct to levodopa for patients with early and late Parkinson's disease. ⁷ Demonstrates possible neuroprotective effects.
Preladenant	A highly selective nonmethylxanthine adenosine A2A receptor antagonist (A2A receptors are highly enriched in the striatum, and their blocking results in a reduction of the postsynaptic effects of dopamine depletion).	Phase II studies suggest a modest reduction in the OFF time, with no significant worsening of dyskinesias. ⁸
IPX066	A novel levodopa/carbidopa formulation that rapidly attains and maintains therapeutic plasma concentrations for a more prolonged duration compared with regular immediate-release levodopa/carbidopa.	Shows promise in increasing ON time compared to standard levodopa formulations. ⁹
AFQ056	A glutamate receptor 5 antagonist aimed at reducing levodopa-induced dyskinesias. ⁸	Phase II studies show an antidyskinetic effect without a worsening in parkinsonism. ¹⁰
VR040	An inhaled form of apomorphine (traditionally a rapidly acting dopamine agonist that can be given only subcutaneously).	Shows promise as a novel rescue therapy in patients with unpredictable ON/OFF fluctuations.
Safinamide	A monoamine oxidase B inhibitor that also inhibits glutamate release.	Shows promise in improving motor ON time without worsening dyskinesias. ¹¹
L-dihydroxyphenylserine	A prodrug of noradrenaline.	Shows promise in improving the symptoms of orthostatic hypotension. ¹²

achieves a more continuous stimulation of brain dopamine receptors and thus reduces the 'wearing-off' effect.

A combination formulation comprising levodopa, carbidopa and the COMT inhibitor entacapone is currently approved for use in Parkinson's disease patients affected by motor fluctuations (indicated by the emergence of end-of-dose 'wearing off'). A patient's levodopa/DDCI doses can be switched individually for similar or slightly smaller levodopa equivalent doses of this combination product.

The recent availability of several fixed-dose combinations of levodopa/carbidopa/

pa/entacapone allows greater flexibility of individual patient dosing. A relatively common side effect of the combination is diarrhoea. This may affect about 4% of individuals, but resolves on stopping the drug.

Dopamine agonists

Dopamine agonists act directly on brain dopamine receptors and have a longer action than levodopa. Initiation of dopamine agonist treatment, such as pramipexole, in patients with early Parkinson's disease delays the emergence of 'wearing off' and dyskinesias.

Addition of a dopamine agonist to levodopa can improve motor symptoms and reduce time spent in the immobile OFF state.

Precautions and side effects

Doctors should counsel patients taking dopamine agonists about the small potential risk of unheralded sleep attacks (including when driving) and compulsive behaviours, such as gambling, hypersexuality, overeating and shopping. Confusion, paranoia, hallucinations and peripheral oedema may also be more frequent in patients being treated with dopamine agonists.



Monoamine oxidase B inhibitors

Monoamine oxidase B deactivates dopamine in the brain. Inhibitors of monoamine oxidase B therefore increase dopamine levels in the brain and are an additional therapeutic option for the treatment of Parkinson's disease. Two monoamine oxidase B inhibitors are indicated for the treatment of Parkinson's disease: selegiline and rasagiline.

Selegiline

Selegiline should be used in low doses (5mg twice daily) as higher doses may also inhibit monoamine oxidase A and result in side effects such as hypertension. Selegiline was commonly used in early-onset disease and in combination with levodopa for maintenance. However, concerns over cardiac side effects have been raised, and there is a potential risk of adverse effects when it is used in combination with selective serotonin re-uptake inhibitors and tricyclic anti-depressants. Selegiline is generally well tolerated as monotherapy, although side effects such as nausea, dizziness, headaches and dry mouth may occur.

Rasagiline

Rasagiline is indicated for the symptomatic treatment of idiopathic Parkinson's disease as monotherapy (without concomitant levodopa/DDCI therapy) or as adjunct therapy (with concomitant levodopa/DDCI therapy). In patients with Parkinson's disease receiving monotherapy with a monoamine oxidase B inhibitor, the effects on motor symptoms are modest.³ In patients with Parkinson's disease receiving treatment with levodopa/DDCI therapy, the addition of a monoamine oxidase B inhibitor has similar effects as the addition of entacapone in reducing daily OFF time.⁴

Future directions

Pharmacological dopamine replacement is generally very effective in early disease but it is only a symptomatic therapy. Future therapeutic strategies should focus not only on ameliorating the symptoms of Parkinson's disease but on neuroprotective or neurorescue therapies that can favourably modify the natural course of the disease and slow the progression of both motor and non-motor manifestations.

Strategies pursuing restorative approaches to Parkinson's disease

therapy involve attempts to replace the degenerating nigrostriatal dopaminergic network with cells. Fetal ventral mesencephalic tissue transplants are under continuing investigation and the stem cell field is advancing rapidly. However, further development and optimisation of the safety and efficacy of techniques involved in generating and manipulating these stem cells, and other cell sources, will be essential before any further clinical trials are done. Other experimental strategies currently under investigation include anti-apoptotic strategies and implantation of genetically engineered cells.

Future advances will include novel medication delivery systems such as transdermal or inhaled therapies (eg, VR040); novel levodopa/carbidopa formulations with prolonged action (eg, IPX066); enzyme inhibitors that can prolong the duration of action of levodopa (eg, safinamide); anti-Parkinson medication with novel receptor targeting (eg, preladenant); safinamide, and medications that improve non-motor symptoms (eg, L-dihydroxyphenylserine); or levodopa-induced dyskinesias (eg, AFQ056).

A list of references is available on request.

Patients Post Myocardial Infarction

Continued from page 22

of bleeding.⁵⁷ The modern DAPT era has complicated the management of patients with concurrent acute coronary syndrome and/or recent stenting and atrial fibrillation – in these patients, the use of triple therapy (DAPT plus anticoagulation) significantly increases the risk of adverse bleeding events.⁵⁸

Should this patient be considered for device therapy?

