

THE JOURNAL OF CLINICAL MEDICINE

MODERN MEDICINE

VOLUME 38 NUMBER 2
FEBRUARY 2013

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Here & Now

ECG of the Month

RoundUp

Get Your Ethics Points Inside!



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- A fixed combination for simple administration ⁴
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References: 1. Scholze J, Breitstadt A, Cairns V, *et al.* Ramipril and hydrochlorothiazide combination therapy in hypertension. A clinical trial of factorial design. *J Hypertens* 1993;11:217-221. 2. Seedat YK, Rayner BL. South African hypertension guideline 2011. *S Afr Med J* 2012;102(1):57-84. 3. Tritace Plus Package Insert. 4. Heidbreder D, Froer K.L, Bauer B, *et al.* Combination of Ramipril and Hydrochlorothiazide in the Treatment of Mild to Moderate Hypertension – Part 2: An Open Long –Term Study of Efficacy and Safety. *Clin Cardiol* 1993;16:47-52.

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Lifelong Learning

ETHICS



Ethics and the Elderly

KEITH BOLTON

This is the first in a series of ethics-related CME articles; written to appear bi-monthly in *Modern Medicine*.

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WOUND CARE

Wound Care Benefit of Instillation Therapy

STAFF WRITERS

Over the past decade the concept of proper wound bed preparation as a means to improve wound healing has gained increasing attention. The principles of wound bed preparation include proper wound debridement, managing wound exudates, and managing bioburden.

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CARDIOLOGY

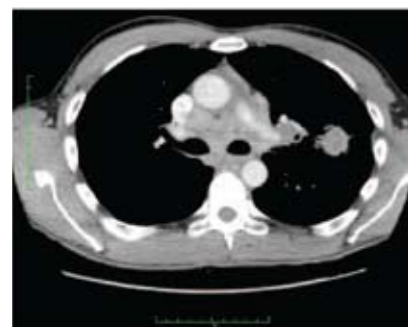


Update on Lipid Management: Commonly Asked Questions

IAN HAMILTON-CRAIG

Target levels for LDL-cholesterol (LDL-C) in patients with cardiovascular disease (CVD) are being lowered. New statin combinations will be more cost effective than present combinations and will help to achieve LDL-C targets. These and other drugs in development promise a new era in CVD prevention.

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CARDIOLOGY

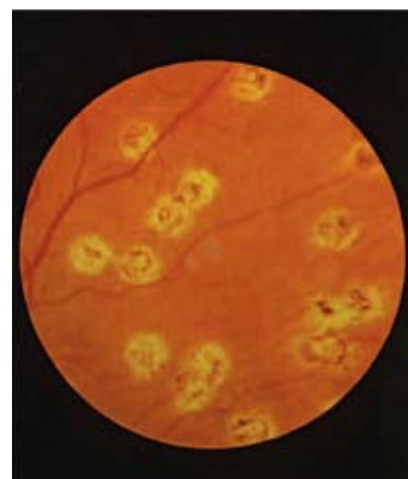


ECG of the Month

ROB SCOTT MILLAR

A previously active 80 year old man presented with a one month history of tiredness and shortness of breath on exertion. He had been hypertensive for 10 years, on treatment with an ACE inhibitor and a diuretic. His pulse was 120/minute, irregular, and BP 170/90 mmHg.

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TRAVEL MEDICINE

Travel Vaccines: A Comprehensive Guide

PETER VINCENT

Vaccine requirements and recommendations for specific countries change, so it is important to be kept up to date by reliable information sources.

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ONCOLOGY



Diagnosis and Treatment of Lung Cancer: A Focus on the GP's Role

PO YEE YIP, DAVID BARNES, BRIAN MCCAUGHAN, MICHAEL BOYER

The lung cancer epidemic has mirrored changes in smoking patterns in many countries and has caused innumerable deaths. Approaches to identification, diagnosis and treatment of the disease are changing and are discussed in this article.

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STROKE



Stroke in the Elderly: Predictable, Preventable and Treatable 33

BILL O'BRIAN, RICHARD LINDLEW, CHRISTOPHER R. LEVI

Stroke is the second most common cause of death worldwide, with most of the disease burden falling to the elderly and the very elderly.

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Game Changers in Type 2 Diabetes: The Implications of Panretinal Laser Therapy 37

PAT PHILLIPS

Panretinal laser therapy, an effective treatment for sight-threatening diabetic retinopathy, should prompt a major review of diabetes management because retinopathy suggests that other microvascular disease is present, and probably macrovascular disease too.

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- Blood flow restored to thrombosed arteries and veins
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- Better epidural postoperative pain management
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- Health tracking innovation promotes doctor / patient interaction
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- An idea whose time has come
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- HPCSA axes 1500 medical and dental practitioners from its register
- Corruption watch, TAC want to see Gauteng health probe info
- South African innovation acknowledged at Davos

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On the **Horizon**

Anaesthetic Agent Delivery and Recycling Simplified

AnaConDa technology, Sweden, has made the administration of anaesthetic agents simple and safe without use of expensive specialist equipment.

The device, inserted between the ET-tube and the Y-piece of the ventilator circuit, has a high capacity miniature vaporiser that uses the patient's body heat to vaporise clinical amounts of isoflurane or sevoflurane, and a high efficiency conserving medium in the form of active carbon. The device's unique function eliminates the need for the CO₂ absorber and one-way valves normally included in an anaesthetic machine. It is now possible to deliver anaesthetic agents easily and safely with a standard ventilator.

Needed to use the device are a syringe pump, gas monitor and standard ventilator. Special adapters and valves are available for filling the syringe. It is recommended that the gas monitor exhaust and ventilator exhaust be connected to a scavenging system, although 90% of the agent delivered will be recycled.

During expiration, oxygen and CO₂ pass the active carbon into the ventilator circuit and out through its exhaust. The anaesthetic agent is absorbed by the active carbon. During inspiration, the anaesthetic agent is desorbed and transported with oxygen to the patient, with agent evaporated from the evaporator.

This device replaces both the circle system, which allows exhaled gases from the patient to be re-circulated, and the vaporiser used in conventional anaesthetic machines. It can also be used as a humidifier.





On the
Horizon

Tiny Rechargeable Neurostimulator Treats Intractable Chronic Migraine



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Keywords:
Eon mini
neurostimulator

Intractable chronic migraine is one of the most difficult to treat headache disorders. This type of migraine is defined as headache lasting at least four hours per day for 15 or more days per month, causing at least moderate disability, and not responding to three or more preventative drugs. The Eon Mini neurostimulator released by St Jude Medical is expanding doctors' options for helping manage patients who suffer from these disabling symptoms.

The device operates through peripheral nerve stimulation (PNS) by delivering mild electrical impulses to the occipital nerves. A small electrical lead or leads are placed under the skin and connected to the neurostimulator which produces the pulses of stimulation. This device is the world's smallest neurostimulator. It has a 10mm profile and weighs 29 grams. Its small size allows for a smaller incision, making the implant location site less visible and more comfortable for patients.

The device provides high power output with long periods between recharges. The rechargeable battery is rated to last at least ten years before battery replacement surgery is needed.

The device features enhanced microchip and software technology which continuously selects the most efficient power management mode. This preserves the battery's capacity to deliver therapy. The advanced programming capability allows doctors to treat up to eight pain areas simultaneously. The device has been approved in many countries for the management of chronic pain of the body and limbs and from failed back surgeries.

Blood Flow Restored to Thrombosed Arteries and Veins



The AngioJet mechanical thrombectomy by Medrad is the only FDA cleared endovascular treatment option that actually removes a thrombus associated with DVT from the body. This procedure quickly restores blood flow and resolves symptoms within minutes.

The system is designed to remove thrombus by using the Venturi-Bernoulli effect where multiple high-velocity high-pressure saline jets which are introduced through orifices at the distal tip of the catheter. This creates a localised low pressure zone resulting in a vacuum effect which breaks up the

thrombus. Fragments of thrombus are propelled back through the catheter and evacuated from the body.

The system's console features an advanced control system that automatically detects the catheter model and configures the console to meet the requirements of each catheter. Throughout the procedure, the console monitors system performance and displays information regarding runtime and infused fluid volumes. The system is capable of removing large thrombus burden from a range of vessel diameters.

There is a full range of compatible catheters with indications for native coronary arteries and grafts, peripheral arteries and veins, and AV access grafts.



More on...
YouTube
Keywords:
Angiojet
drjuancueto

Recent medical publications on pharmacomechanical thrombectomy (combination of catheter-delivered thrombolytics and mechanical thrombectomy) have reported the advantages of faster symptom relief, less procedure time, reduced time in ICU, a shorter hospital stay and subsequent cost savings.



Patients in Chronic Pain? Set Them Free with Adco Tenyl

Adcock Ingram has launched Adco Tenyl, a fentanyl transdermal therapeutic system designed to deliver fentanyl through intact skin in a controlled manner over a period of 72 hours.¹

Adco Tenyl is indicated in the management of chronic intractable pain that requires opioid analgesia which cannot be managed by a lesser means such as paracetamol-opioid combinations, non-steroidal analgesics or as required dosing with short acting opioids.¹

Adco Tenyl is available in 25µg/h, 50µg/h, 75µg/h and 100µg/h. Dosage must be individualised and assessed regularly. The rate at which tolerance develops varies widely among individuals.¹

Practitioners are cautioned to consult the full package insert before prescribing Adco Tenyl.

Adco Tenyl patches are packed in cartons containing five individually packed closure systems.



Product	NAPPI Code	Pack Size	Schedule	Price ²
Adco Tenyl 25µg/h	716797001	5 Patches	S6	R287.16
Adco Tenyl 50µg/h	716798001	5 Patches	S6	R475.36
Adco Tenyl 75µg/h	716799001	5 Patches	S6	R654.80
Adco Tenyl 100µg/h	716800001	5 Patches	S6	R838.24

References: 1. Adco Tenyl approved package insert.

2. Blue Book price list September 2012.

Better Epidural Postoperative Pain Management

Epidural analgesia has traditionally been provided to patients by manual bolus injections from a doctor, continuous infusions from an IV bag or intermittent infusions controlled by the patient. This may result in inconsistent and ineffective pain relief as well as frequent doctor interventions. The Cadd-Solis pain management system with programmed intermittent bolus (PIB) delivery has been launched by Smiths Medical, Minnesota, in countries outside the USA. The new customisable system will help doctors overcome the challenges in maintaining effective analgesia for labour and delivery or for post-operative pain management patients.

The pain management system consists of:

- An ambulatory infusion pump – a small lightweight pump promotes mobility and doctor convenience. The versatile pump can be used for a variety of pain management therapies and patients. The large colour graphic display screen helps doctors view and verify pump programmes, identify and respond to alarms and interpret therapy trends and patient activity. The pump's task-based software and cell-phone design make it easy to use.

- Medication safety software – this is designed to reduce the risk of medication delivery errors. The software allows pharmacists to enter custom therapy-based protocols, drug names, concentrations and dosing limits for standardised programming downloads to the pumps.
- Medication cassette reservoirs and administration sets – exclusive reservoirs and sets contain or connect to medication and fit securely onto the pump, to promote increased medication security. The pump with reservoirs can easily fit into a pouch to allow patient mobility during therapy.





On the
Horizon

Effective Dense Breast Screening System



Screening mammography has long been the mainstay for detecting non-palpable breast cancer. However, breast density is a major limitation to the sensitivity of mammographic screening.

The Somo-V Platinum automated breast ultrasound (ABUS) system, by U-Systems, California, is designed to automatically scan a woman's breast capturing multiple ultrasound images and displaying them in 3D. The system is ideal for women with dense breasts.

The system has an ergonomic reverse curve transducer that

conforms to the anatomical curve of a woman's breast, for improved comfort and imaging performance during a scan. The transducer uses convergent scan line geometry, enabling ultrasound beams to penetrate the skin perpendicularly. This improves penetration and sharpens focus at depth. The reverse curve also creates uniform compression thickness across the entire breast, enhancing image quality. Overlapping wide field-of-view imaging ensures coverage of the whole breast.

The high frequency ultra-broadband transducer delivers a 3D volume view of 15cm x 17cm x 5cm. The high centre-frequency sharpens detail resolution while the ultra broadband performance delivers contrast differentiation, resulting in precise anatomical detail of complex breast tissue and structures.



The system's patented soft touch breast stabilisation membrane and proprietary positioning protocols enable rapid and reproducible breast exams, saving time and improving consistency. Reproducible breast exams allow for accurate comparison of images obtained from previous studies.

Two New Fixed Combinations from Sanofi

Amaryl Combi: Type 2 diabetes

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

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

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

Amaryl Combi should be taken once or twice daily before or with meals. It is a schedule 3 medicine.



Tritace Plus: Hypertension

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

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

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





Health Tracking Innovation Promotes Doctor / Patient Interaction

FolUp, is a mobile and web-based health communication platform that connects practitioners and patients, allowing each to collaborate and actively participate in improving patient care and satisfaction.

This online tool provides patients with a secure platform where they can actively participate in their health management process through tracking their symptoms, how they feel and how they respond to medication. The use of the platform, either via the web or mobi apps, is free for both the practitioner and patient.

“Managing complex diseases is a difficult undertaking for health professionals and patients alike,” says Simon Spurr, co-founder and director of FolUp South Africa. “Clinicians’ time to allocate to patients is often limited which can leave patients feeling isolated. Through improved patient monitoring and doctor feedback, FolUp provides an overview of the entire health patient experience and has the ability to increase patients’ control over their diseases, levels of emotional well-being and accelerate patient healing.”

Patient dashboard

The platform forms part of a web ecosystem, allowing patients to connect with existing forums, medical apps and software that will interface with a myriad of apps, peripheral devices and self-help tools entering the mobile health (mHealth) market – a market expected to grow 20% annually over the next three to five years.

Through patients’ dashboards, doctors will have access to information, insights and trends collated from unstructured medical, social and quality of life data collected through patient entries, diaries, games and blogs.

“Patient feedback is extremely valuable and technology is the best medium to assist doctors in gathering this information to gain deeper



FolUp is an innovative social platform that connects healthcare practitioners and patients, allowing each to collaborate and actively participate in improving care and patient satisfaction.

insight and improve symptom monitoring, diagnosis, treatment and overall patient care,” adds Spurr. “This new type of communication between doctors and patients will also optimise consultations through providing insight into new symptoms, side effects, mood disorders and quality of life issues.”

The secure platform also allows patients to anonymously build networks, or ‘circles of care’, to find support and engage with patients with similar conditions.

“As more than 20 million South Africans live with a chronic disease, which account for 70% of all deaths, this technology has the potential to fundamentally alter the economics of patient care,” concludes Spurr.

Visit www.folup.com to register.

Insertable Cardiac Monitor Reveals Unpredictable Syncope Causes

In patients with unexplained and unpredictable transient symptoms such as dizziness, syncope, palpitations and chest pains that may suggest cardiac arrhythmia, the Reveal family of Insertable Cardiac Monitors (ICM) by Medtronic can test abnormal arrhythmia as a cause.

Placed just under the skin of the chest in an outpatient procedure, the device captures and stores ECG recordings in two ways: a patient-activated feature allows the patient to press a button and store an ECG reading during a syncope episode; and an auto-activated feature automatically detects and records pre-defined arrhythmic events. The stored information can be transmitted remotely via the Medtronic CareLink Network or revealed during an in-office patient visit.

The devices can detect atrial fibrillation and provide longer-term trended diagnostic data including daily AF burden, patient activity



and average day and night heart rates.

Syncope accounts for 1% to 6% of hospital admissions and about 1% of visits to the emergency department each year. Some causes of syncope are harmless, others may be life-threatening. Fainting may lead to further injuries, as 70% of patients in the PICTURE study (the largest international, multi-centre clinical trial on insertable cardiac monitors) had been hospitalised at least once for syncope and more than a third had experienced significant physical trauma in association with a syncopal episode.

Quoth the Maven



Keith Bolton

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

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

This month's *Modern Medicine* sees the introduction of the first ethics article with an opportunity to get those elusive ethics CPD points. These will be featured every second month and will focus on clinical ethical and legal topics. I hope that they will get you thinking on how to weave your way through the ethical minefield that is modern clinical practice.

Three of the four medical articles featured for CPD points relate to problems common in the elderly, as does the ethics discussion. And what, you may well ask, does a paediatrician know about senescence? Well first I am one and secondly, as the Bard points out;

*"Last scene of all,
That ends this strange eventful history,
Is second childishness and mere oblivion,
Sans teeth, sans eyes, sans taste, sans everything."*

The article on stroke in the elderly emphasises that stroke is often not a sudden unpredictable visitation like lightning from above. Rather the gathering clouds of hypertension, TIAs, atrial fibrillation and atheroma give a window of opportunity for timely intervention.

The curtain drops on McCord Hospital

It is very sad to read the announcement of the 'managed shutdown' of McCord Hospital in Durban as a result of the withdrawal of the grant funding by the Department of Health as well as the cutbacks in PEPFAR funding and funding from elsewhere. Think of a mission hospital and you conjure up a vision of Schweitzer in Lambaréné in deep rural Gabon. SA has its fair share of such bastions of caring throughout the rural provinces. McCord was unusual in that it was situated in urban Durban. It was founded, "for Zulus" 103 years ago by Dr James McCord under the auspices of the American Board for Foreign Missionaries. James' wife, Margaret, established the first nursing school for black women but the graduates could not be registered on account of their race. The situation of the hospital within the city was for decades the cause of running battles with Verwoerd's and Vorster's Group Areas Act which could not countenance black patients in a designated white area. The hospital's first superintendent, Dr Alan Taylor, was the driving force for the establishment of the University of Natal's 'non-European' medical school. More recently, McCord has met the medical needs of thousands of HIV patients.

Mr Kevin Smith CEO of McCord recently wrote; "Whilst this current decision is a very painful one, the board considers it a necessary step....." Your pain, sir, is shared by the medical fraternity and more especially the hundreds of thousands of patients who benefitted from your hospital's care. *Sala kahle sihlobo sami esidala !!*

Zombie syndrome

Have you ever woken up feeling as if you were a zombie? I do regularly; especially after a night of excesses! If this happens all the time then perhaps you have Cotard's Syndrome. This is a rare psychological disorder that leads people to believe they are truly zombie-like creatures - soulless, dead inside, and moving about in an otherwise lifeless body in a world that doesn't exist. Dr Jules Cotard (1840-1889) was a Parisian neurologist. Oh well, I am sure I'll have more life tomorrow.

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References: 1. MYPRODOL® Capsules approved package insert. 2. NDTI Scripted data total market March 2012.

