THE JOURNAL OF LIFELONG LEARNING

MODERN MEDICINE

VOLUME 38 NUMBER 8
AUGUST 2013

Get Your Ethics Points Inside!

MODERN MEDICINE CPD

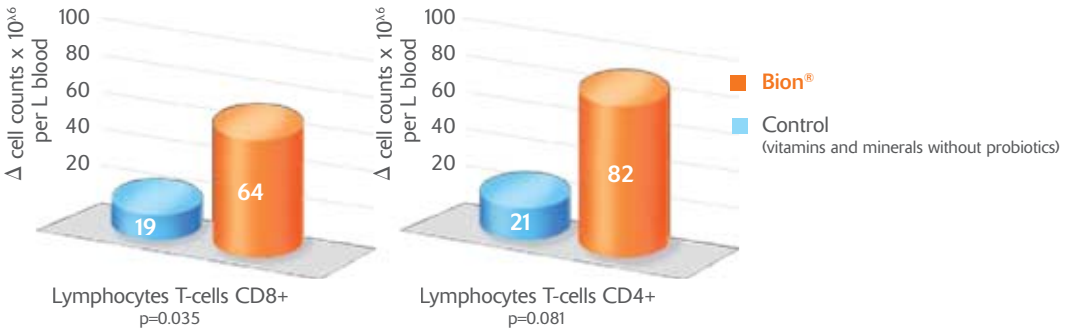
Bion®

Probiotic Multivitamin

Bion® is a well balanced formulation complete with all the essential **vitamins, minerals** and **3 probiotics**. This formulation is proven to help **strengthen immunity**.[1]

- The probiotics in Bion® strengthen immunity by significantly increasing cytotoxic T (CD8+) and helper T-cell (CD4+) counts which are critical for producing antibodies.[1]

3 months of Bion®'s probiotics (TriBion Harmonis®) boost the bodies immune cells by up to 290 %[1]



Adapted from de Vrese et al. [1]

- When Bion® is taken over at least 3 months, studies show significantly shortened duration of common cold episodes by nearly 2 days (p = 0,045) and a reduction in the severity of the symptoms.[1]

Reference:
1. de Vrese M, Winkler P, et al. Vaccine 2006;24:6670-6674.

B.05.13.003

Merck (Pty) Ltd
Reg. No. 1970/004059/07
1 Friesland Drive
Longmeadow Business Estate South
Modderfontein 1645
Tel No: 011 372 5000
Fax No: 011 372 5252
www.merck.co.za

MERCK

MODERN MEDICINE

Volume 38
Number 8
August 2013

Lifelong Learning

Continued on page 2

MODERN MEDICINE

PO Box 84622, Greenside 2034, South Africa
Telephone 011 326 4171
Fax: 086 293 7289

MODERN MEDICINE is published by Modern Media Publishing (Pty) Ltd
Reg No 2012/062379/07

Printed by Tandym Print (Pty) Ltd, Epping, Cape Town.

On the Horizon

Super Strong Synthetic Latex Reduces Allergic Reactions

A synthetic alternative to natural rubber, Cariflex polyisoprene, a product of Kraton Performance Polymers, Houston, Texas, is proving ideal for manufacture of surgical gloves, medical bandages, catheters, tube connectors and other applications requiring high levels of purity, user protection, comfort and product quality. The synthetic latex shows the high tensile strength and tear-resistance of natural rubber without the impurities that cause discolouration, odour and allergic reaction.

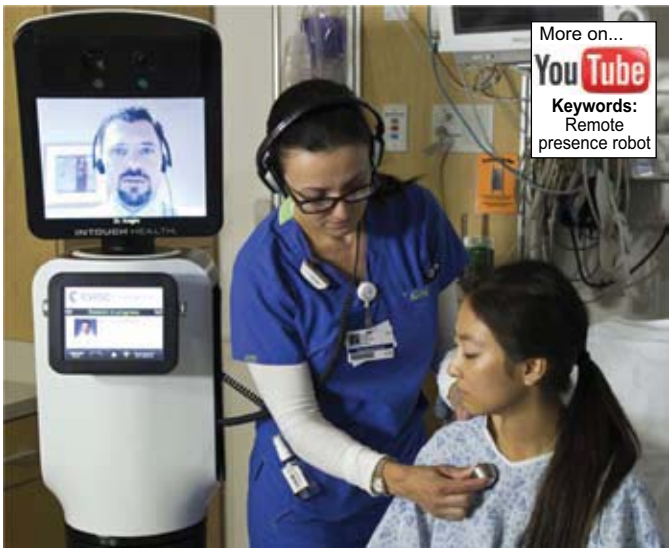
A clean alternative with no impurities

Although replacement of natural rubber latex (NRL) surgical gloves by synthetic alternatives raised some concerns about comfort and protection, when 12 different gloves from a range of suppliers were evaluated for their tensile strength, modulus and puncture resistance, results showed that all the gloves met the required standards for surgical gloves and offered mechanical protection comparable to NRL gloves. Polyisoprene surgical gloves were found to offer greater comfort than other synthetic gloves and were equal to or superior to NRL gloves.

The polyisoprene products can be manufactured on existing production lines designed for natural rubber with modifications only to the compound recipes and process parameters. Because the polyisoprene contains no organic solvents, it is a clean alternative to NRL. It's also free of impurities and of lot-to-lot variations that are inherent with natural products. Being a synthetic material, it can be produced in a precisely controlled environment.

On the
Horizon

Robotic Telepresence Augments Hospital Healthcare



As smart as doctors are, they cannot compete with the volume of knowledge in a robot. In an effort to merge the best of human experience and robotic data, telemedicine robots are being developed that not only allow doctors to reach out to patients kilometres or continents away, but offer immediate information and advice that draw from volumes of medical research and case studies. The telepresence platform RP-Vita, developed by iRobot and InTouch Health and approved by the FDA is operational in seven hospitals across North America.

Diagnoses from a distance

The robot is being used to look in on stroke victims at distant hospitals. With the push of a button on an iPad, the doctor can direct the robot to the patient's bed. Thirty sensors enable the robot to navigate the busy hospital hallways, automatically avoiding personnel and obstacles. If necessary, the robot can plot an alternative course to its destination.

Once it is with the patient, its telepresence interface allows the doctor to check on the patient as if he or she were in the room. A two-way video allows them to see and speak to each other. With the zoom feature, the doctor can read the patient's chart and even check eyes for dilated pupils. The robot can be integrated with live patient data from the electronic medical record and with diagnostic devices such as otoscopes and ultrasound. It comes equipped with the latest electronic stethoscope.

Barrier-Free Examination Table Streamlines Workflow

As health-care practitioners continues to seek benefits from streamlining the exam room workflow, the Midmark 625 Barrier Free examination table offers all the capacity, accessibility and connectivity required for excellent patient care while saving time and reducing strain on medical staff.

Whether transferring a wheelchair patient or assisting an expectant mother, medics can position patients on the exam table more easily and efficiently because of the 47cm to 94cm adjustable table height and powered multi-position actuators that quickly move patients into the required examination position.

Built in digital scale

The exam table, with a 295kg patient-weight capacity, features IQScale, a fully integrated and accurate digital scale built into the unit, which weighs patients quickly, efficiently and discreetly. Handheld controls run the scale functions (including BMI calculation) at the push of a button. Data is sent to update the patient's electronic medical record.

The table includes the IQHub which connects other digital diagnostic devices at the point of care. Diagnostic data is ported directly through the hub to a personal computer. Numerous add-on features make the table fully customisable.

Intelligent Knife Improves Tumour Removal

Scientists have developed an 'intelligent knife' that tells surgeons immediately if the tissue they are cutting is cancerous. The iKnife, developed by Medimass, London, though not yet commercially available, is showing promising results.

In solid tumours, surgical removal of the cancer is generally the best treatment, but normally a margin of healthy tissue is removed with the tumour. It is often impossible to tell by sight which tissue is cancerous. In cases of uncertainty, the removed tissue is sent for lab analysis while the patient remains under general anaesthetic.

Smoke reveals tissue health

The iKnife combines an electro-surgery knife with a mass spectrometer. Electric current used to cut tissue produces smoke that is sucked into a tube and fed to the spectrometer, which analyses the smoke's molecular composition. Software compares the results to a large database of known tissue types, telling the surgeon in seconds what the knife is cutting.

During tests in surgery, the knife diagnosed with 100% accuracy

tissue samples from 91 patients, instantly providing information that lab tests normally take up to half an hour to reveal.

Endoscopic Suction Irrigator Removes Bacteria from Infected Sinuses

Medtronic has developed the Hydrodebrider System to treat chronic sinusitis, a common inflammatory disease affecting nearly 35m people in the US alone, causing them uncomfortable symptoms and repeated doctor visits.

Its powerful irrigation is designed to remove persistent bacterial infection that causes on-going sinus infections.

For many patients, standard medical and surgical treatments are effective. Others continue to experience bouts of infection, despite repeated antibiotics, steroids, surgeries or other sinus treatments. Numerous studies implicate biofilms as a contributory agent in chronic sinusitis and in these cases traditional medical and surgical therapies may not provide long-term sinusitis treatment.

Disrupting and removing biofilm bacteria

The system's innovative flex-tip features high-powered spray, suction and 270° articulation-enabled access for both direct saline irrigation and fluid removal from sinus mucosal surfaces. The hand piece delivers a powerful, safe, rotating spray of pressurised saline at 5ml/sec. This sinus treatment can be used in the operating room during endoscopic sinus surgery or in the doctor's rooms to disrupt and remove bacteria from the paranasal sinuses.

The system has two hand pieces: a standard hand piece with the 270° articulation and suction for irrigation and fluid removal (ideal for accessing the maxillary, ethmoid and sphenoid sinuses) and the

More on... YouTube
Keywords: Hydrodebrider video

new frontal hand piece with a 2.2mm diameter for irrigating the hard-to-reach frontal sinuses. This may be used with olive-tip suction for fluid removal.

Subscription Form

MODERN MEDICINE CPD

Subscribe NOW to receive EVERY ISSUE of Modern Medicine. Access 55 clinical CPD points and 10 ethics CPD points per year.

NON SUBSCRIBERS ONLY RECEIVE OCCASIONAL ISSUES.

Please complete this form in block letters, select your subscription option and, along with your payment, return to Modern Medicine, PO Box 84622, Greenside, 2034.
Tel: 083-325-8947, Fax: 086-293-7289.
e-mail: veronica@modernmedia.co.za

SUBSCRIPTION OPTIONS (PLEASE TICK)

12 Month subscription	R550,00	☐
24 Month subscription	R960,00	☐
36 Month subscription	R1 250,00	☐

Full name: .....

Medical registration: MP.....

Year of qualification: .....

Postal address: .....

..... Code: .....

Tel: (.....)..... Fax: (.....).....

e-mail: .....

PLEASE SELECT YOUR PREFERRED PAYMENT OPTION

☐ Cheque – Enclosed, made payable to MODERN MEDICINE. Please post together with this completed form to the above address.

☐ Direct deposit – Fax this form together with a copy of your proof of payment to 086-293-7289.

Bankers	First National Bank
Branch Code	254905
Account Name	MODERN MEDICINE
Account Number	62365011809

NOTE: THE ABOVE PRICES ARE FOR SOUTH AFRICA ONLY. INTERNATIONAL RATES AVAILABLE ON REQUEST.

On the Horizon

New Wheelchair Streamlines Patient Transport

The Prime TC transport chair by Stryker Medical has changed the look of patient transport in hospitals. Its safe, simple and reliable design answers the needs of patients and caregivers. Obvious touch points make operation intuitive for all users. Backsmart ergonomics reduce the bending and reaching that physically stresses caregivers. The rigid frame enhances durability, while reducing the risk of theft as the chair cannot be folded and placed in a vehicle.

Features and benefits:

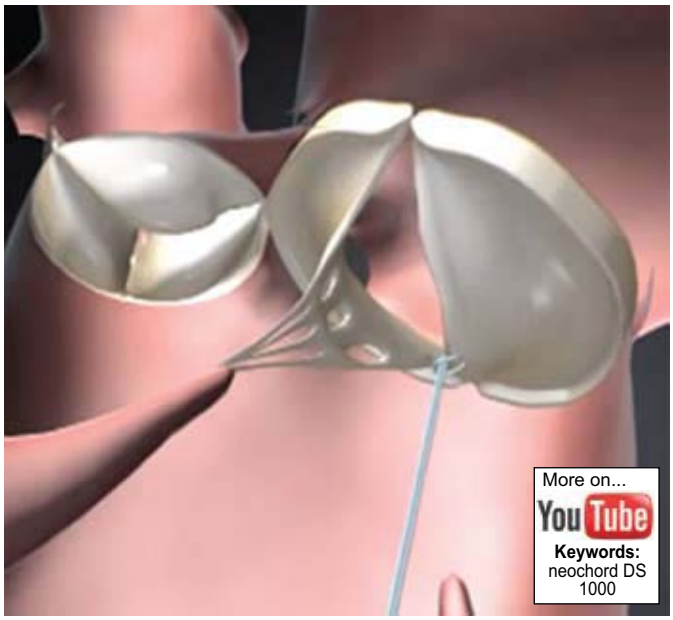
- Big-wheel manoeuvrability makes steering and cornering easier
- StandAssist armrests fold back easily for better patient access
- Backsmart push handles accommodate virtually any caregiver's height

- Flick-up footrests with optional swing away functionality maximise patient access
- One-touch central braking reduces bending to lock brakes
- Anti-tip wheels are standard
- Seamless components make for easy cleaning
- Functional components are movable but not removable, which reduces loss or theft
- Upright O_2 tank holder for easier use
- Durable chrome-plated IV pole features enclosed bag hooks
- Has a safe working load of 227kg
- Rigid nesting frame design saves space and reduces theft.

Now, Mitral Valve Repair Without Bypass

No longer does chordae replacement require open-heart surgery with bypass to stop the patient's heart while the repair is made. NeoChord DS 1000 (Eden Prairie, MN) enables surgeons to replace damaged chordae by placing artificial chordae tendinae or 'neochords' in a beating heart using minimally invasive techniques.

The procedure is performed through a 5cm-8cm incision between the ribs. With ECG guidance, the device is introduced through the apex of the heart into the left ventricle to between the mitral valve leaflets. The expandable jaws of the device grasp the prolapsed leaflet and when the monitor confirms that the leaflet has been adequately captured, the ePTFE suture is deployed and attached to the leaflet. The suture is then pulled through the apex of the heart as the device is removed. The correct length of suture is determined by real-time ECG guidance that observes the improvement in mitral valve regurgitation in the beating heart. The suture is then secured to the apex of the heart.



Immediate confirmation of reduced regurgitation

This system has been designed to restore natural leaflet motion and to preserve a large valve opening with leaflets that fit well together. Use of minimally invasive surgical techniques helps to avoid the complications associated with open-heart surgery on a stopped heart, especially in patients whose condition will not allow open-heart surgery. With this procedure, confirmation that the regurgitation is reduced is immediate.

Classic Antibiotic and Infectious Disease Reference now a Smartphone App

The Sanford Guide to Antimicrobial Therapy, a classic antibiotic and infectious disease reference, is now available on mobile devices using iOS 5.1 or Android 2.2. It is a high value application for medical students, residents and attending doctors who prescribe antibiotics regularly.

The comprehensive, treatment-focused coverage includes:

- Bacterial, fungal, mycobacterial, parasitic, viral infections and HIV/AIDS
- Anti-infective drug information and prevention
- Useful tables and tools, including spectra for antibacterial, antifungal and antiviral agents
- Calculators to assist with dosing.

Monthly updates for the latest content

The guide works on a 12-month subscription of $29.99 that includes monthly updates. The guide is downloaded from the Apple iTunes store, Google Play store or, if the user already has a licence key, as a Chrome App. The licence allows the user to access the guide on up to three mobile devices, regardless of the device's operating system (Apple iOS or Android).

An internet connection is needed initially to install subscription content and to receive the monthly updates but is not required for use of the mobile subscription content. Access to external web resources, such as PubMed abstracts, requires internet connectivity.

Off to a Flying Start with Konica Minolta Medical

Jayshree Parbhoo, owner of Tshepong X-Rays, using her KMMSA equipment.

The REGIUS direct digitiser fits neatly into the rooms.

Parbhoo is thrilled with the image quality of the x-rays.

When Jay Parbhoo, owner and manager of Tshepong X-Rays, started her practice three months ago, Konica Minolta Medical SA (KMMSA) was the company she chose for her medical imaging needs.

Using the company's REGIUS direct digitiser and the computed radiography (CR) image pilot, Parbhoo manages a quick patient turnaround. "Often, when the second view of the patient is being done, the first is already processing," she said.

With the CR software, all the imaging is digital. If there's a mistake, the x-ray can be rejected and a new one taken. "We only print what we want, which saves money," Parbhoo said.

The REGIUS image pilot features tools to rotate the image, lighten and adjust contrast. One can also type in notes for each image. The printer is there to produce hard copies, which patients prefer, or we can send x-rays to the referring doctor digitally. CDs can also be burned for patients to take with them. Parbhoo described the x-rays as being 'great quality'.

Another radiographer who came to visit her practice recently was very impressed with the products.

The REGIUS direct digitiser is compact, and fits neatly in her work area. "It doesn't interfere with patients, and I don't have to leave the room to process the x-ray," Parbhoo affirmed.

In terms of service and support from Konica Minolta Medical, Parbhoo gave a glowing report. "There is no downtime, as most software problems can be dealt with offsite. Those frustrating times when support staff wasn't able to get to us quickly because of traffic are a thing if the past: now they can log in and help offsite. Whenever I've needed support, they have been very helpful.

"The system is also exceptionally user friendly. KMMSA's applications specialist Nicolene Voget came through and had set aside a week to train me. However, after just one day I had learned it," Parbhoo said.

Affordable excellence

Parbhoo has found the software, film and equipment very affordable, compared to what else is on the market. She also likes the door-to-door film delivery service, which is within two days, "Even though I'm in the bundu," she joked. (She is situated in Boksburg).

The patients that Parbhoo serves are underprivileged. Using Konica Minolta imaging products makes it possible for her to do so with inexpensive x-rays (about R200 for a chest x-ray).

A similar article appears in the August edition of Medical Chronicle.

"I'd Recommend Konica Minolta Medical to Anyone" - *Dr Sotirios Divaris*

Outstanding service was the major impact felt by Dr Sotirios Divaris, a radiologist at Vaalpark Hospital in Sasolburg, when he installed a new computed radiography (CR) system from Konica Minolta Medical SA recently.

He purchased the REGIUS Sigma CR mini-PACS (picture archiving and communication system) when he opened a second branch of his practice at Medpark Medical Centre.

Konica Minolta's CR system was perfect for his needs, with its Image Pilot mini-PACS software and easy-to-operate desktop CR reader. The lightest, safest and strongest CR reader on the market, the compact and affordable CR reader maintains superior image quality and reliability and provides simple operation and the smooth workflow that he was looking for. Displaying images within four seconds, the REGIUS Sigma can read up to 60 plates per hour.

Image Pilot pioneers the true meaning of an integrated digital radiography system as it combines CR acquisition, patient registration, image viewing and storage in one easy-to-use and cost effective system.

But it was the personal attention provided by Konica Minolta Medical personnel and their ability to listen to his requirements that really helped him make up his mind.

"I've dealt with really large corporates before and always felt like a number," he said. "It was a very pleasant surprise to experience the responsiveness and personal attention from the people at Konica Minolta Medical. I've never come across anything like it before."

He also installed a Konica Minolta Bizhub printer which prints out high quality, clear colour images. With these, together with CDs for doctors to view x-rays from their computers, Dr Divaris is able to provide doctors in the area with excellent service and a quick turnaround time.

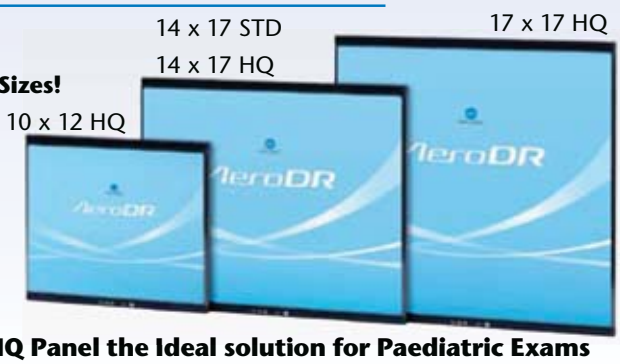
"I'm very happy with the system," he said. "And I'd recommend Konica Minolta Medical to anyone who asks."

AeroDR X70

- The complete versatile Digital X-ray system
- High image quality and lower doses
- Light and easy handling, minimising positioning times
- Flexible wallstand
- Removable grid and tilting bucky
- Built-in foot control for easy access
- AutoTube tracking
- Panel auto tracking function
- Exam Auto Focus function

AeroDR

Available in 3 Sizes!



- Excellent image quality, high detective quantity efficiency (DQE) delivery and low dose
- No battery replacements
- Lightest panel in the world (2.9kg)
- No safety risks
- Displays image in less than 3 seconds
- Maximum patient load over the effective image area is 300kg.

10 x 12 HQ Panel the Ideal solution for Paediatric Exams

- Small size and superior dose efficiency
- Cesium Iodide (CsI) scintillator that boasts ultra-high detective quantum efficiency (DQE)
- High-quality images even with minimum x-ray dose exposure.

RamSoft
RIS PACS Teleradiology

PACS | RIS/PACS | TELE | DICOM

Mammography | Power Server | Gateway Router | Power Server Tele Plus | Power Server PACS

RamSoft
RIS PACS Teleradiology

We understand the needs of busy radiology practices and are able to provide you with fully customisable, feature rich imaging IT solutions for imaging healthcare providers.
Find the best solution for your practice with our RamSoft products.

- Unlimited licensing, number of users, workstations, worklists or modality licences
- Access to the system anytime, anywhere, without losing productivity
- Lower IT costs (management of multiple servers)
- Reduced RIS/PACS administration time
- Decreased service and training costs - one application to learn.

Visit our stand at the RSSA/ SORSA congress (Hall2D stand B), and stand a chance to win a SAMSUNG WB100 camera.

Product information: Chrizelle van der Westhuizen | 011-661-9401 | Chrizelle@kmmsa.com
Sales information: Merinda de Kocks | 011-661-9402 | mdk@kmmsa.com
www.kmmsa.com

adcock ingram

There's something magical about a great comeback story. **Schumacher, Trump, Elvis.** Despite the challenges and negativity, they returned with **a fighting spirit**, **more determined** than ever before. And now, Synaleve® adds its name to the list. Humbled and apologetic, this analgesic will prove that it is undeniably **much better and more prepared** than ever before. **Trust us to cut the long story of pain short.**

Great comebacks. Always *much better* on their return.

THE LONG STORY of PAIN CUT SHORT

Active Ingredients:

- **Meprobamate 200 mg**
- **Codeine phosphate 8 mg**
- **Paracetamol 400 mg**

S5 SYNALEVE® CAPSULES. Each capsule contains: Meprobamate 200 mg; codeine phosphate 8 mg; paracetamol 400 mg. Reg. No. B/2.8/80.
For full prescribing information refer to the package insert approved by the medicines regulatory authority. ZA.13.PAI.140 07/2013.
Adcock Ingram Limited. Reg. No. 1949/034385/06. Private Bag X69, Bryanston, 2021. Tel. +27 11 635 0000. www.adcock.com

adcock ingram
healthcare

1 New Road, Midrand, 1685, South Africa
Private Bag X69, Bryanston, 2021, South Africa
Telephone: +27 11 635 0000
Telefax: +27 86 553 0000
GPS Co-ordinates: S 25 58 25.3 E 28 06 18.8

www.adcock.com

1 July 2013

In 2011 Synaleve was launched onto the South African analgesic market and it was positively received by doctors and patients alike. The properties of the drug allowed it to effectively service the needs of patients who were being treated for moderate to severe pain. We could not have anticipated the complications and challenges that we have experienced with the manufacturing of the product.

- Granules were sticking to the encapsulation machine.
- Separation of capsule shells due to vacuum pressure differentials.
- Variable uniformity in blends due to different particle sizes.

These technical challenges resulted in uneven capsule filling. Adcock Ingram is a manufacturer that constantly strives to uphold the highest standards of manufacturing. We thus took a decision to temporarily discontinue Synaleve until these manufacturing challenges were overcome. We called on technical experts from around the world to assist in resolving the problem.

We improved our manufacturing process, even gaining FDA accreditation at our facility in the interim. Synaleve underwent a complete R&D review to optimize the manufacturing process. Subsequently the product was taken through a stringent validation to ensure that process was infallible and consistent. We also invested in new equipment that would ensure a high quality product could be released to the market.

The outcome has been an improved process of manufacturing the analgesic that you know and trust. It was only once we were 100% certain of our ability to seamlessly meet the market's demands that we made the decision to relaunch Synaleve.

We apologise for the protracted out of stock situation but the Pain of not having our effective analgesic is finally over!

Colin Sheen
Commercial Executive

Dr Abofele Khoele
Drug Management Development Executive

Flordis SA Set to Benefit From the Buyout of Two Renowned International Companies

Natural medicines pharmaceutical company, Flordis SA, is spreading its wings due to the buyout of two international companies – Ginsana and ProThera – by Soho Flordis International (SFI) based in Australia. The acquisition of these companies promises to double both the product range and sales volumes generated by Flordis SA.

Ginsana has been bought from Pharmaton, a Boehringer Ingelheim Group company, a leader and innovator in natural medicines with headquarters in Bioggio, Switzerland. ProThera is a specialist nutraceutical company based in Reno, Nevada, with over 50 years of formulation experience and a comprehensive product line of probiotics and dietary supplements distributed exclusively by healthcare providers.

Having marketed eight of the SFI products to date, Flordis SA has grown exponentially since its debut in South Africa in 2005, doubling its turnover successively for the past two years. Having started out with only sales offices in George and Johannesburg, the company now has branches countrywide, and distribution through all major pharmacy chains, country pharmacies, wholesalers and distributors.

Milestone

According to SFI CEO, Nigel Pollard, "The acquisitions of Ginsana and ProThera mark an important milestone in establishing the SFI Group as a leading global provider of clinically proven natural medicine."

Co-founded in South Africa in 2004 by local pharmacist, Deon Jurgens and Pollard, both formerly of the German pharmaceutical company Knoll AG, Flordis SA was established in order to market the natural medicine and anti-depressant, Remotiv. This product had formerly been marketed by Knoll, which was bought in 2000 by Abbott Laboratories.

"At the time, Abbott Labs did not have an interest in marketing natural medicines. However, Nigel Pollard and I recognised that a growing consumer demand for natural alternatives to chemical medicines was taking root in South Africa," says Flordis SA CEO, Deon Jurgens.

Trial-tested naturals

"What gives Flordis SA an edge is that it markets only natural medicines proven to be efficacious in robust clinical trials, with quality and uniformity of product guaranteed by stringent seed to patient controls."

Deon Jurgens, MD of Flordis SA

Jurgens explains, "SFI is building an international community of leading companies, herbal and medical experts, scientists and researchers to collaborate in the development of natural medicines with high specific evidence."

"SFI advocates the concept of 'specifically clinically proven natural medicines' meaning that the clinical evidence is specific to the finished product. SFI has been involved in two of the largest herbal medicine trials ever supported by the Australian Government. These were a comparison of Iberogast and esomeprazole/Nexiam for functional dyspepsia costing $643,680 and a three-year trial investigating whether Ginsana can improve lung function for patients with chronic obstructive pulmonary disease costing $590,000."