The early implantation of an ICD in patients who have had an MI has been shown not to deliver any additional benefit.⁵⁹ Patients who have had ventricular fibrillation during the early hours of their MI do not need an ICD. Those who had an infarction more than 40 days previously and whose ejection fraction is persistently below 35% should have an ICD implanted, although there are healthcare access and economic limitations to this recommendation. Patients should be on maximal toler-

ated medical therapy prior to re-evaluation of LV function to prevent unnecessary device implantation and potential morbidity from the device.

Conclusion

Contemporary post-MI management should be tailored according to patient characteristics and local access to coronary angiography or noninvasive imaging modalities. Aggressive medical management has a proven benefit for secondary prevention. Coronary revascularisation is indicated for persisting symptoms and high-risk, extensive ischaemia. Implantable defibrillators should be considered in those patients who have persisting severe LV dysfunction (ejection fraction less than 35%).

References are available on request.

Cost-effectiveness of saxagliptin in type 2 diabetes in South Africa

Saxagliptin (Onglyza®) is a dipeptidyl peptidase-4 (DPP-4) inhibitor used for the treatment of type 2 diabetes mellitus (T2DM).¹ Saxagliptin plus metformin provides similar blood glucose-lowering effects to the glipizide plus metformin, but is associated with fewer treatment-limiting side-effects.¹ Compared with SUs, saxagliptin has a beneficial weight profile and carries a significantly lower risk of hypoglycaemia (3.0% vs. 36.3%; $p < 0.0001$).¹ Since weight gain and hypoglycaemia are challenges in the treatment of T2DM, therapeutic regimens that offer benefit in these areas represent treatment advances.¹

A cost-effectiveness analysis was undertaken to estimate the long-term economic and health impact of T2DM on South African patients who were not well-controlled on metformin monotherapy and who were receiving either saxagliptin in combination with metformin or the SU, glimepiride plus metformin.² A SU in combination with metformin is the most common oral antidiabetic treatment strategy in patients that fail on metformin monotherapy and therefore an appropriate comparator for saxagliptin.² The cost-effectiveness model used was a previously published^{3,5} simulation model designed to evaluate the impact of new therapies for T2DM patients based on the UKPDS 68.^{5,6}

Compared with SU plus metformin, the cost per quality-adjusted life year (QALY) gained with saxagliptin plus metformin is approximately R20 848.² The comparison against SU + metformin builds on head-to-head data (a non-inferiority HbA_{1c} trial) comparing saxagliptin and glipizide.^{1,7} The cost-effectiveness results in this analysis were mainly as a consequence of differences in hypoglycaemic events and weight gain between saxagliptin + metformin and SU + metformin.²

The analysis revealed that it is important to consider not only a drug's effect on HbA_{1c} in the treatment of T2DM, but also its effect on hypoglycaemia and weight.² Even in the most conservative scenarios, these variables have an important effect on the health of patients and the healthcare resources they consume.² Based on this analysis, the positive impact of saxagliptin on weight and hypoglycaemia may be underestimated for the following reasons:

- Hypoglycaemia and fear of hypoglycaemia impede achievement of tight glycaemic control, either because of suboptimal dosing, poor compliance, or a combination thereof. This, in turn, increases the risk of macrovascular events.^{8,9}

- Only direct medical costs were included in this analysis.² However, weight and hypoglycaemia impact on health-related quality of life and should also be considered.² The average age of patients in the cohort analysed was approximately 52 years.²
- The analysis may underestimate the problem of hypoglycaemia with the SU + metformin combination in real life. Whereas saxagliptin has shown a low rate of hypoglycaemic events, observational studies report hypoglycaemia to be a serious problem with SUs in clinical practice.^{1,10,11} One study found a 4% risk of severe hypoglycaemia over six months with the SU + metformin combination,¹⁰ whereas Van Staa *et al.*¹¹ estimate the annual risk of severe hypoglycaemia to be 1.8% with SU monotherapy.

The analysis may also underestimate the time patients treated with saxagliptin have well controlled HbA_{1c} levels, since the analysis did not consider data from the two-year follow up of the trial.² This follow-up trial confirms that saxagliptin + metformin performs similarly to SU (glimepiride) + metformin in lowering HbA_{1c}, but is associated with a smaller rise in HbA_{1c} from week 24 to week 104 (adjusted mean change: 0.004% vs 0.008% with glimepiride; 95% CI for mean difference: -0.005%, -0.002%).¹²

The analysis considered a lifetime horizon and since there were an increasing number of patients with missing data over the two-year study follow-up period, a conservative scenario applied identical glucose profiles to the treatment and control groups, namely the glucose profile seen in the UKPDS trial.²

In conclusion, even under the most conservative scenarios for saxagliptin, the results (R20 848 per QALY gained) reveal that treatment with saxagliptin+metformin can be considered a highly cost-effective alternative for T2DM patients in the private sector in South Africa.² Treatments that generate an incremental cost/QALY below ZAR 120 000 are generally considered to be cost-effective in the private health care setting in South Africa.²

This is a summary of the key findings of the analysis.

Full text with expanded reference list available on request

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Preventing Falls and Fall-related Injury in Older People: How GPs can Help

Falls and fall-related injury are common in older people, with some events having a direct impact on the person's ability to function and live independently. There is good evidence that falls and fall-related injury can be prevented, and GPs have a key role in screening, assessment and implementing effective intervention strategies.

The size of the problem

Falls are the leading cause of injury-related hospitalisation and injury-related death in people 65 and older. In a study undertaken in New South Wales, Australia, it was shown that 17% of all presentations of older people to the emergency department were fall-related and, of these, about 50% were admitted to hospital.¹ Falls are also the most common reason why an older person calls for an emergency ambulance and the most frequently cited reason for admission to residential aged care. A fall may be a manifestation of acute or chronic underlying pathology or an unintended event resulting from the interaction of a person with his or her surrounds (such as tripping on a pavement).

There is a wealth of literature² regarding the most effective strategies that can be used to prevent falls and injury. However, despite this, a large number of older people at risk of falls are not being appropriately assessed or offered interventions to minimise risk.