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Reg. No. T/2.8/244. [S3] MYPRODOL® Suspension. A2.8. Each 10 ml contains paracetamol 250 mg; ibuprofen 200 mg; codeine phosphate 10 mg. Reg. No. T/2.8/199. For full prescribing information refer to the package insert approved by the medicines regulatory authority. ZA.12.PAI.145

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New Single Pill Combination Offers Exciting New Treatment Option for Type 2 Diabetes Patients

Demonstrating its commitment to caring for patients and offering therapies that meet the needs of modern-day patients, Novartis has launched Galvus Met[®], a new single-pill combination therapy for the treatment of type 2 diabetes.

Galvus Met combines the efficacy of widely prescribed medications vildagliptin and metformin in a single-pill combination therapy.

Galvus Met is a new oral antidiabetic (OAD) treatment, the first single pill combination (SPC) of a Dipeptidyl peptidase-4 (DPP-4) inhibitor and metformin, available in South Africa.

It is used to treat the pathophysiological hallmarks of type 2 diabetes which consist of progressive insulin resistance, pancreatic β -cell dysfunction, and excessive hepatic glucose production.¹

Galvus Met combines two antihyperglycaemic agents with different mechanisms of action to improve glycaemic control in patients with type 2 diabetes: vildagliptin, a member of the DPP-4 (dipeptidyl-peptidase-4) inhibitor class and metformin hydrochloride, a member of the biguanide class.² Vildagliptin and metformin have complementary actions by managing both islet dysfunction and insulin resistance.^{2,3} When vildagliptin is combined with metformin, it helps to improve glycaemic control with a low risk of hypoglycaemia and weight gain.⁴

Vildagliptin

Vildagliptin is a potent and selective dipeptidyl-peptidase-4 (DPP-4) inhibitor that improves glycaemic control. In patients with type 2 diabetes, administration of vildagliptin leads to the inhibition of DPP-4 enzyme activity for a 24-hour period. Inhibition of DPP-4 results in increased fasting and postprandial endogenous levels of the incretin hormones GLP-1 (glucagon-like peptide 1) and GIP (glucose-dependent insulinotropic polypeptide).²

By increasing endogenous GLP-1 levels, vildagliptin enhances the sensitivity of α cells to glucose, resulting in more glucose-appropriate glucagon secretion. The reduction in inappropriate glucagon during meals in turn attenuates insulin resistance.²

Metformin hydrochloride

Metformin hydrochloride improves glucose tolerance in patients with type 2 diabetes, lowering both basal and postprandial plasma glucose. Metformin hydrochloride decreases hepatic glucose production, decreases intestinal absorption of glucose and improves insulin

sensitivity by increasing peripheral glucose uptake and utilisation. With metformin hydrochloride therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may actually decrease.²

Independently of its action on glycaemia, metformin hydrochloride has favourable effects on lipid metabolism. This has been shown at therapeutic doses in controlled, medium-term or long-term clinical studies: metformin hydrochloride reduces total cholesterol, LDLc and triglyceride levels.²

Simplified treatment regimen

Studies show that only a small fraction (2,8%-11,9%) of adults diagnosed with diabetes are achieving the currently recommended levels of control of blood glucose levels, blood pressure and cholesterol levels.⁴

By combining different treatments into a single pill, non-compliance has been shown to reduce by 24%-26%, translating into better clinical outcomes for patients.⁵

Studies show that the combination of metformin and vildagliptin is effective at improving glycaemic control for at least one year in patients with type 2 diabetes and appeared to be well tolerated.⁶ Galvus Met also significantly improves blood glucose between and after meals⁷ and resulted in sustained HbA1C reduction of **1,1%** after one year of treatment.⁶ The treatment has shown to be as effective as Sulphonylureas (SUs) with lower risk of hypos or weight gain.⁸

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Ethics and the Elderly

Scenario

Dr Slick Snyman is an orthopaedic surgeon with a special interest in hip replacements. He has a 5/8th post at the local government hospital and a busy part-time private practice in a private clinic. On the same day last week he saw two patients with hip fractures which he considered should be managed with hip replacement. Both patients were elderly.

The first patient was seen in the public sector hospital. This patient was a 69 year old African man, Mpho V. He had a long history of alcoholism with a number of medical and surgical admissions. He was knocked down by a car and sustained numerous lacerations and bruises but his most serious injury was a displaced intra-capsular fracture of the femoral neck. Despite mild emphysema, Mpho is considered a good anaesthetic risk. He consented to surgery with an 'X' on the form.

There is however, a limited budget allocated to prostheses in the hospital and an informal selection process is used to allocate hips. There is also concern regarding the quality of hip prostheses supplied on contract to the hospital. The device on contract is a 'less expensive', metal-on-metal joint. Similar prostheses have been withdrawn from use elsewhere.

The second patient is a 89 year old white woman, Anne. She was seen in the private hospital. She has a previous history of hypertension, hypothyroidism and a left haemiplegia. She fell while engaging stairs and fractured her right hip. She appears somewhat confused and disoriented. She has made an attempt at signing the consent for surgery form administered by the nurse aid. She is no longer covered by medical insurance but her children are contributing to her care.

These cases bring to the fore many ethical issues that arise in the treatment of the elderly as well as dilemmas of a more general nature.

Some ethical issues

Informed consent

In both of these cases, it appears that the process of informed consent has likely been subverted. One of the pre-existing requirements for informed consent is that the patient should be competent to consent. It is common that elderly patients may not be fully competent (or more p.c. 'capacitated') to understand the choices at their disposal. Competence is not an all-or-none business and the patient's autonomy may be improved by instituting many processes. Simple matters like addressing the patient in the home language, avoiding medical jargon, talking clearly and loud enough to assist the hard-of-hearing and treating pain may often improve understanding. This may take time and patience; often both are in short supply!

More formal assessment of competence in the elderly may be aided by utilising one of the structured tools designed



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for this purpose.¹ If, even after optimising the situation, the patient still appears unable to make a competent decision, then the doctor must rely on either a valid advance directive or more commonly surrogate consent. The next-of-kin should make the decision using 'substitute judgement' values (as opposed to the 'best interest standards' used in surrogate consent in children). The question is asked, "Knowing Anne (or Mpho), what do you think that she would have requested under the circumstances?" Surrogates may have conflicting interests or even if well-intentioned often get it wrong - about 40% of the time.²

Cost containment

In both these scenarios, costs must be considered. There is increasing realisation that even for well-resourced or insured patients, there are limits to affordability. Hip fractures are common in the elderly and the incidence rises with increasing age. The cost per case in the Netherlands is about €20,000³ (R240,000). Rationing of healthcare is a reality in both the public and private domains. Who should decide, and using what criteria, whether Mpho should receive one of the prosthetic hips?

Resources and scarce resources

The allocation of medical resources is often a haphazard process all the way from the treasury down to the clinic. In the private sector highly profitable activities often take huge precedence over more mundane, basic, cost-effective care. Cross subsidisation is practised in both the private and public sectors. Often those who shout the loudest get the most. There may be a brand new scanner in the imaging department while there is only amoxicillin in the pharmacy.

The allocation of especially scarce resources requires pre-existing guidelines or protocols and these protocols need regular review as conditions change. There are a variety of factors that may be considered when drawing up a protocol. Equality and equity should recognise that all lives are inherently equal. If this were the only consideration then a simple lottery could be used to allocate. However, most health care workers would prioritise certain patients above others. The sickest patients may demand urgent allocation but prognosis should also be factored into the decision.

Quality- or disability-adjusted life years (QALYS/DALYS) could be used. It may be just to consider social usefulness of the potential recipient or even 'punish' previous high risk behaviour. In this respect, for example, a person who has previously regularly donated blood may 'reciprocally' receive a scarce resource ahead of another patient or conversely a chronic smoker may be denied a lung transplant.

The main responsibility of central government is to decide on macro-allocation such as Education vs Health vs Defence. Provincial government should then prioritise how the health allocation is divided; Primary vs Secondary vs Tertiary. The allocation of scarce clinical resources is usually the responsibility of the local institution and thus follows the budget. The decision on, for instance, who gets the ICU bed is the responsibility of the ICU managers. Community representation in the process is essential. It is disappointing that hospital adminis-

trators often wash their hands of these decisions and give little support in this regard, probably fearing litigation.

In the case of Anne, conservative treatment and safe bed rest may well be a more humane practical and ethical alternative to operative intervention. The case of Mpho may be more difficult. Hip replacement and attention to his addiction seems a feasible option.

Societal inequity

The poor (and the rich) are always with us and there will always be disparities between the medical care available to those in the private and public sectors. Our ethical responsibility is to ensure that at least a reasonable level of care is available to all. In this scenario, for example, the standard of the hip prosthesis available in the public sector is called into question. It has been recognised that there is an ethical need to maintain an orthopaedic joint registry to ensure that interventions are more effective than alternatives.⁴ Perhaps the largest ethical elephant in the room is the wide disparity between sectors in SA. It remains to be seen whether the NHI will successfully address this.

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Wound Care Benefit of Instillation Therapy

What is installation therapy?

Over the past decade the concept of proper wound bed preparation as a means to improve wound healing has gained increasing attention. The principles of wound bed preparation include proper wound debridement, managing wound exudates, and managing bioburden. Proper wound bed preparation creates an optimal wound healing environment; the presence of necrotic tissue or eschar is known to impede healing. Likewise, the presence of abnormally high levels of bacteria may also impede healing. These impediments to wound healing may in part be removed by practices such as wound irrigation.

Cleansing the wound by using an irrigant to remove loosely attached bacteria and cellular or other debris may decrease wound complications thereby allowing the wound to heal in a timely fashion. Typically wound irrigation is conducted at moderate pressures (less than 103.4 kPa) using an irrigant that does not cause trauma to the surrounding tissue.

Typical devices used to deliver irrigants to wounds include spray bottles, syringes, squeeze bottles and pulsatile lavage devices. All these types of approaches to fall under the category of instillation therapy.

Advances in instillation therapy

The clinical application of instillation therapy for treating wounds was first described by Fleischmann et al in 1998. Since then, several clinical articles have described various applications of instillation therapy, most of which address the treatment of wound infections. For example, Gabriel et al reported the use of instillation therapy for treating soft tissue infection. They showed that instill-

ing silver nitrate was effective at reducing bioburden, time to wound closure, and time to hospital discharge. Others have followed with similar clinical results. Schintler et al and Timmers et al showed that instilling polyhexanide solution was effective at treating soft tissue necrotising fasciitis and osteomyelitis.

Risk of cross-contamination from splatter

Even though the utility of wound irrigation for infected wounds is an accepted practice, cross-contamination from the splatter, which may be caused during the instillation process, is a safety concern to both the patient and the clinician. In a recent study, Angobaldo et al showed that bacteria from pulsatile lavage treated wounds could be captured a meter away from the wound. The spread of organisms and especially resistant organisms in the hospital environment is a growing concern. Studies have demonstrated that methicillin-resistant *Staphylococcus aureus* or vancomycin-resistant enterococci can be detected on the protective gowns and gloves of up to 67% of health-care workers tested.

With the increasing prevalence of antibiotic-resistant organisms and nosocomial infections it is important that techniques be used to prevent the spread and possible cross-contamination of infection. This is especially true with any type of instillation therapy where outbreaks of infection have been traced back to facility contamination caused by the therapy itself. It is likely that such outbreaks could be prevented by better containment of splatter during the instillation procedure.

Clinical benefits

In addition to the treatment of infection, there are a number of other potential uses for instillation therapy. The medi-

cal and scientific community recognises additional clinical benefits for instillation therapy. Nagai et al reported that instilling the protein sericin has a potent effect on wound healing and corneal epithelialisation in a rodent model. Jerome suggested using instillation therapy to provide pain management during and after dressing changes.

The addition and removal of a liquid solution from a wound bed may have other clinical benefits. Instilling a wound with lactated Ringer's solution or saline may dilute the bioburden and prevent potential clinical infections. At the same time instillation therapy with saline may help remove necrotic tissues and reduce the level of pro-inflammatory mediators, leading to a shift toward the proliferative phase of healing.

Reducing the amount of early inflammation may also lead to better tissue remodeling and tissue quality. Recently Acosta et al postulated that chronic and hyper-inflammation is detrimental to the repair of diabetic foot wounds. They highlighted the need for smart prophylactic interventions to reduce chronic inflammation. Instillation therapy may address this clinical need for a therapeutic intervention.

Historically there have been few product options to help clinicians easily deliver instillation therapy. Furthermore current saline lavage treatments can lead to the inadvertent spread of microbial cross-contaminations and increase the risks of nosocomial infections. With an appropriate instillation therapy system (therapy unit and dressings), clinicians can more safely use these tools while minimising the risk of inappropriate microbial transmissions thus leading to better treatment and healing of difficult wounds.

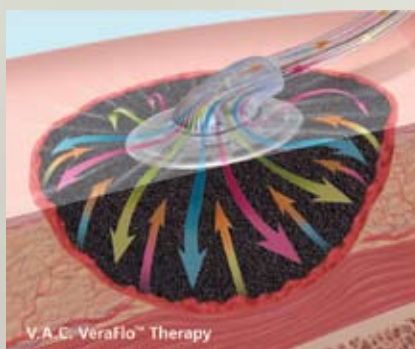
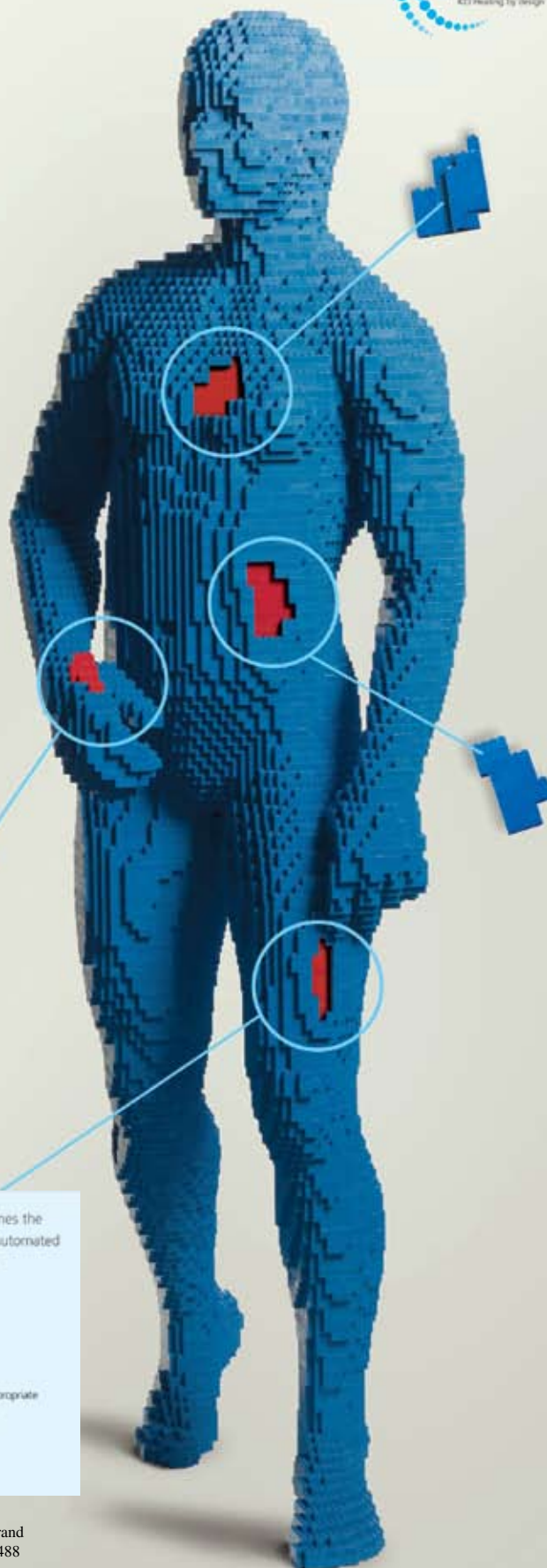
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Update on Lipid Management

Commonly Asked Questions

Target levels for LDL-cholesterol (LDL-C) in patients with cardiovascular disease (CVD) are being lowered. New statin combinations will be more cost effective than present combinations and will help to achieve LDL-C targets. These and other drugs in development promise a new era in CVD prevention.

Lipid management is a common reason for consultation in general practice, and management is now securely grounded on evidence-based guidelines for optimisation of lipid levels and reduction in cardiovascular disease (CVD) risk. This article provides answers to common questions arising in lipid management.

What are the four types of lipid disorder?

Lipid disorders are classified on the basis of a 12-hour fasting lipid profile into the following four types:

- hypercholesterolaemia (HC) – with predominantly elevated LDL cholesterol (LDL-C) levels
- hypertriglyceridaemia (HTG) – with high triglyceride (TG) levels and near-normal LDL-C levels
- combined or mixed hyperlipidaemia – with elevated levels of both LDL-C and TG
- isolated low HDL cholesterol – with low HDL cholesterol (HDL-C) levels and near-normal TG and LDL-C levels.

This classification replaces the older Frederickson classification of types I to V hyperlipidaemias. Lipid phenotypes are further subdivided, according to severity, as listed below.

About the author

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- Hypercholesterolaemia
 - mild (total cholesterol [TC], 5.5 to 6.4mmol/L)
 - moderate (TC, 6.5 to 7.4mmol/L)
 - severe (TC, 7.5mmol/L and higher).
- Hypertriglyceridaemia
 - mild (TG, 2.3 to 4.4mmol/L)
 - moderate (TG, 4.5 to 11.0mmol/L)
 - severe (TG, 11.0mmol/L and higher).
- Low HDL-C
 - below 0.9mmol/L in men
 - below 1.1mmol/L in women.

The occasional patient has an anti-atherogenic lipid profile such as very low levels of LDL-C or very high levels of HDL-C, presumably on a genetic basis as the family history is often one of longev-

ity. In the author's experience, the management of patients with high levels of both LDL-C and HDL-C and a normal TC:HDL-C ratio can often be resolved using imaging. Lowering the LDL-C level is indicated in those patients with positive calcium scores, carotid plaques or increased carotid intima-media thickness.