The Flordis range includes products sourced from Zeller (Switzerland), Steigerwald (Germany) and Ginsana SA (Switzerland). These companies have emerged as leaders in scientific research into herbal medicine over the past 135, 45 and 35 years of their existence, respectively.

Flordis products meet the stringent requirements of medicine regulatory authorities of various countries, including the EU, Switzerland, Germany and Australia and South Africa.

flordis
clinically proven natural medicines

Premium Quality
Clinically Proven Efficacy & Safety

Iberogast®
IBS & Dyspepsia

Remotiv®
Anxiety & Depression

KeenMind®
Memory & Mental Clarity

ReDormin®
Sleeplessness

Ginsana®
Energy & Immunity

Premular®
Premenstrual Syndrome

Gincosan®
Memory & Mental Fatigue

Femular®
Menopause

flordis
clinically proven natural medicines

Flordis South Africa (Pty) Ltd | Tel 044 874 2927 | **www.flordis.co.za**

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.

Another recent case of herbal toxicity admitted in our unit has caused me to reflect again on the relationship between conventional Western medicine practitioners and alternate and complementary medicine.

The majority of South Africans (>80%) will consult a traditional healer (TH) prior to seeking our help. Viewed simplistically, the TH may be mainly involved in diagnostic divination (sangomas) or may be predominantly engaged in herbal treatment with muti (inyangas). Although most traditional medicines may be innocuous or even efficacious, there are some powerful poisons which are being used. *Impila* is derived from the pretty ox-eye daisy, *Callilepis laureola,* and this potent toxin is responsible for causing acute hepatic, renal and cerebral symptoms in a spectrum similar to Reye's syndrome. Cases of more chronic poisoning are seen following ingestion of medicinal teas derived from *Senecio species* containing pyrrolizidine alkaloids. This causes hepatic veno-occlusive disease from sinusoidal obstruction. We have had a spate of such cases lately. Some recent studies have shown the addition of salicylates or ibuprofen to local muti.

It is not only Africans who seek complimentary or alternate practitioners (CAM). More than 70% of Germans use CAM; mostly by visiting a "Heilpraktiker". Many German GPs also practice a combination of conventional medicine and untested alternative therapies such as ozone-therapy, colon-hydrotherapy or bioresonance-therapy. The Geschworenen are still out on the pros and cons of CAM[1]. It is not a cheap option. Inyangas often charge hundreds of rand for a consult, both here and in Germany!

Seasonally appropriate

This month sees another collection of useful articles. It is timely (in our winter) to review the diagnosis and management of sinusitis. The use and abuse of antibiotics in upper respiratory infections is always a matter for concern. There are very few new antibiotics in the pipeline and the bugs are getting smarter and smarter. Some of that resistance is a consequence of inappropriate prescribing.

Also common but often not discussed is the problem of erectile dysfunction (ED) in men. The discovery of effective phosphdiesterase-5 inhibitors has, of course, revolutionised management. The investigation and management of ED is reviewed with important guidelines for who needs referral. Some of same group of males who seek attention for ED may well have other problems related to aging, a sedentary lifestyle and poor diet which predisposes to the "metabolic syndrome". There is still some dispute around the relationships and risk factors that are associated with hyperlipidemia, hypertension, type-2 diabetes, abdominal girth and cardiovascular risk. This article goes a way to clarifying these modern scourges.

Enjoy this month. Spring is around the corner.

Reference

1. *Musselmann B, Miksch A, Rosemann T et al. The role of complementary and alternative medicine (CAM) in Germany – A focus group study of GPs. BMC Health Serv Res. 2008 Jun 12;8:127. doi: 10.1186/1472-6963-8-127*

BUILDING A BETTER SOCIETY
THROUGH EDUCATION AND DEVELOPMENT

Registered with the Department of Education as a Private Institution of Higher Education under the higher education act, 1997. Registration number: 2002/HE07/013.

in association with

FPD
SCHOOL OF
HEALTH SCIENCES

HSA
HEALTH SCIENCE
ACADEMY

DISPENSING COURSE

30 CEU'S

This course is based on the recommended standard for the dispensing course for prescribers in terms of Act 101 of 1965 as amended, which was developed by the South African Pharmacy Council, in consultation with the other statutory health councils. Licensing with the relevant authority as a 'Dispensing Health Care Professional' can only take place once the certificate is awarded.

The Dispensing Course is available through the Foundation for Professional Development (FPD) in association with the Health Science Academy.

COURSE STRUCTURE
The Dispensing course leads to a certificate at a National Qualifications Framework (NQF) level 6. To obtain the certificate a minimum of 30 credits must be obtained. Each credit represents about 10 notional learning hours. The course is taught through distance education, training workshops are provided on request.

ENTRANCE REQUIREMENTS
All Medical Practitioners.

ASSESSMENT
Participants will be assessed through
- Portfolio of evidence
- Written Questionnaire
- Dispensing Practical Exam

Participants should complete all the above within 6 months.

COURSE OBJECTIVES
To enable health professionals to dispense and ensure the quality use of medicines prescribed to the patient.

At the end of the course the participants will be able to:
- Identify and apply ethical, legal and therapeutic considerations in all facets of dispensing.
- Evaluate prescription and assess patient profile.
- Dispense the prescription.
- Manage the procurement and storage of medicines.
- Advise patients to ensure quality use of medicines and improve health status.

STUDY MATERIAL
Participants will receive a comprehensive 'resource guide' covering all the study units and annexure containing 'additional' information which may be required. You will also receive an 'assessment documentation guide', consisting of learning activities, multiple choice and short questions that need to be completed.

CERTIFICATION
Successful participants will receive a Course Certificate from the Health Science Academy should they successfully complete the assessment process. This certificate must then be submitted in terms of regulation 18 of Act 101 of 1965, as amended. The course is accredited through FPD for 30 CPD points.

COURSE FEE
R 2 622.00 (Inclusive of all VAT and taxes where applicable)
The course fee includes all study material, assessment and certification. Study material will be posted as soon as full payment has been received.

LEARNING OPPORTUNITIES
EARN YOUR CPD POINTS

TO REGISTER CONTACT: MELANY MANOHARUM
Tel: 012 816 9000 / 9100, Fax: 086 558 5433, Email: melanym@foundation.co.za

Lifelong Learning

Ethics

Ethical Aspects of Withdrawing or Withholding Treatment

Should health care practitioners (HCPs) preserve all lives, at all cost and for as long as possible? This view is attractive to many theologians and arm-chair philosophers who proclaim the sanctity of life. There is comfort and security for HCPs holding this view as it removes the responsibility for making some very difficult decisions and leaves all in the hands of a "Higher Being". There is no need to consider others in the decision, costs or the quality of life under review.

Most bioethicists reject this absolutist premise. The duty of care is not an absolute duty to preserve life by all means. There is no obligation to provide life sustaining treatment if:

a) Its use is inconsistent with the aims and objectives of an appropriate treatment plan, and

b) The benefits of that treatment no longer outweigh the burdens to the patient.

Is the Equivalence Thesis valid?

Before going much further, we need to consider whether withholding treatment (that is, never starting) is ethically the same or different from withdrawing treatment. As predictable, there are two schools of thought.

The dominant opinion currently favours the Equivalence Thesis. This states that: If it would have been morally permissible to have withheld a therapy (that has in fact already been started), then it is now morally permissible to withdraw that therapy and If, in the future, it would be morally permissible to withdraw a therapy (that has in fact not yet been started), then it is now morally permissible to withhold that therapy. While the ethics gurus have mostly pronounced that there is no moral difference between withholding and withdrawing, most clinicians do not concur. A Non-Equivalence corollary might sound like this: All things being equal, it would at least sometimes be ethical to withhold critical treatment from a patient whereas it might not be ethical to withdraw the same treatment if already started.

People who oppose the Equivalence Thesis use a number of arguments to justify their position. One theory holds that a person who acquires a holding in accordance with the principle of justice in acquisition is entitled to that holding. (Nozick's Principle of Original Acquisition of Holdings).

This certainly fits with the way many or even most clinicians think[1]. An example of this could be constructed using the following scenario:

There is one last bed in ICU and two requests for that single bed. Both patients will likely die if not given the bed. The one patient is Jack, who is 25 years of age and has a predicted intact survival with ICU of 70%. The other is Harry, 65 years of age and he has a predicted intact survival of 30%. Dr Sensible, the ICU consultant, opts for Jack based on distributive justice and utilitarian principles. By doing so, he effectively withholds treatment from Harry.

However, prior to the admission to ICU, the family of Jack decide to transfer him to a facility in another city, closer to home and thus Harry gets the bed. Harry has a stormy course but is hanging in there on a ventilator and his prognosis for intact survival is still about 30%.

Enter another patient, Tertius. He is young, with a good prognosis (70%), and needs ICU to survive. The ICU registrar, Dr Uppity, argues that if withholding and withdrawing are ethically equivalent then Harry should be removed from the ICU bed and palliated and Tertius should get the bed. Understandably Dr Sensible overrides this.

What an unmanageable situation would exist if ICUs were managed by withdrawing treatment from a patient when someone with a better prognosis came along! In this scenario, using Nozick's Principle, Harry is entitled to hold on to the bed that he originally and justly acquired.

Best interest standard

Adults who have the capacity to make their own rational decisions are judged as ideally positioned to assess their own best interests and they are protected under the law and ethically from treatment that will inappropriately prolong their lives. In fact, in SA, treatment of such persons against their will or without their consent would legally constitute assault. The physician does however have an advocacy and oversight responsibility to assess the patient's understanding of the

About the author

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 the University of the Witwatersrand. He has been an academic paediatrian in Johannesburg for about 30 years.*
He worked in private paediatric practice between 1989-1998.

medical condition. Is the patient's decision to decline treatment a decision that many or most rational people might make under the circumstances; or is their decision something that few or no rational persons might make? If the latter, then is their decision evidence of an acute lack of capacity?

Capacity (or in old terminology competence) should not be simply assumed. It is best assessed by a third party and this function is often delegated to a psychiatrist. There are many factors that may affect competence. Besides obvious elements such as intellectual capacity, education and knowledge, factors such as fear, depression or substance abuse may acutely impair capacity.

Persistent vegetative state (PVS)

Many of the widely publicised cases involving withdrawal of treatment involve patients in a PVS. A vegetative state is defined[2] as a clinical condition of complete unawareness of the self and the environment, accompanied by sleep-wake cycles, with either complete or partial preservation of hypothalamic and brain-stem autonomic functions. In addition, patients in a vegetative state show no evidence of sustained, reproducible, purposeful, or voluntary behavioural responses to visual, auditory, tactile, or noxious stimuli; show no evidence of language comprehension or expression; have bowel and bladder incontinence; and have variably preserved cranial-nerve and spinal reflexes.

The *persistence* of such a state should be for at least one month to satisfy the definition. In various cases, both surrogates and care-givers have applied to the courts for legal authority to continue or withdraw life-supporting or life-sustaining treatments for patients with PVS. Usually the arguments have invoked 'death with dignity', 'patient's best interests', 'conditions worse than death' and/or 'futility'.

Although a patient in PVS is apparently beyond personal concern for dignity, it goes without saying that those who love and care for them should uphold their dignity during life and as death nears and this should not be used as a reason for shortening the process.

The best interests of the patient standards can also not logically be applied to someone who in the nature of the condition can have no interests, best or worse.

It is not ethically acceptable that a patient, especially one with an apparently futile prognosis, be left to suffer severe pain or discomfort: but these situations can be managed. Consensus on what constitutes futility has not been reached but in each case there should be general medical consensus on futility of further management by a medical team.

Of course, loving family members, especially those with fervent religious beliefs, would hope and pray for a miracle cure. In an increasing secular society, it is unacceptable that such beliefs should be pervasive with regard to withdrawing treatment. As Savulescu has stated[3]; the elephant in intensive care is distributive justice. He recognises the convenient fiction we use when we tell patients and surrogates that treatment is not in their interests because we can't face up to the elephant of distributive justice and the inevitable limitations of our medical resources.

Children

Children are not supposed to die. The Royal College of Paediatrics and Child Health has produced a booklet governing the choices for withdrawing or withholding treatment in children[4]. This is a comprehensive and useful document. It suggests five situations where withdrawal or withholding treatment may be pertinent. These are:

- The brain dead child
- The permanent vegetative state
- The 'no chance situation'
- The 'no purpose situation'
- The 'unbearable situation'.

The authors emphasise that where uncertainty exists then the care-givers should always safeguard the life. Decisions should not be rushed and the most senior opinions obtained. There should always be attention to palliation and terminal care needs which includes symptom alleviation and care, and which maintains human dignity and comfort.

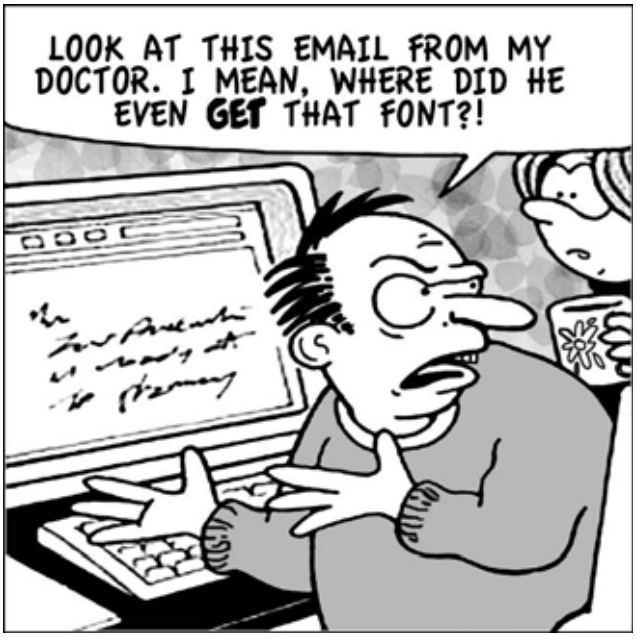
References

1 *Wilkinson D & Savulescu J. A costly separation between withdrawing and withholding treatment in intensive care. Bioethics; ISSN 5 JUL 2012, DOI: 10.1111/j.1467-8519 .2012.01981.x*

2. *The Multi-Society Task Force on PVS. NEJM 1994; 330:1499-1508*

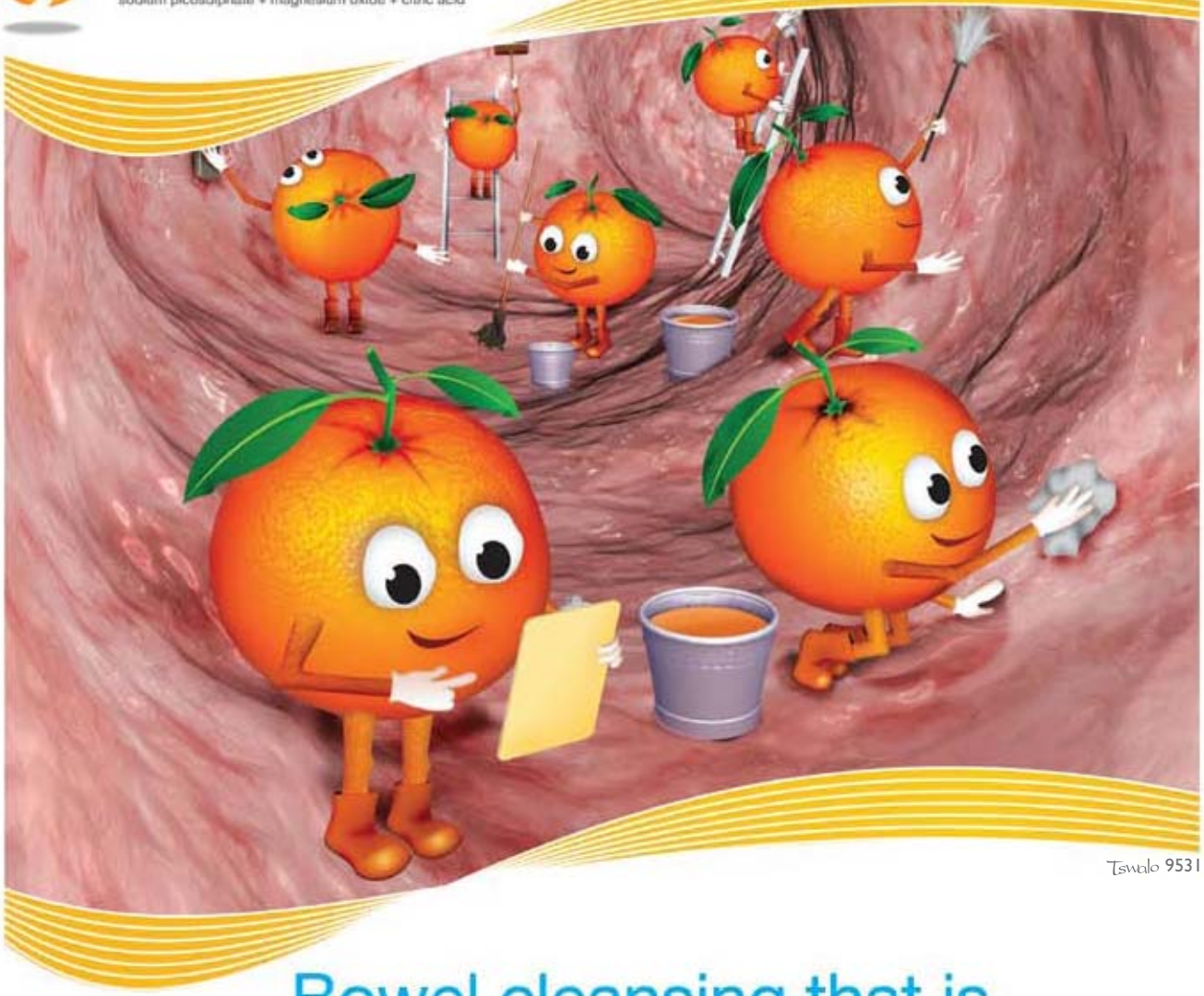
3. *Savulescu J. Just dying: the futility of futility. J Med Ethics doi:10.1136/medethics-2012-10068*

4. *Royal College of Paediatrics and Child Health. Withholding or withdrawing life sustaining treatment in children: A framework for practice. 2nd Edition 2004. ISBN 1 900954 96 6*



PICOLAX®

sodium picosulphate + magnesium oxide + citric acid



Tswalo 9531

Bowel cleansing that is easy to take[1]

- PICO**LAX**'s dual action ensures effective bowel cleansing [2]
- Pleasant orange taste [1,4]
- Low volume of medicine to drink [1,2]
- Low incidence of nausea and vomiting [2,3]
- Can be administered to children above the age of 2 years [4]
- Contains no aspartame [4]

REFERENCES: 1. Hookey LC and Vanner SJ. Pico-Salax Plus Two-Day Bisacodyl is Superior to Pico-Salax Alone or Oral Sodium Phosphate for Colon Cleansing Before Colonoscopy. Am J of Gastroenterol 2009;104:703-709. 2. Regev A et al. Comparison of Two Bowel Preparations for Colonoscopy: Sodium Picosulphate With Magnesium Citrate Versus Sulphate-Free Polyethylene Glycol Lavage Solution. Am J Gastroenterol 1998;93(9):1478-1482. 3. Renaut AJ et al. A randomized controlled trial comparing the efficacy and acceptability of phospo-soda buffered saline (Fleet®) with sodium picosulphate/magnesium citrate (Picoprep®) in the preparation of patients for colonoscopy. The Association of coloproctology of Great Britain & Ireland, Colorectal Disease 2007;10:503-505. 4. South African Registered Package Insert for Picolax dated 02/03/2012.

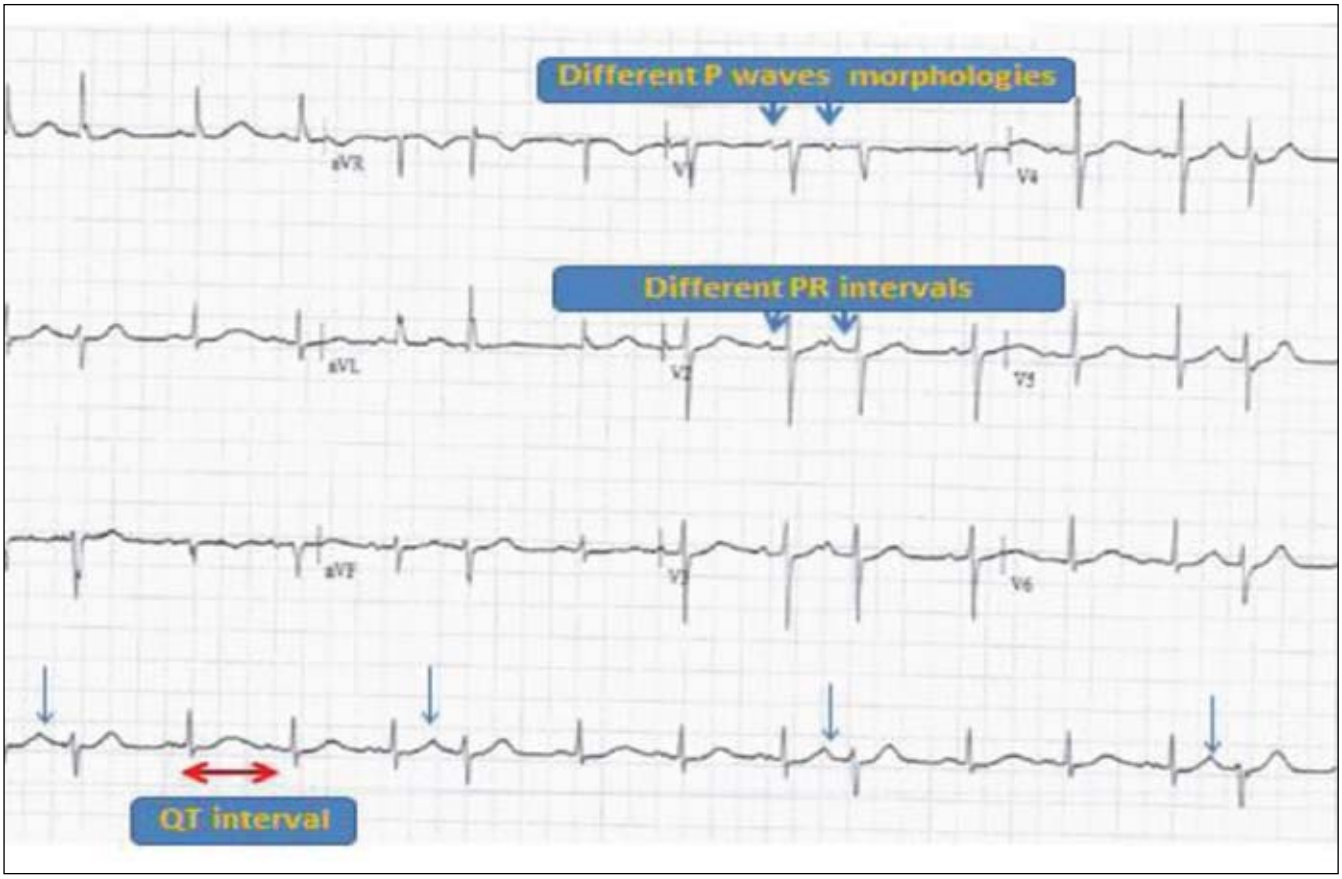
S3 PICOLAX® Powder for oral solution. Each sachet contains the following active ingredients: Sodium picosulphate 10,0 mg, Magnesium oxide, light 3,5 g and Citric acid anhydrous 12,0 g. Reg. No. A39/11.5/0058. Full prescribing information as registered by the MCC can be requested from your Ferring representative.

FERRING PHARMACEUTICALS

NAME AND BUSINESS ADDRESS
FERRING (Pty) Ltd. Route 21 Corporate Park, 6 Regency Drive, Irene Ext 30. Pretoria, South Africa. Tel: +27 12 345-6358/9 Fax: +27 12 345-1156. 2013/007

ECG Challenge: Test Your Interpretive Skills

Dr ZB Vezi, Cardiac Electrophysiologist, Inkosi Albert Luthuli Central Hospital and eThekwini Hospital



ECG 1: 12 lead ECG showing sinus rhythm with 4 premature atrial complexes (PACs). Every 4th beat is a PAC giving an appearance of the irregular rhythm. The PACs get into the AV node during the relative refractory period, thus a relatively prolonged PR interval. The QT interval is well beyond the halfway point between R-R interval suggestive of the prolonged corrected QT interval (QTc).

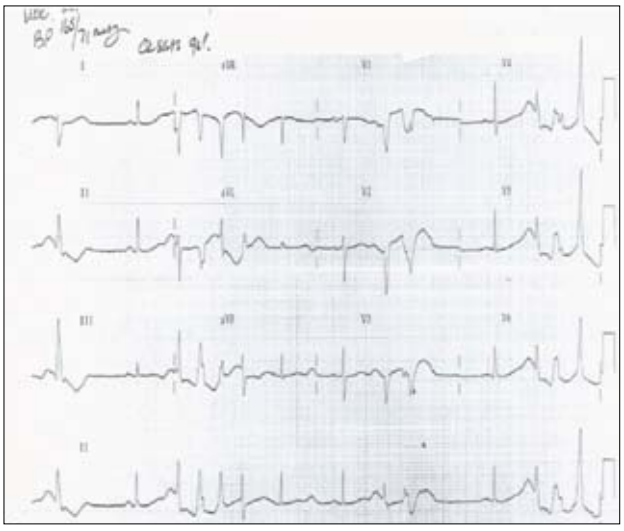
A 36 year old male experienced sudden onset fast palpitations followed by shortness of breath and pre-syncope while he was driving. He sustained a minor accident and later consulted his family physician. It turned out that he had experienced a similar event while riding a bicycle a few months earlier. He didn't have any traditional risk factors for coronary artery disease. His sister, then aged 23 years, died suddenly while swimming; presumable from a heart attack. The physical examination was uneventful. He was immediately referred to a cardiologist for further investigations.

Statements for consideration (true or false):

1. Patient has atrial fibrillation as the R-R interval is irregular.
2. The QRS morphologies differ due to the premature ventricular complexes (PVCs).
3. Patient has had previous myocardial infarction as evidenced by Q waves in LIII.
4. There is evidence of acute myocardial ischaemia and patient requires urgent coronary angiography.
5. There is a great need to carefully select any medication(s), prescribed or over the counter, due to the ECG abnormality noted.

Earn a CPD point

Fill in the answers on the CPD answer sheet at the back of this issue.



ECG 2: 12 lead ECG showing frequent non-sustained polymorphic (different QRS morphologies) ventricular tachycardia (NS-PMVT). The initiation of the NS-PMVT is with the premature ventricular complex (PVC) which occurs during T wave of the preceding beat. This is an example of the R-on-T phenomenon which can give rise to ventricular tachycardia.

Discussion and Diagnosis

1. History and assessment

This patient has a sinister sounding story and the diagnosis is unclear from the history alone. It was correct to immediately refer him for further investigations.

From the history of fast palpitations, one has to assume the diagnosis of tachyarrhythmia; either supraventricular tachycardia (SVT) or ventricular tachycardia. From the history alone, there is no way one can differentiate the SVT from VT. The presence or absence of (pre)-syncope does not make one diagnosis more likely.

We cannot ignore the grave family history. One has to carefully consider tachyarrhythmias that are familial, eg, hypertrophic cardiomyopathy (HCM), long QT syndrome (LQTS), short QT syndrome, Brugada syndrome, arrhythmogenic right ventricular cardiomyopathy (ARVC), etc.