About the author

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Case scenario

Mrs A, aged 78, has been brought to the emergency department by ambulance, having tripped on a tree root while out shopping. She has sustained a left distal forearm fracture, which is reduced and then put in a back slab pending outpatient orthopaedic review. Mrs A's husband is willing and able to help her with both domestic and personal care while her arm is out of action and so she is discharged from the emergency department with simple analgesia and told to see her GP for further assessment of falls and fracture risk.

What can the GP do?

Since Mrs A has fallen and sustained a fracture, it is not necessary to screen her for falls risk. Instead, an assessment looking for modifiable risk factors and tailored intervention is required.

How to identify who is at risk of falls

Screening is a process that aims to identify people at increased risk of falls. It does not necessarily show why someone is at risk of falls. It should be a simple and quick process. For busy GPs, the simplest screen to use in older people is to ask them whether they have fallen two or more times in the past year or have sustained a significant injury from a fall.

There is a multitude of other screening tests available, but the reality is that few have been properly evaluated for reliability and predictive validity. Anecdotal information about them suggests that GP uptake is poor.

Key points

- GPs have a key role in screening and assessment of the risk for falls in older people.
- GPs have direct responsibility for medication use and the prescription of drugs that both increase and decrease risk of falls and fractures.
- Medications to be avoided in the older person where possible are the centrally acting medications, especially sedative hypnotics, antidepressants, antipsychotics and opiate-containing analgesics.
- Exercises that challenge balance are important for falls prevention and must be undertaken continually. The benefits of appropriate exercise should be conveyed to patients, particularly those who have chronic diseases for which different approaches to exercise are required.
- Residents in residential aged care should be seen as having a high risk of falls. At a very minimum, all residents should be vitamin D replete. Several additional strategies can be used to reduce both falls and fracture risk.

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chotics and opiate-containing analgesic agents – with an increased risk of falls and fractures. Sedative hypnotic use is also linked with motor vehicle accidents and, more recently, has been shown to be associated with an increased mortality and cancer risk.³ Clearly, some people have justifiable clinical indications for some of these medications, but ongoing need should be reviewed regularly.

In addition, abrupt withdrawal of any of these medications is contraindicated and many would see withdrawal as a futile exercise unless the older person is a willing participant and has a full understanding of the nature of the risk of using such medication. Hospitals also have a responsibility for reducing the use of sedative hypnotics. Figure 1 shows the results of a sustained training, education and support programme aimed at reducing in-patient falls and which included targeted teaching around the risks of sleeping tablet use at a large metropolitan teaching hospital in Sydney.

In addition to stopping older patients from taking harmful medications, doctors have a requirement to ensure that people are taking medications from which they stand to benefit. Many older people are vitamin D deficient from a combination of limited sunlight exposure and a reduced ability to synthesise vitamin D in the skin. Vitamin D receptors are found on muscle (including cardiac myocytes) and nervous tissue, and there is evidence that vitamin D replacement to achieve serum levels more than 50nmol/L can reduce falls in older people. Low levels of vitamin D are also associated with increased risk of cardiac events and certain malignancies,³ so there are multiple reasons to ensure that people are vitamin D replete.

Both vitamin D and calcium are essential for bone health, and when dietary intake is insufficient, these should be supplemented. However, neither are mainstay treatments for osteoporosis and all too often people who fall and fracture are not offered evidence-based treatments for osteoporosis.⁵

There is no requirement to undertake a bone mineral density (BMD) scanning in an older person who has sustained a low trauma fracture. Several treatment options exist for osteoporosis, and these should be considered in any older per-

TABLE 1

Examples of linking assessment to evidence-based interventions

Risk factor	Intervention
Medication	Stop any CNS medication unless ongoing clinical indication. Ensure calcium and vitamin D intake is sufficient. If not, consider supplementation. Aim for serum vitamin D level >50nmol/L. Offer treatment for osteoporosis for any older person sustaining a fracture from standing height unless there is a clinical contraindication to all the therapies available. Refer for home medication review if concerns about management of medications.
Vision	If cataracts are causing impaired vision, refer for extraction. If using bifocal or multifocal glasses – recommend use of a separate pair of single lens glasses for use outdoors.
Impaired balance or mobility	Consider home or group-training based programme for strength and balance training. Ensure any underlying cause for impaired balance and mobility is addressed where possible – eg, vitamin D deficiency, vitamin B12 deficiency, CNS medication use, pain, etc.
Syncopal/dizziness	Check lying and standing blood pressure. Review any medications contributing to orthostatic hypotension. Consider Epley manoeuvre if dizziness thought to relate to benign paroxysmal positional vertigo. Refer if unexplained dizziness and/or syncope.
Painful feet	Treat pain and consider referral to podiatrist for provision of ankle strengthening and mobility exercises.
Cognition	Document cognitive performance using a simple tool – eg, GPCog, AMTS or MMSE. Consider the impact of any cognitive deficits on ability to engage in an intervention.
Environment	Refer to occupational therapist for modification of the home environment, with provision of support and advice regarding safety within and outside the home for those at highest risk of fall.

ABBREVIATIONS: AMTS = abbreviated mental test score; CNS = central nervous system; GPCog = general practitioner assessment of cognition; MMSE = mini-mental state examination.

son with a low trauma fracture or at high risk of fracture (eg, people taking high doses of corticosteroids). These are detailed in Table 2.

Review of use of bifocal or multifocal glasses

The use of bifocal and multifocal glasses has been shown to increase the risk of falls and evidence exists to support people using single lens glasses for outdoor mobility. Wearing bifocal or multifocal glasses is particularly hazardous during stair descent, where the varying focal lengths can lead to inaccurate foot placement.

Many older people when told about the hazards of wearing bifocal and multi-

focal glasses outdoors will respond by telling the practitioner that they have been wearing them for years. Although true, what will have changed over the years are basic physiological measures of strength, balance and reaction time, which have a direct impact on the ability to respond to a sudden and unexpected challenge to remaining upright.