Each lipid phenotype needs to be classified according to its predominant cause:

- Primary
 - familial (genetic cause identified)
 - sporadic (no cause identified)
- Secondary
 - hypothyroidism
 - diabetes
 - renal failure
 - nephrotic syndrome
 - hepatic disease (especially cholestasis)
 - pregnancy
 - anorexia nervosa
 - alcohol excess
 - drugs causing abnormal lipids – including oestrogens, anabolic steroids, glucocorticosteroids,

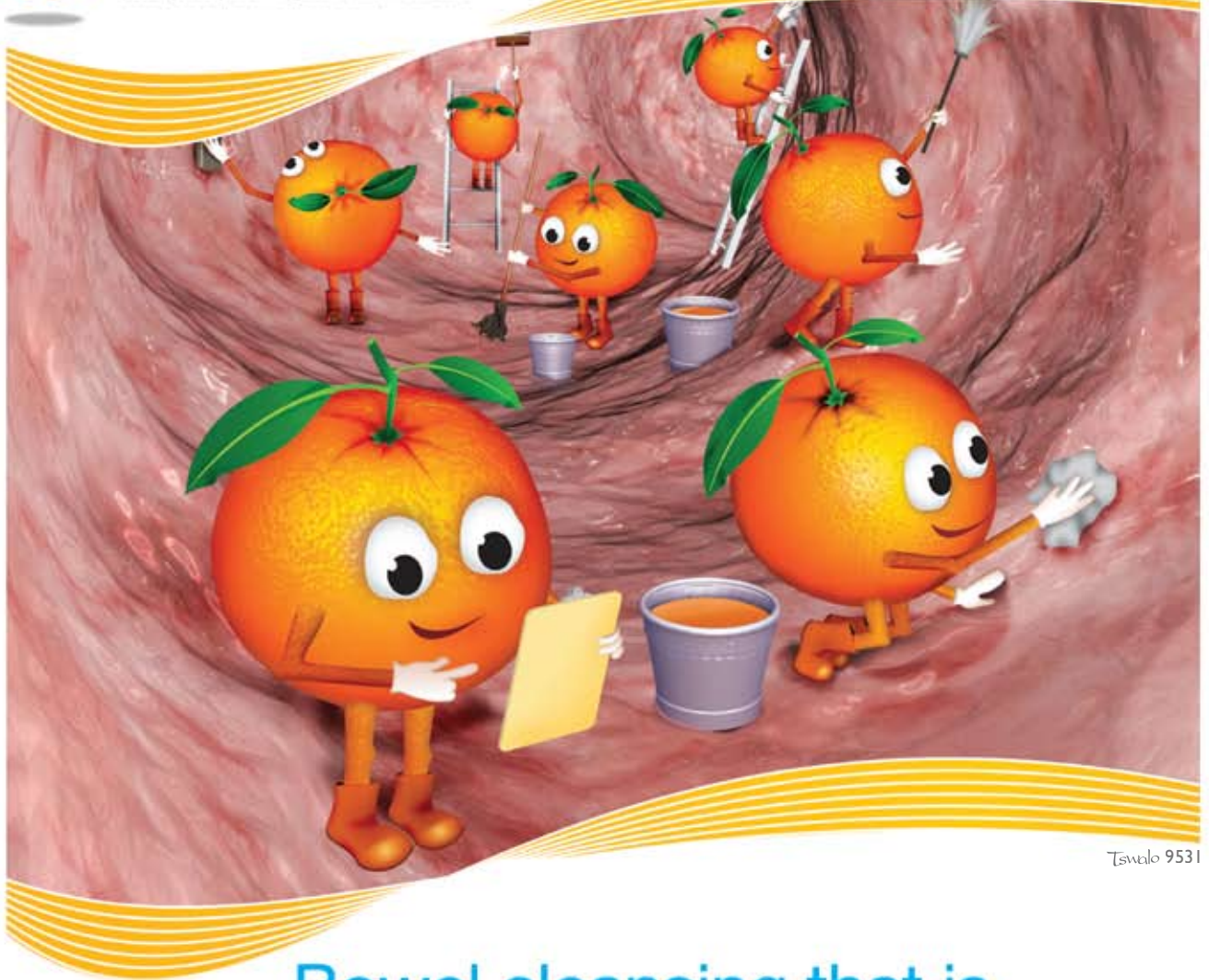
Key points

- Always repeat an abnormal lipid profile when checking for secondary causes of dyslipidaemia.
- Initiate statin therapy at a dose to achieve target LDL-C levels without dose titration. Check lipid profile, creatine kinase, liver enzymes and symptoms 6 to 12 weeks after statin initiation or up-titration.
- Add ezetimibe if target LDL-C is not achieved on maximum tolerated dose of statin.
- Check alcohol, refined carbohydrate and fat intakes in patients with high TG levels.
- Fibrates and high-dose fish oils are more effective than statins at lowering TG levels.
- Fenofibrate is preferred to gemfibrozil for combination with statins.
- A low HDL-C level is often secondary to a high TG level; the TG level should be controlled before treating to raise the HDL-C level.
- Any move towards target levels is of potential benefit, even though targets may not be reached.



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Figure 1. Atherosclerosis of abdominal aorta.

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Figure 2. Early arcus senilis.

COURTESY OF PROFESSOR J BURNET AND PROFESSOR G. WATTS, PERTH, WA.

retinoids, beta-blockers, protease inhibitors and thiazides.

Which lipid disorders are usually encountered in general practice?

About 50% of the general population has cholesterol levels over 5.5mmol/L and can be regarded as having HC, although fewer than 5% have TC levels greater than 7.5mmol/L. The most common lipid disorder (about 25% of cases in general practice) is mild mixed hyperlipidaemia (TC, 5.5 to 6.4mmol/L and TG, 2.3 to 4.4mmol/L) in association with obesity, the metabolic syndrome or diabetes. Levels of HDL-C are often low in patients with these conditions, and may respond to TG control. Levels of TG above 4.5mmol/L are uncommon and occur especially in those people with uncontrolled diabetes and/or excessive alcohol intake.

What is the clinical significance of lipid disorders?

Accelerated atherosclerosis and increased risk of ischaemic CVD are the major complications of HC, mild-to-moderate HTG and low HDL-C (Figure 1).¹ Each of the lipid components appears to be atherogenic by somewhat different mechanisms, and may therefore act independently and additively to increase CVD risk. Severe HTG, although not proatherogenic, may cause potentially fatal acute pancreatitis.

How do lipid disorders present?

Most lipid disorders are asymptomatic, causing subclinical atherosclerosis with no overt clinical signs (the iceberg phenomenon).

Hypercholesterolaemia

Patients with moderate and severe HC may present with premature arcus senilis resulting from corneal LDL-C deposition (Figure 2). Early arcus is often difficult to visualise. Arcus is nonspecific, may occur in elderly patients who

have normal cholesterol levels and does not regress with therapy. After several decades, the usual presentation of HC is ischaemic CVD, especially coronary heart disease (CHD). The risk of CHD increases by about 1% for every 1% increase in LDL-C level, and for every 1mmol/L reduction in LDL-C level with statins there is about 22% reduction in CVD events (Figure 3).

Patients with severe HC may present with tendon xanthomas, cutaneous (tuberous) xanthomas, xanthelasmas (also nonspecific) and premature CHD (Figures 4 to 6). This is the typical sce-

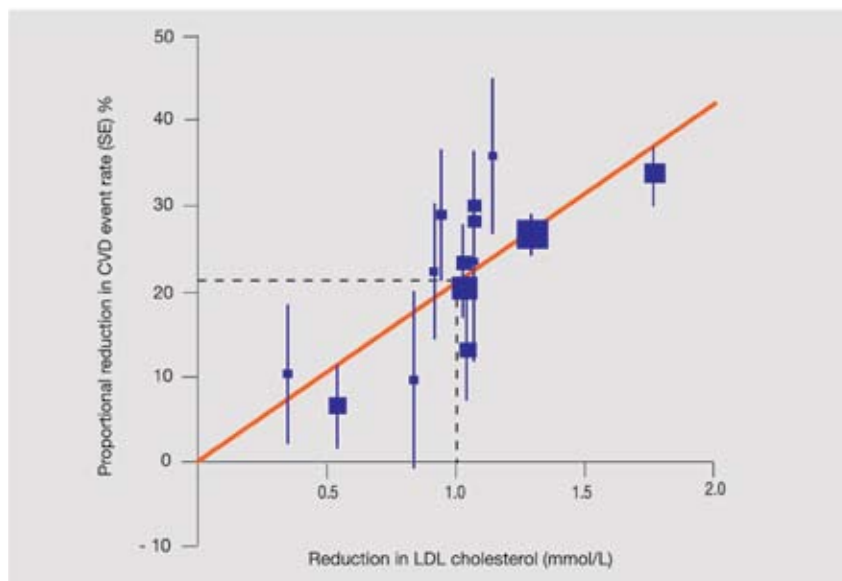


Figure 3. Percentage reduction in cardiovascular disease (CVD) events according to mean absolute LDL cholesterol reduction in 14 statin trials. For each mean 1.0mmol/L reduction in LDL cholesterol there is a 22% reduction in CVD events.¹

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Figures 4a and b. Tendon xanthomas. a (left). Extensor tendon xanthoma. b (right). Achilles tendon xanthoma.

COURTESY OF PROFESSOR J. BURNETT AND PROFESSOR G. WATTS, PERTH, AUSTRALIA.

nario for patients with familial hypercholesterolaemia (FH).

Hypertriglyceridaemia

Patients with moderate-to-severe HTG may present with eruptive xanthomas (Figure 7), but this condition is usually asymptomatic. Planar xanthomas of the palmar skin creases are specific for apolipoprotein (apo) E2/2 homozygosity (familial dysbetalipoproteinaemia). This condition is suspected when levels of TC and TG are elevated to a similar degree (to about 8mmol/L). TG-rich lipoproteins in mild-to-moderate HTG are atherogenic and increase CVD risk.

Severe HTG may present with acute pancreatitis and lipaemia retinalis; in the laboratory, the plasma is noted to be lipaemic.

Isolated low HDL-C

Findings of very low levels of HDL-C (below 0.2mmol/L) are rare; they are usually of genetic origin and may be associated with specific signs such

as corneal opacity. The usual levels in patients with isolated low HDL-C (0.6 to 0.9mmol/L) are asymptomatic and independently associated with increased CVD risk, and are frequently seen in patients with premature CVD.

What lifestyle measures can be prescribed?

Hypercholesterolaemia

HC is treated predominantly by modification of dietary fats, as follows.

- Reduce intake of cholesterol to less than 300mg/day:
 - reduce egg yolk intake (each yolk contains about 250mg cholesterol)
 - avoid full-fat dairy products; use low-fat products instead
 - reduce intake of red meat (red meat and dairy products are major sources of cholesterol and saturated fats)
 - eat vegetarian or fish meals two to three times a week
 - avoid foods high in saturated fats

(eg, pastries, commercial cakes, visible animal fat)

- substitute polyunsaturated fats (safflower oil, sunflower oil) or mono-unsaturated fats (olive oil, canola oil) for saturated fats.
- Increase intake of plant sterols to 2 to 3g/day
 - foods supplemented with plant sterols are available (eg, incertain margarines, about 1 tablespoon contains 2 to 3g sterols).
- Increase intake of plant and vegetable foods
 - these contain soluble fibres which reduce cholesterol absorption.

Hypertriglyceridaemia

HTG is treated predominantly by dietary modification, specifically of the intakes of refined carbohydrates, fats and alcohol, as follows.

- Restrict alcohol (one standard drink a day in women, two in men).
- Substitute complex carbohydrates for refined carbohydrates.



Figures 5a and b. Cutaneous (tuberous) xanthomas on the hands (a, above) and feet (b, right).

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Figure 6. Xanthelasma

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Figure 7. Eruptive xanthomas

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- Reduce intake of saturated fats.
- In severe HTG, reduce intake of all fats.
- Increase exercise levels.
- Lose weight – initially aim for 5% weight loss, which will improve fat metabolism due to predominantly visceral fat loss.

Isolated low HDL-C

Isolated low HDL-C is often resistant to treatment as it frequently has a genetic basis with low levels of apo A-1 as the primary cause. The following may be tried:

- Weight loss
- Reduced high refined carbohydrate intake
- Increased exercise.

What drug therapy can be used?

On the basis of absolute risk, a case can be made for providing statins to all high-risk patients (five-year CVD risk greater than 20%) and to consider treatment for those at intermediate risk (five-year CVD risk of 10 to 20%) if they have associated conditions such as diabetes, chronic renal disease or subclinical atherosclerosis.

Which drug should be used first?

Table 1 provides an overview of the effects of various lipid-modifying drugs on lipid levels. Note that each drug has an effect on all lipid classes. Details of when each drug should be used as first-line therapy are listed below.

- Statins are first-line therapy for all

lipid disorders except moderate/severe HTG and isolated low HDL-C. High doses of more potent statins (with regard to LDL-C lowering) are usually required for controlling HTG.

- For patients not reaching target LDL-C levels on maximum-tolerated doses of statin, and for statin-intolerant patients, ezetimibe is next-line therapy.
- Fibrates are first-line therapy for moderate-to-severe HTG. Fenofibrate is usually preferred as it is likely that add-on statin therapy will be required in many cases and fenofibrate has less risk of muscle adverse effects with statins than does gemfibrozil.
- Omega-3 fatty acids (fish oils) in high dose (six to 12 capsules of 1g daily or the equivalent liquid formula) are an alternative to fibrates for HTG, and can be added to fibrates or statins for TG control.
- Niacin (nicotinic acid) is poorly tolerated and is rarely used in the absence of extended-release preparations.
- Bile acid resins raise TG levels and are relatively contraindicated in HTG, but can be useful when added to ezetimibe for controlling LDL-C levels in patients intolerant of statins.
- Fibrates or niacin are first-line therapy for isolated low HDL-C.

The flowcharts accompanying this article provide algorithms based on current European guidelines for the management of HC in two situations:

- The patient on a statin with controlled LDL-C levels and elevated TG and/or low HDL-C levels¹
- The patient with elevated LDL-C levels and controlled TG and HDL-C levels.

The former situation is the more common scenario as it often accompanies obesity, the metabolic syndrome and diabetes. The abnormal TG and HDL-C levels contribute to the increasingly important problem of residual risk (CVD risk occurring with statin therapy in spite of LDL-C reduction).

What are the targets for treatment?

Treatment targets for the various lipid disorders are:

- For HC, the LDL-C target level is below 2.5mmol/L in high-risk patients and below 2.0mmol/L in very high-risk patients. These targets are based on epidemiological data and results of statin clinical trials.
- For severe HTG, the target TG level is below 11mmol/L (ideally below 8mmol/L) in order to prevent acute pancreatitis.
- For mild and moderate HTG, the target TG level is below 1.7mmol/L on the basis of epidemiological data (no clinical trial has been conducted to validate this).
- For isolated low HDL-C, the target HDL-C level is above 1.0mmol/L on the basis of epidemiological data (as for HTG, no clinical trial has been conducted to validate this target).

How is drug therapy monitored and how are side effects managed?

Table 2 describes the monitoring of lipid-lowering drug therapy and the management of patients who have adverse drug reactions.



TABLE 1

Efficacy of lipid-lowering drugs in modifying lipid profile

Drug	LDL-C	TG	HDL-C
Statin (5 to 80mg/day)	++++ * Note rule of 6% (6% added LDL-C lowering for each doubling of the statin dose) Maximum LDL-C lowering, about 55%. One extended-release (fluvastatin) formulation available	++ Effect greater for higher baseline TG, more potent statins with regard to LDL-C reduction, and higher statin doses	++ Dose dependent, especially simvastatin, and pravastatin and rosuvastatin
Ezetimibe (10mg/day single dose)	++ Average 20% LDL-C reduction. Well tolerated and additive to statin	Minimal	Minimal
Fibrate (62.5 to 1200mg/day)	Variable (0/+) Use fenofibrate not gemfibrozil with statin Reduce fenofibrate dose in renal impairment	++++	+ / ++
Omega-3 fatty acids (high dose, 6 to 12g/day)	Variable (may increase)	+++	+
Niacin (2 to 3g/day optimal)	++ / +++ Dose dependent Poor tolerance unless extended-release formula	++ Dose dependent	++ Dose dependent
Bile acid resins (4 to 20g/day)	+ / ++ Poor tolerance in higher doses	Minimal (increase if baseline high TG)	Minimal
Plant sterols (2 to 3g/day)	+	Minimal	Minimal

ABBREVIATIONS: HDL-C = HDL cholesterol; LDL-C = LDL cholesterol; TG = triglycerides.

* + = extent of beneficial effect.

Statin-induced myalgia

Myalgia associated with statin use occurs more commonly in patients with pre-existing muscle aches and pains, and after exercise. It may mask underlying hypothyroidism (and respond to thyroid replacement) or skeletal muscle pathology (which may require a biopsy to determine). Statin-induced myalgia may occur in patients with normal creatine kinase levels and therefore can be difficult to diagnose without drug with-

drawal and rechallenge.

There is no validated therapy for statin-induced myalgia other than dose reduction or statin withdrawal. Anecdotal benefit has been described for several supplements and drugs (including COX-2 inhibitors, magnesium and coenzyme Q10) but convincing evidence for efficacy is lacking, as is knowledge of the mechanism(s) of statin-induced myalgia. Low levels of vitamin D may aggravate the myalgia; this aggravation may respond to the taking of vitamin D

supplements and allow continuation of statin therapy.

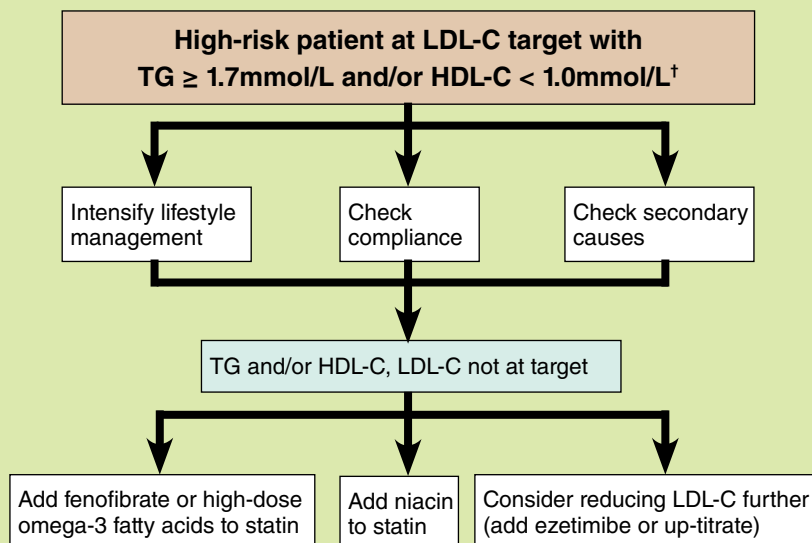
Which drugs should be used in diabetes?

Statins are indicated for all patients with diabetes who are at high risk of CVD (those with other CVD risk factors, renal impairment or proteinuria or those aged over 60 years), with a strong evidence base for CVD benefit.