2. ECG analysis

In ECG 1 we see the patient is in sinus rhythm (ie, P waves are positive in LII and negative in aVR). However, there may be left atrial enlargement as evidenced by bi-phasic P waves in V1 (normally only-positive or has terminal small negativity) and bifid in LII.

Every fourth P wave is a premature/ectopic atrial complex beat (PAC) occurring earlier than expected and of different morphology. In LII, the PACs may be difficult to appreciate but one notices different T-wave morphologies indicative of PAC "buried" within T waves. These PACs create irregular R-R intervals. Due to these PACs, the AVN and the bundle branches receive depolarisation during the relatively refractory period, hence the prolonged PR intervals with slightly different QRS morphologies. This is a normal phenomenon.

There is a slight ST depression in V2-6, however the ST is up-sloping (rather than horizontal or down-sloping) therefore, not indicative of pathological ischaemia. The LIII shows isolated Q wave and this is not abnormal. The QT interval is prolonged. This can be immediately appreciated by the fact that the end of previous T wave is closer to the next P wave, ie, on the other side of the half-way point between R-R intervals. Please note not to assess QT interval after the QRS post PAC.

The next ECG (ECG 2) confirms the presence of non-sustained ventricular tachycardia (NS-VT) which is the most likely cause of his symptoms. His sister most likely died of VT which is known to be triggered by swimming as well as exercise, especially competitive exercise.

3. Diagnosis

Long QT syndrome (LQTS)

4. Management

The patient needs full evaluation - preferably as an inpatient in a monitored bed - to exclude reversible causes of LQTS, ie, drugs (like macrolide antibiotics, tricyclic antidepressants, anti-arrhythmics like sotalol), cardiac ischaemia, heart failure, etc.

The management options will include β-blockers, implantable cardioverter defibrillator (ICD) and left cervical sympathectomy. All these options need to be carefully discussed with the patient (and family) so that he may make an informed decision.

His family and first degree relatives will have to be assessed for "sub-clinical" LQTS.

Lifelong Learning

NMDA Receptors and Central Sensitisation in Acute and Chronic Pain

As we discovered in the previous article (*Modern Medicine*, May 2013), N-methyl-D-Aspartate (NMDA) receptors are important in mediating central sensitisation - as well as peripheral sensitisation - in the dorsal horn of the spinal cord and in the brain. Central sensitisation is an increase in excitability of spinal neurons in the dorsal horn. This facilitates pain impulse processing.

Central sensitisation: Activity dependent

Central sensitisation is **activity dependent**. In acute pain such as postoperative pain - especially when the condition is inadequately managed - the persistent exposure (afferent barrage) to nociceptive input from peripheral neurons in the injury site causes postoperative hypersensitivity. This can be:

- **Primary hyper-analgesia:** at the site of the injury, or
- **Secondary hyper-analgesia:** recruitment of fibres in surrounding, non-injured tissue.

In chronic pain these changes can become permanent, making chronic pain resistant to normal analgesics and requiring other agents to resolve the pain.

Role of NMDA and NMDA receptors in central sensitisation

The identification of the NMDA receptors in the late 1980s has been a relatively new addition to the understanding and treatment of pain, especially chronic pain. Initially it was discovered that NMDA receptor antagonists inhibited the hyper-excitability of spinal cord neurons induced by C-fibre stimulation. This led to the conclusion that activation of NMDA receptors after tissue injury and inflammation enables facilitated processing in the spinal cord. Subsequently it was discovered that NMDA receptors occur not only in the spinal cord but also in the periphery and supra-spinally.

Research tool

The question often asked is: 'If there are NMDA receptors in the body, then where does NMDA naturally or physiologically occur in the body?' The answer is: 'Nowhere.' It is merely a synthetic substance used solely in research to identify different types of receptors. The truth is that the NMDA receptor is, physiologically, a glutamate receptor (Figure 1).

Glutamate is an excitatory receptor in the nervous system that exerts its pre- and post-synaptic effects via a large and diverse group of transmembrane receptors. Activation of the glutamate receptors can have one of two possible effects depending on the receptor's effect:

- **Metabotropic**: effect on the metabolism of the cell, or
- **Ionotropic:** effect on ion shifts across the membrane and action potentials.

The NMDA receptors are Ionotropic receptors (Figure 1).

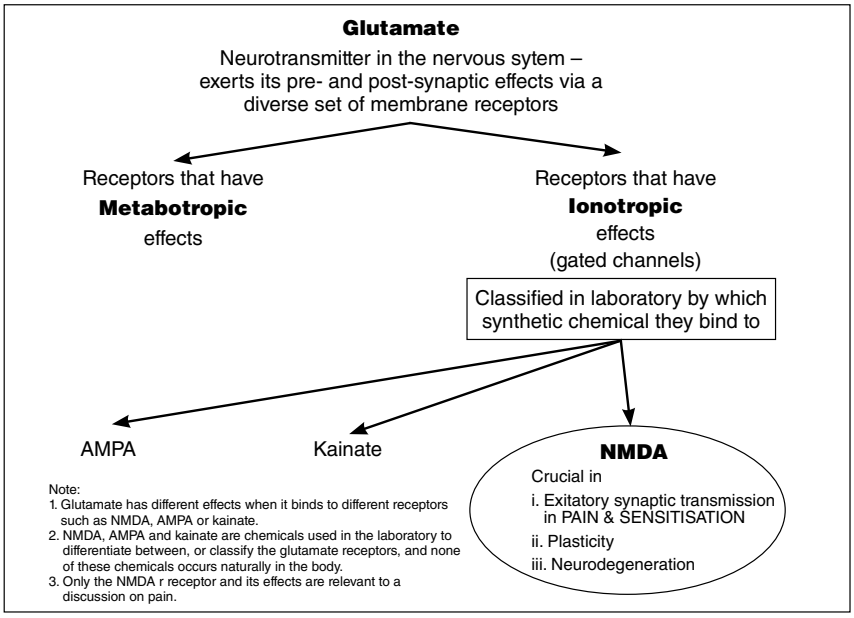


Figure 1: Glutamate receptors and the role of the NMDA receptor

About the author

Dr Russell Raath *MbChB, M Med. (Anaes.), FIPP is an anaesthesiologist and chronic pain interventionalist in private practice at Jakaranda Hospital, Pretoria.*

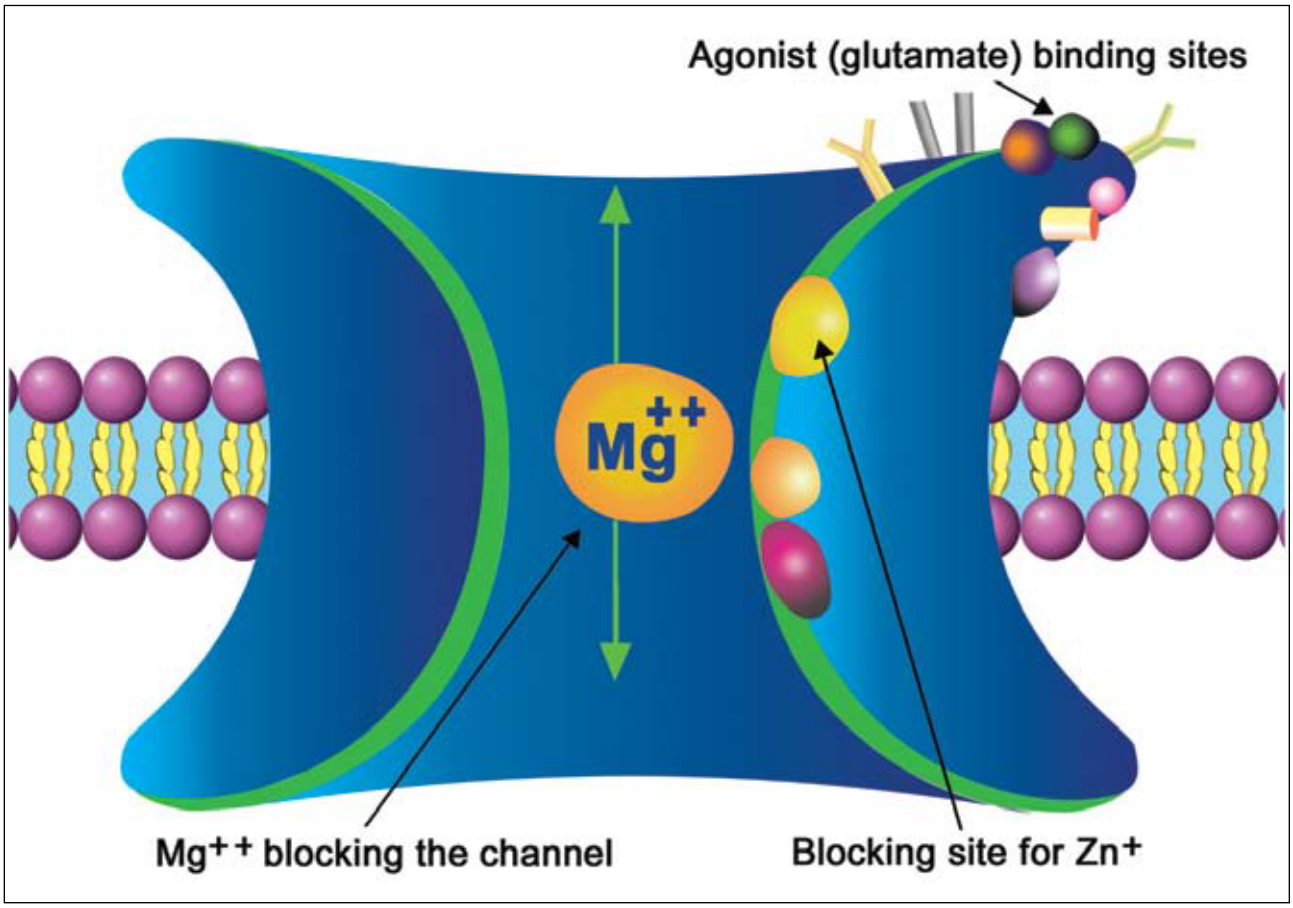


Figure 2: How magnesium and zinc prevent and reverse central sensitisation.

The NMDA receptor is a trans-membrane calcium (Ca^{++}) channel (Figure 2). This channel can be blocked by certain substances. It is physiologically blocked by magnesium (Mg^{++}) as well as zinc (Zn^{+}). For this reason both these substances play a big role in preventing and reversing central sensitisation.

Action of NMDA receptors: How they increase pain sensitisation and diminish opiate effectiveness

In figure 3 we see that:

1. NMDA receptors occur both pre-synaptically AND post synaptically. (Especially on C-fibres in the dorsal horn of spinal cord.)
2. When a nerve impulse reaches the pre-synaptic membrane of a C-fibre pain fibre, glutamate is released from the vesicle in the pre-synaptic membrane. Some of it 'doubles back' to stimulate the pre-synaptic NMDA receptors (blue arrow). This sensitises the pre-synaptic membrane and facilitates the release of increased glutamate when the next nerve impulse arrives. This positive feedback loop is one mechanism whereby NMDA receptors sensitise the transmission of pain.
3. When the released glutamate binds with the post-synaptic NMDA receptor it opens the channel and Ca++ flows through, depolarising the post-synaptic membrane and thus propagating the impulse.
4. However, while the calcium is in the cell, it does two other very important things:
   a. It doubles back on the NMDA receptors and removes the Mg^{++} block from other surrounding NMDA receptors, sensitising the post-synaptic membrane to the next impulse (orange arrows).
   b. It raises the proteinkinase-C in the cell which then doubles back on the membrane and decreases the sensitivity to opiates of the opiate receptors (green arrows). These two effects mean that the C-fibre is more sensitised to pain impulses and at the same time 'resistant' to the effects of opiates.

An excess of excitatory pathway activation via NMDA receptors has been observed in neuropathic pain that responds poorly to morphine.[1]

Overcoming the problem with NMDA blockers

The central sensitisation can be prevented or reversed to an extent by the use of NMDA receptor blockers. **These agents are NOT analgesics but are used to block the NMDA receptors so that traditional analgesics become effective again. In other words they raise the pain threshold of the patient's nervous system.**

Sometimes though, the use of magnesium on its own in high enough doses is

3-WAY ACTION
FOR • PAIN • RELIEF

• ibuprofen 200 mg • codeine phosphate 10 mg • PARACETAMOL 350 mg

MYBULEN® & MYBUCOD® TABLETS

- analgesic
- anti-pyretic
- anti-inflammatory

STILL • THE • STORMS • OF • PAIN

S3 Mybucod® Tablets. Reg. No.: 36/2.8/0379. Each tablet contains ibuprofen 200 mg, paracetamol 350 mg and codeine phosphate 10 mg. S3 Mybulen® Tablets. Reg. No.: 30/2.8/0138. Each tablet contains ibuprofen 200 mg, paracetamol 350 mg and codeine phosphate 10 mg. S3 Mybulen® Capsules. Reg. No.: A38/2.8/0527. Each capsule contains ibuprofen 200 mg, paracetamol 250 mg and codeine phosphate 10 mg. S3 Mybulen® Suspension. Reg. No.: A39/2.8/0237. Each 10 ml contains ibuprofen 200 mg, paracetamol 250 mg and codeine phosphate 10 mg. Preservative: Sodium benzoate 0,1 % m/v.
For full prescribing information please refer to the package inserts approved by the medicines regulatory authority.
Applicant: Pharmacare Limited Co. Reg. No. 1898/000252/06, Building 12, Healthcare Park, Woodlands Drive, Woodmead, 2191. A16056 03/13 124098MH

Healthcare. We Care.

aspen PHARMACARE

Marketed by Aspen Pharmacare
www.aspenpharma.com
Medical Hotline 0800 118 088

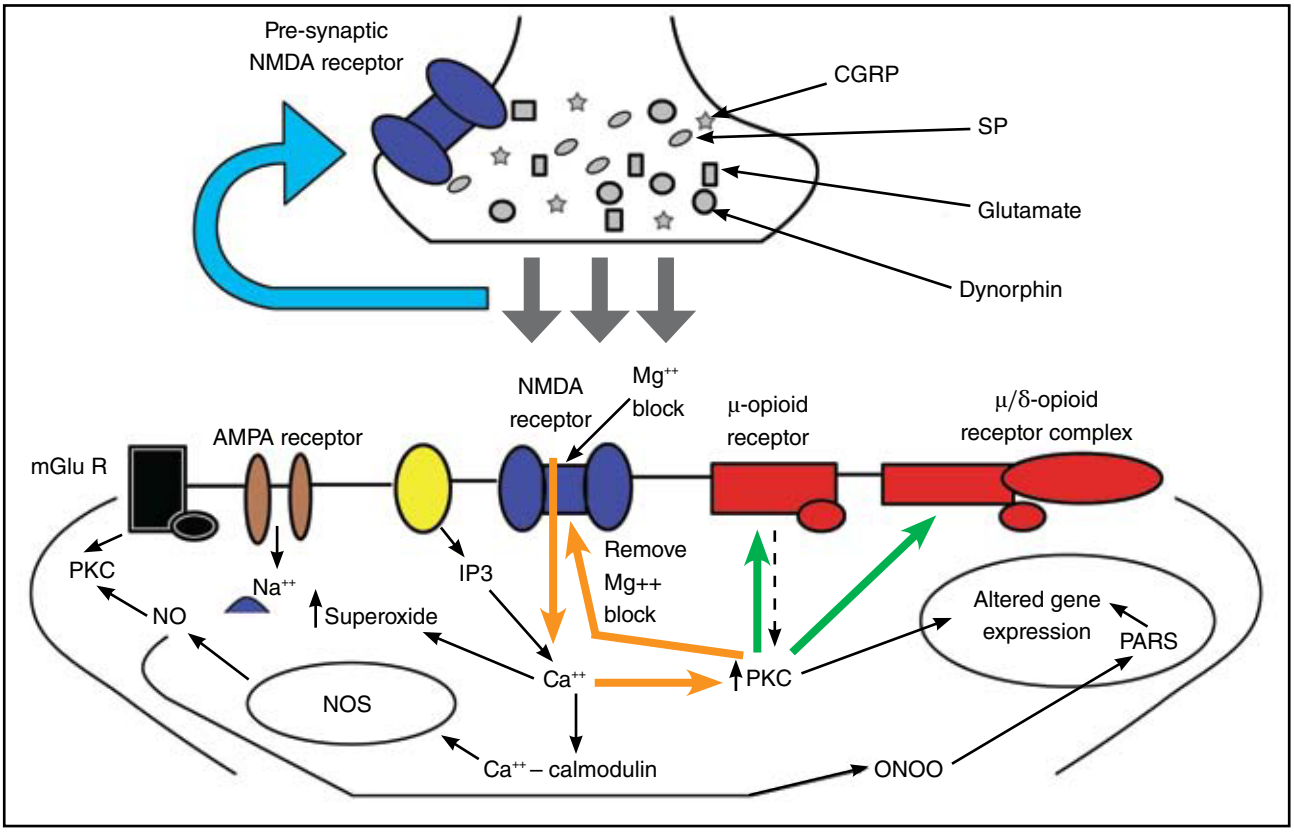


Figure 3: NMDA receptors in the dorsal horn cells of the spinal cord.

enough to be a reasonable analgesic. None of these agents are specifically NMDA channel blockers but have this effect as a side effect. So, we use a drug's **side effect** to our advantage. But we must always bear in mind the **originally intended effect** of the drug - which in this case could be seen as a 'side effect' in patients when used to block the NMDA receptors.

Treatment agents

The treatment of both intense and prolonged acute pain as well as chronic pain should always include an NMDA receptor blocker in the regimen to prevent or reverse central sensitisation. Here are some effective agents:

1. **Magnesium**: Our modern lifestyle and poor soil mean most people have low total body magnesium. As magnesium is an intracellular ion, the plasma levels can remain constant until the cellular magnesium is depleted. Large doses of magnesium are not well absorbed from the gut and can cause diarrhea. Chelated magnesium, that is magnesium bound to amino acids, is the best absorbed of all oral magensium supplements. Intravenous magnesium or trans-dermal magnesium are more efficient ways of restoring magnesium levels. Magnesium has been shown to prevent or reverse tolerance to opiates via its effect on the NMDA receptors.
2. **Zinc**: The NMDA receptor has a binding site for zinc - an antagonist of glutamate. Magnesium and zinc should be supplemented together and there are products on the market that contain both in meaningful amounts.
3. **Memantine** (Alzheimer's drug) and **amantidine** (Parkinson's drug) are also strong blockers of the NMDA receptors.
4. **Dextromethorphan**: There are two cough syrups available in SA that contain **only** dextromethorphan. Giving this along with opiates or any analgesic improves the analgesic effect and could prevent chronic pain and raise the pain threshold.
5. **Ketamine** is probably the most potent NMDA receptor blocker. It should only be administered in a hospital setting by those experienced or trained to do so – in a pain clinic and preferably by anesthesiologists.
6. Ketamine is also administered in low doses by patient-controlled analgesia pumps for post-operative pain as it exerts some of its anaesthetic action via the NMDA receptors as well as being a potent analgesic due to its effects on the NMDA receptors.
7. **Dextro-methadone** is an opiate which also has potent NMDA blocking effects. It is ideal for short-term use to block or reverse sensitisation and to break the pain cycle.
8. **Nitrous oxide (N2O) gas** is a potent NMDA blocker whose effect lasts long after the gas is withdrawn. It too should be administered by a pain clinic or anaesthesiologist.

References

1. *Magnesium increases morphine analgesic effect in different experimental models of pain. Begon S, Pickering G, Eschalier A, Dubray C. Anesthesiology 2002 Mar;96(3):627-32.*
2. *Other references available on request from the author: rpr@mweb.co.za.*

VIMOVO® offers a simple EFFECTIVE pain solution[1]

Sequential delivery of NSAID and PPI[1]

- **Pain reduction** – First arthritis therapy to provide sequential delivery of immediate-release esomeprazole followed by enteric-coated naproxen, in a single convenient tablet[1]
- **PPI gastric protection** – Reducing the risk of NSAID-associated upper GI ulceration[1]

Vimovo® is indicated for the symptomatic relief in the treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis, in patients needing proton-pump inhibitors to reduce the risk of developing non-steroidal anti-inflammatory drugs (NSAIDs) associated gastric and /or duodenal ulcers.[2]

VIMOVO® 500/20 mg	ADMINISTRATION
Adult dose: 1 tablet twice daily[2]	• Swallow tablets whole with water; do not split, chew or crush tablets[2] • ***Take VIMOVO® tablets at least 30 minutes before food[2]*** • Consider dose reduction in patients with mild to moderate renal or hepatic impairment. Do not use in patients with severe renal or hepatic impairment[2] • Use the lowest effective dose for the shortest possible duration[3]

Vimovo®
naproxen/esomeprazole magnesium

References: 1. Wang-Smith L, Fort J, Zhang Y, *et al*. Pharmacokinetics and relative bioavailability of a fixed-dose combination of enteric-coated naproxen and non-enteric-coated esomeprazole magnesium. *J Clin Pharmacol* 2012;52(5):670-680. 2. Vimovo® 500/ 20 mg tablets package insert. April 2013. 3. Dhillon S. Naproxen/ esomeprazole fixed-dose combination for the treatment of arthritis symptoms and to reduce the risk of gastric ulcers. *Drugs Aging* 2011;28(3):237-248.

AstraZeneca

CRRT

The Randomized Evaluation of Normal versus Augmented Level (RENAL) Replacement Therapy Study

Title: Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients

Authors: Bellomo R, Cass A, Cole L, *et al* (The RENAL Replacement Therapy Study Investigators)

Journal: *The New England Journal of Medicine* 2009; **361**:1627-1638.

A clinical summary - all information contained in this document are derived from the article

adcock ingram

Background

- Acute kidney injury (AKI) is associated with substantial morbidity and mortality
- It is a common finding among patients in the intensive care unit (ICU) and is an independent predictor of mortality
- Acute kidney injury severe enough to result in the use of renal-replacement therapy affects approximately 5 % of patients admitted to the ICU and is associated with a mortality rate of 60 %
- The optimal approach to renal replacement therapy, as well as the optimal intensity and timing of such therapy, in critically ill patients remains unclear

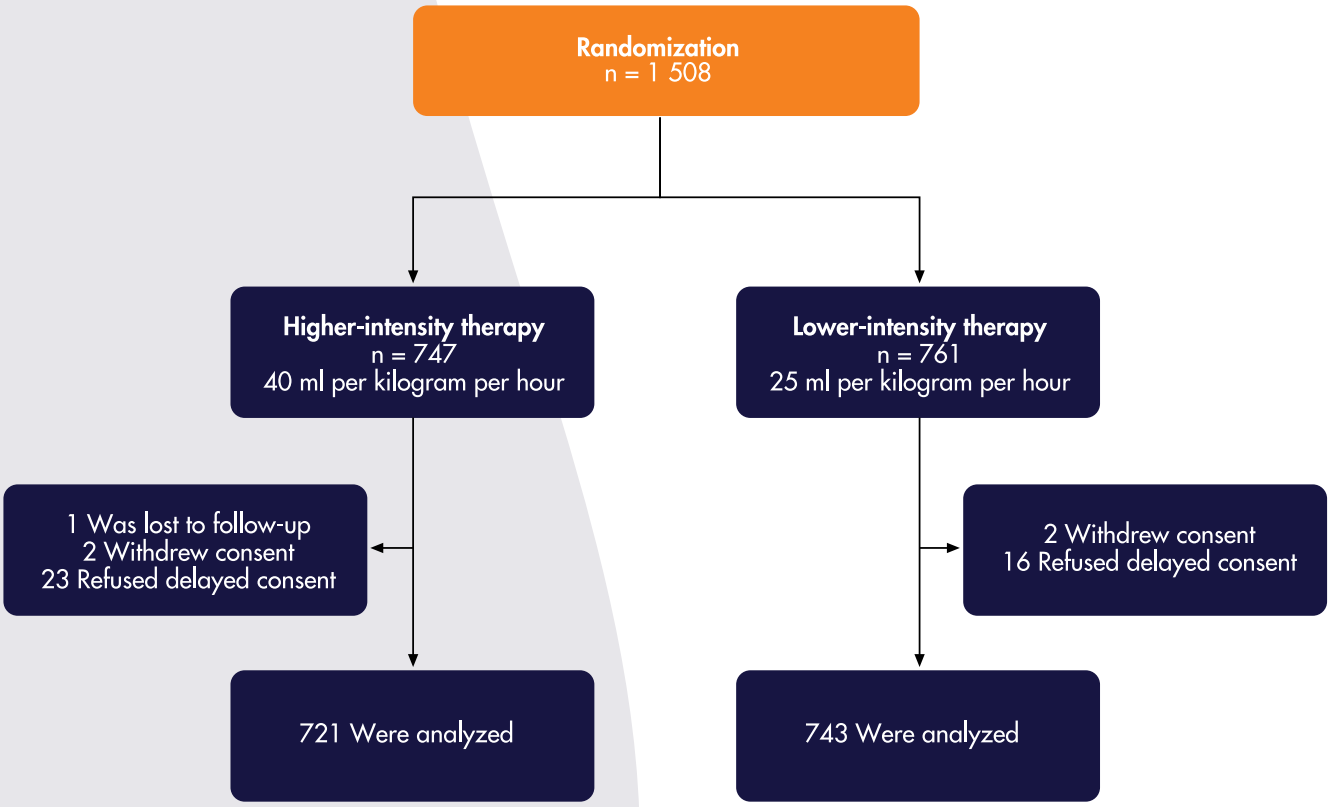
Objective

- Designed to compare the effect of continuous renal replacement therapy (CRRT) at two different levels of dose on 90-day mortality among critically ill AKI patients

Study methods

- Multicenter, prospective, randomized clinical trial
- 1 508 critically ill AKI patients at 35 ICUs in Australia and New Zealand

RENAL Study: Numbers of Patients Randomized in the Study



- 100 % of patients were initiated on CRRT, with exclusive use of continuous venovenous haemodiafiltration (CVVHDF)

RENAL Study: CRRT Initiation Criteria for AKI patients

	Acute Kidney Injury (AKI) Clinical Markers			Other Critical Markers		
	Serum Creatinine	Urine Output	BUN	Serum Potassium	Volume Overload (with AKI)	pH
RENAL Initiation Criteria for CRRT[1]	> 3.4 mg/dl	< 100 ml/6 hr	> 70 mg/dl	> 6.5 mmol/l	Clinically significant organ edema	< 7.2

- Filters with the AN69 membrane (Gambro) were used
- Hemosol BO fluid (Gambro) was used as the dialysate and replacement fluid

Study Outcomes

- The primary study outcome was death from any cause within 90 days after randomization
- Secondary and tertiary outcomes included death within 28 days after randomization, death in the ICU, in-hospital death, cessation of renal-replacement therapy, duration of ICU and hospital stays, duration of mechanical ventilation and renal-replacement therapy, dialysis status at day 90, and any new organ failures

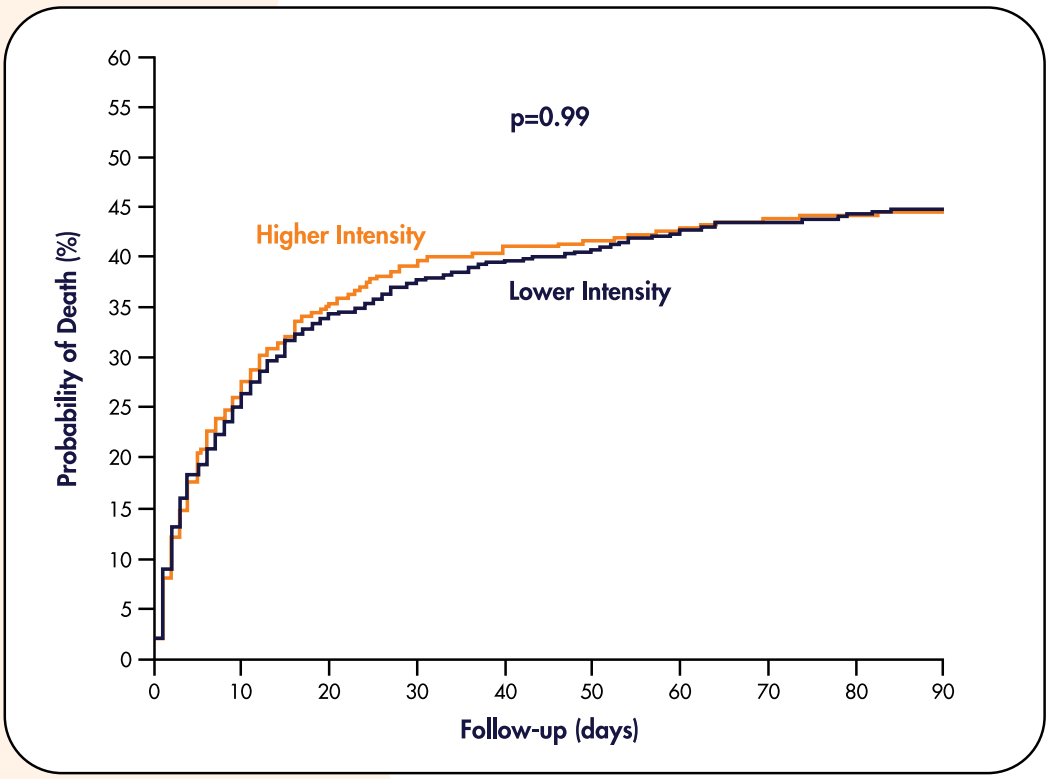
CRRT

Results

Primary Outcome

- Within 90 days after randomization, death occurred in 322 (44.7 %) of 721 patients in the higher-intensity group and in 332 (44.7 %) of 743 patients in the lower-intensity group (p = 0.99)

RENAL Study: Kaplan-Meier Estimates of the Probability of Death



- Mortality was also similar between the two treatment groups in all prespecified subgroups

Secondary and Tertiary Outcomes

- There were no significant differences between the groups in any of the secondary or tertiary outcomes
- At 28 days after randomization, 64 patients (14.5 % of survivors) in the higher-intensity group and 57 patients (12.2 % of survivors) in the lower-intensity group were still receiving renal replacement therapy
- At 90 days, these numbers had dropped to 27 patients (6.8 % of survivors) and 18 patients (4.4 % of survivors), respectively (p = 0.14)
- Oliguria (urinary excretion, <400 ml per day) was present in 59.7 % of patients at randomization

Conclusion

In critically ill patients with AKI, treatment with higher-intensity continuous renal-replacement therapy did not reduce mortality at 90 days

Reference: 1. Bellomo R, Cass A, Cole L, *et al.* (The RENAL Replacement Therapy Study Investigators). Intensity of Continuous Renal-Replacement Therapy in Critically ill Patients. *The New England Journal of Medicine* 2009; **361**:1627-1638.