Assessment of postural hypotension

Postural hypotension and associated symptoms are often related to the use of antihypertensives and other cardiac medications. Postural hypotension should be properly assessed with the

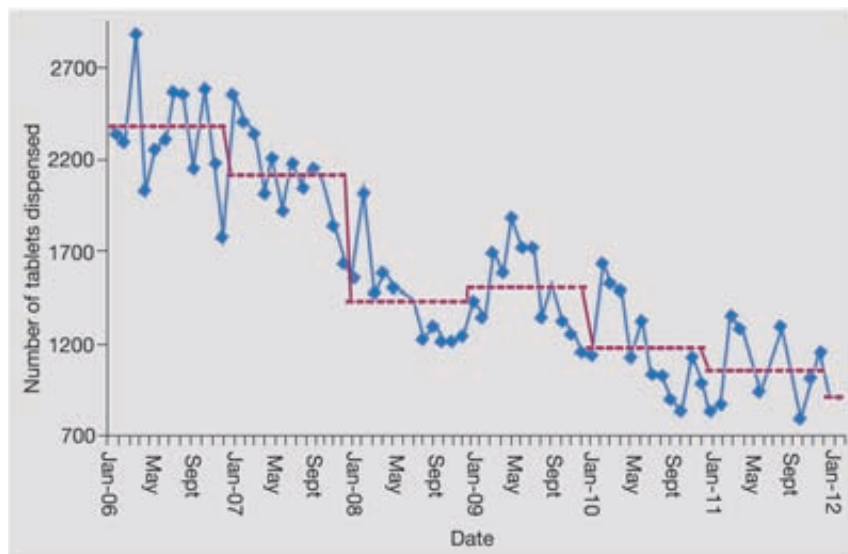


Figure 1. Reduction in sedative hypnotic use occurring over time in a large metropolitan teaching hospital in Sydney following the introduction of a sustained training, education and support programme aimed at reducing in-patient falls. Graph shows the total number of sedative tablets dispensed in all medical and surgical wards between January 2006 and January 2012 [unpublished data].

person lying supine for five minutes and then on standing at one and three minutes. Any changes in pulse and blood pressure should be correlated with symptoms.

When choosing which medications to stop in patients with postural hypotension, most doctors with expertise in the area would recommend stopping peripheral vasodilators and volume-depleting agents if clinically appropriate. In some older people who still have symptomatic postural hypotension despite modifying medications and using standard non-pharmacological treatments, the use of fludrocortisone is required. Fludrocortisone can be helpful but has the main side effect of causing peripheral oedema.

Referral by the GP

As the primary provider of care on an ongoing basis, GPs are in the privileged position of being able to influence the health decisions of their patients. Therefore, in regard to falls prevention it is critical that the GP is proactive in referring older people to evidence-based treatments to minimise falls risk.

Exercise is probably the single most important intervention a person can undertake to reduce the risk of falls and fall-related injury. However, the exercise

needs to challenge balance specifically and preferably improve strength. It also needs to be sustained. Simply advising someone to walk is not an evidence-based approach and, in those with poor balance, may actually increase risk of falling.

Examples of evidence-based exercise interventions include the Otago exercise programme (a progressive exercise programme that includes strengthening and balance exercises) and Tai Chi (Figure 2), both of which can be undertaken on a one-to-one basis or in a group setting, depending on patient preference and availability of services locally.

More recent evidence has emerged on the importance of good foot care and footwear. Painful feet can increase falls risk and there is evidence to support podiatry intervention and the provision of specific ankle/foot exercises.⁶

Referral for other specialist input may be required and may include referral for:

- Cataract extraction.
- Occupational therapy home assessment.
- A home medication review (HMR) when there are particular concerns about compliance and ability to manage medications. In some areas, it will be possible to refer older people to a specialist falls clinic, although the availability of these services is highly variable.

Case continued

When the GP met Mrs A, they addressed a number of issues relating to her identified falls risk profile. This was done over a number of visits rather than overwhelming Mrs A with a large number of recommendations in one session.

The antidepressant and sedative hypnotic had been started a number of years ago after the death of Mrs A's daughter. It was agreed that Mrs A would reduce and then discontinue her antidepressant in the first instance and that this would be reviewed with the potential to slowly reduce and stop the sedative hypnotic.

Her use of bifocals was discussed and she was advised to use single lens glasses when outdoors. She was happy to make this change as she was aware of the distorted visual fields when attempting stair descent.

As her arm was still in a cast, she was reluctant to consider an exercise programme at this point but was happy to do so in the future.

The GP also discussed bone health with Mrs A. She already had sufficient calcium intake in her diet and was taking vitamin D supplements. She was also offered a choice of treatments for osteoporosis.

Preventing falls in nursing and residential aged care facilities

Falls and fall-related injury are more common in residential aged care facilities. It is arguable that there is no indication for screening in this population as all residents are likely to be at increased risk of falls. Interestingly, it should not be assumed that there is a linear relation between falls risk and degree of 'frailty' as those least likely to fall are those who are most 'frail' – ie, unable to transfer or mobilise themselves without assistance.

In this context, assessment should be linked to intervention and several approaches have been shown to be effective. There is evidence that vitamin D supplementation, a single and simple intervention, is beneficial in preventing falls in people living in residential aged care facilities, particularly in those with low serum levels of vitamin D (<50nmol/L).⁷



TABLE 2

Treatment options for older people with low trauma fracture

Treatment	Administration	Comments
Bisphosphonates	Can be given orally (alendronate and risedronate) weekly or monthly or Intravenously (zoledronic acid) annually for three years Avoid in people with impaired renal function (creatinine clearance <35 µmol/L) Check dentition and any requirement for dental work – rare association with osteonecrosis of the jaw Ensure people are calcium and vitamin D replete before administering treatment	For males and females
Strontium ranelate	Given orally daily Caution required if renal impairment	For females only
Raloxifene	Given orally daily. Caution required if renal impairment. Main concern relates to increased risk of venous thromboembolic disease	For females only
Teriparatide	Daily subcutaneous injection for 18 months	Specialist prescription only, or those who have failed on other treatments

Other effective interventions involve a multifaceted assessment of risk, including factors specific to the individual (cognition, physical function, medication use, hydration) and assessing how the person interacts with his or her surroundings (eg, distance to toilet or dining area, adequate lighting at night). People living in residential aged care settings are at high risk of fracture and, despite this, they are often the population least likely to be considered for treatment of osteoporosis.⁸

Limited evidence supports interventions to prevent falls in people with dementia but there is no reason to believe they would not achieve the same fracture reduction benefits from pharmacological treatment of their bone health. Clearly the decision to treat should be based individually and made in the context of the global health of an individual, including potential life expectancy.