A role for fibrates has been demon-



Management of hypercholesterolaemia: High-risk individuals with elevated TG and/or low HDL-C at LDL-C Goal*

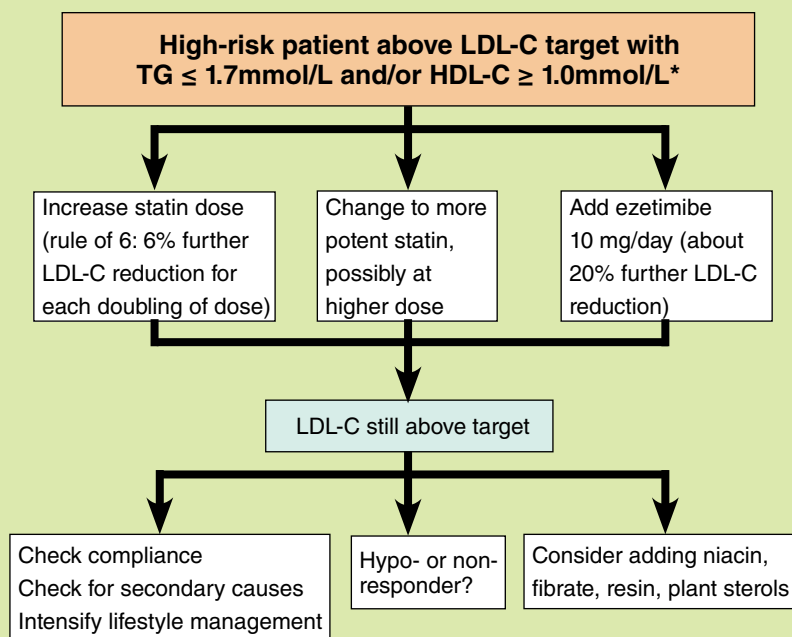


ABBREVIATIONS: HDL-C = HDL cholesterol; LDL-C = LDL cholesterol; TG = triglycerides.

* Adapted from Chapman MJ et al, 2011.2

[†] LDL-C goal is < 2.5 mmol/L in high-risk and < 2.0 mmol/L in very high risk patients.

Management of hypocholesterolaemia: High-risk individuals with elevated LDL-C, normal TG and normal HDL-C levels



ABBREVIATIONS: HDL-C = HDL cholesterol; LDL-C = LDL cholesterol; TG = triglycerides.

* LDL-C goal is < 2.5 mmol/L in high-risk and < 2.0 mmol/L in very high risk patients.

strated in trials with fenofibrate and gemfibrozil in which CVD benefit was confined to those patients with baseline low HDL-C and/or high TG levels (the so-called dyslipidaemic subgroup). The recent ACCORD and FIELD trials also showed microvascular benefits with fenofibrate (reduction in laser therapy for diabetic retinopathy, improved proteinuria, improved sensory neuropathy and reduction in leg amputations) to the extent that fenofibrate should be considered for combination therapy with statins in all high-risk diabetes patients.

When to refer?

When target lipid levels are not achieved in spite of the best efforts of the general practitioner, patients should be considered for referral. Likewise, patients with persistent side effects from therapy should be referred.

It is also appropriate to refer any unusual patient with premature vascular disease, a strong family history of CVD, unusual physical signs or extreme lipid levels (which usually signify genetic disorders of lipid metabolism). Specialised care is important for these patients, and diagnosis may require DNA analysis. Two important patient groups are those with:

- FH, who present with cholesterol levels above 7.0 mmol/L, signs of LDL-C deposition and a strong family history of premature coronary heart disease
- Elevated lipoprotein(a) levels who present with premature CVD (this condition is usually inherited).

When are special lipid tests required?

The literature suggests that apoA-1 (the main protein of HDL) and apoB (the main protein of LDL) may be more predictive of CVD risk than their lipid counterparts. It suggests that a target apoB level of below 0.8 mg/dL may be more appropriate than an LDL-C target in high-risk patients.

ApoA-1 and apoB are not included in international lipid guidelines and measurement of their levels incurs additional costs. For practical purposes, measurement of the levels of LDL-C and HDL-C will suffice.



TABLE 2

Lipid-lowering drug therapy: monitoring and adverse effects

Drug	Monitoring	Adverse effect and prevalence	Adverse effect management
Statins	Six to 12 weeks after initiation or dose escalation: check muscle symptoms, CK and transaminases. Six to 12-monthly: check lipids and adjust dose if target levels not achieved	Myalgia (CK more than three times ULN): 1% to 17% depending on study. Myositis (CK more than three times ULN): less than 1% in controlled trials. Rhabdomyolysis (CK more than ten times ULN with myoglobinaemia and myoglobinuria): rare. Increased transaminases (more than three times ULN): especially in early weeks of treatment; less than 1%	Myalgia and myositis: statin holiday until levels and symptoms normalise, then reintroduce lower dose or alternative statin, consider ezetimibe or other therapy; refer for chronic myalgia. Rhabdomyolysis: cease statin, admit to hospital, rehydrate, monitor renal function
Niacin	As for statins Monitor glucose levels (HbA1c in people with diabetes)	Increased transaminases (more than three times ULN): common in early weeks of treatment, less than 1% after 8 to 12 weeks; dose dependent. Increased glucose: usually not clinically significant	Drug holiday until levels normalise then reintroduce at lower dose or consider alternative therapy (eg, statin)
Fibrates	Monitor lipids six to 12-monthly	Generally well tolerated	—
Fish oils	As for fibrates	Platelet function inhibition rarely of clinical significance; GI disturbance <5%, dose dependent	Dose reduction
Resins	As for fibrates	Constipation; GI effects	Dose reduction
Plant sterols	As for fibrates	—	—
Ezetimibe	As for fibrates	—	—

ABBREVIATIONS: CK = creatine kinase; GI = gastrointestinal; ULN = upper limit of normal.

New combination drugs

A new statin combination with ezetimibe (Inegy - MSD) is now available in SA. It promises to make the task of achieving LDL-C targets easier.

A niacin combination (Tredaptive - MSD) contains extended-release niacin, laropiprant (a specific prostaglandin inhibitor that reduces the skin flushing associated with niacin use) and simvastatin.

What drugs are in the pipeline?

Two novel classes of drugs are in clinical trials. The first class is the second-generation cholesterol ester transport protein

(CETP) inhibitors, of which anacetrapib and dalcetrapib are the most advanced in clinical trials. These have short-term safety and efficacy in raising HDL-C levels by up to 150% or more. They are likely to be used in combination with statins. The second class is the anti-sense RNA compounds ('silencing RNAs'). The apoB anti-sense RNA, mipomersen, is the first of a series of drugs to target messenger RNAs and thereby inhibit synthesis of specific proteins. Mipomersen inhibits apoB synthesis and reduces LDL-C and lipoprotein(a) levels by 20% to 80%. It is given once weekly by subcutaneous injection and is being trialled initially in patients with FH in combination with a statin.

Summary

The use of statins for secondary CVD prevention is now well established and the drugs have an excellent record of safety, tolerability and clinical efficacy. We now have the ability to prevent CVD if lipid therapy is used in appropriate patients at appropriate doses, and early enough in the stage of the disease to significantly reduce atherosclerosis progression rates.

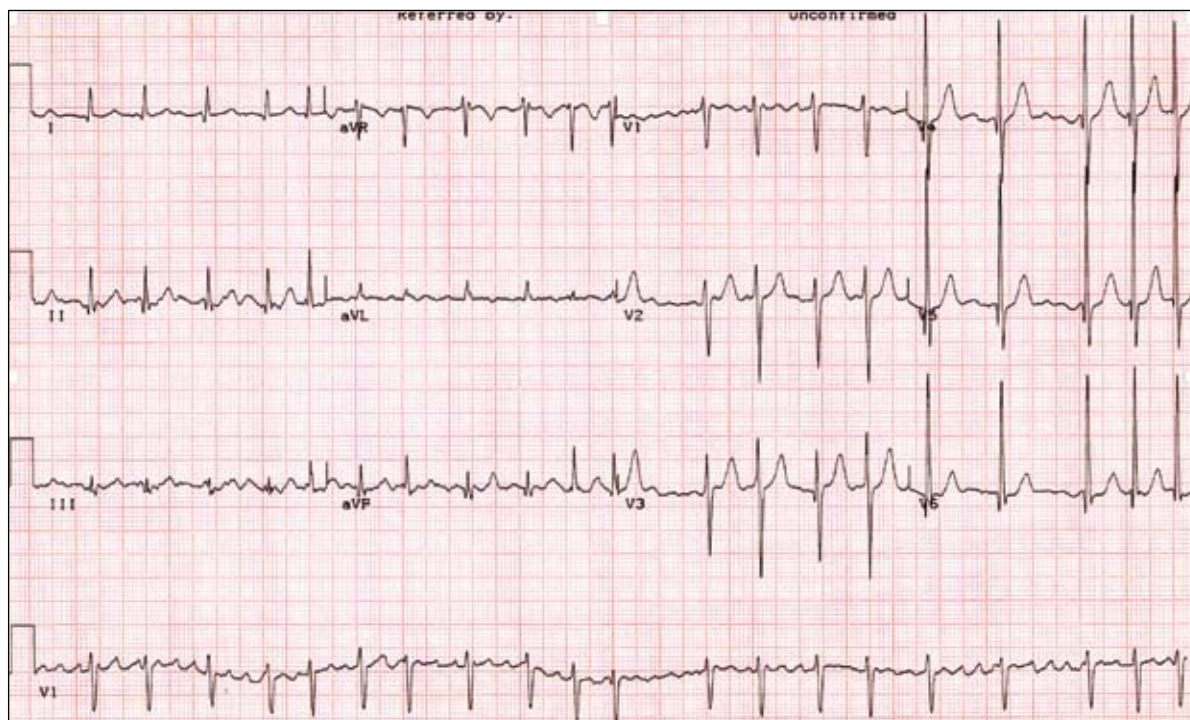
A new post-statin era of lipid therapy is on the horizon with the CETP inhibitors, drugs targeting RNA and other therapies in development.

References available on request



ECG of the Month

Prof Rob Scott Millar, cardiologist – University of Cape Town and Groote Schuur Hospital



A previously active 80 year old man presented with a one month history of tiredness and shortness of breath on exertion. He had been hypertensive for 10 years, on treatment with an ACE inhibitor and a diuretic. His pulse was 120/minute, irregular, and BP 170/90 mmHg.

Statements for consideration (true or false):

1. In view of the rhythm abnormality, he should be started on amiodarone.
2. At this age, the risk of bleeding is too great to consider warfarin anticoagulation.
3. Adding a beta blocker to his treatment will help to control his heart rate.
4. His thyroid function should be checked, even though he has no signs of hyperthyroidism.
5. Better control of his blood pressure is likely to restore his normal rhythm.

Before committing yourself, look carefully at the rhythm. Is it regular or irregular? Are the QRS complexes narrow or wide? What is the atrial rhythm? What are the possible consequences of this rhythm in this patient? What can you do to help him?

A detailed discussion on the above ECG can be seen on the next page.

If you know the answers, fill them out on the CPD answer sheet on page 46 to score a CPD point.

Have you looked beyond the obvious?



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Discussion

Diagnosis

The ECG shows a randomly irregular rhythm at 120/minute (20 QRS complexes in 10 seconds x 6=120). The QRS complexes are narrow, about 90ms (just over 2 small blocks), indicating a supraventricular origin. The most common cause of a randomly irregular tachycardia is atrial fibrillation (AF). Atrial flutter or atrial tachycardia with variable AV block are less common causes; multifocal atrial tachycardia is rare. A search for P waves in lead II shows some inconsistent waves between the T waves and QRS complexes, but no regular, uniform P waves. Look at the longer pauses (figure below) in the V1 rhythm strip at the bottom of the recording. There are rapid (up to 600/min.), irregular waves which vary in morphology and amplitude. This confirms AF – flutter is characterised by uniform waves at 240-360/minute.

Management

The 2 main hazards faced by this man with AF are embolic stroke and heart failure. His stroke risk is significant, on account of his age (over 75) and hypertension, as assessed by a CHA²DS²-VASc score of 3 (table below). Warfarin anticoagulation (or a new agent, such as dabigatran) is strongly indicated to reduce the risk of this devastating and potentially fatal complication. His risk of bleeding is also significant but less than the risk of stroke and the risk-benefit ratio with warfarin is still favourable. Aspirin is much less effective.

The risk of heart failure relates mainly to the rapid ventricular rate. While digoxin was the mainstay of treatment for rate control, it is of value only at rest as its effect depends on enhancing vagal tone. Any exertion causes catecholamine release which negates its effect. Beta blockers, on the other hand, are effective both on exercise and at rest. At the same time as warfarin is started, a small dose of a beta blocker (eg, 25mg atenolol) can be given, increasing the dose until the rate is under 100 at rest and no more than 120 after a brisk walk.

Restoration of sinus rhythm is of no benefit in this case. He is unaware of the rhythm and should do well with the addition of warfarin and atenolol. Use of amiodarone or other antiarrhythmic will expose him to unnecessary side effects. If it converted him to sinus rhythm before warfarin was effective, it may provoke a stroke.



CHA²DS²-VASc

- Congestive heart failure – 1 point
- Hypertension – 1 point
- Age ≥75 years – 2 points
- Diabetes mellitus – 1 point
- Sex, female – 1 point
- Vascular disease – 1 point
- Age 65 – 74 years – 1 point
- Stroke or thromboembolism – 2 points

His blood pressure should be better controlled, although it will not reverse the rhythm. This can be reassessed once his beta blocker dose is sufficient to control his rate. Despite lack of signs to suggest hyperthyroidism, thyroid function must be checked, to exclude this reversible cause of AF.

Have you looked
beyond the obvious?



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Travel Vaccines: A Comprehensive Guide

Vaccine requirements and recommendations for specific countries change, so it is important to be kept up to date by reliable information sources.

At the core of any productive pre-travel encounter is the process of assessing travel-related risks, and addressing them through an individualised risk management plan. These risks can be further categorised into four groups as follows:

Preventable risks: Those risks identified pre-travel that can be nearly completely eliminated by interventions such as immunisation or chemoprophylaxis.

Avoidable risks: Risks that can be avoided through counselling leading to behaviour change such as safe sex practices, or staying out of fresh water sources to avoid schistosomiasis.

Manageable risks: Those risks that can be self managed through stand-by treatment for such conditions as traveller's diarrhoea.

Unexpected risks: These risks may not be anticipated pre-travel but with appropriate contingency planning such as carrying adequate travel medical insurance.

Travel vaccines therefore fall under the preventable management plan.

Routine immunisations

Before considerations for travel to specific destinations it is important to ensure the traveller is up-to-date with their routine immunisations for their appropriate age, according to our Expanded Programme for Immunisation schedule [EPI]. It is important to realise that the common

diseases of childhood do cause serious illness in nonimmune adults, whether they are travelling or at home. Cost of vaccinations is far less than running the risk of hospitalisation or possible medical evacuation.

Routine vaccinations by disease

Diphtheria, tetanus, pertussis and polio

Diphtheria vaccination is recommended for most developing countries and especially for travel to eastern Europe and the Russian states.

One of the most common injuries whilst travelling is a simple cut or abrasion. Hence travellers to countries where health services may be difficult to access should be offered a booster if they have not had a tetanus vaccination in the last five years.

Pertussis outbreaks are becoming common and reports of travelling groups being infected are not unusual.

Polio outbreaks are being continually reported in the Indian subcontinent, parts of Africa and the Middle East. Therefore all travellers older than 18 years should receive a booster vaccination, which will give lifelong immunity.

Vaccination for all of these diseases are combined in one injection, Adacel Quadra or Boostrix Tetra, which are also known as the 'travellers tetanus' vaccines.

SA is one of the few countries in the world where a single tetanus vaccination is still available, Tetovax.

Measles, mumps and rubella

Measles and mumps outbreaks continue to be recorded in the developed world due to breakdown in childhood immunisation. Therefore it remains a significant threat to non-immune children and adults and vaccination is recommended. Priorix and Trimovax are the vaccinations available. Egg sensitivity is no longer considered a contraindication to vaccination.

Varicella

Varicella can have very serious sequelae in both children and adults and immunisation is recommended at 18 months of age. Varilrix is the available vaccine. It can be given as a single vaccine up to 13 years of age thereafter two doses are recommended to be administered at least six weeks apart.

Influenza

Influenza is one of the most common vaccine-preventable illnesses suffered by travellers and far more vaccine coverage needs to be provided, as many trips have been adversely affected. This is especially important for travel to continents in the winter months (which is the traditional flu season). Vaxigrip, Fluarix and Inluvac are our available influenza vaccines.

