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Femtosecond Laser Aids Cataract Surgery Precision

The LenSx Laser, by Alcon Surgical, is the first femtosecond laser cleared for use in cataract surgery, bringing image-guided, computer-assisted precision to refraction cataract surgeons and automating some of the most challenging manual steps of cataract surgery.

The fully integrated, image-guided laser uses a three dimensional surgical platform that allows the surgeon to visualise, customise and perform anterior capsulotomy, lens fragmentation and all corneal incisions with great precision. The laser has many high tech features:

- Real-time video with integrated optical coherence tomography (OCT) provides three dimensional visualisation of the entire anterior segment during docking, planning and the procedure. A disposable, single-use curved patient interface is used to dock with the patient’s eye.
- Curved patient interface is designed for patient comfort, ease of use and optimal laser performance.
- Intuitive touch screen graphic user-interface allows each step of the process to be planned, customised and executed easily.
- True image-guided surgical planning enables the surgeon to programme precisely the size, shape and location of each incision.

The unique shape of the patient interface helps to maintain a more natural curvature of the patient’s cornea, improving surgical accuracy during the procedure. A display panel allows pinpoint decisions to be made on the size, shape and duration of each cut.

The surgical panel combines a video microscope with an OCT and can visualise multiple views, including side views of the capsule bag and cornea and a topographical view of the lens.

Studies have found that surgeons using the laser have made smaller, more precise incisions with improved capsulotomies that allow for a more secure intraocular lens placement.
Hand-held Optical Scan for Melanoma

Researchers at Polartechnics and The Sydney Melanoma Unit (SMU) of the Royal Prince Albert Hospital, Australia, have created the SolarScan Sentry system to overcome clinician-inexperience with melanomas.

Melanoma is the most deadly form of skin cancer and the most treatable, but because many benign or even natural skin spots or blemishes superficially resemble melanomas and most general practitioners see only a handful of melanoma cases in their careers, false-positives can arise.

The Australian system combines a dermascope with a machine-vision system to run software that very accurately differentiates benign spots from early-stage melanoma.

The scanner unit has a dermascope optical system that focuses light, piped from an LED via optic fibre to form a ring source, onto a three CCD colour mini-camera with LVD output built into the camera head. A glass plate closes the unit’s front end and serves as the dermascope’s glass plate. Scan image frames are captured by a PROPCI frame grabber in a desktop pc and forwarded to the image-analysis software.

The scanner uses four colour swatches as calibration targets at the field-of-view corners to provide an accurate colour reference for the image-processing unit. These swatches are later masked out of the image, as are hairs and air bubbles trapped between the skin and glass.

A significant variable in subsequent statistical analysis is colour, with melanomas having a larger scatter over the RGB colour space than benign lesions. Developers have found both absolute and relative colours to be useful diagnostically. A hundred characteristic features can, if taken together, distinguish melanomas from benign lesions with a false-negative rate below eight percent and a false-positive rate under 38%.

SPECT-CT Fusion Imaging Reveals Tiniest Bone Fractures

Single Photon Emission Computed Tomography (SPECT), typically used for imaging soft tissue, is now being combined with low dose CT to create fusion images that reveal otherwise invisible bone fractures – and the benefits are not limited to detecting stress fractures.

Hybrid SPECT-CT combines, in one imaging session, the functional imaging capabilities of SPECT with the precise anatomical overlay of CT images to create precise image fusion, for anatomical referencing and accurate patient-specific attenuation correction, improving localisation and definition of organs and lesions, diagnoses and patient management.

Correcting for patient attenuation requires an accurate measurement of the spatial distribution of attenuation coefficients within the patient. The Hounsfield units from CT data help to provide improved statistical information and greater confidence in detecting abnormalities within deeper organs.

Hybrid systems align the two sets of image data precisely and eliminate inaccuracies caused by variations in patient position, couch surfaces and the internal changes in the patient from one imaging session to the next.

Clinical applications that benefit from using hybrid systems include myocardial perfusion, skeletal, neuroendocrine, adrenal, lymphomas and infections, sentinel node mapping and parathyroid adenomas. In Oncology, the SPECT/CT can localise tumour sites, assess invasion into surrounding tissues and demonstrate their functional status. Quality CT images allow radiologists to compare structural detail with isotope activity, potentially giving a differential diagnosis with no further imaging.