Challenges to implementing the evidence

Despite the evidence supporting fall risk assessment and intervention, the literature suggests that assessment is not routinely undertaken and that people who could benefit from falls and fracture

interventions are not receiving this level of care.⁸

The multifactorial nature of falls and the need to assess multiple domains and involve several health care professionals can seem overwhelming for both the patient and the person undertaking the initial screen or assessment. Time pressures are a reality for the GP and it may be necessary, and more appropriate, to address one risk factor at a time and review progress in subsequent consultations. Many older people do not openly embrace the need for ongoing specific

targeted exercise. It is crucial that all health practitioners describe and prescribe exercise as a life-long activity with many health benefits, including falls and fracture prevention.

There is still limited evidence of effectiveness for fall prevention strategies in some high-risk populations, including people with dementia, Parkinson's disease, depression and stroke, although research is ongoing in all of these areas.

Conclusion

GPs can have a huge impact on an older person's risk of falls and fall-related injury. This in turn can have a dramatic effect on an older person's ability to function and live independently, and their quality of life. To date, and despite evidence and guidelines, there is limited evidence of systematic screening, assessment and intervention in many parts of the world. More work is required for a better understanding of the barriers to delivering effective falls prevention strategies in general practice and appropriate levels of support to implement best practice. The benefits are compelling for patients – fewer deaths, fewer fractures and fewer moves to residential care.

References are available on request



Figure 2. Tai Chi is an example of a suitable evidence-based exercise intervention to help reduce falls.

Our branches reach far,
while our roots run deep.

- ACE inhibitors
- Angiotensin receptor antagonists
- Bezafibrates
- Alpha/beta-receptor blockers
- Centrally acting vasodilator
- HMG-CoA reductase inhibitors (statins)
- Beta-receptor blockers

- Calcium Channel blockers
- Organic Nitrates
- Anticoagulants
- Peripheral vasodilators
- Minerals and Electrolytes
- Diuretics

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90 Dubious Tests and Therapies to Avoid

Seventeen American medical societies have collaborated to produce a list of almost 90 common but often unnecessary tests and procedures, many of them ordered for a peculiar kind of patient — the one without symptoms.

Such services, which are not rooted in evidence-based medicine, contribute to the high cost of healthcare and sometimes harm a patient's health, as in excessive radiation exposure in the course of diagnostic imaging or complications of a surgery after a false-positive test result.

Examples

No fewer than 12 of the guidelines caution doctors that asymptomatic patients probably do not need a given treatment. A few examples follow, along with the American society that recommended them:

- Don't screen for carotid artery stenosis in asymptomatic adult patients (Academy of Family Physicians).
- Don't automatically use computed tomography scans to evaluate children's minor head injuries (Academy of Pediatrics).
- When prescribing medication for most people aged 65 years and older who have type 2 diabetes, avoid attempting to achieve tight glycemic control (Geriatrics Society).
- Don't routinely order imaging tests for patients without symptoms or signs of significant eye disease (Academy of Ophthalmology).
- Don't screen for ovarian cancer in asymptomatic women at average risk (College of Obstetricians and Gynecologists).
- Avoid using stress echocardiograms on asymptomatic patients who meet "low-risk" scoring criteria for coronary disease (Society of Echocardiography).

Dr Christine Cassel said such rules of thumb seek to change the mindset in doctors and patients alike that "more is better," which leads to wasteful spend-



ing and sometimes puts the patient at risk. "What you're talking about is a culture change," Dr Cassel told MMN.

Choosing wisely

The 2013 selection for the guidelines campaign, dubbed "Choosing Wisely", extends a batch proposed last year by a smaller group of medical specialties. One recommendation that two societies include cautions doctors not to schedule elective, nonmedically indicated induction of labour or cesarean deliveries before 39 weeks and zero days of gestational age.

"Sometimes patients request a treatment they don't need," said Dr William Zoghbi, president of the American College of Cardiology. "It takes much longer to dissuade a patient from asking for test than actually ordering the test."

Unnecessary

Other commonly ordered but often unnecessary tests and procedures include:

- Do not order a stress test for asymptomatic patients who are at low risk for

coronary heart disease.

- Do not obtain imaging studies in patients with nonspecific low back pain.
- Do not order imaging studies as an initial test for patients with low pretest probability of venous thromboembolism; instead, first obtain a high-sensitive D-dimer measurement.
- Do not obtain a preoperative chest x-ray when lacking any clinical suspicion for intrathoracic pathology.
- Do not send a person who has experienced a simple fainting spell for a brain imaging scan when there is no evidence of seizures or other neurological signs and symptoms.
- Avoid nonsteroidal anti-inflammatory drugs in individuals with hypertension, heart failure or chronic kidney disease from all causes, including diabetes.
- Don't initiate chronic dialysis without ensuring a shared decision-making process between patients, their families and their caregivers.

Diagnostic imaging "Don'ts" dominate

Not surprisingly, warnings against unnecessary diagnostic imaging also abound in the lists for the other specialties. Doctors should not perform positron emission tomography, computed tomography, and radionuclide bone scans in the staging of early prostate cancer with a low risk for metastasis. There is no evidence to suggest that such scans improve the detection of metastatic cancer or survival.