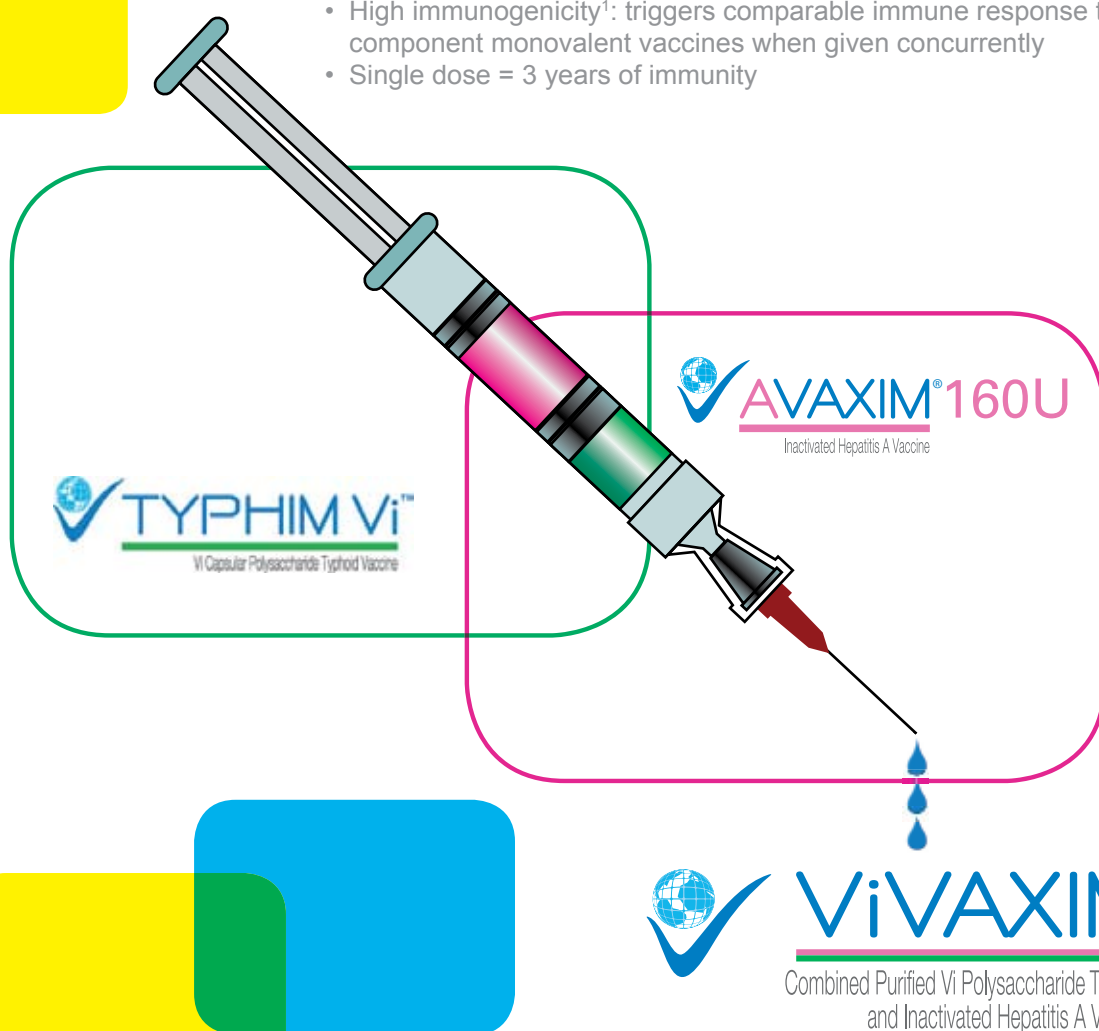


About the author

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The smart dual protection against Hepatitis A and Typhoid Fever

- Dual chamber: an advanced technology that guarantees no interference between the two components of the vaccine
- High immunogenicity¹: triggers comparable immune response to its component monovalent vaccines when given concurrently
- Single dose = 3 years of immunity



REFERENCE: 1. Overbosch D, Peyron F, Picot N et al. Combined typhoid fever and hepatitis A vaccine: comparison of immunogenicity and safety to concomitant monovalent vaccine over 3 years. *J Travel Med.* 2005; 12:319-26.

[54] **VIVAXIM**®. Hepatitis A (inactivated, adsorbed) and Typhoid polysaccharide vaccine. Each immunizing dose (1.0 ml) contains purified *Salmonella typhi* Vi (Ty 2 strain): 0.025 mg, phosphate buffer solution containing: sodium chloride, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate and water for injection. Traces of endotoxin: not more than 150 IU/mg. Hepatitis A virus (inactivated): 160 units. Preservatives (phenoxylethanol 2.5 µl, and formaldehyde 12.5 µg), aluminium hydroxide hydrated: 0.3 mg of Al, medium 199 (Hanks) in water for injection supplemented with polysorbate 80, traces of neomycin, and traces of endotoxin: not more than 10 IU/ml. Reg No.: 41/30.1/0025. **NAME AND ADDRESS OF BUSINESS APPLICANT:** sanofi-aventis South Africa (Pty) Ltd., Reg no.: 1996/10381/07, 2 Bond Street, Grand Central Ext. 1, Midrand, 1685. Tel: (011) 256 3700. Fax: (011) 256 3707. www.sanofi-aventis.com ZA150.12.08.05



Pneumoccal disease

Pneumonia remains one of the common reasons for travel health insurance claims. Therefore, for large travelling groups and those over 65 years, Pneumovax 23 should be offered. It is also advised for all travellers with chronic medical conditions especially cardiorespiratory disease and those with diabetes.

Hepatitis B

In SA universal vaccination is routine for neonates and adolescents. Given the risk of hepatitis B infection becoming chronic in the younger age group, with risk of cirrhosis and hepatocellular carcinoma. Hepatitis B vaccination should be offered to all non-immune travellers. Engerix B, Herbiovac and Euvax are the available vaccines. The combined hepatitis A and B vaccine Twinrix 720/20 can be given as a three dose schedule: 0, 1 and 6 months apart for children aged 1 to 15 years. The same formulation has been approved for rapid administration consisting of four doses at 0, 7 and 21 days, with a booster one year later. This accelerated regime should be restricted to adults, and only when there is limited time to departure.

Area specific vaccines

Hepatitis A

Hepatitis A is the most common vaccine-preventable disease occurring in travellers. The risk of contracting hepatitis A has been estimated as 1 in 1000 per month of travel to an endemic area and as much as 1 in 50 for those trekking through high endemic areas. Avaxim and Havarix are vaccines available with paediatric formulations as well. One booster after six months will give long term immunity. Avaxim 80 can be used in individuals from two years upwards.

The active vaccine can be given on the day of departure as immunity is achieved faster than the incubation period, should exposure occur. Hepatitis A vaccine should be offered to virtually all travellers. A recently launched combination with Salmonella typhi (Typhoid Vi) polysaccharide vaccine, Vivaxim, is suitable for travellers aged 16 years and older and is proving a very useful combination for travellers into Africa and

Asia. The follow-up booster for Hepatitis A is given as a single vaccine 6-8 months later to get long term immunity. The typhoid protection lasts for three years.

Typhoid

Typhoid is a food- and water-borne disease and can result in severe illness and death. If untreated, mortality rates of 10%-20% can occur due to toxemia, bowel perforation and haemorrhage.

Typhoid vaccination is recommended for travellers to endemic areas, where drinking water is unsafe or hygiene poor. Due to resistant strains in SE Asia vaccination is strongly recommended for all backpackers. Typhim Vi and Typherix are the two vaccines available and give protection 2-3 weeks after dose.

Rabies

Rabies carries the highest fatality rate of any vaccine-preventable disease. If one considers all the possible travel activities anticipated in a country where rabies is an endemic problem, the potential for animal bites is much larger than one realises.

Many cases of travel-related rabies infection are associated with the exposed person grossly underestimating the significance of the incident and not seeking medical care until the onset of symptoms.

Rabies exposure during travel could be viewed as avoidable, manageable and potentially preventable using different strategies, including bite avoidance counselling, rabies vaccine post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP).

Pre-exposure prophylaxis simplifies the management of subsequent exposure as it obviates the need for rabies immunoglobulin. It needs to be done well in advance of departure as vaccines are administered on days 0, 7, 21 or 28. There is no need for travellers to have regular boosters: only boost in event of exposure. Verorab and Rabipore are the vaccines available.

Meningococcal disease

The tetravalent meningococcal polysaccharide vaccines, Mencevax and Menomune are recommended for travellers to areas in which meningococcal disease is endemic, like the sub-Saharan African meningitis belt. It is also a

mandatory vaccination for all pilgrims attending the Hajj or Umrah.

Yellow fever

Vaccination for yellow fever is a legal requirement for all travellers travelling to or from, or transiting through, yellow fever endemic countries. A yellow fever vaccination waiver letter may be issued only on well-considered medical grounds. Stamaril is the vaccine available and should be administered 10 days prior to departure. The vaccine should only be given if it is definitely required for travel to at-risk areas and then only following careful appraisal with the patient regarding need and possible contraindications. Travellers to yellow fever areas should be advised that the relevant certificate should be carried at all times to avoid possible revaccination at a border post and/or quarantine.

Cholera

Long term travellers to highly endemic countries may be at increased risk of contracting this water-borne disease. Travellers with lowered gastric immunity such as achlorhydria associated with prolonged proton pump inhibitor medication or who wish to have a higher level of protection should be offered the vaccine.

Dukoral is an oral, killed recombinant B subunit/whole cell vaccine effective against both cholera and enteropathic *Escherichia coli*. It is given in two doses, one week apart. If the time lapse between doses is greater than six weeks the dose schedule must start again. Protection begins one week after last dose and lasts for six months.

Japanese encephalitis and European Tick-borne encephalitis vaccines are not discussed as they are not available in SA.

In conclusion

If travellers are unable to recall whether they have been vaccinated then assume they have not and vaccinate them. Primary immunisations need never be repeated, booster doses are all that are required. If previous vaccine courses have not been completed then complete the course.

References on request.



Diagnosis and Treatment of Lung Cancer: A Focus on the GP's Role

The lung cancer epidemic has mirrored changes in smoking patterns in many countries and has caused innumerable deaths. Approaches to identification, diagnosis and treatment of the disease are changing and are discussed in this article.

Lung cancer is the second most common cancer and leading cause of cancer death worldwide, with an incidence of 1.6 million new cases annually and 1.38 million deaths in 2008.¹ However, there have been major changes in the epidemiology of lung cancer and the treatment of patients with lung cancer has become more complex. Therefore, this article offers an update on diagnosis and treatment of lung cancer with a specific focus on the role of GPs in the management process.

Epidemiology

The overall incidence of lung cancer in men is decreasing whereas the incidence in women, after increasing in the past decade, is now plateauing. There is an increase in the incidence of lung cancer among never-smokers, particularly among females, but smoking remains the major cause of lung cancer.

Squamous cell carcinoma was previously the predominant histology in patients with smoking-related lung can-

cer. However, adenocarcinoma has now become the predominant histology, both in smokers and non-smokers.

Presentations and initial investigations

The presentations of patients with lung cancer are variable. Patients can be completely asymptomatic and have an incidental finding of a lung nodule on a chest x-ray carried out during a preoperative anaesthetic assessment or CT scan for another purpose. Some patients may present with non-resolving or recurrent pneumonia with persisting consolidation on chest x-ray whereas others may present with cough, chest pain, shortness of breath or haemoptysis, which may or may not be associated with constitutional symptoms, such as lethargy or loss of appetite or weight. Since as much as 50% of lung cancer has metastasised at the time of presentation, the symptoms may be those of meta-

static disease, distant from the thorax. Patients with lung cancer may be current smokers, ex-smokers or lifelong non-smokers. Regardless of smoking history, non-resolving or unexplained symptoms warrant further investigation.

A chest x-ray is the most appropriate initial investigation. Not all x-ray detected solitary lung nodules are malignant; other possibilities include hamartoma or post-infection granuloma. Comparison with previous chest x-rays, if available, may assist in understanding the nature of lung nodules. Further investigation of the thorax with a CT scan is usually required to characterise the lung nodule and assess whether it is solitary, its location and its relationship with other structures. CT scans of other regions (eg, abdomen or brain) may be needed depending on the symptoms.

All patients with evidence or suspicion of lung cancer should be referred to a specialist with a specific interest in, and knowledge of, lung cancer. Most commonly this will be a respiratory physician or thoracic surgeon who will be in a position to determine the need for further evaluation, including lung function testing and biopsy. Newly confirmed cases of lung cancer should be

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Key points

- Patients with non-resolving respiratory symptoms warrant investigations to exclude malignancy.
- Staging is the cornerstone of lung cancer prognosis and guides treatment.
- Patients with lung cancer are best managed by multi-disciplinary teams, often with multimodality treatment.
- Early palliative care input for patients with advanced lung cancer improves quality of life.
- Smoking cessation is the most effective intervention to prevent lung cancer.



Essential components in lung cancer management

Establish a tissue diagnosis

- Sputum cytology
- CT-guided fine-needle aspiration/biopsy
- Bronchoscopy with biopsy
- Endobronchial ultrasound and transbronchial needle aspirations

Assess the extent of the disease

- Clinical assessment
- CT scan of thorax with or without abdomen, brain and bone scan
- PET scan

Assess the patient's cardiorespiratory fitness for surgery and subsequent treatment modalities

- Exercise tolerance
- Lung function
- Performance status

Key points in lung cancer treatment

Non-small cell lung cancer

- Stage I: surgery
- Stage II: surgery + adjuvant platinum-based chemotherapy +/- radiotherapy
- Stage IIIA: induction chemotherapy followed by surgery and radiation or concurrent chemoradiotherapy
- Stage IIIB: concurrent chemoradiotherapy
- Advanced or metastatic: palliative chemotherapy, targeted therapy and radiotherapy

Small cell lung cancer

- Limited stage: sequential or concurrent chemoradiotherapy +/- prophylactic cranial irradiation
- Extensive stage: palliative chemotherapy +/- prophylactic cranial irradiation

a CT scan of the thorax and whole body positron emission tomography (PET) scanning. Staging investigations of SCLC include CT scans of the brain, thorax and abdomen, and bone scans. A PET scan is able to provide valuable information and would preclude the need for other investigations.

A detailed description of the staging system for lung cancer is beyond the scope of this article, and details are available elsewhere.² NSCLC is staged according to the TNM (tumour, node, metastasis) staging system. Broadly, stage I is localised to the lungs and stage II is localised to the lungs with ipsilateral local lymph node involvement or a large primary, whereas stage III disease is locally advanced with mediastinal lymph node involvement. Stage IV disease indicates the presence of distant metastases or a malignant pleural effusion. Although the same staging system can be used for SCLC, more commonly a two-stage system is used. Limited SCLC describes disease confined to one hemithorax and the ipsilateral supraclavicular nodal, whereas extensive SCLC refers to any greater extent of disease.

managed by clinicians who are members of a multidisciplinary team (usually including thoracic surgeons, respiratory physicians, pathologists, radiologists, nuclear medicine physicians, medical and radiation oncologists, palliative care physicians and nurses). Depending on the stage of the disease and the patient's cardiovascular fitness levels, patients will be referred either to surgeons for resection or to medical and radiation oncologists for chemotherapy and/or radiotherapy. In an increasing number of cases, multimodality treatment is appropriate.

Diagnosis

It is important to make a prompt and accurate diagnosis of suspected lung cancer and to manage the patient by adhering to best practice guidelines. In most patients, a tissue diagnosis is of great importance because the histological type of cancer has an impact on further management. Non-small cell lung cancer (NSCLC) accounts for 80% of cases of lung cancer, whereas small cell lung cancer (SCLC) accounts for approximately 15% to 20%, with rare tumours

such as carcinoid accounting for less than 5%. In some situations it is possible to treat patients without a tissue diagnosis but this should be the exception.

Lung tissue is commonly obtained by one of several methods, depending on the location of the tumours. For peripherally located lesions, tissue is obtained by radiologically guided fine-needle aspiration or core biopsy of a lung nodule. For centrally located lesions, bronchoscopy with brushings, washings and biopsy is performed. Sometimes, surgical biopsy of mediastinal lymph nodes using mediastinoscopy is required, either as the primary method of obtaining a tissue diagnosis or as a means of confirming or excluding malignancy in enlarged nodes. A less invasive procedure for this, recently developed, involves endobronchial ultrasound and trans-bronchial needle aspiration. Finally, a biopsy of metastatic sites (eg, liver or distant lymph nodes) may be used to make a diagnosis.

Staging

The prognosis of patients with lung cancer depends on the stage of the disease. Staging investigations for NSCLC include

Treatment

Patients with stage I to IIIA NSCLC and those with limited stage SCLC have a potentially curable disease and should be assessed and treated by clinicians who are part of a multidisciplinary team. Treatment approaches depend on the stage of the disease, the cell type and fitness of the patient (see the boxes on this page).

Non-small cell lung cancer Early (stage I and II)

Surgery remains the mainstay of treatment for patients with early NSCLC. The extent of surgery is dependent on both the fitness of the patient and the characteristics of the tumour, including its size and location and the extent of local spread. Surgical procedures include pneumonectomy, lobectomy or lesser resections, such as wedge resection or segmentectomy. Overall, 70% of patients with stage I disease and 50% of those with stage II disease will be cured.

Following surgical resection, adjuvant chemotherapy may result in further improvement in outcomes, particu-



larly in patients with stage II disease. However, the size of the additional benefit is modest (approximately 5% improvement at five years)³ and patients need to be fit enough to tolerate treatment. Typically, four cycles of chemotherapy are administered over 12 to 16 weeks.

For those patients who have undergone complete surgical resection for a localised peripheral tumour, there is no evidence that postoperative radiotherapy improves outcomes. Surgery is not always possible because of impaired lung function or the comorbidities that patients may have. Radiotherapy is an alternative for these patients. Stereotactic radiotherapy, a relatively recent development, may result in better outcomes for these patients.

Locally advanced (stage IIIA and IIIB)

Patients with stage IIIA NSCLC have tumours in the lungs, with involvement of ipsilateral mediastinal lymph nodes. Possible management approaches for these patients include trimodality treatment with induction chemotherapy, followed by surgery and then radiotherapy or concurrent chemoradiation. There is controversy concerning the optimal approach and decisions as to how these patients are treated often depend on the expertise and experience of the treating team. Approximately 25% of patients with stage IIIA disease are cured.⁴

In stage IIIB disease there is bilateral mediastinal nodal involvement that is not amenable to surgical resection (Figure 1). Similarly, tumours that involve structures, such as the mediastinum or vertebral bodies, are also not amenable to surgical resection even if there is no nodal spread. These patients, if fit enough, are treated with concurrent chemotherapy and radiation, delivered over about six weeks. The intent of treatment is cure or long-term disease control, with less than 10% of patients being cured.⁴

Advanced or metastatic (stage IV)

Chemotherapy, new targeted therapies and radiotherapy are the primary treatments available for 50% of patients who present with metastatic disease or



Figure 1. CT scan of a patient with locally advanced (stage IIIB) adenocarcinoma of the lung, with bilateral mediastinal lymph nodal involvement.

develop it after failure of treatment during the early stages of NSCLC. Although these patients will ultimately succumb to their disease, there is good evidence that both prolongation of survival and improved quality of life occur with modern chemotherapy regimens, whereas radiotherapy is effective in controlling symptoms, including pain, cough, haemoptysis and the symptoms of cerebral metastatic disease. Irrespective of the treatment approach used, good palliative care support involving the patient's GP, with specialist medical and nursing palliative care services, is important.

A major change in the approach to advanced NSCLC has been the recognition that tumour characteristics such as histology and the presence of genetic changes can be used to guide and 'personalise' therapy. Examples include the preferential use of pemetrexed-based chemotherapy in patients with non-squamous tumours (and its avoidance in those with squamous histology), and the first-line use of targeted therapies in patients whose tumours have mutations in genes, such as the epidermal growth factor receptor gene (EGFR) and echinoderm microtubule-associated protein-like 4 and anaplastic lymphoma kinase genes (EML4-ALK).

Somatic mutation at the tyrosine kinase domain of the EGFR gene has been shown to be important in the pathogenesis of some forms of lung cancer. Therapy with oral tyrosine kinase inhibitors, such as erlotinib, has been associated with a rapid response and significant progression-free survival in patients who possess the EGFR mutation (approximately 15% to 20% of adenocar-

cinomas in western countries). However, resistance eventually develops after nine to 13 months of treatment. Furthermore, about 5% of NSCLC contain a fusion of oncogenes (EML4-ALK), which is mutually exclusive from the EGFR mutation and occurs more commonly in non-smokers.