Adcock Ingram Healthcare (Pty) Ltd. Reg. No. 2007/019928/07
Private Bag X69, Bryanston, 2021, South Africa
Telephone + 27 11 635 0000
www.adcock.com
ZA.13.REN.003 07/2013.

adcock ingram

S3 accord metformin

metformin hydrochloride

- Accord Metformin is a biguanide oral anti-hyperglycaemic agent which acts by increasing peripheral glucose utilization through increasing insulin sensitivity and decreasing hepatic and renal gluconeogenesis.[1]
- Accord Metformin is indicated for type 2 (non-insulin dependent) diabetes mellitus when diet has failed and especially if the patient is overweight.[1]

Get the balance right

accord healthcare

Accord Healthcare (Pty) Ltd
Building 5, Tuscany Office Park, 6 Coombe Place,
Rivonia, Gauteng, SOUTH AFRICA. Tel: +27 11 234 5701 Fax: +26 11 234 5700
Postnet Suite 182, Private Bag X51, Rivonia 2128, medinfo@accordhealth.co.za

S3 Accord Metformin 500 Reg. No.: 41/21.2/0639. Each tablet contains 500mg Metformin Hydrochloride.
S3 Accord Metformin 850 Reg. No.: 41/21.2/0640. Each tablet contains 850mg Metformin Hydrochloride.
Applicant: Accord Healthcare (Pty) Ltd; email: medinfo@accordhealth.co.za
Reference 1. Package insert - Accord Metformin.

www.accord-healthcare.co.za

Lifelong Learning

The Practical Value of the Metabolic Syndrome

The presence of the metabolic syndrome can be a useful tool to help practitioners identify patients at higher risk for cardiovascular disease and type 2 diabetes. To help reduce such risks, patients with the metabolic syndrome should be targeted with interventions following a multifaceted approach.

Vascular inflammation, hyperglycaemia, elevated blood pressure and dyslipidaemia are all known to be risk factors for cardiovascular disease and type 2 diabetes. That the same risk factors underlie both diseases suggests they share a common pathophysiological pathway: obesity. In obesity (especially abdominal obesity), increasing levels of free fatty acids drive resistance to insulin action on peripheral glucose utilisation, while inflammatory cytokines produced by abdominal adipocytes cause vascular endothelial dysfunction. This understanding has advanced from a concept of shared pathophysiology to the recognition that the clinical clustering of cardiovascular and metabolic risk factors could be understood as a common clinical entity.[1-3] This clinical clustering has previously been referred to as the 'insulin resistance syndrome', the 'deadly quartet' and 'Syndrome X' (not to be confused with syndrome X whereby symptomatic angina pectoris develops despite normal coronary arteries) but is now widely known as the metabolic syndrome.

This article discusses recent updates to the definition of the metabolic syndrome and its associated risks, while providing a clinical framework for practitioners to use in approaching and managing patients with the metabolic syndrome.

Defining the metabolic syndrome

The metabolic syndrome is made up of individual cardiovascular disease and metabolic risk factors, including:

- Increased waist circumference
- Abnormal fasting blood glucose levels
- Abnormal LDL cholesterol, HDL cholesterol and triglyceride levels
- Elevated blood pressure.

Various historical definitions of the metabolic syndrome have placed emphasis on different individual risk factors. The two most widely used and accepted definitions of the metabolic syndrome in current research and clinical practice are those of the US National Cholesterol Education Program/Adult Treatment Panel (NCEP/ATP) III and the International Diabetes Federation (IDF); (see box).[4,5] The definition preferred by the authors is that of the IDF because it uses central adiposity as the common factor, is practical to apply and offers ethnic-specific reference ranges.

Epidemiology and associated risks

The staggeringly high rates of global overweight and obesity are mirrored in the high prevalence of the metabolic syndrome,[6] with a prevalence up to

About the authors

Dr Namson S Lau *BMed, BMed Sci(Hons), FRACP is an Honorary Fellow at the Metabolism and Obesity Services, Royal Prince Alfred Hospital, Sydney, and an NHMRC Scholar and Doctoral Candidate at the Boden Institute at The University of Sydney;*
Nicholas R Fuller *BA(HMS), MNutrDiet, APD, ESSAM AEP is a Dietitian, Exercise Psychologist and Clinical Trials Research Officer at the Boden Institute at The University of Sydney; and*
Prof Ian D Caterson *AM, MB BS, BSc(Med), PhD, FRACP is the Boden Professor of Human Nutrition, Director of the Boden Institute at The University of Sydney and a former Head of the Metabolism and Obesity Services at Royal Prince Alfred Hospital, Sydney, Australia.*

Key points

- The metabolic syndrome represents a link between abdominal obesity, a clustering of the major individual cardiovascular and metabolic risk factors, and an increased risk of cardiovascular disease and type 2 diabetes.
- Practitioners should regularly screen the metabolic profile of all adult patients; patients who are older and at higher risk should be screened bi-yearly.
- The presence of one cardiovascular risk factor should lead to a careful assessment of the patient for the presence of the other cardiovascular and metabolic risk factors that characterise the metabolic syndrome.
- Patients with the metabolic syndrome should be carefully assessed for related comorbidities.
- Treatment should follow a multidisciplinary approach, addressing the common underlying cause (excess weight) and intensively targeting individual risk factors.
- Successful weight loss and regular physical activity can help reduce the risk of cardiovascular disease and type 2 diabetes in patients with the metabolic syndrome.

NCEP/ATP III and IDF definitions of the metabolic syndrome

The NCEP/ATP III criteria (2001, revised 2005) defines the metabolic syndrome as the presence of any three of the following traits:[4]

- Abdominal obesity (waist circumference*): ≥ 102cm in men; ≥ 88cm in women elevated serum triglyceride levels: ≥ 1.7mmol/L; or if the patient is taking medication for elevated triglyceride levels
- Decreased serum HDL cholesterol level: < 1mmol/L in men; < 1.3mmol/L in women; or if the patient is taking lipid-modifying medications elevated blood pressure: ≥ 130/85mmHg; or if the patient is taking antihypertensive medications
- Elevated fasting plasma glucose levels: ≥ 5.6mmol/L; or if the patient is taking medication for hyperglycaemia.

The IDF definition of the metabolic syndrome includes as its central element ethnicity-specific abdominal obesity (waist circumference*)[5]

- Europid: ≥ 94cm in men; ≥ 80cm in women, with the same for sub-Saharan Africans currently, until more data are available;
- South East Asians, Chinese and Japanese: ≥ 90cm in men; ≥ 80cm in women.

Plus any two of the following:

- Elevated serum triglyceride levels: ≥ 1.7mmol/L; or if the patient is taking medication for elevated triglyceride levels
- Decreased serum HDL cholesterol levels: ≤ 1.03mmol/L in men; ≤ 1.29mmol/L in women; or if the patient is taking lipid-modifying medication
- Elevated blood pressure: systolic blood pressure of ≥ 130mmHg; diastolic blood pressure of ≥ 85mmHg; or if the patient is taking antihypertensive medication
- Elevated fasting plasma glucose levels: ≥ 5.6mmol/L; or a prior diagnosis of type 2 diabetes.

*Waist circumference is assessed by locating the top of the right iliac crest, placing a measuring tape horizontally around the waist at the level of the iliac crest, ensuring the tape is snug and parallel to the ground. Measurements are made at the end of expiration. The wearing of light clothing is acceptable.

ABBREVIATIONS: IDF = International Diabetes Federation; NCEP/ATP III = National Cholesterol Education Program/Adult Treatment Panel III.

22% in a 2007 Australian study.[7] In the USA prevalence is even higher, with over one-third of adults shown to have the metabolic syndrome in the 2009 United States National Health and Nutrition Examination Survey.[8]

Studies have also confirmed an increased risk of cardiovascular disease and type 2 diabetes among patients with the metabolic syndrome compared with patients without the syndrome. The AusDiab study reported an odds ratio of 3.5 to 6.6 for 10-year cardiovascular disease risk, whereas a 2007 review of the Framingham Offspring cohort of 2800 patients showed a relative risk of 1.7 to 1.8 for cardiovascular disease and 2.1 to 3.5 for type 2 diabetes.[7,9] This increased risk for cardiovascular disease and type 2 diabetes has been convincingly demonstrated in a large meta-analysis of 950,000 patients, which showed that the metabolic syndrome was associated with more than a twofold increase in risk for cardiovascular disease and more than one and a half-fold increase in all-cause mortality.[10]

Controversies

Debate continues within parts of the cardiology and endocrine communities as to whether the metabolic syndrome represents anything beyond its constituent cardiovascular and metabolic risk factors and whether it is indeed a 'real' or useful clinical construct. The specific details of the controversy are beyond the scope of this article, but reference articles are available for further reading.[11-13] More useful than rehashing ontological arguments is to acknowledge that experts agree that the clustering of common metabolic risk factors for cardiovascular disease and type 2 diabetes is real, and that the presence of one component of the metabolic syndrome should lead to a clinical assessment of the patient for the other associated risk factors.

Overweight and obesity are common factors in the clinical cluster of the metabolic syndrome and may be a key underlying pathogenic cause of the condition (along with attendant abnormal lipid levels and glucose metabolism). However, although numerous studies and real world clinical experience have shown that most patients who are obese also have the metabolic syndrome, it should be noted that not all people who are overweight or obese necessarily have the condition.

Despite these controversies, the metabolic syndrome continues to be widely used as a research and clinical tool in the field of obesity, cardiovascular disease and type 2 diabetes.

Clinical implications

Screening for the metabolic syndrome

For practitioners, the metabolic syndrome can represent a useful framework to help identify patients in need of early, aggressive and targeted multifactorial interventions that reduce weight, increase physical activity and treat individual cardiovascular and metabolic risk factors. The goal of such interventions is to reduce a patient's long-term risk of developing cardiovascular disease and type 2 diabetes.

Online cardiovascular disease risk calculators

Framingham Heart Study

www.framinghamheartstudy.org/risk/index.html

HeartSCORE: cardiovascular risk assessment and management

www.heartscore.org/Pages/welcome.aspx

During routine patient consultations, practitioners should consider whether patients have had a metabolic profile assessment of weight, waist circumference, blood pressure and measurements of fasting lipid and blood glucose levels.

Current expert guidelines offer a range of screening protocols, such as bi-yearly assessments of body mass index and waist circumference for all overweight adults, and comprehensive health checks for all patients aged 45 years or older every two to five years (including assessment of their metabolic profile).[14] The US Endocrine Society suggests metabolic screening of all adult patients every three years, with more frequent evaluations for individuals at higher risk (eg, patients who are overweight or obese, smokers, of older age or members of at-risk population groups).[16]

At the authors' complex obesity clinic services, the metabolic profile of all obese patients is assessed annually. In the authors' opinion, it is reasonable to assess the full metabolic profile of all overweight and obese adult patients at least bi-yearly.

TABLE 1

Lifestyle management goals and recommendations

Risk factor	Goals and recommendations
Waist circumference abdominal obesity	7% to 10% weight loss from baseline • Low-calorie diet (a reduction of 500kcal to 1000kcal per day)
Physical inactivity	At least 150 minutes per week of moderate intensity exercise • 30 to 60 minutes per day of brisk walking, at least five days per week • Increase levels of incidental activities to over 10,000 steps per day (using a pedometer to measure steps) • Encourage higher levels of exercise
Diet	Reduce intake of saturated fats, trans fat, cholesterol and simple sugars • Reduce total fat intake to below 30% of daily energy intake • Reduce saturated fat intake to below 7% of daily energy intake • Reduce overall trans fat and cholesterol intake
Cigarette smoking	Cessation of smoking • Refer patient to a quitting programme • Refer patient for motivational counselling • Pharmacotherapy

Screening for comorbidities

Patients identified with the metabolic syndrome may benefit from a five- to ten-year cardiovascular risk assessment using one of the validated online cardiovascular disease risk calculators, such as the Framingham Risk Score[17] and the European HeartSCORE.[18]

Physicians treating patients with a moderate-to-high risk of cardiovascular disease (estimated at greater than or equal to 15% risk for a cardiovascular event) should apply a reduced threshold for prescribing medical therapy when targeting the individual cardiovascular and metabolic risk factors.

As well as being an indicator of increased risk for cardiovascular disease and type 2 diabetes, the metabolic syndrome has been associated with a higher risk of developing other disorders, including nonalcoholic steatohepatitis,[20] obstructive sleep apnoea,[21-24] chronic kidney disease (CKD),[25-28] hyperuricaemia, gout [29-31] and polycystic ovary syndrome.[32-35] GPs should consider tailoring the clinical history, examination and investigations of patients with the metabolic syndrome to screen for these associated conditions.

Targeted, multifactorial management

As described in the 2005 US National Heart, Lung, Brain Institute guidelines for the diagnosis and management of the metabolic syndrome, the two major clinical goals in the management of the metabolic syndrome are:[4]

- Treating one of the underlying causes of the metabolic syndrome (abdominal obesity) by instituting weight management that includes dietary changes and increased physical activity
- Managing other individual cardiovascular disease and metabolic risk factors.

Lifestyle management

Weight loss

Effective weight loss can improve cardiovascular and metabolic risk factors associated with the metabolic syndrome and reduce the risk of type 2 diabetes in patients with the syndrome.[4,36] A combined lifestyle management approach of a low-calorie diet, increased physical activity and behavioural change is the cornerstone of successful treatment leading to sustained weight loss. Patients who adhere to lifestyle recommendations (Table 1) can generally expect to lose between 7% and 10% of their initial body weight over a period of six to twelve months.[4,37]

Dietary changes

A reduction of the daily food intake by 500kcal to 1000kcal can lead to a weight loss of about 0.5kg to 1kg a week. General dietary principles include recommending lower intakes of saturated fats, trans fats, cholesterol and rapidly absorbed simple carbohydrates (sugars), in addition to increasing the intake of vegetables, fruit and whole grains. Both the Mediterranean diet,[38] with a high intake of fruits, vegetables, nuts, whole grains and olive oils, and the Dietary Approaches

TABLE 2

Recommendations for the management of metabolic cardiovascular factors

Metabolic cardiovascular risk factor	Therapeutic goals	Recommendations
Elevated blood pressure	• Below 130/80mmHg	• Modify blood pressure through lifestyle changes and/or antihypertensive medication
Elevated lipid levels	**Primary target:** • LDL cholesterol levels below 2.0mmol/L (or below 1.8mmol/L if known cardiovascular disease and lipid-modifying medication) **Secondary targets:** • Total cholesterol levels below 4.0mmol/L • Triglyceride levels below 1.5mmol/L • HDL cholesterol levels above 1.0mmol/L	• Improve lipid profile through lifestyle changes and lipid-modifying medication
Elevated glucose levels	• Fasting blood glucose levels of below 5.5mmol/L • If pre-diabetes is present, regularly monitor for progression to type 2 diabetes • If type 2 diabetes is present, aim for HbA1c of below 7.0%	• Avoid type 2 diabetes through lifestyle changes to achieve target blood glucose levels • Improve blood glucose levels through lifestyle changes and medications as required (eg, metformin first-line)
Prothrombotic state	–	• Consider low-dose aspirin as primary prevention after balancing the patient's risk of cardiovascular disease with the risk of major bleeding

to Stop Hypertension (DASH) diet,[39] of low salt intake with high consumption of fruits, vegetables, nuts, legumes and low-fat dairy, can form the nutritional basis to moderate risk factors for metabolic cardiovascular disease. Both diets have supportive clinical evidence to warrant specific recommendation as dietary management for patients with the metabolic syndrome.

Physical activity

Regular moderate intensity exercise can facilitate weight loss and improve the metabolic risk factors associated with the metabolic syndrome. Reaching and sustaining the exercise target of at least 150 minutes of moderate-intensity exercise per week (eg, achieved by 30 to 60 minutes per day of brisk walking on most, if not every, day of the week) will aid weight loss and is the key to maintaining such loss. Increasing the physical intensity of exercising will also enhance its beneficial effects. A pedometer to measure incidental activity levels can be a useful tool to help patients achieve the recommended incidental activity target of 10,000 steps or more per day.

Smoking cessation

Given the clear link between cigarette smoking and cardiovascular disease, any lifestyle intervention for smokers must recommend smoking cessation.[40]

Treatment challenges

Overweight and obesity constitute a chronic and relapsing condition, for many patients find it challenging to achieve and maintain weight loss. Although recent evidence confirms that practitioners can assist their patients to lose weight through routine clinical care, the importance of a multidisciplinary approach for weight loss is well established, particularly in patients with the metabolic syndrome.[36,41,42] practitioners should therefore consider using the skills of:

- Dietitians and exercise physiologists (to help patients refine diet and exercise programmes)
- Self-help groups and psychologists (to assist patients with behavioural modifications)
- Specialist obesity services (for patients who fail to lose weight despite compliance with a lifestyle approach).

The long-term effects of bariatric surgery in patients with the metabolic syndrome are unresolved. Evidence demonstrates that the significant weight loss associated with bariatric surgery is due to the high short-term rates of remission of the metabolic syndrome. However, rates of long-term remission following the surgery remain unknown.[43]

Management of specific risk factors

Recommendations for the management of specific cardiovascular and metabolic risk factors include aggressive treatment of hypertension, dyslipidaemia and dysglycaemia (Table 2).

Blood pressure

Lifestyle modification and weight loss can often improve high–normal blood pressure (eg, 120/80 to 139/89mmHg), but in patients with hypertension

of any grade (greater than or equal to 140/90mmHg) antihypertensive therapy is generally required. Current guidelines for patients without end-organ damage suggest a target level for blood pressure of 140/90mmHg or lower. However, given the link between the metabolic syndrome and cardiovascular disease, it is the practice of these authors to aim for a lower blood pressure target of 130/80mmHg or lower, which is the level recommended for patients with cardiovascular disease, CKD and type 2 diabetes.[44]

There is evidence to support the use of ACE inhibitors or angiotensin II receptor blockers as first-line antihypertensive therapy in patients with type 2 diabetes and mild CKD. However, the superiority of these agents in patients with the metabolic syndrome who do not have cardiovascular disease or type 2 diabetes remains unclear. Furthermore, thiazide diuretics have been associated with an increased risk for new onset type 2 diabetes and should be used with caution in patients at risk of dysglycaemia.[45]

Dyslipidaemia

Following current practice guidelines, target lipid levels for patients with the metabolic syndrome include an LDL cholesterol level of less than 2.0mmol/L. This can be achieved through a combination of lifestyle modification and, if required, lipid-modifying medical therapy.[15] Secondary lipid treatment targets are a total cholesterol level of less than 4.0mmol/L, a HDL cholesterol level of greater than 1.0mmol/L and a triglyceride level of below 1.5mmol/L.

Dysglycaemia

The Diabetes Prevention Programme clearly demonstrated that intensive lifestyle changes that focused on weight loss and increased physical activity delayed or prevented type 2 diabetes in patients with dysglycaemia and the metabolic syndrome.[42] The same study also demonstrated that lifestyle changes were superior to metformin in preventing type 2 diabetes and reducing rates of the metabolic syndrome.

In the authors' clinical practice, in selected patients with the metabolic syndrome who have dysglycaemia and/or polycystic ovary syndrome, metformin can be used as an adjuvant to lifestyle modification. However, metformin should not be the initial or sole therapy used to prevent type 2 diabetes. The cost-effectiveness of using metformin to prevent type 2 diabetes is currently unknown.

Although thiazolidinediones are known to improve insulin sensitivity and reduce progression to type 2 diabetes, their use is associated with weight gain and fluid retention and they can exacerbate cardiac failure. Rosiglitazone has been associated with an increased risk for cardiovascular events. Thiazolidinediones may also increase the risk of fracture and low bone density. These issues suggest it is prudent to avoid using thiazolidinediones in all patients without type 2 diabetes, or only after careful consideration of the alternative treatment options in patients with type 2 diabetes.

In patients with the metabolic syndrome, there is no firm evidence to indicate whether treatment of insulin resistance with medications that potentiate insulin action (ie, metformin and thiazolidinediones) further lowers risk of cardiovascular events beyond the reduction associated with lifestyle changes and weight loss.

Aspirin for primary prevention

Several American expert committees have recently reviewed the use of aspirin for the prevention of cardiovascular disease.[46,47] In summarising their positions, they concluded that aspirin should be considered for primary prevention in patients with a high ten-year risk of cardiovascular disease (as calculated by cardiovascular disease risk tools) following an individualised clinical judgement made after balancing the risk of cardiovascular disease with the risk of major bleeding. In patients with a previous cardiovascular event, aspirin should be used for secondary prevention unless there is a specific contraindication.

The 2009 United States Preventative Task Force reported on the magnitude of aspirin benefit compared with the risk of major bleeding.[47] The data suggest that aspirin doses ranging from 75mg to 325mg are equally effective for reducing the risk of cardiovascular disease in treated patients, however, both a 2006 meta-analysis[49] of twenty-two studies and a 2009 meta-analysis [50] of six large studies demonstrated that low-dose aspirin was as likely as high-dose aspirin to cause major bleeding.[47] Although, as indicated in the 2009 meta-analysis, the benefits of aspirin as primary prevention in low-risk patients (including those with uncomplicated type 2 diabetes) remain unclear, with the results of several long-term studies pending.

Summary

The controversy about whether the metabolic syndrome is a 'real' entity clouds the consensus that the rates of hypertension, dyslipidaemia and dysglycaemia increase as worldwide obesity increases. The clustering of metabolic risk factors for cardiovascular disease and type 2 diabetes is established and the presence of one risk factor should lead to an evaluation for the presence of the other risk factors and comorbidities associated with the metabolic syndrome.

Practitioners are recommended to assess their patients' cardiovascular and metabolic risk profile regularly. Patients identified with the metabolic syndrome are at an increased risk of developing cardiovascular disease and type 2 diabetes. However, this risk can be reduced by the introduction of a multifactorial clinical management plan, targeting patients' lifestyle and their individual cardiovascular and metabolic risk factors.

References are available on request.

Lifelong Learning

Glycaemic Control and Weight Loss in Type 2 Diabetes

Globally it was estimated in 2010 that there were 285m people living with type 2 diabetes, making up approximately 90% of diabetic cases. Traditionally considered a disease of adults, type 2 diabetes is increasingly diagnosed in children due to rising obesity rates. Type 2 diabetes is diagnosed as frequently as type 1 diabetes in teenagers in the US. It is recognised as a global epidemic by the World Health Organization.

Type 2 diabetes is characterised by beta-cell dysfunction in the pancreas, against a backdrop of obesity-related insulin resistance. When lifestyle measures and oral blood glucose-lowering medication fail to sustain glycaemic control, current guidelines recommend the use of basal insulin. Data from the UK Prospective Diabetes Study suggests that glycaemic control progressively worsens over time. This deterioration has been attributed to a progressive loss of beta-cell function that occurs irrespective of currently used medications such as metformin, sulfonylureas, or insulin.

'Lizard spit'

Exenatide is the synthetic version of exendin-4, a hormone found in the saliva of the Gila monster. It displays biological properties similar to human glucagon-like peptide 1 (GLP-1). This regulates glucose metabolism and insulin secretion. Exenatide is a GLP-1 agonist and belongs to the group of incretin mimetics. It enhances glucose-dependent insulin secretion by the pancreatic beta-cells, suppresses inappropriately elevated glucagon secretion and slows gastric emptying.

Indication

Exenatide has been approved by the MCC as an add-on therapy for use in patients whose diabetes is not well-controlled on other oral medication or by lifestyle modification. The medication is injected subcutaneously twice a day using a filled pen-like device.

Mechanism of action

Exenatide is thought to facilitate glucose by:

1. Augmenting pancreas response by increasing insulin secretion in response to meals being eaten. The result is a release of a higher, more appropriate amount of insulin which helps lower the rise in blood sugar resulting from eating.
2. Suppressing pancreas glucagon in response to eating which stops the liver from producing unnecessary sugar, thereby preventing hyperglycaemia.
3. Slowing down gastric emptying which decreases the rate at which meal-derived glucose appears in the bloodstream.
4. Exerting a subtle, yet prolonged, effect that reduces appetite. This promotes satiety via hypothalamic receptors. Clinical trials have demonstrated that the weight-reducing effect continues at the same rate with continued use. When separated into weight loss quartiles, the highest 25% experienced substantial weight loss, and the lowest 25% experienced no loss or small weight gain.
5. Reducing liver fat content. Fat accumulated in the liver or non-alcoholic fatty liver disease is common in several metabolic diseases. It is common for patients with type 2 diabetes to have low HDL cholesterol and high triglycerides.