One item in the list encourages, rather than discourages, testing. It advises not to diagnose or manage asthma without spirometry. Basing the diagnosis merely on symptoms is problematic, because the symptoms may stem from causes other than asthma.

For the full lists visit <http://www.abim-foundation.org>

Very early ART Achieves HIV Cure in Mississippi Infant

During the March Conference of Retroviruses and Opportunistic infections (CROI) in Atlanta, US, a team led by Dr Deborah Persaud of Johns Hopkins University reported on the first thoroughly documented case of functional cure in an HIV+ infant and suggested that very early ART may prevent establishment of a latent reservoir and achieve cure in children.

Maternal infection with wild-type subtype B HIV was verified. The mother and infant shared HLA haplotypes. Infant infection was confirmed by positive HIV DNA and RNA testing on two separate blood samples obtained on the second day of life.

30 hours after birth: Aggressive treatment started

The mother arrived at a rural hospital in the autumn of 2010 already in labour and gave birth prematurely. She had not seen a doctor during the pregnancy and did not know her HIV status. When a test showed the mother might be infected, the hospital transferred the baby to the University of Mississippi Medical Centre, where it arrived at about 30 hours old.

ART treatment was immediately initiated.

Age 29 days: Virus undetectable

Three additional plasma viral load tests were positive before reaching undetectable levels at age 29 days. Plasma HIV RNA remained undetectable. Plasma viral load, PBMC DNA, and HIV-specific antibodies remained undetectable with standard clinical assays, confirming a state of functional HIV cure.

Mother and child disappear at 18 months

"Virus levels rapidly declined with treatment and were undetectable by the time the baby was a month old," said Dr Persaud. "That remained the case until the baby was 18 months old, after which the mother stopped coming to the hospital and stopped giving the drugs."

Five months later: Still negative

"When the mother and child returned



five months later staff expected to see high viral loads in the baby. But the tests were negative. Suspecting a laboratory error more tests were ordered. To our great surprise, all of these came back negative," Dr Persaud said.

Two and a half years later: Functional cure

The researchers, sponsored by AmfAR, the American Foundation for AIDS Research, put the baby through a battery of sophisticated tests. They found tiny amounts of some viral genetic material but no virus able to replicate, not even lying dormant in so-called reservoirs in the body.

Today the child is two and a half years old and has been off drugs for a year with no sign of functioning virus.

SA HIV clinicians respond

Dr Leon Levine of the Child and Adolescent Committee of SAHIV Clinicians Society responded: "This announcement at the CROI conference in Atlanta of the functional cure of a 26 month old child with HIV infection is very exciting because it provides proof of concept that if an HIV infected infant is started on antiretroviral therapy early enough there is a chance that the infection can be eradicated before it takes hold in the body."

"This child was started on treatment exceptionally early at the age of 30 hours of life. Usually in SA a child is started on antiretroviral treatment following a diagnosis of HIV infection at 6 weeks. For this reason it is very unlikely that there will be any babies in SA in the same situation as this child."

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How Long Does a Cough Last? Patients' Expectations Are Unreasonable

An interesting study has identified a mismatch between patients' expectations regarding the duration of acute cough illness (ACI) and the actual duration based on the best available evidence.

To test a hypothesis that antibiotic overuse for acute cough illness (ACI) is in part due to a mismatch between patients' expectations and the natural history of ACI, Dr Mark Ebell and others undertook a study in Georgia, US.

They phoned a random sample of 493 adults to determine their expectations regarding the duration of ACI. Next they performed a systematic review of observational studies and the placebo or untreated control groups of randomised controlled trials to determine the duration of ACI from the published medical literature. They

included studies of otherwise healthy adults with undifferentiated ACI, no clear bacterial cause, data on at least one cough outcome, and at least one week of follow-up.

The mean duration of cough in the published literature was 17.8 days. Survey respondents reported a median duration of five to seven days and a mean duration of 7.2 to 9.3 days depending on the specific scenario. Patients expecting a longer duration of illness were more likely to be white, female, and have self-reported asthma or chronic lung disease.

Independent predictors of the belief that antibiotics are always helpful included nonwhite race, some college education or less, and previous antibiotics for ACI.



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Play to Become a Surgeon : Wii Games Boost Performance

Playing console games improved the performance of surgeons learning minimally invasive surgery in a study that suggests the device could have a role to play in educating doctors.

In a trial among 42 post-graduate surgeons in Italy, those who were asked to play Wii games such as Tennis and a 3D battle game an hour a day, five days a week for four weeks did better at 13 out of 16 measures on a surgical simulator than those who didn't play the games, researchers from Sapienza University of Rome wrote in the journal PLoS One.

Trainee surgeons commonly hone their laparoscopic surgery skills on computer simulators. However, the expense of the machines, combined with the difficulty of a technique that involves maneuvering tiny operating tools through very small incisions, as well as increased risks of lawsuits, have raised the need for training outside the operating theater, researchers led by Gregorio Patrizi from the University's Department of Surgical Sciences wrote.

Gallbladder removal

"It is hard to suggest that academic institutions adopt a video-game console as a didactic tool for surgery," Patrizi and colleagues wrote. "We hope this may be a trigger to develop dedicated software aimed to help young surgeons as the economic impact of these consoles is significantly lower than traditional laparoscopic simulators and they provide basic didactic value."

The researchers said they chose the Wii for the trial because its motion-sensing interface resembles the movements required for keyhole surgery more closely than other video-game consoles.

They used the Symbionix's LAP Mentor simulator [R810 000] to test all 42 participants before and after the four-week trial. In one task that simulated moving a camera inside a patient, those who had played the Wii [R3500] were 83% more accurate after four weeks, compared with a 10% improvement in those who didn't play the Wii.

In another task that simulated cholecystectomy the Wii group had a 35% improvement in performing safe cauter-



ies compared with a 12% gain for the other group.

"The Nintendo Wii may be adopted in lower-budget institutions or at home by younger surgeons to optimise their training on simulators before performing real procedures," Patrizi and colleagues wrote.