Fusion imaging combines morphological studies with functional ones, overcoming the drawbacks of both modalities and emphasising their individual strengths.
Under-mattress Monitoring Improves Hospital Patient Care

The EarlySense System is an innovative, continuous patient monitoring solution that monitors patients’ heart rate, respiratory rate and movement without having to touch the patient. The contact free sensing capability and immediate data transfer enables medical staff proactively to provide personalised patient care while reducing potentially adverse events, such as patient falls, pressure ulcers and infection. The system provides information for timely intervention to reduce escalations to a higher level of care, so shortening hospital stays.

A plate with an integrated piezo-electric sensor, placed under the mattress, uses ground-breaking signal processing techniques - developed on a database of more than a million patient-monitoring hours – in an embedded algorithmic engine that converts patients’ cardio ballistic effect, respiratory motion pattern and large body movements into vital signs. Oximetry integration monitors oxygen saturation of the patient.

Accurate results are transmitted to, and displayed automatically at, the bedside, the nurses’ station and on additional displays in central areas. Data are also sent simultaneously to handheld devices to enable intervention by caregivers.

As preventable adverse events often occur if protocols are not fully implemented, the system provides a toolset to enhance nursing management efficiency and ensure consistent quality of care. Managers can receive reports automatically, via email or on demand, of pressure ulcer prevention protocol compliance, fall prevention activity and vital sign vigilance. Reports are created automatically to obviate additional chores or changes to workflow.

MRI Guided Ultrasound Approved to Treat Bone Metastases

The FDA has approved ExAblate, from Israeli company Insightec Inc, for treatment, with MRI guided focused ultrasound, of bone metastases in patients who are not candidates for or refuse to undergo radiation treatment. ExAblate received FDA approval in 2004 for its non-invasive outpatient therapy for uterine fibroids.

The system, compatible with GE Healthcare’s normal and wide bore systems, combines acoustic ultrasound waves with continuous guidance and treatment monitored by MRI in a combination of technologies called Magnetic Resonance guided Focused Ultrasound therapy (MRgFUS). The focused ultrasound acoustic energy destroys the nerves causing the pain from bone metastases, bringing rapid pain relief.

With MRgFUS, the focused ultrasound beam can be seen during the treatment to ensure it travels a safe pathway to the focus and is targeted accurately. Sonification parameters can be adjusted to optimise the treatment. Temperature maps display the relative tissue temperature in colour, superimposed on the anatomical MR image, to allow the doctor to monitor temperature changes continuously through the treatment. Based on the observed temperature changes, treatment parameters can be adjusted to ensure safe and effective thermal ablation. The system tracks regions that have reached thermal dose, enabling the doctor to determine if heating has been sufficient.

No incisions are required and there is no ionising radiation. Patients can have multiple treatments. For applications in which patients are able to undergo the ablation with conscious sedation (such as bone, breast, and fibroids), recovery time is generally less than an hour after the procedure.
New Alternative for Airway Clearance

The CoughAssist T70, Philips Respironics’ latest airway clearance technology for enhanced patient care in hospitals or at home, provides an effective, comfortable alternative to traditional suctioning methods and may minimise the risk of pneumonia and infections that can lead to hospital readmissions.

The device clears secretions from the lungs by gradually applying positive air pressure to the airway and then rapidly shifting to negative pressure, creating a high expiratory flow that simulates a deep, natural cough. Air is delivered - rather than through a suction catheter in the airway - through a facemask, mouthpiece or simple adapter that allows the device to function with an endotracheal or tracheostomy tube, reducing discomfort and risk of infection.

A Cough-Track feature with automatic sensitivity allows patients to initiate therapy and synchronise treatment with their own breathing patterns.

The device is compact and easy to transport, has AC and DC power options and a detachable lithium ion battery that allows up to four treatments on a single charge. The user-friendly digital interface and preset prescriptions simplify setup and initiation of therapy. New data management software can monitor tidal volume, peak cough flow and oxygen saturation levels.

App Ends Delays in Clinical Assessment and Patient Treatment

A new application from Airstrip Technologies, Airstrip Patient Monitoring, securely sends patient information directly from hospital monitoring systems, bedside devices and electronic health records to a doctor’s mobile device.

Doctors gain access to critical patient data or regular bedside monitoring data without being physically present, through an application powered over wireless networks, delivering virtual real-time and historic interactive waveform and relevant clinical data.