Clinical studies

An open-label, crossover study of exenatide or insulin glargine[1] showed similar significant improvements from baseline HbA1c independent of treatment order. Improvements in HbA1c from baseline did not significantly differ between treatment groups. Exenatide therapy was associated with significant reductions in body weight and PPG excursions compared with insulin glargine. Insulin glargine was associated with a significantly greater reduction in FSG compared with exenatide.

A study by Bunck MC *et al*[2] found that traditional blood glucose lowering agents do not sustain adequate glycaemic control in most type 2 diabetic patients. Exenatide significantly improved beta-cell function during a one year treatment programme compared with titrated insulin glargine. After cessation of both exenatide and insulin glargine therapy, beta-cell function and glycaemic control returned to pre-treatment values, suggesting that ongoing treatment is necessary to maintain the beneficial effects of either therapy.

A study published by Kelly AS *et al*[3] from the University of Minnosota Medical School, showed that GLP-1 receptor agonist treatment reduces BMI and elicits a meaningful reduction in systolic blood pressure in adolescents with severe obesity.

References

1. *Barnett AH et al. Tolerability and efficiency of exenatide and titrated insulin glargine in adult patients with type 2 diabetes previously uncontrolled with metformin or a sulfonylurea. Clin Ther 2007,29:2333-48*
2. *Bunck MC, Diamant M et al. One year treatment with exenatide improves beta-cell function, compared with insulin glargine, in metformin-treated type 2 diabetic patients. Diabetic Care 2009 May; 32(5): 762-768*
3. *Kelly AS et al. The effect of glucagon-like peptide 1 receptor agonist therapy on body mass index in adolescents with severe obesity: A placebo-controlled clinical trial. JAMA Pediatrics 2013, 167(4):355-360*

Not at HbA_{1c} goal

Rising HbA_{1c} > 8%

Struggling with their weight

Byetta®
exenatide injection

Improve & sustain HbA_{1c} control in your type 2 patient not at goal...

- Improved HbA_{1c} in patients failing on maximally-effective doses of MET or SU or combined MET/SU[1,2,3]
- As effective as insulin glargine[4,5]
  - Comparable reductions in HbA_{1c} vs. insulin glargine in patients stratified by baseline HbA_{1c} ≥ 9% or < 9%[5]
- Sustained HbA_{1c} improvement
  - Over 3 years, HbA_{1c} reduction of -1.0% sustained from baseline[6]

... With the additional benefit of weight loss

- Weight loss of -5.3 kg achieved over 3 years[6]

Recommended in the SEMDSA guidelines for the treatment of hyperglycaemia in patients with type 2 diabetes, who are inadequately controlled by other oral antidiabetic therapy[7]

SEMDSA - Society for Endocrinology, Metabolism and Diabetes of South Africa
MET - Metformin
SU - Sulphonylurea

Bristol-Myers Squibb
1054ZA13PRO5177-01.

AstraZeneca

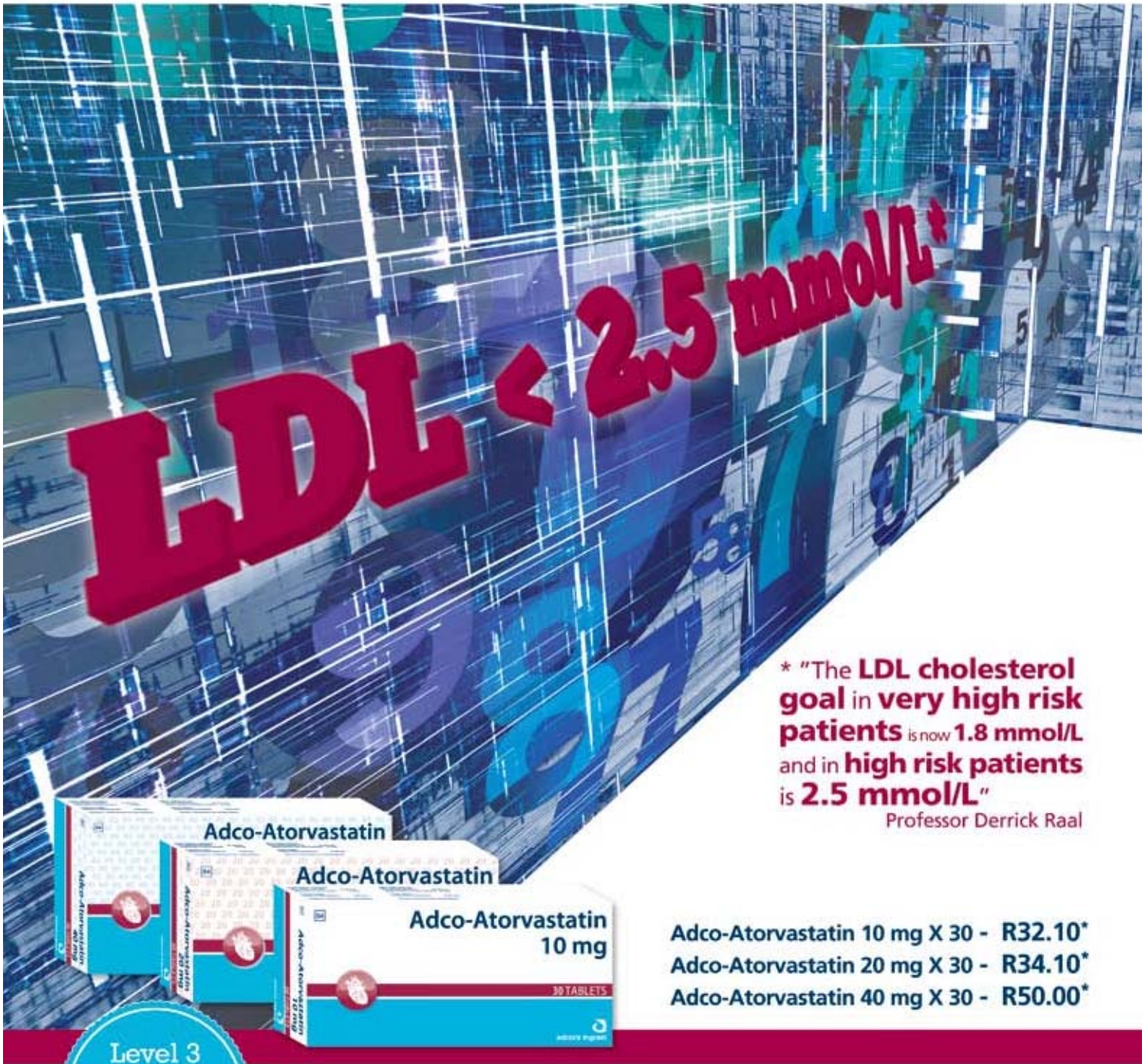
Byetta®
exenatide injection

References:

1. DeFronzo RA, Ratner RE, Han J, *et al.* Effects of exenatide (exendin-4) on glycaemic control and weight over 30 weeks in metformin-treated patients with type 2 diabetes. *Diab Care* 2005;28(5):1092-1100. 2. Buse JB, Henry RR, Han J, et al. Effects of exenatide (exendin-4) on glycaemic control over 30 weeks in sulfonylurea-treated patients with type 2 diabetes. *Diab Care* 2004;27(11):2628-2635. 3. Kendall DM, Riddle MC, Rosenstock J, *et al.* Effects of exenatide (exendin-4) on glycaemic control over 30 weeks in patients with type 2 diabetes treated with metformin and a sulfonylurea. *Diab Care* 2005;28(5):1083-1091. 4. Heine RJ, Van Gaal LF, Johns D, *et al.* Exenatide versus insulin glargine in patients with suboptimally controlled type 2 diabetes: a randomized trial. *Ann Intern Med* 2005;143(8):559-569. 5. Barnett AH, Burger J, Johns D, *et al.* Tolerability and efficacy of exenatide and titrated insulin glargine in adult patients with type 2 diabetes previously uncontrolled with metformin or a sulfonylurea: a multinational, randomized, open-label, two-period, cross-over noninferiority trial. *Clin Ther* 2007;29(11):2333-2348. 6. Klonoff DC, Buse JB, Nielsen LL, *et al.* Exenatide effects on diabetes, obesity, cardiovascular risk factors and hepatic biomarkers in patients with type 2 diabetes treated for at least 3 years. *Curr Med Res Opin* 2008;24(1):275-286. 7. Amod A, Ascott-Evans BH, Berg GI, *et al.* The 2012 SEMDSA guideline for the management of type 2 diabetes (revised). *JEMDSA 2012*;17(2):S1-95.

S3 Byetta® Soln for Inj. Each ml contains exenatide 250µg. 5(10) µg/dose 1.2(2.4) ml prefilled pen. Reg. No: 41/34/0068, 0069. Holder of certificate of registration: Eli Lilly (SA) Pty Ltd. Marketed by: Bristol-Myers Squibb (Pty) Limited. Reg. No. 1956/001115/07. Woodmead North Office Park, 54 Maxwell Drive, Woodmead, 2191, South Africa. PO Box 227, Sunninghill, 2157. Tel: (011) 808 5000. Fax: (011) 808 5301. AstraZeneca Pharmaceuticals (Pty) Limited. Reg. No. 1992/005854/07. Building 2, Northdowns Office Park, 17 Georgian Crescent West, Bryanston, 2191, South Africa. Private Bag X23, Bryanston, 2021. Tel: (011) 797-6000. Fax: (011) 797-6001. www.astrazeneca.co.za. Expiry Date: March 2015. Log No: BYE 07/13/003.

The SA Lipid Guideline goal[1]...
...can now be achieved with our affordable treatment



* "The **LDL cholesterol goal** in **very high risk patients** is now **1.8 mmol/L** and in **high risk patients** is **2.5 mmol/L**"
Professor Derrick Raal

Adco-Atorvastatin 10 mg X 30 - R32.10*
Adco-Atorvastatin 20 mg X 30 - R34.10*
Adco-Atorvastatin 40 mg X 30 - R50.00*

Level 3 **BBBEE** contributor
SANAS ACCREDITED

*Prices as per DOH website and include VAT. www.doh.gov.za

Reference: 1. A joint statement from the South African Heart Association (SA Heart) and the Lipid and Atherosclerosis Society of Southern Africa (LASSA). South African Dyslipidaemia Guideline Consensus Statement. *S Afr Med J* 2012; **102**: 177-188

Adco-Atorvastatin 10 mg, 20 mg, 40 mg. Each tablet contains 10 mg, 20 mg, 40 mg atorvastatin respectively. Reg. No. 43/7.5/1116, 43/7.5/1117, /43/7.5//1118 respectively. ZA.12.CVS.004. 06/2012. For full prescribing information refer to the package insert approved by the medicines regulatory authority. Adcock Ingram Limited, Reg. No. 1949/034385/06. Private Bag X69, Bryanston, 2021. Tel +27 11 635 0000 www.adcock.com

adcock ingram generics

Lifelong Learning

Erectile Dysfunction: A Guide for GPs

Erectile dysfunction is a serious matter. Not only can this cause great distress for a man and his partner, but it is an important marker of underlying comorbidities, including future cardiovascular disease.

Erectile dysfunction (ED) is a persistent or recurrent inability to attain and/or maintain a penile erection sufficient for satisfactory sexual activity and intercourse. It is a common condition with one in five men over the age of 40 reporting significant ED in an Australian study.[1] Although 88% of men in this study had visited a GP in the past 12 months for various reasons, only 30% of men with ED had actually discussed this important symptom with the GP.[1]

ED is associated with chronic diseases, including cardiovascular disease (CVD), and with CVD risk factors (eg, diabetes, hypertension, high lipid levels, smoking, obesity and low level of physical activity). ED is now known to be an early warning sign of future CVD in otherwise healthy men[2] and in those with diabetes.[3] A study of men aged 20 and older reported a more than twofold higher incidence of atherosclerotic events in men with ED compared with men in the general population.[4] Moreover, the relative risk conferred by ED is higher in younger men.[4,5] These data suggest that in a man presenting with ED there is a compelling need for medical assessment, and treatment for the ED.

Lack of sexual activity associated with ED can significantly affect the well-being of men and their partners, whose needs are often overlooked. In older patients doctors may sometimes not consider sexual health a priority and the impact of ED is underestimated. Fortunately, for most men presenting with ED and who desire restoration of sexual function simple, safe treatments are available.

Role of the GP

It is important for GPs to understand the implications of ED: both the need for a full clinical assessment and the potential benefits of restoring sexual function.

GPs should be the point of first contact and must be prepared to enquire about a patient's sexual health. Men still appear reluctant to bring up what they perceive as an embarrassing subject. Some GPs are also hesitant to approach their patients about ED. There are various ways (see box) of initiating a discussion about sexual function, either by direct questioning or positioning the question in a specific context relevant to the man's situation. The patient usually appreciates a flexible and confident approach. An experienced GP will know if a patient does not want to engage in discussion.

Men with ED might circumvent contact with their usual GP, going to the internet to buy drugs or to clinics that do not follow appropriate clinical guidelines. These practices may mean that underlying medical problems and comorbidities go undetected, and that ineffective and expensive treatments are prescribed. Deaths from contaminated counterfeit medication have been reported.[6] GPs should promote their willingness to deal with ED, so their patients are not exposed to these risks.

Once the symptom has been raised, the GP has all the skills required to assess the man and to initiate treatment. Patient information resources (fact sheets and booklets) and professional guidance (clinical summary guides) on ED are available from various reputable health sources.

Assessment

The steps to be taken in assessing a man with ED include:

Key points

- Erectile dysfunction (ED) is a common symptom, which increases in incidence with age.
- All men with ED need to be assessed, even if there is no desire to restore sexual function, because there may be serious comorbidities.
- For those men with ED who desire restoration of sexual function, effective and safe treatments are available.
- It is important that GPs fully understand the role of phosphodiesterase-5 inhibitors for ED and be confident prescribing them and monitoring their effectiveness.
- Patients with ED should be referred to an appropriate specialist if more specialised treatments are necessary.

About the author

Dr Douglas Lording *BMedSci, MB BS, FRACP is a Consultant Endocrinologist and Andrologist at Cabrini Health, Cabrini Hospital, Malvern, a board member of Andrology Australia and an Honorary Adjunct Professor of Medicine at Monash University, Melbourne, Australia.*

Initiating discussion about sexual function

Introductory question

'Many men (of your age/with your condition) experience sexual difficulties. If you have any difficulties, I am happy to discuss them.'

Direct questions

'Are you sexually active?'

'Do you enjoy an active sexual life?'

Contextual questions

To a younger man:

'Do you have any concerns about your development? Does everything down there work OK?'

To a man in a reproductive age group:

'Are you thinking of having a family soon? Do you have any concerns about your fertility? Do you think there could be any problems?'

To a middle aged or older man having a general assessment:

'Are you still getting a good erection? This is an age where medical problems may be interfering.'

To a man with diabetes during review of complications:

'I want to check you in relation to the effects of your diabetes. Have you noticed any problems with your eyes…feet…erections?'

To a man with cardiovascular disease or risk factors:

'It is common for men with diabetes/high blood pressure/heart disease to experience erectile problems. I can help you, if you are having problems.'

'I want to assess your risk of future heart disease. There are lots of things that might prompt me to look more closely at your situation. Can you tell me what your erections are like?'

- **Clearly defining the nature of the sexual dysfunction.**
  It is important to distinguish ED from premature or delayed ejaculation and loss of libido. When it has been established that the man has ED, a history of the development and severity of this symptom will help with the diagnosis. Specific questions (see box) may be useful in evaluating the man with ED. If these questions (or similar) are asked, a comprehensive picture of the problem will be evident. Organic and psychogenic ED have typical features that are worth comparing (see box).
- **Understanding the psychosocial issues.**
  It is important to know whether the man's partner has any sexual or medical problems. Single or young men may have issues with ED different from a man in a long-standing sexual partnership. Important ethnic or religious factors may impinge on the issue. It may be important at this point to know why the man presented at this stage and whether his partner will be involved in the assessment.
- **Undertaking a thorough clinical evaluation.**
  A thorough clinical evaluation is necessary, focusing on the key medical and psychiatric associations of ED. Men with ED may have previously undiagnosed diabetes, hypertension or hyperlipidaemia, and comorbid medical conditions.
- **Evaluating the importance of restoring sexual function.**
  Not all men presenting with ED will seek treatment. However, most men who voluntarily present with ED will at least try simple treatments. The view of the man's partner is helpful in this assessment, but not all men will involve their partners in this decision.

Clinical evaluation

Medical history

Medical history should cover general health and well-being, any specific illnesses from which the patient suffers and medication history. Specific attention should be paid to the presence of vascular diseases and risk factors for CVD (eg, diabetes, hypertension, high lipid levels, smoking, obesity and low level of physical activity). Drug and alcohol use should also be assessed. Previous reproductive health is important. Developmental issues, previous infertility and gonadal disease may suggest hypogonadism. Pelvic trauma, including trauma experienced from bike riding, should be noted. Pelvic surgery and radiotherapy may cause ED. The GP should ask if the penis has changed shape or has become bent with an erection. Depression, and medications used to treat depression and other psychiatric disorders, often impact significantly on ED. Depression is a common cause of ED and the GP should be alert to clues when taking a history from patients.

Physical examination

Physical examination should focus on the known causes of ED, with emphasis on a vascular and genital examination. This examination should include blood pressure, heart rate, abdominal aortic aneurysm, carotid bruits, foot pulses and an assessment of body weight. Examination of the penis and testes is mandatory.

Unexpected neurological disease is not commonly found when assessing men with ED, but weakness, sensory symptoms and any lower limb signs might prompt investigation. Depending on the age of the man, this consultation is an opportunity to broach other important issues, such as prostate disease.

Investigations

It is important that the glucose and lipid status of men with ED is known, and morning total testosterone level

Questions used to understand the sexual function of a man with ED

- Tell me what happens when you try to have intercourse? Is your erection hard? Can you penetrate easily? Does your erection stay until sex is completed?
- How often are you having intercourse? How does that compare to the past? Past year? Five years ago? Why do you think this change has occurred?
- How often do you masturbate? What are your erections like then?
- Are you aware of erections through the night or early morning? What are those erections like?
- Are you able to climax when you want? Does that feel the same as before? Is it painful?
- Tell me about your overall interest in sexual things? Movies, books, girls in the street?
- What about your partner? Are you still sexually attracted?
- How long would you say that all this has been happening?
- What do you think is the cause of this problem?
- What does your partner think of all this? Have the two of you discussed this problem?
- Does your partner have an interest in sex? Enjoy sex? Does your partner have any sexual problems?
- What effect is this problem having on you?
- What effect is it having on your partner?

Presentation of Organic and psychogenic causes of ED

Organic

- Gradual onset (except trauma and surgery)
- Persistent and progressive
- Masturbatory, nocturnal and morning erections similarly affected
- Medical cause identifiable
- Often older men

Psychogenic

- Sudden onset, precipitating event identified
- Often intermittent or variable
- Masturbatory and/or nocturnal and morning erections usually spared
- Absence of medical cause
- Often younger men

should be measured. If testosterone levels are low a full assessment for hypogonadism should be completed before contemplation of testosterone replacement. This will include measuring levels of follicle-stimulating hormone and luteinising hormone, and then further testing depending on whether the cause is gonadal or pituitary in origin. Other investigations, such as measurement of prolactin levels and thyroid, liver or kidney function tests, should be performed in appropriate clinical circumstances.

Special vascular or neurological testing is rarely helpful in determining the most appropriate treatment and is usually not indicated. Vascular assessment might help following pelvic trauma or in men who have always had ED, particularly if simple treatments are ineffective. Suspicion of spinal disease, such as multiple sclerosis, will require appropriate testing.

Diagnosis

At the end of the clinical assessment, the GP can formulate a diagnosis, particularly looking for causes of ED that are specifically treatable. Comorbidities in men with ED are important to define and manage.

Management

A management plan should be established. Ideally the man and his partner should be involved in formulating it. It is important to recognise conditions for which there is a specific treatment. For restoration of sexual function, the potential treatment strategies and options should be discussed with the patient. Treatment options (see box) vary according to the level of complexity and need for referral. A significant issue is for the man to understand the costs of treatment.

Even if the ED is predominately physical, most treatments will be enhanced by supportive counselling. This is not always easy in general practice, in part because of time constraints but also because of lack of training. However, basic reassurance, support and follow up are important to men with ED. Because of the strong association between ED and CVD, it is important for the GP to consider whether the man is fit enough to resume sexual activity, before restoring sexual function. Usually the clinical history will give sufficient information to reassure the GP that starting treatment is safe, but screening for asymptomatic CVD may be required.

Modifiable risk factors and causes

Presentations in which specific treatment may restore normal erectile function include a pattern of psychogenic ED associated with an obvious precipitating factor, a prescribed medication leading to a change in sexual function, depression, and presence of hypogonadism. It is important to note that testosterone is indicated for treatment of ED only in men with hypogonadism and is not a treatment for ED in its own right. Acute medical conditions of any cause may lead to a deterioration of sexual function and it is important to reassess the patient after a full recovery.

Other factors may impinge on ED and some benefit may result from modification. These factors include obesity, cigarette smoking, lack of exercise and drug and alcohol use. The appreciation of CVD implications in men with ED may motivate the patient to a more committed approach to his general health and well-being.

It is common in the middle aged and older man to identify a number of factors that may have a bearing on ED, the primary cause of which may be vascular. Often these factors will include rela-

tionship issues that will need resolution before sexual function is improved.

For most men, a specific treatment to promote erections will be required. It is usual to start with simpler first-line options that can be managed by the GP and then to use other treatments if these fail (see box).

Phosphodiesterase-5 inhibitors

Phosphodiesterase-5 inhibitors (PDE5) are the cornerstone of treatment for men with ED. The three PDE5 inhibitors available in tablet form (sildenafil, tadalafil and vardenafil) are widely used, well tolerated and safe to use. There are no other approved oral agents for ED, and other medications available in other forms, such as nasal sprays, are not supported by clinical trial data.

PDE5 inhibitors all work by promoting the normal response to sexual stimulation, usually leading to a harder, more sustained, erection. Across a large number of trials the success rate in allowing intercourse to occur satisfactorily is about 70%.[7] There is no convincing evidence that one PDE5 inhibitor is more efficacious than the others, but in an individual patient they may have different efficacy. The main difference is that tadalafil has an average half-life of about 17 hours compared with four to five hours for the others. This means that tadalafil gives the potential to allow a longer window for successful intercourse, which is important for some couples.

PDE5 inhibitors have been traditionally used 'on demand', taken in preparation for intercourse over the following few hours. More recently, low-dose tadalafil has been available for 'daily dosing', with the view that sexual activity can be more spontaneous. For men who respond to a PDE5 inhibitor, and who use two or more doses a week, daily dosing is cost neutral and a logical choice. Other men will choose this approach after they have weighed up what is best for them, particularly those troubled by the timing issues surrounding 'on demand' dosing.

There are significant ways in which to ensure the best possible success when using PDE5 inhibitors (see box). Most importantly, men must understand that sexual stimulation is required for erection and enough time must elapse after taking the medication for it to be at a therapeutic concentration. The response will often improve with experience of use, and the common practice of judging success on the basis of one or two 'samples' is flawed.

Nitrate medications may potentiate the hypotensive effects of PDE5 inhibitors and concomitant use is contraindicated. Some men get disturbed vision with sildenafil and backache with tadalafil. Other adverse effects include flushing, nasal congestion, headaches, dyspepsia and myalgia. A small number of men will not continue use of PDE5 inhibitors because of these effects. There remains a misconception that these medications have adverse CVD effects. Clinical trials did not support this, although men with recent cardiovascular events, severe heart failure and uncontrolled hypertension were generally excluded from trials. Therefore, caution should be exercised when considering PDE5 inhibitors for men with active coronary ischaemia, congestive heart failure, borderline low blood pressure, borderline low cardiac volume status, a complicated multi-drug antihypertensive regimen or drug therapy that can prolong the half-life of PDE5 inhibitors.

Vacuum devices and penile rings

A penile ring alone or in conjunction with a vacuum device, may be suitable for men who have partial ED. These could be a first choice for some men, or for those who have an unsuccessful trial of a PDE5 inhibitor. Penile pain, numbness, coldness and difficulty ejaculating may occur, and men need to be careful not to fall asleep with the ring in place.

Intracavernosal injection of vasoactive drugs

If the above treatments fail or are contraindicated, self-injection of vasoactive drugs into the corpora will usually lead to a strong erection. Intracavernosal injection of alprostadil is highly effective but may cause penile pain. Intracavernosal injections of atropine (off-label use) and papaverine, in various combinations, can also be used for ED. These may be used in combination with alprostadil, if alprostadil alone is unsuitable. Many GPs will choose to refer a patient with ED at this stage. However, there is no reason why a GP cannot initiate injection of vasoactive drugs, particularly GPs in rural areas or those working in isolation from specialist urological services. It is important to teach men how to inject and to carefully establish the best dose, working upwards from about 5µg. In this way a prolonged erection (priapism), which is potentially damaging, is avoided. Men who do inject themselves with this treatment should always be given a strategy for intervening if the erection is unduly prolonged.

Men with limited manual dexterity or

Treatments for ED

First-line treatment

- Modify medication, if applicable (eg, antidepressants, antihypertensives)
- Diagnose and manage hypogonadism (note, this may not always improve ED)
- Address psychosexual issues (eg, anxiety, stress, relationship issues)
- Address modifiable lifestyle risk factors (eg, smoking, obesity, unhealthy diet and lack of exercise)
- Discuss sexual misinformation (eg, realistic expectations for age)

Second-line treatment

PDE5 inhibitors

- Tadalafil: 10mg and 20mg for on demand use and 5mg for once a day use
- Sildenafil: 50mg and 100mg for on demand use
- Vardenafil: 10mg and 20mg for on demand use

Penile rings and vacuum devices

- Suitable for men with partial ED, in those who are not interested in or have contraindications to PDE5 inhibitors

Third-line treatment

Intracavernosal injection of vasoactive drugs

- Alprostadil: 10µg and 20µg preloaded syringes

Fourth-line treatment

Penile prosthetic surgery and vascular surgery

- Require referral of patient to an experienced urologist

who are visually handicapped or obese may find this procedure beyond them. It is possible to involve the partner in these circumstances. There are no significant systemic complications of this treatment. However, if vasoconstrictive drugs are used to treat priapism, hypertensive crisis has been reported.

Penile prosthetic and vascular surgery

The implantation within the corpora cavernosa of paired cylinders, attached to a scrotal pump and subcutaneous fluid reservoir (penile prosthesis), is another approach to allow restoration of sexual activity, and is highly effective in well-chosen patients. It is usually considered after other treatments have been tried. This procedure is associated with a small risk of infection and other surgical complications, and sometimes mechanical failure. Referral of patients to an experienced urologist is appropriate in these situations.

Arterial and venous surgery is rarely indicated for men with ED. Very occasionally, younger men with ED following pelvic injury will have surgically treatable disease. These procedures are highly specialised.