Eye-hand coordination

Previous studies have shown playing video games can enhance spatial attention and eye-hand coordination. Ben

Challacombe, a consultant urologist at Guy's and St Thomas' Hospitals in London, said that on the basis of the study he'd recommend his students spend time playing the Wii to refine their skills.

"We already knew that people who are good at video games are more easily trainable at laparoscopic keyhole surgery," Challacombe said in a telephone interview. "What this has shown is that if you train using a computer game you get much better more quickly."

New Blood at iNova

Kym Hampton is the new Country Business Manager at iNova. She joined the company in February 2013, bringing with her a wealth of experience in the health care sector that she has cultivated since 1984.

Hampton started her career in nursing before moving into the commercial aspect of health care in 1994. She has held several positions in sales, marketing, customer relations and key accounts and from 2008 was the Managing Executive, Hospital Products of Adcock Ingram.

iNova is well established and has been operating in SA since 1953. It was at one

time known as 3M Pharmaceuticals, but in 2006 3M sold the business globally and it was renamed. It is now owned by Canada's Valeant Pharmaceuticals.

"At iNova, we believe that our speed, efficiency and simplicity of action are essential to achieving our objectives and satisfying market needs. Kym is a welcome addition to the team and her rich background and leadership will help us remain committed to making everyday life better for all our people, customers and consumers by providing quality, high-end products that meet individual needs," said a company spokesperson.

No Difference in Extrapyramidal Effects Between First and Second Generation Antipsychotics... Except the Expense

Second-generation antipsychotics (SGAs) became the mainstay of treatment for psychotic disorders after pre-licensing trials suggested they induced fewer extrapyramidal side effects (EPS), and might provide advantages in efficacy and cognition. A growing body of evidence suggests that the advantages observed in some of these trials may have been at least in part due to their design, said an article in the *British Journal of Psychiatry*.

High-dose haloperidol was a common choice as a first-generation antipsychotic (FGA) comparator, ensuring a high risk of EPS compared to the SGAs. Given that many SGAs cause weight gain and metabolic abnormalities, it is not clear that their risk/benefit balance is superior to that of FGAs for the treatment of psychotic disorders.

Pragmatic clinical trials have pro-

vided mixed results, but generally have not supported substantial real-world advantages for most SGAs over FGAs. Peluso and colleagues reported a secondary analysis of data from CUTLASS-1, a pragmatic clinical trial, to evaluate whether SGAs provided any advantage over FGAs in terms of EPS liability.

Early benefits not sustained

Trends towards resolution of Parkinsonism and akathisia, and a higher rate of tardive dyskinesia in the SGA group at 12 weeks became null by 52 weeks. The authors concluded that there was no real-world advantage of SGAs in reducing EPS risk.

It is important to note that 22% of patients in the FGA group received adjunctive anticholinergic medication, compared with only one in the SGA

group. Cognitive outcomes were not measured, so it is unclear as to whether the anticholinergic drugs had any adverse cognitive effects. Quality of life was similar, so the clinical significance of any differences is questionable.

This study adds to the evidence that many SGAs have no real-world advantage over their FGA counterparts. The story is far from over, but it appears possible that the last 15-plus years of antipsychotic market dominance by SGAs, and massive associated expense, may have done little to improve schizophrenia outcomes. It may in fact have caused more harm than help due to metabolic problems induced by SGAs.

The authors concluded, "It is imperative that the new generations of psychiatrists become familiar with the larger array of antipsychotic options and consider FGAs as viable."

Two New Fixed Combinations from Sanofi

Amaryl Combi: Type 2 diabetes

Sanofi has introduced Amaryl Combi 2/500mg tablets, a fixed drug combination of glimepiride 2mg and metformin hydrochloride 500mg.

Amaryl Combi is indicated as an adjunct to diet and exercise in noninsulin-dependent diabetes mellitus (type 2 diabetes) patients who are well controlled and stabilised on the individual components in the same ratio as contained in Amaryl Combi. The combination medication is applicable:

- In cases where the monotherapy with glimepiride or metformin did not result in adequate glycaemic control.
- Replacement of combination therapy of glimepiride and metformin.

Amaryl Combi should be taken once or twice daily before or with meals.

It is a schedule 3 medicine.



Tritace Plus: Hypertension

Sanofi has announced the launch of Tritace Plus 5/12.5mg, 5/25mg and 10/12.5mg tablets, a fixed drug combination of ramipril and hydrochlorothiazide.

Tritace Plus is indicated for the treatment of essential hypertension in patients stabilised on the individual components at proposed doses, for whom this combination therapy is appropriate.

Tritace Plus is a schedule 3 medicine that should be taken in the morning as a single dose. Titration will be based on physician's judgment according to severity of hypertension and other associated risk factors.





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Month of issue
MARCH 2013

Please return by June 30, 2013

Fill in the answers from the question page to the block below.

PATIENTS POST MYOCARDIAL INFARCTION	DIABETES-RELATED FOOT PROBLEMS	THERAPEUTIC PROGRESS IN PARKINSON'S DISEASE	PREVENTING FALLS AND FALL INJURIES
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Answer the following questions as either true or false. All the answers are to be found in the CPD articles in this issue.

PATIENTS POST MYOCARDIAL INFARCTION (Pg 15)

1. Coronary CT Angiography has replaced cardiac catheterisation as the usual method of assessing coronary anatomy in the patient who has had a coronary event.
2. Bleeding, as a complication of aspirin therapy post-coronary, is dose-related.
3. Atorvastatin 80mg is the usual statin used for lowering cholesterol post-coronary.
4. Digoxin remains a pillar of standard medical post-coronary treatment.
5. Coronary artery bypass grafting is very useful in the face of LV dysfunction due to extensive scarring.

DIABETES-RELATED FOOT PROBLEMS (Pg 24)

1. If the diabetic foot is pink then it is reasonable to assume perfusion is adequate.
2. An MRI is the best pre-operative modality for assessing deep fascial infection.

The first entry received that scores full-marks will receive a hamper of goods sponsored by OTC PHARMA SA.