The app is a native solution on the iPhone, iPod Touch and iPad. The iPad version offers such functionality as dynamic and interactive patient monitoring surveillance screens that allow a user to follow the real-time waveforms of several patients at once.

The AppPoint software development platform is reusable, scalable and independent of information systems, and allows the entire hospital enterprise to use the app via integration with existing patient monitoring and clinical information systems.

With this technology, clinicians can immediately communicate by their mobile devices and collaborate to develop a more timely treatment plan, improving clinical outcomes. Disagreements can be escalated up the chain of command immediately, regardless of the location of the providers involved.

The service has a web server, mobile device and a measuring interface connected to existing hospital monitoring devices, that read and then send patient data such as blood pressure, heart rate and temperature securely over the internet to the web server. Doctors have access to the web server through the app on their mobile devices and can view data trends and receive alerts if something goes wrong, saving time by having to launch only a single app.
ENTREPRENEURSHIP FOR HEALTH PROFESSIONALS’ PRACTICE (EHP²)

EHP² facilitates the development of entrepreneurial competencies of health practitioners to successfully start up, manage and grow their practices to establish professional businesses that deliver quality health services to clients.

About the programme:
The EHP² is a pioneering initiative between the Centre for Entrepreneurship at Wits Business School and Wits Faculty of Health Sciences, aimed at equipping health professionals, administrators and managers in health practices, with perspectives, knowledge and skills to effectively and efficiently start up, manage, grow and professionalise their practices/businesses.

Programme Output: Certificate of Competence (NQF level 8)
CPD Points

Programme objectives:
The course is designed to develop multiple competencies of health practitioners to:
• To nurture an entrepreneurial paradigm among health practitioners;
• Increase efficiency and effectiveness of systems, administration and management of a practice and people;
• Professionalisation of the practice.

Who should attend:
• Health professionals and practitioners;
• Health administrators and managers;
• Health accountants;
• Health PR and marketing personnel.

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One of the articles reviewed for CPD this month revolves around the risks of ionising radiation as a potential cause for both premature cancer and genetic damage in our patients.

The article is written from the perspective of a Sports Physician and largely reflects the risks to a fit young adult with an injury or recurrent injuries. The author stresses the need use two important principles when considering ordering an x-ray:
• Justify the need for the investigation and
• Optimise the (minimal) dose of irradiation.

The first principle is mostly the responsibility of the clinician and the second requires input from the radiologist and radiographer.

As a paediatrician, I am even more concerned about radiation. Obviously the young child (or fetus) has a potentially longer life to accumulate radiation and the rapidly growing child is more sensitive to DNA damage. What are not mentioned in this article are the individual sensitivities in certain patients. We are aware that certain gene mutations predispose to certain cancers (such as BRCA genes and breast cancer) but less well-known are the inherited susceptibilities to damage from ionising radiation. There are some unusual or rare genetic syndromes known to be associated with increased sensitivity to ionising radiation but there is also good evidence to suggest that genetic sensitivity to radiation may be far more common.

About 30% of individuals may show increased chromatid breaks in response to a radiation challenge but whether this equates to a risk for developing cancer is not yet certain. If we could identify the individuals at risk, then this might influence our clinical practice. New genetic screening techniques like GWA (genome-wide associations) may help identify the at risk groups. This type of screening is, however, expensive and opens up an ethical “can of worms”.

Global concern over diabetes

Also of interest in this month’s edition, is an article dispelling some of the diabetic myths that are “out there”. Of real concern is the increase in all types of diabetes, especially in children. A lot of attention has been given to the emergence of type 2 diabetes; mostly paralleling the obesity and sedentary lifestyle that pervades our era. The American Academy of Pediatrics has recently seen fit to publish guidelines for the management of type 2 diabetes as many primary care doctors will be unfamiliar with treating children and adolescents. The bottom lines of the recommendations are: when in doubt and if there is ketoacidosis, then give insulin. If you are sure that the child has type 2, then introduce lifestyle modifications and metformin is the drug of choice.

From the other side of the pond, the EURODIAB study group have been monitoring a striking increase in type 1 diabetes in children. There is much speculation regarding the cause for this increase. A number of environmental triggers have been suggested, including caesarean delivery, higher birth weights, early obesity, viral infections, cow’s milk proteins, the hygiene hypothesis, vitamin D deficiency; you name it!

How these factors, alone or in concert, act to produce autoimmunity is a matter of speculation. Time will tell as a number of large prospective studies are underway.