Referral

GPs will often want to refer men with specific ED problems to appropriate specialists. Men with Peyronie's disease or other penile problems can be referred to an experienced urologist, men with hypogonadism to an endocrinologist, and men with depression or other mental health issues to a psychiatrist or psychologist.

Another reason for referral of men with ED is failed treatment with PDE5 inhibitors. Some GPs prefer not to manage any men with ED. If necessary, patients could be referred within a multi-doctor practice to a colleague who has a special interest in ED or to an ED specialist, which will usually be a urologist, an endocrinologist with an interest in andrology, a sexual health physician or a GP 'specialist'.

Follow up

It is common for the first attempts at treatment of ED to be not completely successful. Follow up will help enhance the outcome, particularly checking dosing techniques, side effects and partner's response. Concomitant psychosocial factors are more likely to be detected and resolved. Many potential treatment failures may be averted with a comprehensive follow up.

Conclusion

Erectile dysfunction is a serious medical problem. It is important that GPs are open to talking about ED with their patients and prepared to ask about sexual function, when appropriate. Many important underlying conditions will be detected with appropriate evaluation.

For men and their partners who want to restore sexual function, PDE5 inhibitors will usually be indicated. GPs can confidently prescribe these drugs, thereby successfully treating most men presenting with ED. It is important to recognise that basic support and counselling, together with follow up, will enhance the outcome.

References are available on request

Optimising use of PDE5 inhibitors for ED

- Explain how the drugs work
- Encourage men to discuss medication use with their partners
- Emphasise the need for normal sexual stimulation
- Suggest not to take with, or soon after, a fatty meal, particularly when using sildenafil
- Suggest avoiding significant alcohol intake for first attempts
- Recognise that for some men manual stimulation is more effective
- Ensure enough time is allowed between dosing and stimulation, at least 30 minutes for first attempts
- Start with the highest dose in most men
- Consider initial dosing without a partner in anxious men
- Consider small starting doses in men who are concerned about side effects
- Try at least four doses to determine effectiveness
- Try a different PDE5 inhibitor if one PDE5 inhibitor is not effective
- Try a lower dose if it is working well
- Encourage men to have sexual activity sooner after dosing or later after dosing to better understand their response window once a response has been achieved.

Adcock Ingram Healthcare (Pty) Ltd. Reg. No. 2007/019928/07
Private Bag X69, Bryanston, 2021. Tel. +27 11 635 0000. www.adcock.com

Save the date

Tuesday 15th October 2013

Upgradethics 2013

Brought to you by

adcock ingram generics

Send an e-mail to **Generics@Adcock.com**
to receive further information.

Lifelong Learning

Management of Cytomegalovirus and Herpes Zoster in Immunocompromised Patients

Cytomegalovirus (CMV) is a double-stranded DNA virus belonging to the Herpesviridae family. Other family members include herpes simplex virus type1 and herpes simplex virus type2, varicella zoster virus, human herpes virus HHV-6, HHV-7 and HHV-8. CMV shares many of the attributes of the other herpes viruses, including genome, virion structure, and the ability to cause latent and persistent infections. CMV has the largest genome of all herpes viruses. Multiple genetically distinct strains of CMV exist which may account for the differences in virulence. Infection with more than one strain of CMV is possible.

Clinically significant CMV disease is not uncommon in patients immunocompromised by HIV infection, solid-organ or bone-marrow transplantation, those receiving high-dose steroids, tumour necrosis antagonists, or other immunosuppressing medications for conditions such as systemic lupus erythematosus, rheumatoid arthritis, Crohn's disease, or psoriasis, among others.

Organ transplantation and cytomegalovirus

CMV infections can have direct or indirect effects. Direct effects include bone marrow suppression, myocarditis, pneumonia, GI disease, hepatitis, pancreatitis, nephritis, retinitis, and encephalitis, among others. Indirect effects may include acute and chronic graft rejection, accelerated atherosclerosis (heart transplants), secondary bacterial or fungal infections, EBV-associated post-transplant lymphoproliferative disease and decreased graft and patient survival.

In support of the diagnosis, CMV antigen or inclusions are found with histological examination. CMV isolated from clinical samples in the absence of clinical symptoms may represent viral colonisation or subclinical replication. This may warrant antiviral suppressive therapy. In patients infected with HIV, antiviral therapy is often not required in the absence of clinical apparent disease.

HIV and cytomegalovirus

In patients with HIV infection, CMV involves the entire GI tract. In the upper GI tract, CMV has been isolated from oesophageal, gastric and duodenal ulcers. Upper GI tract oesophageal disease can present with painful dysphagia, while lower GI tract disease may present with colitis. For an accurate diagnosis, a full colonoscopy with multiple biopsies is necessary.

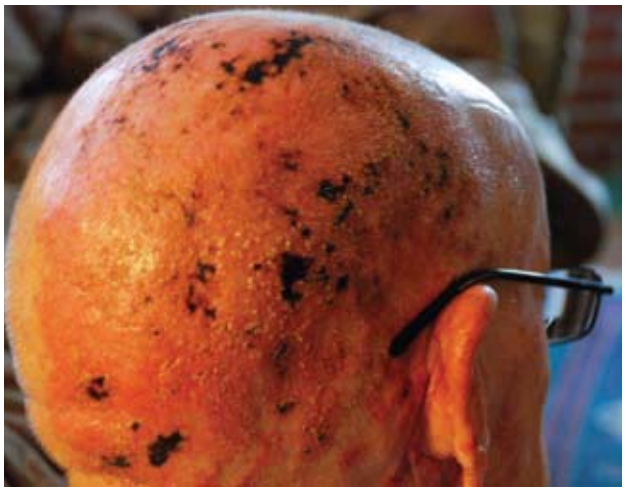
Retinitis is the most common manifestation of CMV disease in HIV positive patients. Affected patients report decreased visual acuity, floaters, and loss of visual field on one side. This frequently progresses to bilateral involvement that may be accompanied by systemic CMV disease.

Treatment

The best option for treatment and prevention is ganciclovir and valgariciclovir with foscarnet or cidofovir and off label leflunomide as a second line. Prophylactic treatments include high dose valaciclovir, penciclovir, famciclovir and aciclovir. There is no consensus at this time as to whether prophylaxis or pre-emptive treatment is better in solid-organ transplants.

Herpes zoster (HZ)

HZ infections are more common and often more complicated in immunocompromised patients. The key clinical objective is to reduce the incidence of cutaneous and visceral dissemination that can lead to life-threatening complications. For localised disease, oral valaciclovir, famciclovir or acyclovir with close outpatient follow-up is best. Intravenous acyclovir therapy is reserved for those with disseminating varicella zoster virus infection, ophthalmic involvement, very severe immunosuppression or the inability to take oral medication. Foscarnet is the drug of choice to treat aciclovir-resistant HZ. Appropriate analgesic therapy with early antiviral treatment reduces the incidence and severity of acute zoster pain and post-herpetic neuralgia.



Herpes zoster immunocompromised patient.

Some things are DESIGNED to RETURN

Others are DESIGNED for RELIEF

vavirex® 500
valaciclovir tablets
Prevents Recurrence of Herpes

VAVIREX® 500 is indicated for:

- The treatment of
  - herpes zoster (shingles)
  - recurrent genital herpes in immunocompetent adult patients
- The prevention of
  - recurrent herpes simplex infection of the skin and mucous membrane of the ano-genital area
- The prophylaxis of
  - cytomegalovirus (CMV) infection, CMV disease and other herpes infections following organ transplantation where a special risk exists

S4 VAVIREX® 500 Tablets. Reg. No.: 43/20.2.8/0388. Each film-coated tablet contains valaciclovir hydrochloride equivalent to 500 mg valaciclovir. For full prescribing information refer to the package insert approved by the medicines regulatory authority. Applicant: Pharmacare Limited. Co. Reg. No.: 1898/000252/06. Building 12, Healthcare Park, Woodlands Drive, Woodmead, 2191. A 15428 07/13.

aspen PHARMACARE

Healthcare. We Care.

Marketed by Aspen Pharmacare
www.aspenpharma.com
Medical Hotline 0800 118 088

Whatever the reason,
whatever the season,

Avamys®
fluticasone furoate

S4 **AVAMYS** Nasal Spray (Suspension). **REGISTRATION NUMBER:** 41/21.5.1/0968. Each 50 µl spray contains 27,5 µg of fluticasone furoate. Preservative: Benzalkonium chloride 0,015% m/m. **PHARMACOLOGICAL CLASSIFICATION:** A.21.5.1 Corticosteroids and analogues. **APPLICANT:** GlaxoSmithKline South Africa (Pty) Ltd, 57 Sloane Street, Bryanston 2021.

aspen PHARMACARE

Healthcare. We Care.

gsk GlaxoSmithKline

Marketed by Aspen Pharmacare
www.aspenpharma.com
Medical Hotline 0800 118 088

GlaxoSmithKline South Africa (Pty) Ltd, (co. reg. no.: 1948/030135/07), 57 Sloane Street, Bryanston 2021. Tel: +27 11 745 6000. Fax +27 11 745 7000. Marketed by Aspen Pharmacare, Building 12, Healthcare Park, Woodlands Drive, Woodmead, 2191. All adverse events should be reported by calling the Aspen Medical Hotline number or directly to GlaxoSmithKline on +27117456000. For full prescribing information refer to the package insert approved by the medicines regulatory authority. AVA/0911/12 A15959 03/13 13123

Lifelong Learning

Treatment Decisions in Adult Rhinosinusitis

Adult rhinosinusitis is one of the most commonly diagnosed conditions and patients will often present to their GP for treatment. A thorough patient history is important for the diagnosis of acute and chronic rhinosinusitis and for guiding appropriate medical therapy.

Many patients present to their GPs with rhinosinusitis symptoms, as both acute and chronic rhinosinusitis have an adverse effect on quality of life. Rhinosinusitis often imposes significant medical costs on patients, while also creating additional indirect costs to society through loss of work and reduced workplace productivity. This article reviews the diagnosis and management of acute and chronic rhinosinusitis in adults.

Nasal anatomy

The paranasal sinuses are a group of air-filled chambers in the face that are named according to the bone by which they are located (Figure 1). They include:

- Maxillary sinuses – located in the maxillary bone, behind the cheeks
- Frontal sinuses – located in the frontal bone, above the eyes
- Ethmoid sinuses – a group of six to 12 small sinus cells located between the orbits
- Sphenoid sinus – the most posterior sinus, located in the central skull base below the pituitary gland.

The paranasal sinuses are lined by ciliated respiratory epithelium and produce about 500mL of mucus a day that helps remove trapped dust particles and bacteria that have been inhaled. This mucus, which is normally watery thin, drains through a series of channels, eventually entering the nasal cavity through a final common drainage pathway (known as the osteomeatal complex) that is located lateral to the middle turbinate (Figure 1). The mucus then drains into the posterior nasal cavity and down the throat, where it is swallowed.

About the author

Dr Ron Bova *MB BS, MS, FRACS is a Consultant ENT Head and Neck Oncology Surgeon at St Vincent's Hospital, Sydney, Australia.*

Rhinosinusitis

Rhinosinusitis is defined as inflammation of the nose and paranasal sinuses and can be classified as:

- Acute rhinosinusitis, in which symptoms last less than 12 weeks
- Chronic rhinosinusitis, in which symptoms last longer than 12 weeks
- Recurrent acute rhinosinusitis, in which patients experience more than three to four episodes of acute rhinosinusitis per year, but remain free of sinus symptoms between acute exacerbations.

Various international task forces have used evidence-based methodology to provide guidelines for the diagnosis and treatment of rhinosinusitis and nasal polyps. As rhinitis nearly always coexists with sinusitis, the term sinusitis has now been replaced by the more accurate term rhinosinusitis.

Acute rhinosinusitis

Acute rhinosinusitis is a bacterial infection of the sinuses. Most cases of acute rhinosinusitis develop when a viral upper respiratory tract infection (URTI), usually the common cold, causes nasal congestion and impairs sinus drainage. If the mucosal oedema in the sinus drainage pathways is particularly severe, it can impede mucus transport resulting in the retention of mucus in the sinuses. This trapped mucus then becomes secondarily infected by bacteria, causing acute rhinosinusitis. It has been estimated that about 0.5% to 2% of common colds are complicated by acute rhinosinusitis.

Key points

- Acute and chronic rhinosinusitis are common disorders that can adversely affect patient quality of life.
- Most patients with mild acute rhinosinusitis can be treated expectantly using analgesics in conjunction with oxymetazoline hydrochloride or intranasal corticosteroids.
- Antibiotics are indicated in patients with severe acute rhinosinusitis or with mild acute rhinosinusitis not responding to treatment with nasal sprays.
- Chronic rhinosinusitis is treated with a protracted course of saline irrigations and intranasal corticosteroid therapy.
- Referral is indicated when severe acute and chronic rhinosinusitis do not respond to appropriate medical therapy, when acute rhinosinusitis is recurrent, and if the diagnosis is in doubt or complications are suspected.
- A sinus CT scan is recommended before referral, as patients may require functional endoscopic sinus surgery.

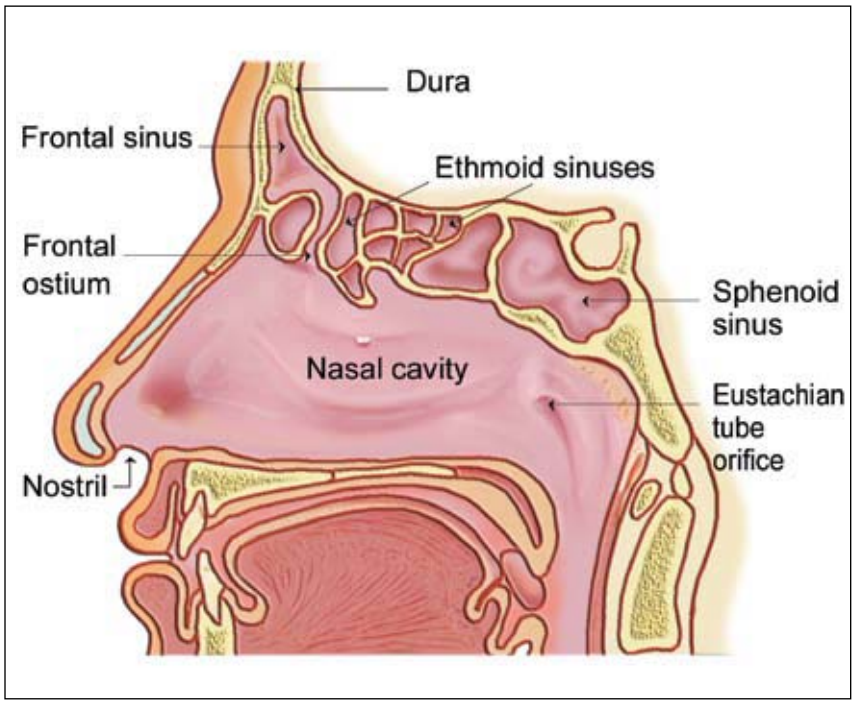


Figure 1. Sinus anatomy.

Diagnosis

A diagnosis of acute rhinosinusitis in general practice rests largely on a history of a common cold that persists or progresses for longer than seven to 10 days. Symptoms of acute rhinosinusitis include:

- Nasal congestion
- Facial pressure, especially when leaning forward
- Yellow or green mucopurulent rhinorrhoea and/or postnasal drip
- Facial pain, including malar pain (maxillary sinus), nasal bridge pain (ethmoid sinuses), frontal pain (frontal sinus) and occipital or vertex pain (sphenoid sinus)
- Halitosis
- Loss of smell
- Cough, particularly at night
- Referred dental pain (the premolar tooth roots extend towards the maxillary sinus floor, hence referred dental pain is relatively common in inflammatory sinus disorders)
- A feeling of disequilibrium due to secondary Eustachian tube dysfunction.

Physical examination of the nose and sinuses is limited in general practice. Possible physical signs of acute rhinosinusitis may include tenderness over the affected sinuses and observation of purulent discharge on anterior rhinoscopy (best achieved using an otoscope inserted into the anterior nasal cavity).

Radiographic imaging of the sinuses is unnecessary for patients who meet the diagnostic criteria for acute rhinosinusitis, unless a complication or alternative diagnosis is suspected. CT scanning remains the gold standard imaging modality for evaluating the sinuses and has replaced standard x-rays.

Treatment

Treatment options for acute rhinosinusitis include analgesia, topical decongestants, intranasal corticosteroids and antibiotics.

Topical decongestants

Commercially available topical decongestants, such as oxymetazoline hydrochloride nasal spray, for three to five days, help to decongest the nasal mucosa and open the sinus drainage pathways. This, in turn, facilitates sinus drainage and improves sinus ventilation. However, use of oxymetazoline hydrochloride decongestants for longer than a week should be discouraged, as prolonged use can lead to significant rebound nasal congestion which can be difficult to treat (rhinitis medicamentosa).

Intranasal corticosteroids

A course of an intranasal corticosteroid (two to six weeks) provides an alternative treatment option to oxymetazoline hydrochloride. A recent Cochrane review supports the use of intranasal corticosteroids as monotherapy or as an adjuvant therapy to antibiotics in treating acute rhinosinusitis.[1]

Antibiotics

There is moderate evidence that antibiotics provide only a small benefit in patients who are not immunosuppressed with community-acquired uncomplicated acute rhinosinusitis. Routine antibiotic treatment can reduce the duration of symptoms; however, 80% of patients treated without antibiotics will improve within two weeks. The small benefit to the patient from treatment with antibiotics should be balanced against their potential for adverse side effects.[2] However, there are some situations when antibiotic treatment is clearly indicated. These include:

- Patients presenting with severe symptoms
- Acute rhinosinusitis that remains refractory to other, more conservative treatment measures
- Patients who are immunosuppressed
- When complications are suspected (eg, periorbital cellulitis).

The most common bacteria isolated from the maxillary sinuses of adults with acute rhinosinusitis are Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis. Amoxycillin (seven to 14 days) is appropriate first-line therapy for adults with acute rhinosinusitis.

For patients with penicillin hypersensitivity, antibiotic treatment options include sulphamethoxazole trimethoprim, cefaclor monohydrate or doxycycline.

If patients fail to respond to first-line antibiotic therapy within three to five days, second-line therapy should be considered. Appropriate antibiotic choices include amoxycillin clavulanate, cefaclor monohydrate or cefuroxime axetil.

Recurrent acute rhinosinusitis

Recurrent acute rhinosinusitis is diagnosed when upwards of three to four

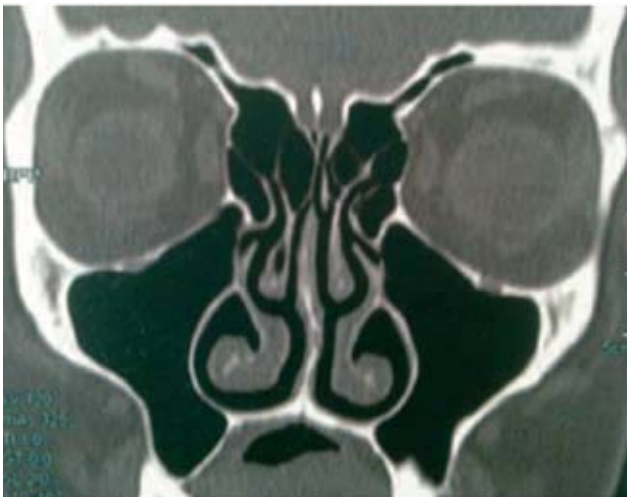


Figure 2. CT scan demonstrating well aerated sinuses with no mucosal thickening (normal CT scan).

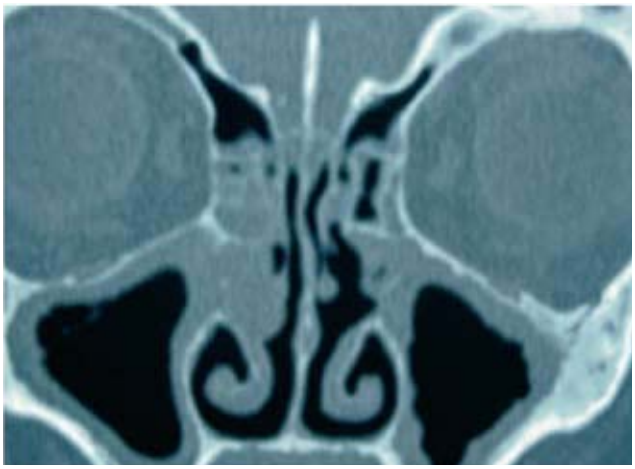


Figure 3. CT scan demonstrating mucosal thickening throughout the ethmoid and maxillary sinuses in a patient with chronic rhinosinusitis.

episodes of acute rhinosinusitis occur per year, without signs or symptoms of rhinosinusitis between these episodes. Factors that may increase the risk of recurrent acute rhinosinusitis include allergic rhinitis, immunodeficiency and anatomical variations in sinus drainage pathways that may predispose to sinus obstruction and inflammation (eg, septal deviation, pneumatisation of middle turbinate [concha bullosa], hypoplasia of maxillary sinus and narrowing of the osteomeatal complex region).

Treatment strategies to prevent recurrent acute rhinosinusitis include smoking cessation, optimising the management of allergic rhinitis and daily nasal saline irrigations. Functional endoscopic sinus surgery (FESS) is also effective in reducing the frequency of recurrent acute sinusitis; patients should have a CT scan performed prior to referral.

Referral

Most patients with acute rhinosinusitis are managed by the GP, but referral is indicated when:

- Patients are not responding to medical therapy – a sinus CT scan is recommended before referral to confirm the diagnosis. ENT surgeons can perform a nasal endoscopy to confirm the presence of pus draining out of the osteomeatal complex region and a pus swab can be taken for culture to guide further antibiotic therapy
- Acute rhinosinusitis is recurrent
- A complication of acute rhinosinusitis is suspected, such as periorbital cellulitis, meningitis, localised osteomyelitis or oroantral fistula.

Differential diagnosis

The symptoms of acute rhinosinusitis overlap with other conditions, making the diagnosis difficult at times. Differential diagnoses to consider for acute rhinosinusitis include:

- Viral URTI – these commonly cause nasal congestion and clear rhinorrhoea, but rarely cause purulent rhinorrhoea or facial pain
- Allergic rhinitis
- Sinonasal or nasopharyngeal tumours – these rare tumours can cause progressive nasal obstruction and sometimes epistaxis, but typically do not cause pain or purulent rhinorrhoea
- Acute migraine – classic migraine symptoms include photophobia, aura, unilateral headache with pain usually associated with visual disturbance. Some patients may experience migraine without classic symptoms but instead may present with mid-facial pain
- Atypical facial pain syndrome – this refers to pain within the territory of the trigeminal nerve. Facial pain is usually unilateral, poorly localised and deep-seated, and often described as a severe ache or a crushing or burning sensation. Clinical examination and imaging studies are normal. Depression and anxiety are prevalent in this population
- Dental infection – a periapical infection involving the upper molar or premolar teeth will typically cause unilateral facial symptoms similar to acute rhinosinusitis. Pain and fevers are common. In severe dental infections facial swelling can result (it is very rare for acute rhinosinusitis to cause facial swelling). Sometimes a periapical dental abscess can cause secondary acute rhinosinusitis, particularly when the infected tooth root extends into the maxillary sinus.

Chronic rhinosinusitis

Chronic rhinosinusitis is inflammation of the sinuses that persists for longer than 12 weeks. The condition is commonly seen in general practice. Some patients with chronic rhinosinusitis may experience mild symptoms for years without seeking medical advice. However, other patients may have chronic fluctuating symptoms that can exert a substantial negative impact on health and which can be associated with a reduced quality of life.

Although acute rhinosinusitis is considered to be primarily a bacterial infection, the pathogenesis of chronic rhinosinusitis remains poorly understood. There is an enormous amount of ongoing research examining the immunological mechanisms underlying chronic rhinosinusitis. Aetiological factors that are thought to play a role in chronic rhinosinusitis include:

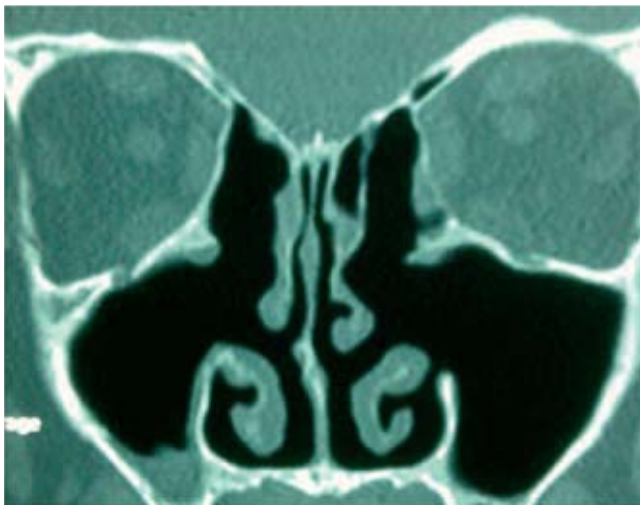


Figure 4. Postoperative FESS CT scan demonstrating widely patent maxillary and ethmoid sinus drainage pathways with well.

- Mucosal inflammation secondary to chronic allergic rhinitis or smoking that leads to congestion in the osteomeatal complex region
- Immunodeficiency disorders, including immunoglobulin IgA and IgG subclass deficiency
- Mucociliary disorders such as cystic fibrosis
- Nasal polyps obstructing the sinus drainage pathways
- Anatomical factors, such as a septal deviation, which may impinge onto the lateral nasal wall and exacerbate congestion around the osteomeatal complex region. Similarly, paradoxical lateral curving middle turbinates can also cause obstruction in the osteomeatal complex region.

Diagnosis

The diagnosis of chronic rhinosinusitis in general practice is determined largely by the patient's clinical history. Symptoms, in order of prevalence, include:

- Nasal congestion or obstruction
- Facial pain, fullness or pressure
- Mucopurulent rhinorrhoea or post-nasal drip – often associated with a cough, especially at night
- Reduced smell
- Headaches
- Referred dental pain
- Halitosis
- Intermittent ear pain due to secondary Eustachian tube dysfunction
- Fatigue and chronic mild disequilibrium.

Chronic rhinosinusitis is defined as two or more symptoms for 12 or more weeks. One of:

- Nasal congestion/blockage/obstruction or nasal discharge (anterior rhinorrhoea or posterior post-nasal drip); along with
- Facial pain/pressure or reduction/loss of smell.

Empirical treatment can be commenced when the diagnosis is suspected A sinus CT scan is currently the most sensitive imaging modality and can be used to confirm the diagnosis before beginning treatment or when patients treated empirically fail to respond to appropriate medical therapy (Figures 2 and 3).

Treatment

The mainstays of medical management for chronic rhinosinusitis include nasal saline irrigations, intranasal corticosteroids, oral antibiotics and FESS. Smoking cessation is important in the management of chronic rhinosinusitis, as smoking has been shown to exacerbate the condition.

Nasal saline irrigations

Nasal saline irrigations (sprays and solutions) can be administered once or twice a day. Saline sprays moisten the nasal and sinus mucosa, which improves mucosal ciliary function and facilitates mucus drainage from the sinuses. Saline irrigations using a syringe or commercially available devices have the additional benefit of achieving more effective mechanical debridement of the crusts and mucus that often collect in the nasal cavity. Patients can mix their own saline solutions using a simple recipe of one and a half teaspoons of sea or rock salt added to 500mL of water. Most commercially available saline irrigation products can be refilled. Saline is safe, cheap and a natural product with no side effects. Patients can use saline treatments for short periods or indefinitely, as needed.