New oral inhibitors, such as crizotinib, are being developed to specifically target this abnormality but are currently available only in the context of clinical trials.

Small cell lung cancer Limited stage

SCLC is highly sensitive to chemotherapy and radiotherapy. Therefore, the primary treatment is chemotherapy (platinum-based with etoposide) combined with concurrent thoracic radiotherapy. A meta-analysis has shown that this approach improves survival and reduces local recurrence.⁵ This is given with curative intent with a five-year survival rate of 10% to 20% and median survival of up to 22 months. Brain micrometastases may be present at the time of diagnosis despite a negative brain scan, and the brain is a common site of relapse after therapy. Therefore, prophylactic cranial irradiation (PCI) is appropriate in those patients who demonstrate a good response to chemoradiotherapy and who remain in good performance status after the completion of their concurrent treatment.

Extensive stage

Platinum with etoposide chemotherapy is the first-line treatment for patients with extensive SCLC. The response rate is up to 70% initially. However, SCLC inevitably progresses. Overall, the response rate to subsequent chemotherapy in recurrent or refractory SCLC is poor. A recent study has demonstrated benefit from PCI in those patients with extensive disease who respond well to initial chemotherapy.⁶ Radiotherapy to the primary site is generally not indicated in the initial treatment of extensive SCLC.

Role of the GP

GPs play a critical role in lung cancer management from the initial phase of diagnosis through to liaising with all members of the multidisciplinary team



and acting as patient advocates (see the box on this page). They act as a bridge between specialists and patients. Their role is multifaceted, including liaison with hospital specialists, management of chemotherapy and radiotherapy toxicities, palliation of symptoms and ultimately end-of-life care. At the time of presentation, GPs have an important role in providing advice and support relating to smoking cessation, which is critical for any patient who is to be considered for surgical resection.

There are some patients who are not suitable for aggressive anticancer therapy, due to advanced disease or severe comorbidities. This may be from the time of diagnosis or after progression of their disease despite therapy. Referral of these patients to a palliative care service is an appropriate option, but GPs continue to play an invaluable role in the palliation of symptoms. Research has shown that early palliative care input improves quality of life, mood and even prolongs median survival.⁷ Therefore, GPs are encouraged to be involved in the palliative and end-of-life care of patients from the early stages of the diagnosis.

Lung cancer screening

Over the years, there have been numerous studies examining screening for lung cancer with chest radiograph with or without sputum cytology. However,

Role of the GP in the management of lung cancer

- Smoking cessation education
- Vigilance in assessing high-risk patients with symptoms
- Liaison with specialists to ensure prompt diagnosis and treatment
- Management of chemotherapy and radiotherapy toxicities
- Palliation of symptoms such as pain and shortness of breath
- End-of-life care

these studies did not show any population mortality benefit. Therefore, population screening with chest radiography has not been recommended.

The recent US multicentre randomised clinical trial published in the *New England Journal of Medicine* has reignited the debate about lung cancer screening.⁸ It demonstrated that screening with a low-dose CT scan resulted in a relative reduction in lung cancer mortality of 20% among current and ex-smokers with a heavy smoking history (30 pack years or more) aged between 55 and 74 when compared with chest radiograph alone. This is the first study that has shown a reduction in lung can-

cer mortality using a low-dose CT scan as the screening tool. This is a promising and exciting result. However, there are a number of unanswered questions that need to be addressed before a low-dose CT scan is accepted as a population-wide screening tool.

The most appropriate duration of screening was not determined by this study. There are no well-defined consensus guidelines on the management and follow-up of suspicious lung nodules. Those who screen positive tend to have early localised disease; therefore, minimally invasive surgical resection may be required. However, the availability of such a service is highly variable. Furthermore, the availability of low-dose CT screening and expertise in interpreting these images are also variable, so until these issues are addressed it is premature to offer low-dose CT screening to all current or past heavy smokers.

Conclusion

Lung cancer is a major health problem. Since prevention of this disease is better than cure, smoking cessation education is vitally important. Lung cancer management is complex and highly specialised; therefore, referral of these patients to a specialist who is part of a multidisciplinary team should be the standard of care.

References are available on request

SAMA Warns Doctors Against Working in the United Arab Emirates

The South African Medical Association (SAMA) has warned local health professionals against applying for positions in the United Arab Emirates (UAE) and similar countries in the wake of the incarceration of respected veteran paediatrician, Prof Cyril Karabus, in Abu Dhabi.

SAMA has also advised doctors already working in the UAE to withdraw their services to avoid the risk of a Karabus-type experience.

"We advise SA doctors and other health professionals to avoid working in the UAE and would ask that those already there, consider withdrawing their services in the interest of their own safety," Dr Mzukisi Grootboom, SAMA chairperson, notes in the statement.

Prof Karabus, a retired Red Cross Children's Hospital

paediatric haematologist, was arrested while in transit through Dubai in August after having been tried and convicted in absentia in 2003 for the death of a three-year-old patient he had treated during a locum at an Abu Dhabi hospital in 2002. He and his family were returning from his son's wedding in Canada and was unaware of the decade old judgment against him.

It took five court appearances and almost eight weeks in prison before the physically unwell 78-year-old medical specialist was finally granted bail in October.

There have been several subsequent hearings, but all have been postponed. One of the main stumbling blocks has been the inability of the prosecution to produce the original medical records of the case.



Stroke in the Elderly: Predictable, Preventable and Treatable

Stroke is the second most common cause of death worldwide, with most of the disease burden falling to the elderly and the very elderly. Effective treatments are available for acute management and for primary and secondary prevention of stroke. GPs are particularly well placed for identifying at-risk patients and for initiating 'triple therapy' of aspirin, a high-dose statin and blood pressure lowering therapy.

Stroke is a common cause of death and disability, especially in elderly patients.¹ The definition of elderly varies widely but most publications refer to the elderly as those older than 65 with 'very elderly' defined as those over 80. Stroke is both predictable and preventable, and treatments exist that can significantly alter the natural history of the disease.² Although major strides have been made in our understanding of the diseases responsible for stroke, and development of treatments to prevent and treat acute stroke, most information comes from studies in a younger population. With an ageing population, stroke is predicted to increase in incidence, emphasising the need to optimise acute and preventive interventions.

Epidemiology

Stroke is the second most common cause of death worldwide. Of those affected by stroke, some 80% are older than 65 and 25% are over 85. The incidence of stroke doubles every decade after the age of 55, and with increasing life expectancy the

incidence of stroke in the population will also increase. Indeed, stroke is a significant cost to society and is predicted to be the leading cause of death in developed countries by 2030.¹

Hypertension, diabetes, smoking and atrial fibrillation have all been identified as modifiable risk factors for stroke. These account for about 60% of stroke cases. The remaining 40% are due to as yet unidentifiable causes, but may involve possible genetic mechanisms.² Age is the main unmodifiable risk factor for stroke and has a profound effect on both incidence and outcome. Age-associated risk factors, such as atrial fibrillation, congestive cardiac disease and carotid

artery atherosclerosis, explain a large part of the increased incidence of stroke among the elderly and comorbidities may explain the poorer outcome. However, even adjusting for these factors, mortality, length of hospital admission and final discharge destination are all poorer in the older patient who has had a stroke.

Aetiology and subtypes

Over 80% of strokes are ischaemic in nature; the remaining causes are secondary to haemorrhage.² Three main stroke subtypes cause 75% of ischaemic strokes, with a roughly equal distribution. These subtypes affect prognosis and treatment.

• **Large vessel atherosclerosis strokes.** These classically affect the origin of the internal carotid but may occur at any point both intra- and extra-cranially. This subtype may result in thrombosis at the site of disease or artery-to-artery distal embolisation. Antiplatelet and antithrombotic therapies are the best treatment options.

Key points

- Stroke is the second most common cause of death worldwide and predominantly affects the elderly.
- Aspirin therapy, referral to a stroke unit and thrombolysis within 4.5 hours of onset are interventions that are of proven benefit for acute ischaemic stroke.
- A transient ischaemic attack (TIA) is a medical emergency and presents an urgent window of opportunity to prevent a completed stroke.
- Stroke prevention can be achieved by urgent diagnostic evaluation of a TIA and by starting 'triple therapy' with aspirin, a high-dose statin and blood pressure lowering therapy.
- Treatment with an anti-platelet agent should be started immediately in patients who have experienced a transient focal neurological event.
- Anticoagulation therapy is vastly superior to treatment with antiplatelet agents for patients with atrial fibrillation.
- Carotid imaging is one of the most critical investigations in preventing stroke and should be performed urgently, followed by referral for surgery if a significant symptomatic stenosis is identified.

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- **Cardioembolic strokes.** These are mainly due to atrial fibrillation but are also caused by mural wall thrombosis following myocardial infarction, left ventricular failure or mitral valve disease. This subtype is an increasingly common cause of stroke in the elderly and anticoagulation is the treatment of choice.

- **Lacunar ischaemic strokes.** These are caused by small vessel disease. This subtype, in general, is associated with a significantly better outcome and much lower recurrence rate compared with other subtypes of ischaemic stroke. Treatment should include an antiplatelet agent.

Most strokes resulting from haemorrhage are caused by hypertensive small vessel lipohyalinotic disease, cerebral amyloid or aneurysm rupture. A minority of cases are secondary to vascular malformations. Prognosis is poor in patients who have had a haemorrhagic stroke, with 50% mortality at one month.

Acute management

Patients with acute stroke should be referred to hospital immediately as treatments are critically time sensitive. There are three proven interventions for acute ischaemic stroke:

- Aspirin given within 48 hours of symptom onset reduces both death rate and further stroke at one month.
- Stroke units have a large effect on reducing mortality and morbidity, are applicable to the vast majority of patients, and are effective across all age groups.²
- Thrombolysis with alteplase is beneficial when given appropriately to those presenting within 4.5 hours of ischaemic stroke symptom onset.^{3,4}

Most evidence for the benefit of these interventions comes from studies in younger patients. There is less evidence, to date, of benefit in those over 80 because of their exclusion from the major trials. The Third International Stroke Trial (IST-3) has investigated thrombolysis for acute ischaemic stroke in those over 80.⁵ Current practice for the acute management of stroke is that age alone is not an exclusion criterion. If pre-morbid physical and cognitive functions are good then thrombolysis should be considered. The outcome is

poor in elderly patients with a significant deficit at presentation, particularly when a vessel occlusion can be identified on imaging. However, if the elderly patient is not independent before the event then alteplase is not generally offered because the aim of treatment is to return the patient to independent living.

Transient ischaemic attacks

A transient ischaemic attack (TIA) presents an urgent window of opportunity to prevent a completed stroke. Early, intensive assessment and treatment of herald events such as a TIA is essential for stroke prevention. This can be achieved by urgent diagnostic evaluation of patients suspected of having a TIA and by starting 'triple therapy' with aspirin, a high-dose statin and blood pressure lowering therapy.⁶

In a patient with a transient focal neurological event that has fully resolved and who is back to normal, immediate loading with aspirin is appropriate – waiting for a CT scan before initiation only raises risk while rarely changing management acutely. This is not the case if neurological signs persist or red flags are present, such as prior malignancy that may have metastasised or if the patient is currently on anticoagulation. A history of paroxysmal atrial fibrillation or identifying atrial fibrillation on an electrocardiogram should prompt immediate anticoagulation rather than antiplatelet therapy.

Urgent assessment of the extra-cranial carotid arteries is the other key step in the management algorithm of TIA because carotid stenosis is a particularly sinister and time-critical cause of transient symptoms. Indeed, a significant proportion of patients will have a completed stroke within days of a herald event if there is a significant carotid stenosis.

A recent focus of research has been identifying 'high-' and 'low-'risk TIAs based on clinical features. The role of these scoring systems is as yet unproven and does little in directing treatment to alter the natural history of individual events. Rapid assessment in specialised clinics, where available, is of proven benefit.

Secondary prevention

Appropriate antithrombotic therapy is the first step of secondary prevention. The choice lies between antiplatelet treatment and anticoagulation. In the setting of a cardioembolic source such as atrial fibrillation, anticoagulation with warfarin is the treatment of choice. Strong evidence now exists that warfarin is superior to aspirin for atrial fibrillation, even in the very elderly, and while the risk of haemorrhage increases with age and comorbidities, so does the risk of ischaemic stroke, with the risk-benefit balance in favour of anticoagulation.⁷ The newer anticoagulant agents (eg, dabigatran, apixaban and rivaroxaban) appear to offer many advantages for secondary prevention of stroke. Caveats exist regarding the use of these newer agents in the elderly, with studies suggesting that adverse events are increased in the older age group. If a cardiac source of stroke cannot be identified, therapy with either aspirin plus slow-release dipyridamole or clopidogrel alone are the optimum treatments, and are equivalent.⁸ The combination of clopidogrel and aspirin offers no additional benefit due to the increased haemorrhagic risk of this combination for those patients with prior stroke.⁹

Hypertension is a main risk factor for stroke and while early intensive treatment in the first week following a stroke may be harmful, controlling blood pressure in the long term is of major importance in preventing further cardiovascular events.¹⁰ Furthermore, blood pressure lowering treatment is appropriate for both ischaemic and haemorrhagic stroke. There are concerns regarding optimum blood pressure targets in the very elderly, for whom a balance is needed between treatment and over-treatment, but benefit has been demonstrated in primary prevention for those over 80, and for all ages in secondary prevention.¹¹

Statin therapy reduces risk of cardiovascular events and is of proven effect in the secondary prevention of stroke, including in the very elderly, in whom atorvastatin has the most robust evidence.¹²

Carotid endarterectomy is one of the most powerful interventions in preventing stroke. In patients with symptomatic

ANTI COAGULANT

- Antiplatelet therapy with clopidogrel, a mainstay of therapy to prevent atherothrombotic events in high risk patients ¹
- Recommended in anti-thrombotic therapy and prevention of thrombosis, 9th edition: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines ²

S3 MISTRO
clopidogrel 75 mg
PREVENTION PROTECTION



moderate (50% to 70%) or severe (greater than 70%) stenosis, early intervention (within two weeks of symptom onset) results in a major absolute risk reduction of further stroke.

The benefit of carotid endarterectomy is even more substantial in the elderly; therefore, age alone should not be an exclusion criterion for this intervention if the patient is otherwise well.¹³ Carotid stenting is inferior to surgery and thus should be performed only if the patient is unsuitable for endarterectomy or because of patient preference.

The presence of other vascular risk factors should also be addressed, including smoking (stopping smoking can reduce future vascular risk by half), diabetes and lifestyle changes such as diet modification and increasing physical activity levels.

Life after a stroke

The sequelae of a stroke are variable and depend, to a large degree, on the extent and location of the infarction or haemorrhage. Recovery is most dramatic in the weeks and months following the event

but significant functional gains can be seen up to a year or more after the initial event, particularly with intensive rehabilitation and input from allied healthcare professionals.

Non-focal symptoms such as fatigue and mood disturbance are very common. These can be particularly troublesome, especially when on a superficial level all other signs have resolved. Typically, patients who have such symptoms launch back into their previous routine only to find that their physical and intellectual reserves are not what they were. Emphasising a graded return to duties and giving reassurance that these symptoms are to be expected and will gradually improve with time is helpful. As these issues can persist for months and even years, a low threshold for initiating an anti-depressant is worthwhile (the best evidence is for SSRIs), especially when mood and irritability are a problem.

Driving can generally be resumed one month after the stroke event, provided deficits do not interfere with ability. Motor function and visual field assessment are important factors in determin-

ing this, but issues with judgement also have a significant impact on safety and can best be assessed on family reports of behaviour. If there are any doubts, an on-road driving test can be helpful.

Conclusion

Stroke is a common cause of death and disability in the elderly, but good treatments now exist for both acute stroke and primary and secondary prevention. Primary care physicians are particularly well placed in identifying at-risk patients, such as those with a TIA and atrial fibrillation, and for commencing therapy. Treatment includes 'triple therapy' (aspirin, a high-dose statin and blood pressure lowering therapy), warfarin for atrial fibrillation and urgent imaging of carotids, with referral for surgery if a significant symptomatic stenosis is identified. In addition, rapid TIA assessment clinics, where available, are an excellent resource.

References are available on request.

Migraine Triggers Fail to Match Patient Reports

The migraine triggers cited most frequently by patients are physical exertion and bright or flickering light, yet in a small prospective study few participants with a history of migraine with aura developed headaches when exposed to those triggers.

Only three of 27 patients (11%) reported attacks of migraine with aura following provocation, and three others reported migraine without aura.

All of the attacks occurred in response to exercise; provocation with light elicited no headaches, Jes Olesen, MD, DMSc, of the University of Copenhagen, and co-authors reported in the journal *Neurology*.

"Experimental provocation using self-reported natural trigger factors causes migraine with aura only in a small subgroup of patients with migraine with aura," the authors wrote in conclusion.

Exertion and light most often blamed

"Naturally, when having an attack, patients will think back to identify possible causes but, just as naturally, patients rarely seek confirmation by exposing themselves to suspected trigger factors," the authors noted in their introduction.

Olesen and colleagues previously reported that more than half of patients with a history of migraine with aura could describe a stimulus that always or often provoked attacks (Cephalalgia 2010; 30: 346-353). Most often, those were

exertion and light.

In the 27 patient study, exercise alone triggered migraine attacks in four of 12 patients (one preceded by aura). Two of seven patients developed migraine with aura after exercise and exposure to light. None of 11 patients had migraine attacks with photostimulation only.

The results were "less than spectacular" as compared with nitroglycerin infusion, which reliably provokes symptoms in about 75% of patients, an accompanying editorial pointed out.

Are patients simply wrong?

"There can be several reasons for this," wrote Dr Peter Goadsby and Dr Stephen Silberstein of the University of California San Francisco. "Perhaps patients are wrong. This is the least attractive option. The reporting is so consistent across the world and so many patients have so many attacks, it is hard to think they are all just incorrect."

A second possibility relates to possible differential effects of triggers on aura and migraine headache.

A third possibility revolves around the classic clinical advice to identify and avoid triggers, advice that could be wrong, as suggested in migraine literature.

"Many questions are unresolved and require continued careful, bedside approaches to studying this common, disabling brain disorder," Goadsby and Silberstein concluded.



Game changers in Type 2 diabetes: The Implications of Panretinal Laser Therapy

Panretinal laser therapy, an effective treatment for sight-threatening diabetic retinopathy, should prompt a major review of diabetes management because retinopathy suggests that other microvascular disease is present, and probably macrovascular disease too.