Speaking of the environment, winter is nearly upon us. Let us conserve energy and hope that ESKOM can cope.

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4. South African Registered Package Insert for Picosulfate dated 02/06/2012.

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Navigating Conflicts of Interest: Waltzing With a Porcupine

In a medical context, a conflict of interest (COI) is a set of circumstances that creates a risk that a health professional’s judgement or responsibility may be deflected from his primary concern (usually the patient) to a secondary party (usually him/herself). It is the ‘set of circumstances’ that define a COI, and these exist whether or not improper actions ensue. To use a religious analogy, a COI is the temptation and not the sin.

Hipocrates
The original Hippocratic oath was not very forceful in recognizing that the patient’s interests may be in conflict with the physician’s interests although the modern oath taken by local medical graduates does go some way towards this recognition; “That I will exercise my profession to the best of my knowledge and ability for the safety and welfare of all persons entrusted to my care and for the health and well-being of the community”.

A wide spectrum
Most COIs hinge around financial gain but they may involve other rewards and motivations such as fame, job promotion, religious beliefs or even personal relationships. COIs may be overt where the doctor is well aware that his action is, or could be unethical, but all-too-often the conflict is covert or subliminal. Most doctors would deny the possibility that the gift of a ballpoint pen or a donated pizza over journal club could influence their prescribing patterns but there is a body of research to the contrary.

Protect the patient
COIs are a normal feature of our human interactions but there are some good reasons why the relationship between a patient and a doctor should engender special consideration and protection:

- Firstly, the patient is usually vulnerable. This vulnerability may arise from a variety factors such as medical ignorance, fear or the patient’s state induced by the illness per se.
- Secondly, we doctors have been substantially empowered by society. This has allowed doctors to invade the patient’s homes, their minds and their bodies.

The balance between the patient and doctor is horribly skewed if compared to, say, the relationship between a prospective home owner and an estate agent.

Pharma’s persuasive power
The biggest potential source of COIs arise from the doctor’s relationship with the pharmaceutical industry; but this is by no means the only source of contention. In the not too distant past, local scandals arose from kickbacks by radiologists for MRIs ordered, and there are numerous examples involving perverse, favoured conditions available to specialists in private hospitals, improper relations with retail pharmacists, special arrangements with funders... The list goes on and on.

I have been wading my way through Bad Pharma by Ben Goldacre and after you have read this tome you will surely be convinced that there isn’t a drug that really works and that there are no honest doctors left on the planet. It makes depressing reading. Perhaps it is over-stated but it’s a fact that the pharmaceutical industry is big business and they have a mandate to maximise profits for the benefit of their shareholders. They spend billions annually on marketing and a substantial part of this is spent on in-person detailing by sales representatives. Many would blame the pharmaceutical industry for the dishonest practices of doctors but this is a bit like blaming provocative clothing for rape!

Clinical practice guidelines - a new front
One of the areas where COIs have recently been brought to the attention of physicians is in the development of clinical practice guidelines (CPGs). We practice in an era where the gold standard of treatment is evidence-based medicine. No longer are we prepared to accept the recommendation of an expert in the field (eminence-based medicine) but we now are expected to understand a whole new jargon. We try to combine multiple sources of data into Cochrane-like systematic reviews and then

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analyse this data using meta-analysis. Forest plots and Funnel plots are displayed with gay abandon. On the surface, this would appear to offer a better chance of getting closer to the truth but we should be aware that there may be hidden bias in the choice of data to be included in the review. Some authors of meta-analyses rarely report their funding sources and their ties to industry.

The next step after sophisticated interpretation of the data is the formation of clinical practice guidelines. These CPGs have the fundamental task of converting data into recommendations and thus have the potential to shape clinical practice worldwide. This may have great advantages to doctors and their patients, but obviously the process has huge economic relevance to drug manufacturers. This is reflected in the fact that in some instances 90% of the authors of a CPG have industry affiliations.

A CPG author with industry connections may have a pro-industry bias; an author who has expertise in performing a procedure may be biased towards procedures while the recipient of research grants may be biased towards academic career advancement. Some authors have used a formal tool to evaluate COIs in CPGs. The domains in which they identified conflicts included: Research, Clinical practice, Personal income, Equity/stock options, Expert testimony, Fiduciary role, Advocacy role, and Patient rights. Other authors have reviewed the management strategies employed when COIs were identified in CPG panel members. The best method of handling this appears to involve utilising an independent monitoring body who then either exclude or limit input from panel members with COIs.