Antibiotics and corticosteroids are sometimes added to saline irrigations (when prescribed by ENT specialists); however, there is currently no evidence to support use of saline additives in patients with chronic rhinosinusitis.

Intranasal corticosteroids

Treatment with intranasal corticosteroids can address underlying allergic rhinitis and help to reduce congestion in the osteomeatal complex region. Intranasal corticosteroids should be continued for at least two to three months. If patients achieve significant symptom resolution after several months of taking intranasal corticosteroids, treatment can be discontinued and nasal saline irrigations continued indefinitely. Intranasal corticosteroids are occasionally associated with minor nose bleeding but studies show no detrimental structural effects to the nasal lining following long-term use.

Antibiotics

The role of antibiotics is controversial in chronic rhinosinusitis. Patients may require short-term treatment with antibiotics to address acute exacerbations of chronic sinusitis. Amoxycillin potassium clavulanate for 14 days is appropriate. Macrolide antibiotics are sometimes prescribed because of their combined anti-bacterial and anti-inflammatory properties, but the appropriate treatment duration remains unclear (varying from two to eight weeks). Currently, there are no adequate placebo-controlled studies to justify the routine use of long term antibiotics in patients with chronic rhinosinusitis.

Functional endoscopic sinus surgery

Referral for FESS is indicated when chronic rhinosinusitis remains refractory to a prolonged trial of medical therapy.

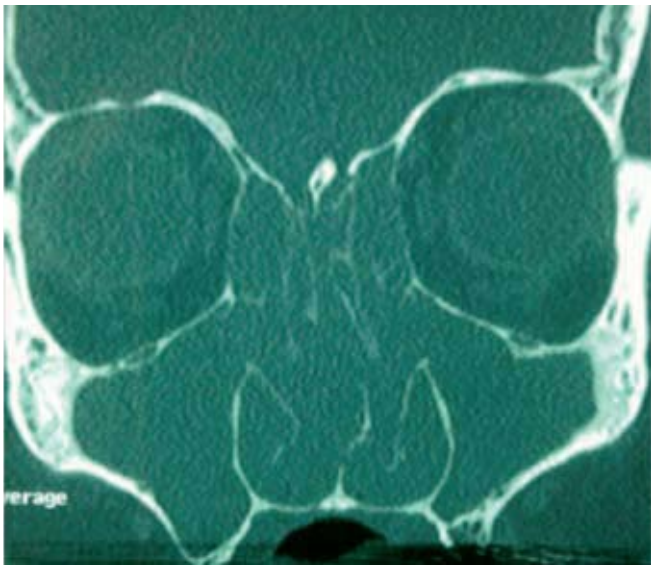


Figure 5. CT scan demonstrating severe nasal polyps completely obstructing both nasal passages resulting in widespread obstructive chronic rhinosinusitis.

The aims of FESS are twofold:

- To enlarge the osteomeatal complex region by creating larger openings into the maxillary and ethmoid. Sinuses, which promotes more effective mucus drainage (Figure 4)
- To create larger sinus drainage pathways, which facilitates the use of long-term medical treatment to prevent chronic rhinosinusitis recurring.

FESS is carried out under general anaesthesia and can be performed as day surgery or as an overnight hospital stay. Sinus surgery has been shown to benefit patients with chronic rhinosinusitis in more than 100 published case series. Major complications are rare, but revision surgery is required within five years in 5% to 10% patients. It is important that patients understand that long-term medical therapy is often required after sinus surgery to prevent chronic rhinosinusitis recurrence. Medical therapy usually includes daily nasal saline irrigations combined with the appropriate medical management of allergic rhinitis.

Specific subtypes of chronic rhinosinusitis

Nasal polyps

Chronic rhinosinusitis associated with nasal polyps is relatively common. Most patients with nasal polyps have allergic rhinitis but the reason why patients with allergic rhinitis go on to develop polyps is unknown. Inflammatory nasal polyps slowly enlarge over many years resulting in progressive nasal obstruction, obstruction of the olfactory fossa – which inevitably leads to a reduced sense of smell – and obstruction of sinus drainage pathways resulting in secondary rhinosinusitis (Figure 5).

Treatment options for patients with benign inflammatory nasal polyps include a trial of corticosteroids. A short course of reducing-dose oral prednisone (for 10 to 14 days), followed by an intranasal corticosteroid spray (for three to four months), often results in dramatic shrinkage of nasal polyps, leading to symptomatic improvement. An example of a simple reducing-dose regimen includes prednisone at a dosage of 25mg daily for the initial five days of treatment, 12.5mg daily for the following five days and 12.5mg on alternate days for the last five days of treatment. Higher corticosteroid doses can be used in patients with severe nasal polyps. Such 'medical polypectomy' with oral corticosteroids facilitates the use of intranasal corticosteroid sprays and nasal saline irrigations by allowing more proximal delivery into the nasal and sinus cavities.

FESS is indicated when patients present with severe obstructing nasal polyps which are unlikely to respond adequately to medical therapy alone. Polyps can descend to the anterior nasal cavity and can often be seen inside the nostrils. Debulking these severe polyps provides immediate symptomatic relief and facilitates the use of long-term medical therapy with intranasal corticosteroids. FESS is also indicated in patients with mild to moderate nasal polyps whose symptoms remain refractory to a trial of corticosteroid therapy.

Allergic fungal rhinosinusitis

Allergic fungal rhinosinusitis (AFRS) is considered the nasal equivalent of allergic bronchopulmonary aspergillosis and is characterised by thick mucus of a 'peanut butter' consistency. Most patients present with peripheral blood eosinophilia and nasal polyps; histology will confirm fungal hyphae and eosinophils embedded within the mucus material. A characteristic radiological feature of AFRS is the presence of hyper-densities within the opacified sinuses, which represents aggregations of fungal organisms and debris (double density sign on a CT scan).

Treatment requires FESS followed by a prolonged trial of intranasal corticosteroids. The use of systemic or intranasal antifungal therapies has yet to be validated.

Samter's triad

Samter's triad is a condition characterised by asthma, severe nasal polyps and aspirin or NSAID intolerance. Patients initially experience allergic nasal symptoms, which progress to adult-onset asthma and severe nasal polyps, with aspirin intolerance developing last. An allergic reaction to aspirin or to NSAIDs in these patients may cause severe asthma exacerbations, urticaria or, rarely, angioedema. Treatment for Samter's triad includes the following: asthma therapy, corticosteroid therapy, FESS for nasal polyps and management of aspirin sensitivity, which can sometimes necessitate aspirin desensitisation.

Differential diagnosis

Many of the symptoms of chronic rhinosinusitis are generally nonspecific and will therefore overlap with other conditions. Differential diagnoses to consider for chronic rhinosinusitis include:

- Neuralgic pain resulting from migraine, cluster or tension headaches and atypical facial pain syndrome – these patients typically present with facial pain and headaches, but have few nasal symptoms to suggest rhinosinusitis. A sinus CT scan will help

Continued on page 60

Lifelong Learning

Who Should Administer Conscious Sedation?

Part Three: Sedation competence

The previous article argued that competence to administer conscious sedation (CS) should move away from competence based on a practitioner's specialty to competence based on skills and knowledge.
The UK's General Dental Council says[1]: "Dentists have a duty of care to administer conscious sedation only within the limits of their knowledge, training, skills and experience and healthcare professionals should have completed relevant postgraduate education and training and have clinical experience of the particular conscious sedation technique." This principle is equally applicable outside dentistry, In fact, all international guidelines agree with the principles expressed above.[2]
This article will outline the competence every sedation practitioner should have when he plans to administer CS.

Sedation competence: practical considerations

Patient assessment and selection

According to the American Society of Anesthesiologists (ASA), only ASA1 (normal, healthy) patients or ASA2 patients (those with well-controlled disease eg, hypertension) are suitable for sedation outside the operating room.

A focused airway examination is a must to rule out any abnormalities that may lead to airway compromise.

About the author

Professor James Roelofse *MB ChB, M Med (Anaes), PhD (Anaes) is Head of Sedation and Pain Control at the University of the Western Cape, Cape Town and Visiting Professor at the University College London, London, UK.*

The value of an up-to-date medical history questionnaire[2] which gives an indication as to the health status of the patient cannot be overemphasised.

Levels of consciousness

A sedation practitioner must understand and be able to recognise the different levels of sedation or levels of consciousness (LOC)[3], as drugs depress the central nervous system and change the LOC. The deeper the level of sedation or consciousness the higher the incidence or risk of adverse events.

Special attention must be paid when administering ketamine. Some contend that ketamine at the doses used for sedation causes dissociative sedation, a level that falls outside the conscious sedation continuum.[4]

The airway

Every sedation practitioner must know, understand, and have respect for maintenance and protection of the airway. He must know the anatomical and physiological differences between adults and children, the effects of drugs on the airway, and be able to manage the airway.[5] In CS, the patient is taken from a state of self-preservation to that of dependence on the skills and knowledge of the practitioner. Regardless of the sedation technique, loss of airway control is always possible. Teams that have recognised, discussed, planned, and prepared for this emergency are more likely to succeed in re-establishing an airway rapidly, effectively, and safely.

The drugs

A sedation practitioner must understand the pharmacokinetics and pharmacodynamics of sedative and analgesic drugs. There is no ideal drug, but there are basic questions to consider when selecting a drug:

- What is desired: sedation or analgesia, or a combination of both?
- How rapid is the drug's onset of action? Some drugs take time to reach peak effect.
- How long must the desired effects last?
- What is the side-effect profile: ie, could the drug induce nausea and vomiting?

With intravenous drugs, safe sedation practice means titration to effect. If too little is given, the result could be an anxious patient. If too much is given, hypoventilation and even airway obstruction may result.

Training

All international guidelines agree that training is essential[2] irrespective of whether the sedation practitioner is:

- An operator sedationist (who gives sedation **and** performs the procedure), or
- A dedicated sedation practitioner (who only administers and monitors the sedation).

Documentation

According to international guidelines[2], all sedation practitioners should keep the following documentation:

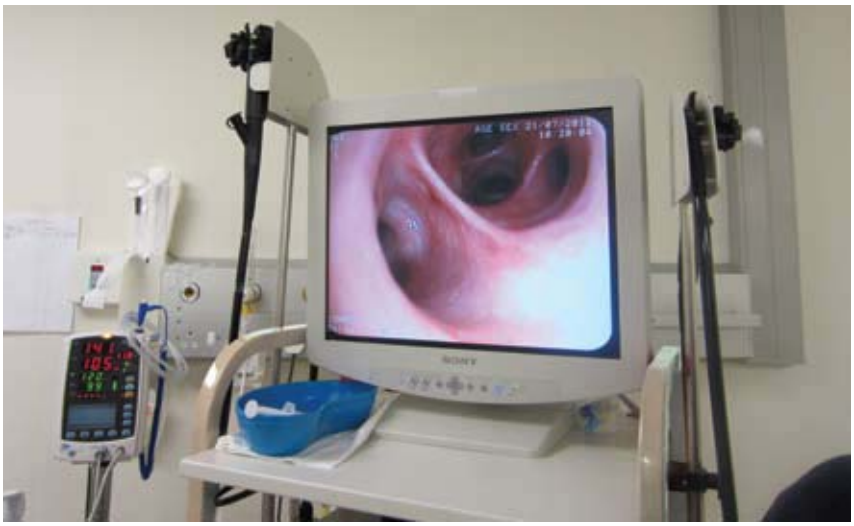
- Medical history questionnaire
- Consent to sedation and analgesia for medical/dental procedures
- Pre-procedural checklist
- Pre- and post-sedation instructions
- Clinical monitoring
- Sedation monitoring chart
- Post-sedation monitoring chart
- Discharge scoring system
- Discharge questionnaire
- Critical incident report

Informed consent is a crucial document. The patient needs to know everything regarding the planned procedure and possible complications. Never ask for consent when sedative drugs have already been administered to the patient!

Fasting

Practitioners should follow the 2-4-6 rule.[2] The patient is allowed to take clear fluids up to two hours before the procedure, breast milk four hours before the procedure, and solids six hours before the procedure.

The American College of Emergency Physicians guidelines state the patient need only fast for three hours before sedation as the possibility of aspiration is not of serious concern.



This patient undergoing bronchoscopy is being monitored electronically while under conscious sedation.

Monitoring

The golden rule is never leave the patient alone. The practitioner's armamentarium includes several electronic monitoring devices:

- Blood pressure
- Pulse oximetry
- ECG
- Capnography
- Depth of anaesthesia or bispectral index (BIS) monitors.

Finally there is the almost forgotten art of clinical monitoring; using one's eyes, ears and fingers.

The premises

No sedation practitioner should proceed with CS before ensuring the premises meet all the guideline requirements for safe sedation.[2]

Airway certification

It is expected of all sedation practitioners to have the necessary up-to-date airway certification as stipulated in international guidelines.

Conclusion

There are no short-cuts in safe sedation practice. Follow the sedation guidelines but remember they are only a guide - not an instruction manual. Never leave the patient alone. Always ensure there is a trained second person present to help monitor the patient and assist with rescue if necessary.

The take home message is: Proper preparation, proper evaluation, appropriate skills to rescue the patient and proper recovery lead to safe and successful sedation.

References

1. *Standards for conscious sedation in dentistry: Alternative techniques. Standing Committee on Sedation in Dentistry 2007; http://www.rcseng.ac.uk/fds/publications-clinical-guidelines/docs/SCSDAT%202007.pdf*
2. *Piercy J, Roelofse JA. Guideline for the safe use of procedural sedation and analgesia (PSA) for diagnostic and therapeutic procedures in adults. S Afr J Anaesthesiol Analg 2010; 16(2): S1-S25*
3. *Roelofse JA. Who should administer conscious sedation? Part one: What exactly is conscious sedation? Modern Medicine 2013; 38(6): 35-37.*
4. *Green SM, Krauss B. Clinical practice guideline for emergency department ketamine dissociative sedation in children. Ann Emerg Med. 2004; 44: 460-471.*
5. *Chung F, Elsaid H. Screening for obstructive sleep apnea before surgery: Why is it important? Curr Opin Anaesthesiol. 2009; 22(3): 405-411.*
6. *Cote C. Round and round we go: Sedation. Ped Anesth. 2008;18: 3-8.*

Lifelong Learning

Effective Treatment of Gram-positive and Gram-negative Bacterial Infections

Even common problems in antibiotic treatment do not have simple solutions. Choosing one antibiotic drug from among several candidates entails balancing the benefits and the drawbacks associated with each. The physician must strike the right balance between effectively treating the current infection and maintaining options for future use in the light of growing drug-resistance. Here are three antibiotics to consider.

Teicoplanin

Teicoplanin is a glycopeptides antibiotic complex isolated from the fermentation broth of *Actinoplanes teichomyceticus*. It is used in the treatment of serious infections caused by aerobic and anaerobic Gram-positive bacteria. It is also effective against methicillin-resistant *Staphylococcus aureus* (MRSA) and *Enterococcus faecalis*. Its effectiveness has been documented in the following infections: endocarditis, septicaemia and osteomyelitis, respiratory infections, skin and soft tissue infections, urinary tract infections and peritonitis associated with chronic ambulatory peritoneal dialysis.

Teicoplanin's mechanism of action is similar to that of vancomycin with a similar spectrum of activity. Its mechanism of action is to inhibit peptidoglycan polymerisation. This results in an inhibition of Gram-positive bacteria cell wall synthesis, consequently resulting in cell death.

Pharmacokinetics

Teicoplanin is rapidly and extensively absorbed from muscle and the peritoneal cavity, but poorly absorbed from the gastrointestinal tract. Following intravenous administration, the majority of the drug is excreted unchanged by glomerular filtration. Concentrations, relative to those in plasma, are high in lung and bone tissue and low in fat. It penetrates slowly and poorly into cerebrospinal fluid, but relatively rapidly and effectively in synovial and pleural fluids and soft tissue.[1]

Levofloxacin

Levofloxacin is a fluoroquinolone antibiotic and is the optical S-negative isomer of the racemic drug substance ofloxacin. It has a broad spectrum of *in vitro* activity against Gram-positive and Gram-negative bacteria, including pathogens such as *Mycoplasma, Chlamydia, Legionella* and *Mycobacteria spp.*

It has been effective in treating the following bacterial infections: acute exacerbations of chronic bronchitis, community acquired pneumonia, sinusitis, complicated and uncomplicated urinary tract infections, acute pyelonephritis, uncomplicated skin and soft tissue infections and complicated intra-abdominal infections.

Pharmacokinetics

The bioavailability of oral levofloxacin is almost 100% and is little affected when administered with food. Oral absorption is rapid and complete, with little difference in serum-concentration profiles following a 500mg oral or intravenous (infused over 60min) dose. Penetration into cerebrospinal fluid is relatively poor (concentrations are approximately 16% of simultaneous plasma values).

The plasma elimination half-life ranges from six to eight hours in individuals with normal renal function. Approximately 80% is eliminated unchanged in the urine through glomerular filtration and tubular secretion.[2]

Ciprofloxacin

Ciprofloxacin is a second-generation fluoroquinolone antibiotic. Its spectrum of activity includes most strains of Gram-positive and Gram-negative bacteria responsible for: lower respiratory tract infections, urinary tract infections, skin and skin structure infections, gastro-intestinal tract infections,

Heliobacter pylori is a common Gram-negative bacterium.

osteomyelitis and gonorrhoea.

Ciprofloxacin is used alone or in combination with other antibacterial drugs in the empiric treatment of infections where the bacterial pathogen is unidentified. It kills bacteria by interfering with the enzymes that cause DNA to rewind after being copied, thereby stopping synthesis of DNA and protein.

Pharmacokinetics

There is a linear effect of 200mg-400-mg of ciprofloxacin given intravenously. Drug accumulation does not occur when administered at 12hr intervals. It is present in active form in the saliva, nasal and bronchial secretions, mucosa of the sinuses, sputum, skin blister fluid, prostatic secretions, lymph, bile and peritoneal fluid. Concentration of diffused drug in the cerebrospinal fluid is generally less than 10% of peak serum concentrations.[3]

References

1. *Rowland M. Clinical pharmacokinetics of teicoplanin. Clin Pharmacokinet 1990 Mar:18(3): 184-209*
2. *Fish DN, Chow AT. The clinical pharmacokinetics of levofoxacin. Clin Pharmacokinet 1997 Feb:32(2):101-19*
3. *www.accessdata.fda.gov/drugsatfda_docs/label/2009/019537s073,020780s03lbl.pdf*

Specpharm's Range of Antimicrobials

SPEC TEICOPLANIN

200 mg

400 mg

Spec-Topistin

ciprofloxacin

400 mg / 200 ml

200 mg / 100 ml

100 mg / 50 ml

Spec Levofloxacin

250 mg / 50 ml

500 mg / 100 ml

SPECPHARM

S4 **SPEC TEICOPLANIN 200** solution for IV; per vial contains 200 mg teicoplanin, Reg No: 42/20.1.1/0888; **SPEC TEICOPLANIN 400**, per vial contains 400 mg teicoplanin, Reg No: 42/20.1.1/0889. S4 **Spec-Topistin** solution for IV Infusion, per vial contains 2,0 mg ciprofloxacin/ ml 0,9% NaCl. Reg No: 37/20.1.1/0655. S4 **Spec Levofloxacin 250** solution for IV; contains levofloxacin 250 mg/ 50 ml bag; Reg no: 42/20.1.1/0440. **Spec Levofloxacin 500** solution for IV contains levofloxacin 500 mg/100 ml bag. Reg no: 42/20.1.1/0428. For further prescribing information please refer to the approved package insert. HCR: Specpharm (Pty) Ltd Reg. No.: 97/00203/07. Cnr 15th and Pharmaceutical Road, Halfway House, Midrand. PO Box 651, Halfway House 1685, Gauteng. Telephone: + 27 11 652 0400. Certification No.: TEICO/15/06-05-2013.

www.specpharm.com

Confounding Predictions, Studies Show Sharp Drop in Dementia

Two recent studies published in Britain in The Lancet offer encouraging signs of a significant decline in the rate of elderly people affected by dementia. One of the studies, the Cognitive Functioning and Ageing Study (CFAS) I and II conducted in England and Wales, shows a dramatic drop in dementia rates in people aged 65 and over. Expectations based on previous data suggested that 8.3% of the subjects would show signs of dementia in 2011, but findings showed evidence of dementia in 6.5%. This decrease of 1.8% has led researchers to conclude that there is a cohort effect: dementia risk is lower for those born later in the previous century.

The Danish study compared two cohorts born ten years apart. It examined the test results of people aged 93 (born in 1905) whose mental ability was tested in 1998, comparing them with the scores from the second cohort of ninety-five year olds (all born in 1915) and assessed in 2010. The same design and assessment instrument was used for both cohorts. Cognitive and physical functioning were tested. Of those assessed in 2010, 23% scored maximum scores, twice as many as those achieving this a decade earlier. Severely impaired patients fell from 22% to 17%, with the later-born cohort showing higher chances of surviving longer with better overall functioning.

Education, heart care get the credit

These new studies seem to show that better health and education could see a fall in dementia rates. Now it seems that, at least in developed countries such as the UK and Denmark, the incidence of dementia reduces among the better educated as well as among people whose cardiovascular risks are well controlled, since some dementia might be caused by vascular damage and mini-strokes.

Given the huge emotional and financial toll that dementia carries, these studies offer a ray of hope amid current projections which calculate a doubling of the dementia rate over the next thirty years. If further studies yield results that confirm the trends noted in the new studies, these projections may change considerably.

Poisons Information at Your Fingertips: New Online Database

Treatment protocols for more than 40 000 potential poisons are now available online via the Afritox Poisons Information System. Continuously updated and based on information which was previously distributed on disk to selected centres in SA and other African countries, the online database is managed by the Poisons Information Centre at the Red Cross War Memorial Children's Hospital in Cape Town. The Centre has been the sole collator and provider of information about poisons and treatment protocols in SA since 1987.

Afritox claims to be the only source of information about the contents of locally found substances and commercial products, making it ideally suited to Southern Africa. However, it also provides comprehensive information about potential poisons, chemicals and drugs encountered globally.

Afritox is available through annual paid subscription to GPs, paediatricians, physicians, ICU and emergency units in two versions:

- Continuous online access is available on any laptop, desktop or smartphone. Treatment protocols are given for both children and adults.
- Alternatively, the downloadable version can be installed on a personal computer, with updates of new data downloaded whenever the internet is accessed. This version is ideal for subscribers who need vital information at their fingertips but might have intermittent internet access.

In addition, Afritox offers a free access webpage for people seeking information about potential poisons. The site lists numerous products which are not toxic so that members of the public can make informed decisions about accidental ingestion of worrisome substances, and avoid needless consultations, admissions or treatment for low-risk or non-toxic substances. Products or chemicals for which no information is given on the public website are those which pose a risk and require treatment. Users are asked to contact the Poisons Information Centre directly for further advice.

Infant Reflux Guidelines: Conservative for GER but Important to Identify and Treat GERD

New American Association of Pediatrics guidelines stress how important it is to distinguish between physiologic gastroesophageal reflux (GER) and gastroesophageal reflux disease (GERD). Effective treatment depends on correctly identifying if an infant is suffering from GER or GERD. For both, lifestyle changes are the first line of treatment, but medicines are explicitly indicated for GERD only. The recent guidelines encourage doctors to avoid unnecessary, costly treatments and take note of risk factors associated with gastric motility promoters and proton pump inhibitors in young patients.

GER is the passage of gastric contents into the oesophagus. However, GERD is reflux associated with more troublesome and worrying symptoms. When reflux symptoms are intractable or life-threatening these complications require more intensive interventions, even surgery in some cases.

GERD symptoms vary and are affected by the age of a patient, but mucosal injury is a key characteristic of the disease. It can lead to a range of symptoms, including poor weight gain, vomiting, dysphagia and esophagitis. There may also be abdominal or substernal/retrosternal pain. Further causes for concern in GERD are wheezing and a refusal to feed in infants, as well as cough, laryngitis, pharyngitis, sinusitis, recurrent otitis media, and dental erosion.

Diagnosis is made complex by the absence of any single test, so a systematic approach is suggested in the newest guidelines, including upper gastrointestinal tract contrast radiography, intraluminal esophageal pH monitoring, multiple intraluminal impedance, astroesophageal scintigraphy scans and endoscopy or esophageal biopsy.

First modify the diet

First-line treatment for infants is lifestyle modification. Breastfeeding mothers should adapt their own diets, and infants' feeding volumes and times can be adjusted. Changing babies fed on formula to a protein hydrolysate formula thickened with a small amount of rice cereal is recommended.

Keeping an infant upright or prone during feeding is helpful, but semisupine positioning should be avoided during and after feeding as it can exacerbate GER.

Possible safety risks are associated with antacid and acid suppressants for chronic treatment, with some agents not having been tested in paediatric patients.

The benefits of prokinetic agents may also be outweighed by possible adverse effects. Proton pump inhibitors necessitate specific timing, while therapies such as H2RAS may show rapid reduction in efficacy over time.

A key point stressed in the guidelines is identifying paediatric patients who are at risk for GERD and its serious complications. However, it is also important to avoid extraneous procedures and therapies in infants with GER who do not present with these complications.

Tip to Keep Eyes Sparkling and Moist

One of the world's top beauties and former Victoria's Secret model, Miranda Kerr, has revealed that she avoids camera flash burn by lubricating her eyes with a nature-based eye drop.

Quoted on website Into The Gloss, Kerr, 30, who shot to prominence in 2007 as a Victoria Secret Angel, said she kept Similasan Dry Red Eye Relief in her handbag at all times for photo shoots.

"I always keep my handbag packed with a few essentials... and I always keep Similasan Dry (Red) Eye Relief on me. My eyes have been burned by flash bulbs twice at photo shoots – like blisters on my eyes – so I try to keep them lubricated now," she said.

Swiss-based Similasan (www.similasan.co.za) produces a high quality homeopathic range of eye, ear, nose and throat products available in SA - through Litha Pharma - and sold across the world.

Dry Red Eye Relief soothes, clears and moisturises dry, red and irritated eyes without the sting. It contains no potentially damaging chemical vasoconstrictors, used in other eye drops to contract and narrow blood vessels in the eyes.

As Popular Medical Procedures are Retested, Reversals Mount

A review by the Mayo Clinic of a decade's worth of research published in *The New England Journal of Medicine* (2001-2010) led researchers to conclude that, in all classes of medical practice, a significant number of new drugs and procedures are either no better than the old ones, or may even be worse.

Although new medical practices become popular and are adopted because there is compelling evidence of their clinical superiority or non-inferiority, the report notes that, "the history of medicine, however, reveals numerous exceptions to this rule." Medical reversals, it argues, "occur when new studies – better powered, controlled, or designed than their predecessors – contradict current practice." Reversals therefore describe a situation in which subsequent research finds that a newer medical practice is "inferior to a lesser or prior standard of care."

The Mayo Clinic study reviewed 2044 original articles, with 1344 focused on a specific medical practice. Of these, 73% investigated new medical practices and 27% tested established practices. Results indicated that, "of the 363 articles that tested an existing medical practice, 146 (40.2%) found it ineffective compared with a previous standard or its omission (reversals), whereas 138 (38%) upheld the practice, and 79 (21.8%) were inconclusive."