Panretinal laser therapy is an important part of the management of diabetic retinopathy. The need for the procedure may be a game changer for diabetes management and the procedure itself is often a life-changer for the patient. Both the diabetes health professional team and the patient are confronted with the reality of visual loss, the potential of future visual loss and blindness, and the virtual certainty of severe microvascular disease in other systems of the body (neuropathy and nephropathy), as well as the likelihood of macrovascular disease (atherosclerotic cardiovascular disease).

This article discusses the implications of requiring and having panretinal laser therapy for proliferative retinopathy. Some background information is given in the box on diabetic retinopathy and panretinal photocoagulation.

Implications of having laser photocoagulation

Visual loss after laser therapy

After panretinal laser therapy, the retina is covered with white blots of ischaemic retina, as shown in Figure 1. It is amazing that the eye can see anything at all but central macular vision is usually pre-

served (recognition of colour and perception of details) although peripheral vision may be lost or severely impaired, especially in dim light.

Loss of visual capacity may mean that people are no longer safe to drive, especially at night. They may also not be safe in the dark if they have the additional microvascular complication of neuropathy, which reduces their proprioception. When they are in dim light or dark, they are totally dependent on their vestibular system to inform the brain of body position and may therefore have difficulty maintaining their balance.

Diabetic retinopathy and panretinal photocoagulation

Diabetic retinopathy

In the early stages of diabetic retinopathy, microaneurysms and small haemorrhages of the retinal arterioles occur and then retinal vessels become blocked, depriving areas of the retina of a blood supply. Visual symptoms are not normally experienced in this nonproliferative retinopathy.

As the retinopathy progresses, the retinal ischaemia causes the production of growth factors, including vascular endothelial growth factor, that stimulate the growth of fragile abnormal retinal vessels – proliferative retinopathy. As these vessels grow, the patient becomes at risk of visual loss due to haemorrhage into the vitreous and/or retinal detachment.

Panretinal photocoagulation

Panretinal, or scatter, photocoagulation is able to destroy ischaemic retinal tissue, and thereby stop the neovascularisation. In the absence of growth factors, the new vessels generally regress and may disappear.

The procedure of panretinal laser therapy involves the placing of multiple laser burns (up to 2000) over the entire retina, avoiding the macula. The treatment is not applied directly to neovascularisation of the optic disc and generally not to neovascularisation elsewhere. A common complication is exacerbation of macular oedema if it is present. Also, because the laser therapy destroys viable retinal tissue, it can cause peripheral visual field defects, reduced night vision, diminished colour vision and decreased contrast sensitivity.

Despite the small risk of some immediate visual loss, timely laser photocoagulation is an effective therapy for sight-threatening diabetic retinopathy.¹ It should be performed as soon as possible for high-risk proliferative retinopathy and when any maculopathy is stabilised in earlier proliferative retinopathy, and be considered for severe nonproliferative retinopathy; for less severe retinopathy, the benefits need to be balanced against the risks.¹

About the author

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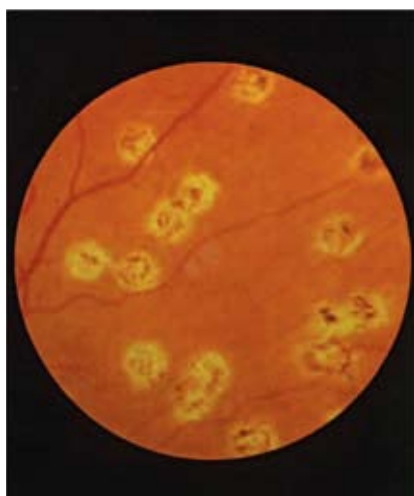


Figure 1. The retina after panretinal laser therapy for proliferative diabetic retinopathy.

These visual limitations can threaten a person's capacity to function independently and their employment. Such losses may be overwhelming, profoundly disorienting and depressing. Yet once these visual threats have been dealt with, there are other threats to be confronted.

Proliferative diabetic retinopathy rarely affects one eye and not the other. One eye may be more affected than the other, but severe retinopathy will be present in both eyes and both will need laser therapy, resulting in bilateral loss of peripheral and night vision. The Diabetic Retinopathy Study (DRS) established the value of laser therapy for proliferative diabetic retinopathy by comparing the

visual outcomes in patients with bilateral proliferative retinopathy who had one eye treated while the other acted as a control (treatment was deferred in the control eye).^{2,3} The trial demonstrated the clear benefit of early laser therapy, with reduction in the incidence of severe visual loss (Figure 2).

However, although laser therapy decreases visual loss compared with the untreated eye, vision continues to decline, causing severe visual loss within a relatively short time in many patients.

Implications of requiring laser photocoagulation

Widespread severe microvascular disease

In a person with severe diabetic retinopathy, severe microvascular disease is likely to be present throughout the body – most notably in the kidneys and nerves but also in other organs, such as the heart. Nephropathy is associated with albuminuria, rising plasma creatinine levels and a series of 'vicious cycles' linked to cardiovascular disease.⁴ Neuropathy is associated with loss of protective sensation in the periphery and changes in the structure and function of the feet, both of which make foot problems more likely.

Probable macrovascular disease

Type 2 diabetes itself is associated with increased cardiovascular risk, and risk factors for diabetic retinopathy include hypertension, dyslipidaemia and smoking, all of which are risk factors for cardiovascular disease as well.¹ Severe dia-

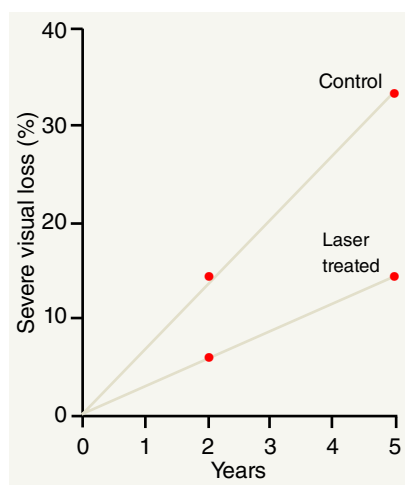


Figure 2. Results of the Diabetic Retinopathy Study (DRS) showing benefit of panretinal laser therapy.^{2,3} (Severe visual loss was defined in the DRS as visual acuity $\leq 20/800$; in Australia, this is equivalent to $\leq 6/240$.)

betic retinopathy suggests that these risk factors had not been well controlled and that widespread macrovascular disease may be present. As noted, cardiovascular risk would be further increased if nephropathy were also present.

Assessing and responding to these implications

Visual loss

Ophthalmologists will almost certainly assess a patient who has undergone laser therapy for diabetic retinopathy for visual limitations and capacity to cope with dark environments and driving. Counselling, arranged by the ophthalmologist or GP, is important in enabling patients to cope with these limitations.

Investigations for microvascular and macrovascular disease

Suspected microvascular disease

- **Nephropathy:** plasma creatinine and estimated glomerular filtration rate (eGFR); urinary albumin-creatinine ratio (ACR) or albumin excretion rate (AER)
- **Neuropathy:** peripheral sensation, reflexes and power
- **Cardiac:** echocardiogram

Suspected macrovascular disease

- **Coronary:** ECG; exercise stress test
- **Cerebral:** carotid ultrasound
- **Peripheral:** ankle brachial pressure indices

TABLE 1

The ABCS of diabetes care^{5*}

Factor	Target
A – Glycosylated haemoglobin (A1c)	<7.0%
B – Blood pressure	<130/80 mmHg
C – Cholesterol	<4 mmol/L
S – Smoking	0

* A further 'S' (salicylate therapy) in the original ABCSS is no longer routinely recommended for those people with diabetes and no known cardiovascular disease.



Common contributors to nephropathy

- Urinary tract infection
- Urinary obstruction
- Current or previous nephrotoxic medication – eg, NSAIDs, radiographic contrast media, aminoglycoside antibiotics
- Renovascular disease (arterial and venous)

Common contributors to neuropathy

- Alcohol
- Entrapment neuropathy
- Vitamin B1 deficiency
- Hypothyroidism
- Neurotoxic medication – eg, nitrofurantoin, statins, vinca alkaloids (chemotherapy)

Widespread microvascular and probable macrovascular disease

Assessment of micro- and macrovascular disease includes establishing the extent of disease and damage and any uncontrolled risk factors for future problems. Indicators include a history of myocardial infarction or angina, transient ischaemic attack, stroke and claudication. Some investigations are suggested in the box on page 38, and the advice of specialist colleagues may be useful.

Reviewing the major targets in managing type 2 diabetes, the ABCS of diabetes care (glycosylated haemoglobin [A1c], Blood pressure, Cholesterol level and Smoking), would identify any specific risk factors that should be addressed

Provision of counselling by a person familiar with the potential problems and possible solutions can minimise any limitations and help the patient cope with an uncertain future. Specialist psychological support will also help the

patient adjust to the situation, and cognitive behavioural therapy will provide skills to cope with future challenges. The patient's family might also value advice about their role in helping the patient live with their limitations.

TABLE 2

Assessment of risk factors for foot problems in diabetes: the foot factor traffic lights

Foot factor traffic lights			
ABCS assessment	Red lights – 'Danger'	Amber lights- 'Caution'	Green lights – 'Healthy'
Anaesthesia			
– Pinprick, light touch (eg, 10g monofilament)	No stimuli felt	Reduced stimuli	All stimuli felt
– Reflexes	No reflexes	Reduced reflexes	Normal reflexes
Blood			
– Pulse palpation	No pulses	Reduced pulses	Normal pulses
Care*			
– Questioning	Foot care and/or footwear inadequate	Foot care and/or footwear could be better	Appropriate foot care and footwear
– Observation	Skin breakdown	Threatened skin breakdown	Normal skin
Structure			
– Observation	Weight-bearing ulcer	Callus or corn	No skin lesions
Patient risk assessment			
Traffic lights	Risk assessment		Recommended action
One or more red lights	High risk		Prompt referral to a podiatrist
One or more amber lights	Moderate risk		Regular podiatry care and assessment
All green lights	Low risk		General foot care advice

* Inadequate foot care in the absence of any other red or amber traffic lights is not a major risk factor for severe foot problems. Adequate foot care in the presence of one or more red or amber traffic lights is essential and can prevent severe foot problems.



Panretinal laser therapy: key points

- Panretinal laser therapy is effective in patients with diabetic retinopathy that is threatening sight, although it may itself cause some visual loss.
- Counselling and support help the patient deal with visual losses and their effect on daily functioning and work, and to cope with future losses.
- The existence of one severe microvascular complication should prompt review of the general risk factors for diabetes complications (the ABCS) and a check for the complications themselves and their severity.
- Efforts to reduce the future impact of microvascular and macrovascular diabetic complications include controlling complication risk factors, assessing the risk of future adverse events (eg, the ABCS of foot risk) and responding to these risks.

in a patient with diabetes, remembering that recommended targets for such patients with existing nephropathy or coronary disease are lower (Table 1).⁵ GPs and patients are probably prepared to invest time and effort in these assessments, and patients are likely to commit to intensifying therapy and coming as close as possible to the general targets of diabetes care.

Particular problems may be identified by the clinical history, examination and investigations. Suggested responses to these include:

- **nephropathy** – assess for other contributors to nephropathy (see the box)
- **neuropathy** – assess for other contributors (see the box), and assess the other risk factors for foot problems requiring more intensive foot care and

specialised footwear (ie, foot sensation and circulation, routine foot care and abnormal foot structure)

- **cardiac dysfunction** – consider referral to a cardiologist
- **coronary artery disease** – consider referral to a cardiologist
- **cerebrovascular disease** – if significant (more than 70% occlusion) or symptomatic, consider referral to a neurologist or stroke physician
- **peripheral vascular disease** – as for neuropathy.

The foot factor ‘traffic light’ guide is a quick way to assess foot risk (the ABCS of foot risk: Anaesthesia, poor Blood flow, routine Care and abnormal Structure), as shown in Table 2.⁶ If all the traffic lights are green (normal), there is no excess risk or need

for specialist podiatric input. If there are any amber or red lights, the patient should be referred promptly for specialist assessment and advice on footwear and foot care. Ongoing specialist podiatric nail care will be needed for patients with peripheral vascular disease and/or abnormally thickened or fungus-infected nails, as well as for those who cannot see or reach their nails.

Conclusion

Despite the small risk of some loss of peripheral and night vision, panretinal laser therapy is an effective treatment for sight-threatening diabetic retinopathy. It is a major life-changing event for the patient, and should prompt a series of life and health preserving measures by the diabetes health professional team because the presence of retinopathy suggests the presence of other microvascular complications of diabetes, and also probably macrovascular complications. The GP plays a key role in coordinating multi-pronged assessment and multi-disciplinary management to control risk factors and minimise the impact of other diabetic complications. Shared care is clearly the best form of care in this situation.

References are available on request

Reaching Cholesterol Goals Now More Affordable

Pharma Dynamics says it has made reaching cholesterol treatment goals more affordable with the launch of Dynator (atorvastatin). Atorvastatin effectively lowers LDL and triglycerides, and is extensively studied in primary and secondary prevention.

The company says Dynator will save patients up to 48% vs the market leader, making intensive and effective management of dyslipidaemia more affordable. This will contribute significantly to reducing the growing cardiovascular disease health burden in line with the 2012 SA dyslipidaemia guideline consensus statement.

Dynator is available in four dosage strengths:

Name	Dose	Pack size	Price (SEP excl VAT)
Dynator 10mg	10mg	30 tablets	R35.00
Dynator 20mg	20mg	30 tablets	R60.00
Dynator 40mg	40mg	30 tablets	R70.00
Dynator 80mg	80mg	30 tablets	R90.00



Sixteen Doc Team Successfully Performs Double Arm Transplant

The most extensive bilateral arm transplant to date has been successfully achieved thanks to an interdisciplinary team of doctors and nurses at Johns Hopkins Hospital, Baltimore, USA. The operation last December lasted 13 hours and involved 16 doctors from orthopaedics, vascular medicine, plastic surgery, and other disciplines from five hospitals.

Today, the 26-year-old patient, Sergeant Brendan Marrocco, can flex his left arm at the elbow along with slightly rotating his wrist, though the feeling in his hands have not returned.

For the procedures, different approaches were involved for each arm to preserve Brendan's residual limbs. As Dr. Andrew Lee, who headed the transplant team, reported, the right arm had "an above-elbow transplant by connecting the bone, muscles, blood vessels, nerves and skin between the donor [arm] and recipient." For the left side, the elbow joint was preserved, as were some of the nerves, so the team "transplanted the entire donor forearm muscles over his remaining tissues, then rerouted the nerves to the new muscle." Because of the complexity, the team practiced on cadaver arms four times over a span of 18 months prior to the surgery.

Innovative anti-rejection treatment

The risk of transplant rejection is high, so the Hopkins team employed an innovative approach by infusing Marrocco with bone marrow cells harvested from the donor's lower vertebrae. This has allowed him to cut back on the standard three-drug regimen used to prevent



Arm transplant teamwork

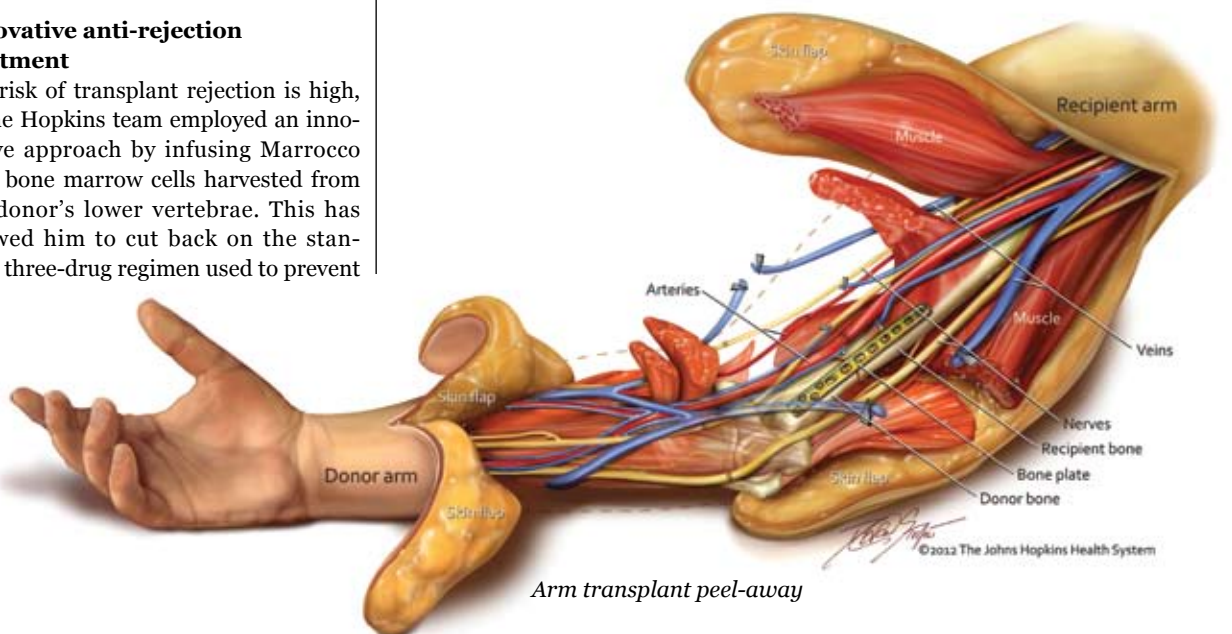
limb rejection; important because the anti-rejection drugs can compromise the immune system and damage organs.

Though the costs of the procedure and rehabilitation are being covered by the army, all the doctors involved volunteered their services.

At a press conference, Dr. Lee made it clear that though Marrocco's progress has exceeded their expectations, it will take many months to years before functionality returns. This is primarily

because "nerves regenerate at the maximum speed of one inch per month." To encourage nerve growth and development, Brendan will undergo six hours of physical therapy a day for the next two years.

In 2009, Sergeant Marrocco was driving an armored vehicle outside Baghdad when it was hit by a roadside bomb. All of his limbs had to be amputated, though he retained more of his left arm than his right.



Arm transplant peel-away

An Idea Whose Time Has Come A Doctor Test Drives Discovery's HealthID App

There are very few ideas that cross my desk and do not quickly end up in the bin under it. Yet HealthID has been one of a handful of game-changing enhancements to my successful private practice. And the sleek shiny iPad makes a stylish addition to my consulting room!

Time saver

Let me share what my experience has been so far with this new application. As many of you who are already using HealthID may have experienced, I find it saves time and generates less admin. My patients generally seem impressed that our practice embraces technology.