Learning to dance

Finally, how should the practising clinician deal with the COIs in the workplace? The doctor's relationship with the pharmaceutical industry has been aptly described as 'dancing with a porcupine'.

First and foremost is the recognition that a COI exists and is pervasive. All the evidence points to the fact that even apparently trivial gifts may have profound influences on behaviour. This is best countered by avoidance of compromising situations; no more pens & Benz. Where a physician is in a position of potential influence over his colleagues, it is important to publicly declare his/her conflicts of interest. This allows the audience to evaluate the message in this light. We should also be vigilant as there are perverse influences around every corner. Our patients trust us to use resources intelligently and to always act in their best interests. Our financial gains are secondary.

Recommendations

Greenberg7 has recommended that clinicians should adopt the following principles to avoid or manage COIs:

• Disclose all relevant COIs to their patients.
• Do not accept anything of material value from 'the industry' except for legitimate work compensated at market value.
• Only act as consultants when performing defined professional services within a written contract.
• When giving presentations, the content should not be created or controlled by industry.
• Drug samples are only acceptable for use by indigent patients.
• Doctors should not accept gifts from industry sources.
• Follow ethical precepts, in the patient's best interest, when choosing treatments.
• Avoid selling healthcare products for profit in their offices.
• Recognise that the behaviour of doctors' staff should fall within the same ethical boundaries.

With regard to the development of CPGs, he also concludes that "the sponsoring organization should not accept direct funding from industry for developing, promoting or publishing guidelines."

These principles were developed for dermatologists but they seem appropriate for all of us in clinical practice.

Potential conflict of interests

Prof Bolton is in full-time academic employment. He is involved in contract research with Nestlé. He has no conflicts of interest recognised in this regard.

References:
3. Roseman M, Milette K, Bero L et al. Reporting of conflicts of interest in meta-analysis of trials of pharmacological treatments. JAMA 2011;305(10): 1008-17
Atrial fibrillation (AF) is the most common cardiac arrhythmia in humans. Its incidence increases with age from 0.1% in patients younger than 55 years of age to 9.0% in patients aged over 80 years. The lifetime risk of developing AF is one in four and its incidence doubles with each decade of life over the age of 55, independent of known predisposing conditions. With ageing population, the prevalence of AF is expected to reach epidemic proportions. AF causes significant impairment in quality of life, primarily from symptoms such as palpitations, fatigue, breathlessness or chest discomfort, often resulting in curtailment of employment, or social or recreational activities.

Furthermore, AF is associated with a four to fivefold increase in the risk of stroke, a tripling of the risk of heart failure and an increased risk of mortality. About 15% of strokes are attributed to AF and these tend to be associated with higher morbidity and mortality, greater disability, longer hospital stays and lower rates of discharge of patients to their own homes.

Three different types of AF are recognised: paroxysmal, persistent and permanent forms (Table 1). Persistent and permanent forms of AF are invariably associated with underlying structural heart disease. When paroxysmal occurs in the absence of structural heart disease or clinical risk factors for AF it is termed ‘lone AF’. In general, management decisions in patients with AF are based on the nature and severity of symptoms and on thromboembolic risk, rather than arrhythmia classification.

The GP frequently encounters patients suffering from AF either as part of long-term management with other comorbidities, as a new diagnosis in the investigation of breathlessness and palpitations, or as an incidental finding.

Significant advances in the pharmacological and percutaneous intervention-al treatment of patients with AF have occurred over the past decade. Being aware of these advances enables doctors to better answer the question ‘what do I do for my patient with AF today?’

**Diagnosis of AF**

The clinical diagnosis of AF is suspected by the presence of a classic irregularly irregular pulse and is confirmed with an ECG. It is important to be aware that for short periods of time the rhythm during AF can be relatively regular and thus mimic sinus rhythm at the pulse. This may particularly occur when AF is either very rapid or slow. Conversely, the presence of multiple ventricular or atrial ectopic beats can mimic AF. Therefore, ECG confirmation is essential. This demonstrates the presence of rapid oscillations or fibrillatory waves (best seen in leads V1 or II on the ECG) that vary in amplitude, shape and timing, accompanied by an irregular and often rapid ventricular response (Figure 1). When
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- Vitamin K antagonists such as warfarin have been trusted in the prevention and treatment of recurrent VTE* and thromboembolism post atrial fibrillation for ~70 years1,2,3,4,5