HRT, asthma, diabetes

One example they cite is the routine use of HRT in postmenopausal women (cardiovascular outcomes were worse for these women than no intervention in other patients). Another relates to the use of impermeable bedcovers to control mite allergen exposure for adults with asthma; this expensive preventive measure was shown to have no clinical or physiologic benefit. A key finding in regard to type 2 diabetes revealed that intensive glucose lowering increased mortality in these patients and did not significantly reduce major cardiovascular events when compared with a less stringent glucose level goal. Another found no efficacy in recommended routine screening of diabetic women for asymptomatic bacteriuria. Greater antibiotic use did not improve outcomes or reduce complications.

With regard to breast cancer treatment, the review threw light on the costly, controversial practice of combining conventional adjuvant chemotherapy with autologous stem cell transplantation and high-dose chemotherapy. No improvement in survival was found, although relapse risk reduced.

When hypothermia isn't cool

Another study showed that mild intraoperative hypothermia during intracranial aneurysm surgery, a practice used in 50% of aneurysm surgeries, did not improve neurologic outcomes, but was associated with some increase in bacterial infections.

Another form of reversal which surprised the researchers was the withholding of potentially beneficial therapies due to unfounded or contradicted concerns, such as not permitting vaccinations for multiple sclerosis patients for fear of a flare-up. Likewise, concerns about oral contraceptives increasing lupus flares persist despite trials in 2005 refuting these worries.

The full list of these 146 reversals can be found at http://download.journals.elsevierhealth.com/mmcs/journals/0025-6196

Treatment Decisions in Adult Rhinosinusitis *From page 53*

exclude chronic rhinosinusitis in these patients.

- Allergic rhinitis – seasonal or perennial allergic rhinitis may exist in isolation, without the presence of chronic rhinosinusitis. If in doubt of the diagnosis, a prolonged trial of intranasal corticosteroids is indicated.
- Vasomotor rhinitis (VMR) – this is a relatively common condition, particularly in the elderly, in which the nasal secretory glands undergo autonomic deregulation, resulting in clear mucoid rhinorrhoea without any other symptoms of rhinosinusitis. Rhinorrhoea is typically exacerbated by changes in humidity, temperature and some foods and chemicals. VMR typically does not respond to intranasal corticosteroids and requires anticholinergic nasal sprays.
- Gastroesophageal reflux disease (GORD) – this can cause a postnasal drip sensation associated with a chronic cough. There is some evidence to suggest that GORD may contribute to the aetiology of chronic rhinosinusitis in some patients due to acid reflux into the posterior nasal cavity.
- Nasal obstruction as a result of adenoid hypertrophy, nasopharyngeal or nasal tumours.

Conclusion

Acute rhinosinusitis and chronic rhinosinusitis are common disorders that are often seen in general practice. Acute rhinosinusitis is a bacterial infection of the sinuses that is nearly always preceded by a viral URTI. A thorough history, with emphasis on symptom duration, is important so that GPs can differentiate between a viral URTI that does not require antibiotics and acute rhinosinusitis that requires antibiotic therapy when symptoms are severe.

Chronic rhinosinusitis represents an inflammatory disorder of multifactorial aetiology. Since symptoms of chronic rhinosinusitis overlap with multiple other nonsinogenic conditions, an accurate history is important. Antibiotic use is controversial in chronic rhinosinusitis; therapy is aimed at addressing predisposing factors such as allergic rhinitis.

A sinus CT scan and referral to an ENT specialist are indicated when acute rhinosinusitis and chronic rhinosinusitis do not respond to appropriate medical management, when acute rhinosinusitis is recurrent, or if the diagnosis is in doubt or complications of sinusitis are suspected.

References are available on request.

Seizure Control Reaches a New Level of Affordability

Epilepsy is one of the most common neurological disorders in South Africa.[1]

In this regard, Pharma Dynamics, a leading supplier of effective, affordable, quality medicines, has launched Dyna Levetiracetam.

Levetiracetam is a unique antiepileptic drug due to its linear pharmacokinetics, minimal drug interactions, seizure efficacy and good tolerability.[1]

Levetiracetam is indicated as adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in adults and children over age 16.

Levetiracetam is now accessible to many more patients as Dyna Levetiracetam offering the patient a cost saving of up to 57% compared with the originator levetiracetam.[2]

The package insert as approved by the Medicines Control Council is available upon request from k.bissolati@pharmadynamics.co.za

Reference:

1. References available on request.

2. Prices as per Department of Health website. http://www.doh.org.za – Accessed 24/05/13.

For convenient titration, Dyna Levetiracetam is available in three dosage strengths:

Product	Active	Pack size	Price (SEP excl VAT)[2]
Dyna Levetiracetam 250mg	Levetiracetam 250mg	60	R121.04
Dyna Levetiracetam 500mg	Levetiracetam 500mg	60	R242.06
Dyna Levetiracetam 750mg	Levetiracetam 750mg	60	R363.10

Konica Minolta Medical – Serving with Passion; Delivering Results

Konica Minolta Medical South Africa (KMMSA), a sister company to Konica Minolta SA, leverages off its membership of the Bidvest Group to give back to communities in this country.

The Bidvest Group is one of SA's biggest success stories - an international services, trading and distribution company that's listed on the JSE and operates across four continents. This footprint gives it more than recognition as a business powerhouse; it provides a strong platform for member companies to become involved in projects that enhance the lives of communities.

Support for Pink Drive

KMMSA has taken up this opportunity and is bringing it to life by joining the Pink Drive initiative.

"Pink Drive is one of SA's foremost breast cancer community carers," explained Chrizelle van der Westhuizen, spokesperson for KMMSA. "Pink Drive is centred around mammography and breast health and the premise that 'early detection saves lives'.

Pink Drive provides free mobile breast cancer screening via its dedicated mobile breast check units, as well as education for underprivileged patients through three mobile educational units. Teams travel through semi-urban and urban areas around SA to give disadvantaged communities information, physical examinations and advice on breast health, early detection of breast cancer and breast self-examination techniques.

Equipping the units

To date, the initiative has provided 4464 free mammograms, undertaken 41 759 clinical breast examinations and educated in excess of 51 600 women on the importance of breast health.

In conjunction with Bidvest's continued support on this exciting initiative, KMMSA's involvement will equip the Pink Drive mobile units to make them digitally compatible. This includes installing state-of-the-art CR multi-slot readers as well as the RamSoft PACS (picture archiving and communication systems) that enables immediate reporting from wherever the units are currently operating.

"Together with the involvement of Pink Drive partners like radiologist, Dr Louella Ritz and KMMSA partners Vertec and RamSoft, our vision is to use our knowledge, technology and resources to give all South Africans the education and support they need to care for their breasts."

"Our motto is 'the business of medical', but our passion is the people of our wonderful country."

MODERN MEDICINE'S CPD JOURNAL PROGRAMME

ANSWER FORM

Accredited by the SAMA Health Care/Policy and CPD Unit.

SURNAME	INITIALS	YOUR HPCSA REG. NO. MP

Postal Address:

Postcode:

Tel: Fax:

E-mail:

INSTRUCTIONS

1. Use a blue or black pen only.
2. Fill in the appropriate circle completely, ie ● – do not use X or ✓ or any other mark.
3. Erase or white out mistakes fully.
4. Answer all the questions.
5. Each group earns 1 CPD point.

Month of issue
AUGUST 2013

Please return by November 30, 2013

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

ECG OF THE MONTH	METABOLIC SYNDROME	ERECTILE DYSFUNCTION	ADULT RHINOSINUSITIS	CONSCIOUS SEDATION
1 T F	1 T F	1 T F	1 T F	1 T F
2 T F	2 T F	2 T F	2 T F	2 T F
3 T F	3 T F	3 T F	3 T F	3 T F
4 T F	4 T F	4 T F	4 T F	4 T F
5 T F	5 T F	5 T F	5 T F	5 T F

Once completed . . .

- Make an accurate and clear photocopy of this answer form for your records.
- Cut this CPD answer form out of the journal carefully, place in a stamped, addressed envelope, and post it to MODERN MEDICINE, PO Box 84622, Greenside 2034, South Africa (Do not register the letter) - OR Scan the completed answer form and email it to CPD@modernmedia.co.za
- The publisher cannot be held responsible for answer forms not received by post.
- Credit for these CPD modules needs to be maintained in doctors' personal records.

I declare that these are my own answers, and I would like to continue receiving Modern Medicine.

Signature: _____

Date: _____

WITHHOLDING & WITHDRAWING TREATMENT (2pts)
1 T F
2 T F
3 T F
4 T F
5 T F

CUT ALONG DOTTED LINE

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

QUESTIONS FOR CPD ARTICLES: AUGUST 2013

CPD: 5 Regular points; 2 Ethics points

Instructions

1. *The answer form is bound into this journal opposite.*
2. *Read the instructions on the answer form and answer the questions carefully.*
3. *Your answers for the August 2013 issue must reach Modern Medicine, PO Box 84622, Greenside 2034 by November 30, 2013.*
4. *You must score at least 80% in a section to be awarded the assigned CPD point for it.*
5. *Modern Medicine will keep track of all CPD points earned and will issue a single, comprehensive certificate to all participants at year-end.*

Answer the following questions as either true or false. All the answers are to be found in the CPD articles in this issue.

WITHHOLDING & WITHDRAWING TREATMENT (Pg 16)

1. Nozick's Principle justifies a non-equivalence view of withholding versus withdrawing treatment.
2. Capacity and Competence are terms used interchangeably in discussions regarding consent.
3. The patient's regular physician is the best person to assess capacity.
4. For a vegetative state to be termed persistent at least 6 months should be allowed.
5. Distributive Justice is most important when deciding to withdraw treatment in cases with PVS.

ECG CHALLENGE (Pg 19)

1. Patient has atrial fibrillation as the R-R interval is irregular.
2. The QRS morphologies differ due to the premature ventricular complexes (PVCs).
3. Patient has had previous myocardial infarction as evidenced by Q waves in LIII.
4. There is evidence of acute myocardial ischaemia and patient requires urgent coronary angiography.
5. There is a great need to carefully select any medication(s) prescribed or over the counter due to the ECG abnormality noted.

METABOLIC SYNDROME (Pg 31)

1. The metabolic syndrome is an inevitable consequence of obesity.
2. Treatment should aim to reduce total cholesterol levels to 5mmol/L.
3. Treatment should aim to get fasting blood sugar levels to less than 5.5mmol/L.
4. The target is to reduce blood pressure to 140/90.
5. Compared to higher dosage regimes, low-dose aspirin (75mg/day) reduces the risk for major bleeding.

ERECTILE DYSFUNCTION (ED) (Pg 39)

1. Persistent ED suggests an organic cause.
2. Psychogenic ED is usually found in older men with depression.
3. Sildenafil is a phosphodiesterase-5 inhibitor.
4. Vardenafil has the advantage of a longer half-life.
5. Alprostadil is the drug of choice for intracavernosal injection.

ADULT RHINOSINUSITIS (Pg 49)

1. In chronic rhinosinusitis the symptoms last longer than 12 weeks.
2. Rhinitis medicamentosa is caused by the use of intranasal steroids for more than 5 days.
3. Antibiotics are the mainstay of treatment for acute Rhinosinusitis.
4. The atypical facial pain syndrome is causes by Moraxella catarrhalis.
5. Nasal polyps and eosinophilia are common in allergic fungal rhinosinusitis.

CONSCIOUS SEDATION (Pg 54)

1. Only ASA 1 and 2 patients qualify for sedation outside the operating room.
2. Only clear fluids should be taken three hours before the sedation procedure.
3. The anatomy of the airway is the same in adults and in children.
4. A patient can still give informed consent after a sedative has been administered.
5. Both electronic and clinical monitoring are important in a patient undergoing sedation.

See answer form opposite

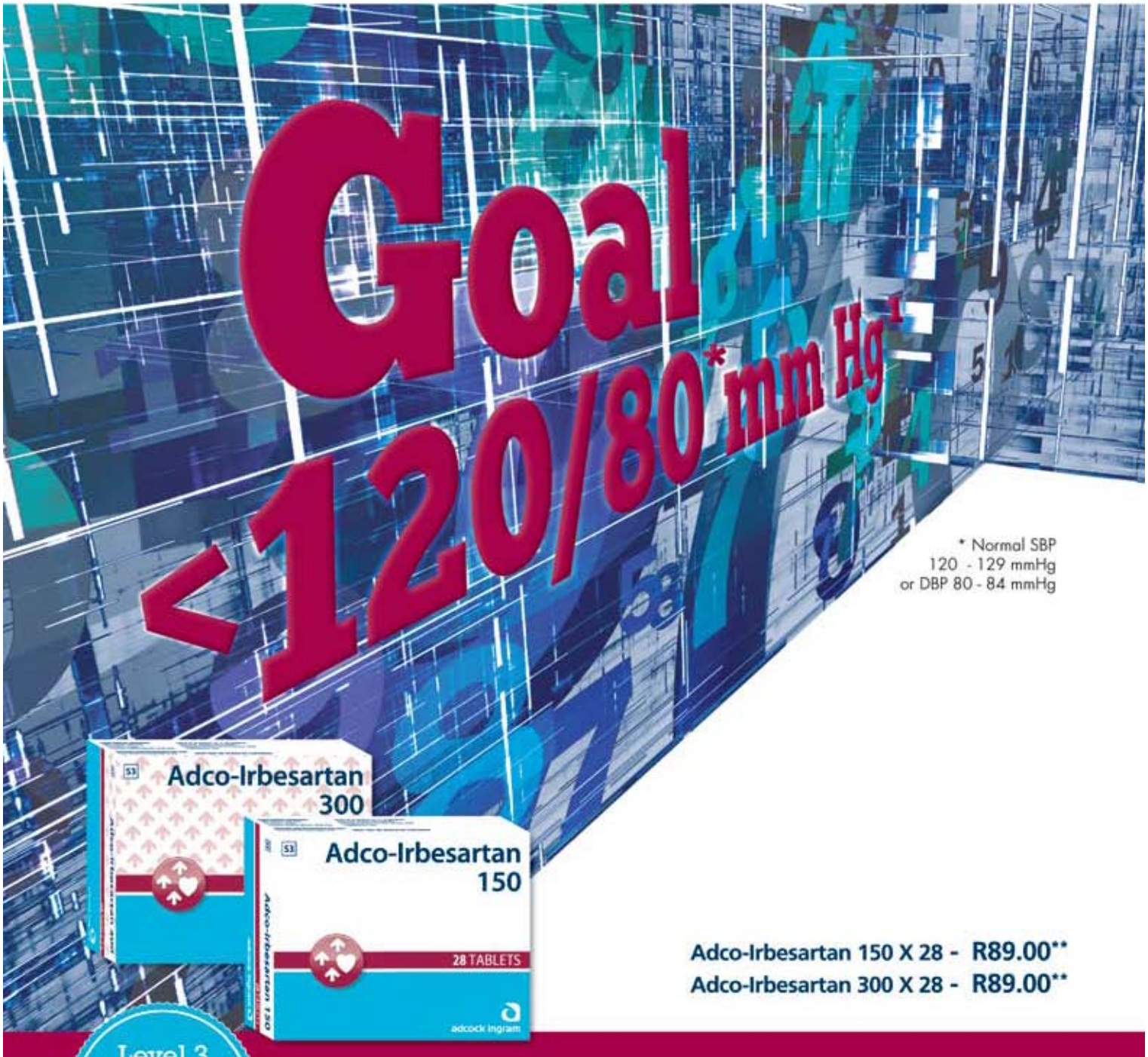
MAY WINNER: CONGRATULATIONS TO DR G STOCKTON OF HOUT BAY WHO WINS THE OTC PHARMA HAMPER!

2013 Medical Conference Planner

Your Reminder

2013		
1 - 2 Sep	**Professional Beauty Johannesburg** WHERE: Gallagher Convention Centre, Midrand, JOHANNESBURG CONTACT: Probeauty • 011-781-5970 • belinda@probeauty.co.za	**EXHIBITION, 10 Speakers** www.probeauty.co.za
2 - 4 Sept	**Rehabilitation Research Conference 2013** WHERE: UCT, CAPE TOWN CONTACT: Bonnie Croeser • 021-406-6401 • bonnie.croeser@uct.ac.za	**CPD, EXHIBITION, 10-50 Speakers** rehabconf2013.uct.ac.za
2 - 4 Sep	**NEA/FUNDISA - Nursing Education Association/Forum of University Nursing Deans Nursing Education Conference** WHERE: Birchwood Hotel, JOHANNESBURG CONTACT: NEA & FUNDISA • 012-333-1415 • admin.nea@edunurse.co.za	**CPD, EXHIBITION, 10-50 Speakers** www.edunurse.co.za / www.fundisaforum.org
2 - 4 Sep	**Burn Society 15th Congress** WHERE: Oysterbox Hotel, Umhlanga, DURBAN CONTACT: Onscreen Conferences • 021-486-9111 • info@onscreenav.co.za	**CPD, EXHIBITION, 10-50 Speakers** www.saburnsociety.org.za
2 - 5 Sep	**SAOA - 59th Congress of the Orthopaedic Association** WHERE: Sun City Resort, SUN CITY CONTACT: ICE Solution • 011-911-1921 • marie@icesolution.co.za or kerrie@icesolution.co.za	**CPD, EXHIBITION, 10-50 Speakers** www.saoa.org.za
5 - 10 Sept	**Options VIII for the Control of Influenza** WHERE: Cape Town ICC, CAPE TOWN CONTACT: Integress Meetings and Events • +1-404-591-3281 info@controlinfluenza.com	**CPD, EXHIBITION, 50-100 Speakers** optionsviii.controlinfluenza.com
7 - 8 Sept	**Management of Cardiovascular Disease** WHERE: PRETORIA CONTACT: FPD • 012-816-9000 /9174 • evelynm@foundation.co.za	**CPD, 10 Speakers** www.foundation.co.za
13 - 15 Sept	**HIV/AIDS Management Course** WHERE: DURBAN CONTACT: FPD • 012-816-9000 /9176 • evelynm@foundation.co.za	**CPD, 10-50 Speakers** www.foundation.co.za
13 - 15 Sept	**The Cutting Edge in Oral and Maxillo-Facial Surgery: Orthognathic Surgery, Facial Cosmetic Surgery & Reconstructive Surgery** WHERE: Hilton, Sandton, JOHANNESBURG CONTACT: Conference Management MECC • +1-305-663-1628 tvalls@meccinc.com	**CPD, EXHIBITION, 10-50 Speakers** www.plasticsurgeons.co.za
16 - 20 Sept	**Aeromedical Evacuation and Transport Course** WHERE: College of Emergency Care, UCT, CAPE TOWN CONTACT: Janet Sirmongpong • 021-406-6348 • janet.sirmongpong@uct.ac.za	**CPD, 10-50 Speakers** www.eci-sa.org
20 - 22 Sep	**COSMEDICA Conference** WHERE: Sandton Sun, JOHANNESBURG CONTACT: Cosmedica Management • 011-958-2261 • info@cosmedica.co.za	**CPD, EXHIBITION, 10-50 Speakers** www.cosmedica.co.za
28 - 29 Sept	**HIV/AIDS in the Workplace** WHERE: PORT ELIZABETH CONTACT: FPD • 012-816-9000 /9174 • evelynm@foundation.co.za	**CPD, 10-50 Speakers** www.foundation.co.za
28 Sep - 1 Oct	**SASLHA/SAAA/ENT - Speech-Language-Hearing Association, Association of Audiologists National and ENT Conference** WHERE: University of the Free State, BLOEMFONTEIN CONTACT: Eastern Sun Events • 041-374-5654 • ent@easternsun.co.za	**CPD, EXHIBITION, 50-100 Speakers** www.entcongress.co.za

When an ARB is required to achieve the ideal blood pressure...
...always remember Adco-Irbesartan



* Normal SBP
120 - 129 mmHg
or DBP 80 - 84 mmHg

Adco-Irbesartan 150 X 28 - R89.00**
Adco-Irbesartan 300 X 28 - R89.00**

Level 3 BBBEE contributor
SANAS ACCREDITED

**Database of Medicine Prices [Online]. Date as on the website [cited 26 April 2013] Available from URL:http://www.mpr.gov.za/PublishedDocuments.aspx

Reference: 1. Seedat YK, Rayner BL. South African Hypertension Guideline 2011. *S Afr Med J* **2012**;102:57-84.

Adco-Irbesartan 150 & 300. Each tablet contains 150 & 300 irbesartan respectively. Reg. No: 44/7.1.3/0530, 44/7.1.3/0531

For full prescribing information refer to the package insert approved by the medicines regulatory authority. ZA.13.GEN.020 05/2013

Adcock Ingram Limited. Reg. No. 1949/034385/06. Private Bag X69, Bryanston, 2021. Tel: +27 11 635 0000 www.adcock.com

adcock ingram generics

adcock ingram

generics

Serez 25, 100, 200, 300. Each tablet contains quetiapine fumarate equivalent to 25, 100, 200, 300 mg quetiapine free base respectively. Reg. No. 43/2.6.5/0796, 43/2.6.5/0797, 43/2.6.5/0798, 43/2.6.5/0799 respectively. Applicant: Lasara Traders (Pty) Ltd. Marketed by Adcock Ingram Healthcare (Pty) Ltd. **Gen-Payne Capsules.** Each capsule contains 10 mg codeine phosphate; 200 mg ibuprofen; 250 mg paracetamol. Reg. No. 35/2.8/0046. **Migroben® 80.** Each film-coated tablet contains 80 mg valsartan. Reg. No. 43/7.1.3/0032. **Migroben® 160.** Each film-coated tablet contains 160 mg valsartan. Reg. No. 43/7.1.3/0033. **Co-Migroben® 160/12,5.** Each film-coated tablet contains 160 mg valsartan and 12,5 mg hydrochlorothiazide. Reg. No. 43/7.1.3/0084. **Co-Migroben® 160/25.** Each film-coated tablet contains 160 mg valsartan and 25 mg hydrochlorothiazide. Reg. No. 43/7.1.3/0085. **Acnetane® 10 mg.** Each capsule contains 10 mg isotretinoin. Reg. No. 34/13.4.2/0356. **Acnetane® 20 mg.** Each capsule contains 20 mg isotretinoin. Reg. No. 34/13.4.2/0357. **Adco-Alzam 0,25 mg.** Each tablet contains 0,25 mg alprazolam. Reg. No. 30/2.6/0212. **Adco-Alzam 0,5 mg.** Each tablet contains 0,5 mg alprazolam. Reg. No. 30/2.6/0211. **Adco-Alzam 1 mg.** Each tablet contains 1 mg alprazolam. Reg. No. 30/2.6/0213. **Adco-Zildem 60.** Each tablet contains 60 mg diltiazem hydrochloride. Reg. No. 30/7.1/0287. **Adco-Zildem 90.** Each tablet contains 90 mg diltiazem hydrochloride. Reg. No. 30/7.1/0288. **Adco-Zildem 180 SR.** Each tablet contains 180 mg diltiazem hydrochloride. Reg. No. 30/7.1/0183. **Adco-Zildem 240 SR.** Each tablet contains 240 mg diltiazem hydrochloride. Reg. No. 30/7.1/0184. **Adco-FEM 35.** Each tablet contains cyproterone acetate 2 mg and ethinyloestradiol 0,035 mg. Each non-hormonal tablet contains sugar: Lactose monohydrate 67 mg. **Adco-Talomil 20 mg.** Each tablet contains 25 mg citalopram hydrobromide equivalent to 20 mg citalopram. Reg. No. 35/1.2/0272. **Adco-Bisocor 5 mg.** Each film-coated tablet contains 5 mg bisoprolol. Reg. No. 37/5.2/0010. **Adco-Bisocor 10 mg.** Each film-coated tablet contains 10 mg bisoprolol. Reg. No. 37/5.2/0011. **Adco-Atenolol 50 mg.** Each tablet contains 50 mg atenolol. Reg. No. W/5.2/115. **Adco-Atenolol 100 mg.** Each tablet contains 100 mg atenolol. Reg. No. W/5.2/116. **Adco-Zetomax 5 mg.** Each tablet contains lisinopril 5 mg (as the dihydrate salt). Reg. No. 33/7.1.3/0513. **Adco-Zetomax 10 mg.** Each tablet contains lisinopril 10 mg (as the dihydrate salt). Reg. No. 33/7.1.3/0514. **Adco-Zetomax 20 mg.** Each tablet contains lisinopril 20 mg (as the dihydrate salt). Reg. No. 33/7.1.3/0515. **Adco-Zetomax Co 10/12,5.** Each tablet contains lisinopril dihydrate (equivalent to 10 mg anhydrous lisinopril) and hydrochlorothiazide 12,5 mg. Reg. No. 37/7.1.3/0160. **Adco-Zetomax Co 20/12.5.** Each tablet contains lisinopril dihydrate (equivalent to 20 mg anhydrous lisinopril) and hydrochlorothiazide 12,5 mg. Reg. No. 37/7.1.3/0162. **Adco-Zopimed.** Each film-coated tablet contains 7,5 mg zopiclone. Reg. No. 33/2.2/0450. **Adco-Dapamax.** Each tablet contains 2,5 mg indapamide. Reg. No. 30/7.1/0092. **Adco-Sporozole.** Each capsule contains 100 mg of itraconazole in a microgranule formulation. Reg. No. 37/20.2.2/ 0559. **Adco-Paroxetine 20 mg.** Each tablet contains paroxetine mesylate equivalent to 20 mg paroxetine base. Reg. No. 36/1.2/0096. **Adco-Omeprazole 20.** Each capsule contains 20 mg omeprazole . Reg. No. 37/11.4.3/0228. **Adco-Amoclav BD 1000 mg.** Each film-coated tablet contains amoxicillin trihydrate equivalent to 875 mg amoxycillin and potassium clavulanate equivalent to 125 mg clavulanic acid. Reg. No. 36/20.1.2/0211. **Ponstel 250.** Each capsule contains 250 mg mefenamic acid. Reg. No. 28/2.7/0703. **Ponstel Forte**. Each capsule contains 500 mg mefenamic acid. Reg No. 28/2.7/0548. **Ponstel S**. Each 5 ml suspension contains 50 mg mefenamic acid. Reg No. 28/2.7/0704. **Adco-Simvastatin 10 mg**. Each tablet contains 10 mg simvastatin. Reg. No. 35/7.5/0277. **Adco-Simvastatin 20 mg.** Each tablet contains 20 mg simvastatin. Reg.No. 35/7.5/0278. **Adco-Simvastatin 40 mg.** Each tablet contains 40 mg simvastatin. Reg. No. 35/7.5/0279. **Adco-Vascard 20 SR.** Each sustained release capsule contains 20 mg nifedipine. Reg. No. 30/7.1/0407. **Adco-Vascard 30 SR.** Each sustained release capsule contains 30 mg nifedipine. Reg. No. 32/7.1/0551. **Adco-Zolpidem Hemitartrate 10 mg.** Each tablet contains 10 mg zolpidem hemitartrate. Reg. No. 36/2.2/0132. **Adco-Mirteron 15.** Each tablet contains 15 mg mirtazapine. Reg. No. A39/1.2/0217. **Adco-Mirteron 30.** Each tablet contains 30 mg mirtazapine. Reg. No. A39/1.2/0218 **Adco-Prednisolone Syrup.** Each 5 ml contains prednisolone 15 mg. Reg. No. 38/21.5.1/0125. For full prescribing information refer to the package insert approved by the medicines regulatory authority. ZA.13.GEN.003 02/2013. Adcock Ingram Limited. Reg. No. 1949/034385/06. Private Bag X69, Bryanston, 2021. Tel. +27 11 635 0000. www.adcock.com