Organised

On a personal note, I love not needing to riffle through reams of handwriting; or search for blood results; or try to piece together an incomplete or confusing referral history.

Portable

Nothing gets lost, information is simple to access and my database is portable – as user friendly in the consulting room as it is in theatre or at home.

Impressive

I particularly enjoy being prepared for patients who have given me pre-consent to access their history. This is efficient and professional, and sets the tone for an effective consultation.

Certainty

No longer do I need to guess what the little round white tablet was that Mrs Henderson took last week for what she thinks may have been her blood pressure! Nor do I need to listen to a loud tuneless recording while holding for blood results from February's admission for cholecystitis.

Informative

Instead, while I wait for her to find her shoes and make her way back to my desk, I can quickly confirm her current cholesterol reading, learn of the aspirin that has been added to her script and begin writing a referral note to the pulmonologist for the musical wheezing that persists in her chest, despite my best efforts.



Dr Gregory Green is a general practitioner in Johannesburg. He has a special interest in asthma. Dr Green has been using HealthID since June 2012. He holds the following qualifications:

- BSc (Wits)(1997)
- MB BCH (Wits)(2001)
- DMH (SA)(2003)

Modern

I think that in future, if we look back, we may just concede that healthID was a tool we didn't yet know we needed. Maybe even one we couldn't do without - in the same way that my one-year old will never know how we lived without Facebook, the internet or mobile phones!

Seamless

Prospective and future healthcare providers may never know a consultation without seamless access to a digital reflection of the patient in front of them. For me, continuity and integrated health care are necessary ingredients for improvement in patient outcomes.

Professional

On a practice level, innovative technology like this allows both my patients and I to enjoy a more professional consultation experience.



the future of your patients' medical history.



Introducing **HealthID**. The technology that puts your patients' health records in your hands. Once they have given consent, you will have access to their medical history, insight into the benefits of their medical aid plan, and be able to make referrals to other healthcare professionals. You can also study their blood test results, write electronic prescriptions and complete Chronic Illness Benefit applications, all with the touch of your finger. It's what healthcare will look like in the future, today.

To learn more about how this innovation can benefit you, go to www.discovery.co.za/healthID or use your smartphone to scan the QR code.



HPCSA Axes 1500 Medical and Dental Practitioners from its Register

The Health Professions Council of South Africa (HPCSA) has been tightening its control of the health professions since legislation was amended in 2007 requiring it to fall in line with the National Health Policy as determined by the Minister of Health.

In its latest clampdown some 1500 medical and dental practitioners will no longer be allowed to practice their professions after they were suspended from the HPCSA register for failure to pay their fees.



In total almost 10,000 healthcare practitioners were suspended for a variety of reasons, including over 6500 emergency care practitioners who failed to comply with the regulations governing the professions. Almost 600 psycholo-

gists were also struck from the register.

According to the Health Professions Act, it is a criminal offence to practice when suspended or erased from the register.

The action against medical practitioners comes after the deadline for payment of annual fees was disregarded despite the council having exhausted all avenues in contacting these practitioners, including letters, telephone calls, SMSs and notification via professional associations.

Antibiotics Cut Deaths Among Severely Malnourished Kids – Malawi Study

Antibiotics added to nutritional therapy helped aid recovery and prevent deaths among severely malnourished children, findings that suggest routine use of the drugs should be considered in kids who suffer from acute hunger.

Children with severe malnutrition who were given amoxicillin had a 25% greater recovery rate and a 35% lower death rate than those who took a placebo, according to the study published in the *New England Journal of Medicine*. Those given the antibiotic cefdinir (Omnicef, Abbott), had a 40% better recovery rate and 45% reduced death rate. Omnicef is not yet registered in SA.

“Childhood malnutrition remains the biggest, and unfortunately, most under-recognised, health problem in the world,” said study author Indi Trehan, a clinical fellow in the Department of Pediatrics at Washington University, St. Louis and a visiting lecturer at the University of Malawi. “No matter what advances we make in HIV or malaria or diarrhea, malnourished children will always be at the highest risk of death from these diseases. In terms of bang-for-buck, this is where we need to focus.”

Amoxicillin cost about R26 per child in the study, while the cefdinir was R70. That expense can be lower if used on a



large scale, the authors said. That compares with R450 per child for traditional nutritional therapy.

The study included 2767 Malawi children ages 6 months to 4 years who had severe acute malnutrition. They were given amoxicillin, cefdinir or placebo for seven days in addition to nutritional therapy, which is a ready-to-use paste that doesn't need to be mixed with water.

Worthwhile investment

Trehan said “The dramatic decrease in the mortality rates seen in this study has convinced us that this investment will be worthwhile for the benefit it provides to child survival worldwide.”

Trehan said it's unclear how the antibiotics work to benefit these children. It could be that their immune systems were so compromised by the malnutrition that they were unable to clear any simple infections on their own. By providing the antibiotics early on, they may have been protected from typical childhood infections that came along during the study.

Another possibility, he said, was maybe the children already had an infection that “tipped them over the edge” into severe malnutrition and the antibiotics treated that condition.

Trehan said in other studies it's been shown that the intestinal barriers of children who are malnourished are weak and porous so intestinal bacteria may be able move into the blood. It's possible that the antibiotics might be helpful in limiting the amount of infection and inflammation in the gut, helping them maximise absorption of the nutritional therapy.

Corruption Watch, TAC Want to See Gauteng Health Probe Info

Corruption Watch (CW) and the Treatment Action Campaign (TAC) are to go to court to challenge the Special Investigating Unit's (SIU) refusal to provide access to any information gathered during its investigation into mismanagement and corruption in the Gauteng health department between 2006 and 2010. The SIU embarked on an investigation into the department following a proclamation by the then-president Kgalema Motlanthe, in 2010.

"Gauteng's health department faces an ongoing financial crisis and the mismanagement of resources meant to realise the right of access to public health

care is a matter of grave concern," says TAC Gauteng chairperson Sibongile Tshabalala. "It causes loss of life on a daily basis, and the refusal of the SIU to provide any information about their three-year investigation is unacceptable and unlawful."

Mismanagement rife

"The Gauteng public health sector has, over a lengthy period, experienced widely acknowledged corruption and mismanagement of public funds. These - a major cause of appalling levels of service delivery - are precisely what the SIU is required to investigate."

CW and TAC requested access to information pertaining to the SIU's lengthy probe in the public interest and in accordance with the Promotion of Access to Information Act (PAIA). The PAIA is intended to promote the right to access information in order to foster a culture of transparency and accountability. The SIU responded to the requests with a blanket refusal.

"We are extremely concerned at the approach of the public authorities to access to information" says David Lewis, executive director of CW. "The default position enshrined in our law is that the public should have access to information."

South African Innovation Acknowledged at Davos

South Africa played a meaningful part at the recent Davos, Switzerland meeting of the World Economic Forum.

One of the groups making up the global talkshop, the Workplace Wellness Alliance, released a report on the latest thinking on workplace wellness and metrics. The report is based on research and data from over two million employees from 25 companies across 125 countries. As one of the Leadership Members of the Alliance, Discovery is recognised in the report for its programme to incentivise healthy behaviours and outcomes and its global collaboration with international partners in China, the UK and the US.

Discovery CEO Adrian Gore facilitated a session on wellness in the workplace that included CEOs of major companies, health ministries, and representatives of the World Health Organization (WHO) and NGOs. The session aimed to connect workplace wellness to the broader discussion of human capital and competitiveness. Gore said: "Global health demands better prevention models. This is critical if we are to address the rapid rise in healthcare costs while at the same time maintain and increase health gains."

Big savings possible

Workplace wellness programmes are increasingly recognised as a means of



Adrian Gore

reducing the impact of chronic diseases of lifestyle on individuals and organisations. Research reported in The Lancet last month indicates that a few risk factors - tobacco use, an unhealthy diet, lack of physical activity, mental ill health and poor adherence to treatment - account for the majority of preventable chronic diseases. Recently published research by Vitality's team showed that if physical inactivity, low fruit and vegetable intake, smoking, obesity, hypertension, hypercholesterolemia and alcohol abuse, were lowered to their theoreti-

cal minimum, the average annual costs per working adult would be reduced by 18.4%.

The benefit of workplace wellness programs has been shown to extend beyond risk factor reduction. Well designed programs also positively impact productivity, competitiveness and economic growth. This is relevant when one takes into account the staggering cost of healthcare for economies. In 2010, Americans spent \$2.5 trillion on healthcare, equating to 19% of gross domestic product (GDP). In SA and the UK, 8% to 9% of GDP is spent on healthcare. An ageing population with higher health risks and associated higher healthcare costs is already placing pressure on economies around the world. Discovery believes that a stronger focus on prevention and health is one way of stemming the tide of chronic diseases and high healthcare costs.

"Workplace wellness programmes offer a long-term solution for organisations. Some organisations and programmes have made significant and measurable progress in improving the health of their workforce and their financial bottom line. What is critical now is collaboration and the sharing of knowledge. This requires a concerted effort and coordination by employers, governments and healthcare professionals," Gore said.



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:

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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
FEBRUARY 2013**

Please return by May 31, 2013

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

LIPID UPDATE

1	<input type="radio"/> T	<input type="radio"/> F
2	<input type="radio"/> T	<input type="radio"/> F
3	<input type="radio"/> T	<input type="radio"/> F
4	<input type="radio"/> T	<input type="radio"/> F
5	<input type="radio"/> T	<input type="radio"/> F

ECG OF THE MONTH

1	<input type="radio"/> T	<input type="radio"/> F
2	<input type="radio"/> T	<input type="radio"/> F
3	<input type="radio"/> T	<input type="radio"/> F
4	<input type="radio"/> T	<input type="radio"/> F
5	<input type="radio"/> T	<input type="radio"/> F

LUNG CANCER

1	<input type="radio"/> T	<input type="radio"/> F
2	<input type="radio"/> T	<input type="radio"/> F
3	<input type="radio"/> T	<input type="radio"/> F
4	<input type="radio"/> T	<input type="radio"/> F
5	<input type="radio"/> T	<input type="radio"/> F

STROKE & THE ELDERLY

1	<input type="radio"/> T	<input type="radio"/> F
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3	<input type="radio"/> T	<input type="radio"/> F
4	<input type="radio"/> T	<input type="radio"/> F
5	<input type="radio"/> T	<input type="radio"/> F

TYPE 2 DIABETES

1	<input type="radio"/> T	<input type="radio"/> F
2	<input type="radio"/> T	<input type="radio"/> F
3	<input type="radio"/> T	<input type="radio"/> F
4	<input type="radio"/> T	<input type="radio"/> F
5	<input type="radio"/> T	<input type="radio"/> 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: _____

ETHICS AND THE ELDERLY

1	<input type="radio"/> T	<input type="radio"/> F
2	<input type="radio"/> T	<input type="radio"/> F
3	<input type="radio"/> T	<input type="radio"/> F
4	<input type="radio"/> T	<input type="radio"/> F
5	<input type="radio"/> T	<input type="radio"/> F



CUT ALONG DOTTED LINE

QUESTIONS FOR CPD ARTICLES: FEBRUARY 2013

CPD: 5 Regular points; 2 Ethics points

The first entry received
that scores full-marks
will receive a hamper
of goods sponsored by
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Instructions

1. The answer form is bound into this journal on page 46.
2. Read the instructions on the answer form and answer the questions carefully.
3. Your answers for the February 2013 issue must reach Modern Medicine, PO Box 84622, Greenside 2034 by May 31, 2013.
4. You must score at least 60% in a section to be awarded the assigned CPD point for it.

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

LIPID UPDATE (Pg 16)

1. The most common lipid disorder is mild mixed hyperlipidemia.
2. In HC, regression of arcus senilis is useful for monitoring clinical response to treatment.
3. Lipaemia retinalis is a feature of severe hypertriglyceridaemia.
4. The target level for treated patients with HC is an LDL-C level of 5 mmol/L.
5. The validated treatment of statin-induced myalgia is Cox-2 inhibitors.

ECG OF THE MONTH (Pg 24)

1. In view of the rhythm abnormality, he should be started on amiodarone.
2. At this age, the risk of bleeding is too great to consider warfarin anticoagulation.
3. Adding a beta blocker to his treatment will help to control his heart rate.
4. His thyroid function should be checked, even though he has no signs of hyperthyroidism.
5. Better control of his blood pressure is likely to restore his normal rhythm.

LUNG CANCER (Pg 29)

1. The predominant histology in lung cancer is adenocarcinoma.
2. There is no role for the GP in the management of lung cancer.

3. Low-dose CT scan is a useful screening test for high-risk groups.
4. Mediastinal lymph node involvement means that this is a least Stage III disease.
5. The cure rate for Stage I non-small cell disease is about 25%.

STROKE & THE ELDERLY (Pg 33)

1. Most strokes have a haemorrhagic etiology.
2. Lacunar ischemic strokes should be treated with an antiplatelet agent.
3. Aspirin is contraindicated in transient ischaemic attacks.
4. Thrombolysis should be deferred for 12 hours following an acute ischemic stroke.
5. Carotid stenting is preferred to endarterectomy in the fit elderly patient.

TYPE 2 DIABETES (Pg 37)

1. Proliferative diabetic retinopathy commonly affects only one eye.
2. Diabetic retinopathy is usually associated with widespread microangiopathy in other organs.
3. Loss of peripheral vision is an important complication of panretinal laser therapy.
4. Hyperaesthesia is a common indicator of foot problems in the diabetic.
5. The GP is usually best placed to coordinate the management of the multisystem pathology in the type-2 diabetic.

ETHICS AND THE ELDERLY (Pg 12)

1. Surrogates should use "best interest standards" when consenting for elderly family members.
2. Surrogates are often wrong in their assessments.
3. The ethical allocation of scarce resources is best facilitated by applying pre-existing guidelines and protocols.
4. In the distribution of resources, reciprocity implies an allocational reward for previous altruistic behaviour.
5. Hospital administrators are usually very supportive of clinicians ethical decisions regarding the allocation of scarce resources.

See answer form opposite

2013 Medical Conference Planner

Your Reminder

2013	    	  
1 - 3 Mar	Paediatric Update 2013 WHERE: Conference Centre of University of Pretoria, Pretoria CONTACT: Erna Stadlander • 011-463-5085 • erna@soafrica.com	CPD, Expo, 10-50 Speakers www.paediatrician.co.za 
2 Mar	SASOP - Society of Psychiatrists - Northern Subgroup Symposium WHERE: CSIR, Pretoria CONTACT: Riana Lombard • 011-768-4355 • riana@londocor.co.za	CPD, Expo, 10-50 Speakers www.sasop.co.za 
2 - 6 Mar	SASA - Society of Anaesthesiologists Congress WHERE: Boardwalk Convention Centre, Port Elizabeth CONTACT: Eastern Sun Events • 031-368-2530 • sasa@easternsun.co.za	CPD, Expo, 10-50 Speakers www.sasacongress2013.co.za 
7 - 9 Mar	SAMS - Menopause Society Congress WHERE: Spier Estate, Stellenbosch CONTACT: Alison Shaw • 031-539-3605 • info@menopause.co.za	CPD, Expo, 10-50 Speakers www.samenopausesociety.co.za 
12 - 14 Mar	SAFHE/CEASA - Federation of Hospital Engineering/Clinical Engineering Association WHERE: Cape Town ICC, Cape Town CONTACT: SBS • 021-914-2888 • natalie@sbs.co.za	CPD, Expo, 10-50 Speakers www.sbs.co.za 
13 - 16 Mar	ASSA - 28th Association of Surgeons - Biennial Congress WHERE: East London ICC, East London CONTACT: Eastern Sun Events • 041-374-5654 • info@easternsun.co.za	CPD, Expo, 50-100 Speakers www.assacongress.co.za 
14 - 17 Mar	OSSA - 43rd National Congress of the Ophthalmological Society WHERE: Cape Town ICC, Cape Town CONTACT: Ryno Kriek • 051-436-7733 • ossacongress@telkomsa.net	CPD, Expo, 10-50 Speakers www.ossa2013.co.za 
14 - 17 Mar	NASA - Neurology Association WHERE: Protea Hotel, Stellenbosch CONTACT: Sonja du Plessis • 011-768-4355 • sonja@londocor.co.za	CPD, Expo, 10-50 Speakers www.mynasa.co.za 
15 - 17 Mar	RSSA/NASCI - Radiological Society/North American Society of Cardiac Imaging CT Angiography - Cape WHERE: Radisson Blue Hotel, V&A Waterfront, Cape Town CONTACT: Consultus • 021-938-9238 • sunevr@sun.ac.za	CPD, 10-50 Speakers www.rssa.co.za 
16 - 18 Mar	ISAPS - International Society of Aesthetic Plastic Surgery WHERE: The Lord Charles Hotel, Somerset West CONTACT: Hendrika van der Merwe • 021-919-4227 • eliteconfer@iafrica.com	CPD, Expo, 10-50 Speakers www.isaps.co.za 
17 - 18 Mar	Professional Beauty Cape Town WHERE: Cape Town ICC, Cape Town CONTACT: Professional Beauty • 011-781-5970 • belinda@probeauty.co.za	CPD, Expo, 10-50 Speakers www.probeauty.co.za 
21 - 22 Mar	Here be Lungs WHERE: Lanzerac, Stellenbosch CONTACT: Mari Horn • 021-938-9082 • mari5@sun.ac.za	CPD, Expo, 10-50 Speakers www.herebelungs.co.za 
21 - 24 Mar	Bushpath - Symposium on Gastrointestinal, Soft Tissue, Bone and Gynaecological Pathology Congress WHERE: Legend Golf & Safari Resort, Waterberg Region, Limpopo Province CONTACT: Karin Kardoos or Yvonne Fernandes • 011-768-4355 • karin@londocor.co.za / yvonne@londocor.co.za	CPD, Expo, 10-50 Speakers www.bushpath.co.za 
22 - 24 Mar	RSSA/NASCI - Radiological Society/North American Society of Cardiac Imaging CT Angiography - Jhb WHERE: Sandton Sun, Johannesburg CONTACT: Sune van Rooyen • 021-938-9238 • sunevr@sun.ac.za	CPD, Expo, 10-50 Speakers www.rssa.co.za 
25 - 27 Mar	TB Vaccines 3rd Global Forum WHERE: Kramer Building, UCT, Cape Town CONTACT: Deidre Raubenheimer • 021-406-6167 • deidre.raubenheimer@uct.ac.za	CPD, Expo, 10-50 Speakers www.tbvaccines2013.org 

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*Including VAT

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.

S4 Adco-Atorvastatin 10, 20, 40 mg. A7.5. Each tablet contains 10, 20, 40 mg atorvastatin respectively.
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