- Warfarin reduces thromboembolic risk in atrial fibrillation by 50 %2

- Long-term preventative therapy with warfarin reduces the risk of thromboembolism by 90 % in patients with VTE3

*VTE = venous thromboembolism;

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AF is intermittent, ECG confirmation of diagnosis can be more difficult. For patients with frequent symptoms (episodic palpitations), AF can be detected by 24-hour Holter monitoring or longer periods of monitoring (usually by seven-day event recorder or seven-day Holter monitor). In patients with infrequent episodes of AF, one strategy is to request that they present for an ECG at the time of symptoms. Alternatively, an implantable monitor (loop recorder) may be useful in occasional cases.

**Risk factors for AF**

AF is frequently associated with cardiovascular or non-cardiovascular risk factors. When these factors are absent, the diagnosis of 'lone AF' may be made (Table 2). The Atherosclerosis Risk in Communities (ARIC) study showed that about 57% of cases of new-onset AF could be attributed to common cardiovascular risk factors. When a patient presents with AF, a search for these risk factors is important as part of an overall management strategy. As part of this initial evaluation, in addition to the ECG, an echocardiogram and routine blood tests are mandatory.

**Anti-coagulation for AF**

The uncoordinated atrial activity during AF predisposes patients to thrombus formation, especially in the left atrial appendage. Issues relating to anticoagulation include: the assessment of thromboembolism risk, the potential benefit to be gained from anticoagulation, the risk of bleeding and patient preference for anticoagulation.

**Thromboembolism risk**

Patients with non-valvular AF have a five to eight times increased risk of stroke; however, the risk is not uniform and is influenced by the presence of certain risk factors. These risk factors have been combined to formulate stroke stratification schema.

Traditionally, the CHADS2 score (cardiac failure, hypertension, age over 75 and diabetes are assigned one point, and prior stroke or embolic event are assigned two points) has been used to categorise the risk of AF. Low-risk patients (score of 0) are recommended to take aspirin alone; those at intermediate risk (score of one) are recommended to take either aspirin or warfarin; and high-risk patients (score of two or more) are recommended to take warfarin (target INR 2 to 3). However, the CHADS2 score has been found to have only moderate predictive value for thromboembolic risk. Furthermore, about 65% of patients would be classified as being at intermediate risk, with uncertainty as to which agent to prescribe (aspirin or warfarin). With the use of CHADS2 scoring, low-risk patients still have an appreciable risk of stroke (1.67 per 100 person years).

Recently, the CHA2DS2VASc score (one point each for cardiac failure/left ventricular dysfunction and hypertension, two points for age 75 years or older, one point for diabetes, two points for stroke, and one point each for vascular disease, age 65 to 74 years and sex category [female]; Table 3) has been advocated as a better predictor of low risk than the CHADS2 score. Patients with a CHA2DS2VASc score of zero have a very low risk of events (0% in one study). Patients with a score of one or more require anticoagulation with warfarin (INR 2 to 3; Table 3). It is important to note that the CHA2DS2VASc score has as yet not been widely adopted in cardiology practice, with many still favouring the CHADS2 score.

**Bleeding risk**

Many clinical risk factors have been reported to be associated with an increased risk of bleeding but the recently reported HAS-BLED scoring system has been used as a simple risk assessment tool in major international guidelines. In this system, one point is given for uncontrolled hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, being elderly (over 65 years) and drugs or alcohol use. A score of three or more suggests a high risk of bleeding.
that requires caution when considering anticoagulation.

**Patient preference**

The risks and benefits of anticoagulation should be discussed thoroughly with patients, and their perceptions and expectations taken into account, along with factors such as patient compliance, cognitive function, alcohol intake, recreational drug use, pharmacological drug interactions, mobility, risk of falls and accessibility to monitoring services.

Frequent re-assessment of stroke risk is also important. The amount of time spent in the therapeutic range (INR 2 to 3) has a key influence on the level of protection against ischaemic stroke and risk of major haemorrhage. Good anticoagulation control (time in therapeutic range 70% or more) is associated with a low risk of stroke and bleeding events.8

**Anticoagulants**

**Warfarin**

Warfarin provides a 62% relative risk reduction for stroke and a 26% relative risk reduction for overall mortality compared with no anticoagulation.9 The benefit of aspirin is less, with a relative risk reduction of 22% compared with no anticoagulation.