3. A single organism is usually responsible for infection in diabetic foot ulcer.
4. Skin breakdown assists in draining the pus and is a good sign in the infected diabetic foot.
5. Good care of the diabetic foot may reduce lower limb amputations by 50%.

THERAPEUTIC PROGRESS IN PARKINSON'S DISEASE (Pg 29)

1. Levodopa prevents the progression of motor symptoms in PD.
2. The peripheral half-life of levodopa is extended by both DDCI and COMPT inhibitors.
3. Pramipexole may cause unheralded sleep attacks.
4. Rasagiline is a monoamine oxidase B inhibitor.
5. Stem cell transplants are now available as neurorescue therapy in PD.

PREVENTING FALLS AND FALL INJURIES (Pg 34)

1. Vitamin D replacement may prevent falls in the elderly.
2. Vitamin D (with calcium) is the mainstay of treatment for osteoporosis.
3. Fludrocortisone is useful for treating resistant cases of postural hypotension.
4. Bifocals or multifocals offer the best visual protection against falls.
5. Exercise programmes such as Tai Chi increase the risk of injury from falling.

See answer form opposite

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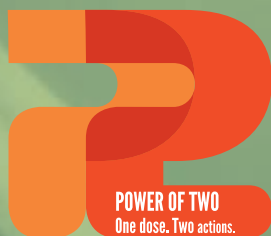
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Your Reminder

2013		 WWW. 
3 - 6 Apr	23rd Biennial Congress of the Rheumatism and Arthritis Association (SARAA) & 7th Annual Congress of the African League of Associations for Rheumatology (AFLAR) WHERE: Elangeni Hotel, Marine Parade, DURBAN CONTACT: Dine Poulton • 011-768-4355 • dine@londocor.co.za	CPD, Expo, 10-50 Speakers www.saraa.co.za www.aflar.net 
9 - 13 Apr	AAGL - Association of Gynaecologic Laparoscopy - 9th International Congress on Minimally Invasive Gynaecology WHERE: Cape Town ICC, CAPE TOWN CONTACT: Turner Conferences and Conventions • 031-368-8000 info@aaglcaptown2013.org.za	CPD, Expo, 10-50 Speakers www.aaglcaptown2013.org.za 
10 - 13 Apr	12th World Federation of Chiropractic Congress WHERE: Durban ICC, DURBAN CONTACT: WFC • +1-416-484-9978 • congress2013@wfc.org	CPD (18), Expo, 50-100 Speakers www.wfc.org/congress2013/ 
12 - 13 Apr	1st Interdisciplinary Academic Conference on the Holistic Support of Children in Healthcare WHERE: Netcare Head Office, Sandton, JOHANNESBURG CONTACT: Annemarie Oberholzer • 082-562-5912 • contact@opssa.org.za	TBC, Expo, 10-50 Speakers www.opssa.org.za 
17 - 19 Apr	Building Children's Nursing for Africa WHERE: Riverclub, Liesbeeck Parkway, Observatory, CAPE TOWN CONTACT: Janet Sirmongpong • 021-406-6348 janet.sirmongpong@uct.ac.za	No CPD, , 10 Speakers www.buildingchildrensnursing2013.co.za 
17 - 20 Apr	22nd Biennial Congress of the Arthroplasty Society WHERE: Champagne Sports Resort, DRAKENSBERG CONTACT: ICE Solution • 082-898-6247 • mel@icesolution.co.za	CPD, Expo, 50-100 Speakers www.saoa.org.za 
18 Apr	Pre-SEMDSA Endo 101 Course WHERE: Wanderers Club, Illovo, JOHANNESBURG CONTACT: Shelley Harris • 011-202-0516 • shelley@semdsa.org.za	CPD, Expo, 10-50 Speakers www.semdsa.org.za 
18 - 22 Apr	Level 2 Diploma Course in Aesthetic Medicine WHERE: JOHANNESBURG CONTACT: Mareli Janse van Rensburg • 012-548-7152 info@aesmedsa.co.za	CPD, Workshop Speakers www.aesmedsa.co.za 
19 - 21 Apr	SEMDSA/LASSA - Society for Endocrinology, Metabolism and Diabetes / Lipid and Atherosclerosis Society Congress WHERE: Wanderers Club, Illovo, JOHANNESBURG CONTACT: Shelley Harris • 011-202-0516 • shelley@semdsa.org.za	CPD, 10-50 Speakers www.semdsa.org.za 
29 - 30 Apr	ICEEWM - International Conference on Environmental, Energy and Waste Management WHERE: Holiday Inn, Sandton, JOHANNESBURG CONTACT: WASET • info@waset.org	No CPD, Expo, 10-50 Speakers www.waset.org/conferences/2013 

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References: 1. Rosak C. The pathophysiologic basis of efficacy and clinical experience with the new oral antidiabetic agents. *J Diabetes Complications* 2002;16(1):123-132. 2. Charpentier G, Fleury F, Kabir M, et al. Improved glycaemic control by addition of glimepiride to metformin monotherapy in Type 2 diabetic patients. *Diabet Med* 2001;18:828-834. 3. Haute Autorité de Santé. French Transparency Committee 10 December 2008. http://www.has.sante.fr/portail/upload/docs/application/pdf/2010-11/galvus_ct_5731.pdf. 4. Holstein A, Plaschke A, Egberts E-H, et al. Lower incidence of severe hypoglycaemia in patients with type 2 diabetes treated with glimepiride versus glibenclamide. *Diabetes Metab Res Rev* 2001;17:467-73. 5. Klepzig H, Kober G, Matter C, et al. Sulfonylureas and ischemic preconditioning. A double-blind, placebo-controlled evaluation of glimepiride and glibenclamide. *Eur Heart J* 1999;20:439-46. 6. Monami IM, Luzzi C, Lamanna C, et al. Three-year mortality in diabetic patients treated with different combinations of insulin secretagogues and metformin. *Diabetes Metab Res Rev* 2006;22(6):477-82.

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