A number of new anticoagulants have emerged, targeting the single coagulation enzymes thrombin (dabigatran) or factor Xa (apixaban and rivaroxaban), although apixaban has not yet been approved for AF treatment in South Africa. These drugs are given in fixed doses without coagulation monitoring.

**Dabigatran**

The major advantage of dabigatran etexilate (direct thrombin inhibitor) is that it does not require INR monitoring and does not have many of the food and drug interactions of warfarin.10 Dabigatran 150mg twice daily was found to be better than warfarin for stroke risk reduction with a similar risk of major bleeding, and dabigatran 110mg twice daily was found to be similar to warfarin for stroke risk reduction with significantly less major bleeding.11,12 For the prevention of stroke and systemic embolism in patients with non-valvular AF, the recommended daily dose of dabigatran is 300mg taken orally as a 150mg cap-

---

**TABLE 2**

**Common factors for atrial fibrillation and associated common diagnostic tests**

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Common diagnostic test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Measurement of resting and ambulatory blood pressure</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Measurement of fasting blood glucose level</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>Echocardiography</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Clinical examination, chest x-ray and measurement of B-type natriuretic peptide</td>
</tr>
<tr>
<td>Obesity</td>
<td>Body mass index</td>
</tr>
<tr>
<td>Sleep apnoea</td>
<td>Clinical history and sleep studies</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>Thyroid function tests</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>ECG and exercise stress test (stress echocardiography, nuclear scan, angiography)</td>
</tr>
<tr>
<td>Pulmonary disease (eg, smoking, chronic obstructive pulmonary disease, chronic thromboembolic pulmonary hypertension)</td>
<td>Chest x-ray and pulmonary function tests</td>
</tr>
<tr>
<td>Pericarditis</td>
<td>Pleuritic chest pain and concave up ST-elevation on ECG</td>
</tr>
</tbody>
</table>

**TABLE 3**

**CHA2DS2VASc scoring system and associated risk of thromboembolic stroke**

<table>
<thead>
<tr>
<th>Factor</th>
<th>CHA2DS2 VASc score</th>
<th>Stroke risk (% per year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure/ left ventricular dysfunction</td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>Age 65 to 74 years</td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>Age ≥ 75 years</td>
<td>2</td>
<td>2.2</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>Stroke/transient ischaemic attack/ thromboembolism</td>
<td>2</td>
<td>2.2</td>
</tr>
<tr>
<td>Vascular disease (previous myocardial infarction, aortic plaque, peripheral arterial disease)</td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>Female sex</td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>Maximum score</td>
<td>9</td>
<td>15.2</td>
</tr>
</tbody>
</table>

*CHA2DS2 VASc score 1=1.3% stroke risk per year; 2=2.2%; 3=3.2%; 4=4%; 5=6.7%; 6=9.8%; 7=9.6%; 8=6.7%; 9=15.2%
<table>
<thead>
<tr>
<th>Drug</th>
<th>Side effects</th>
<th>Contraindications</th>
<th>Caveats</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rhythm control drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flecaïnide</td>
<td>Ventricular pro-arrhythmia (or ventricular fibrillation) in patients with structural heart disease. Atrial pro-arrhythmia (eg,) atrial flutter with 1:1 conduction when used without concurrent atrioventricular nodal blocking</td>
<td>Absolutely contraindicated in patients with left ventricular dysfunction or coronary heart disease</td>
<td>Reasonable first choice for maintaining sinus rhythm in patients with paroxysmal and persistent atrial fibrillation, normal ventricular function and no structural heart disease. Should be used in combination with atrioventricular nodal blocking agent (eg, β-blocker or calcium channel blocker such as verapamil)</td>
</tr>
<tr>
<td>Sotalol</td>
<td>Bradycardia, depression of cardiac pump function, atrioventricular block, ventricular proaryrhythmia (torsades de pointes)</td>
<td>Relatively contraindicated if renal impairment present. Avoid in patients with heart failure. Use with caution in patients with underlying conduction abnormalities</td>
<td>May be used as first choice in patients with paroxysmal and persistent AF</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Thyrotoxicosis (three to six monthly thyroid function tests required), sleep disturbance, cutaneous photosensitivity and tremor. Pulmonary fibrosis and liver dysfunction are rare</td>
<td>Use with caution in patients with underlying conduction abnormalities</td>
<td>First-line agent in patients with atrial fibrillation and heart failure. Second or third-line agent for patients with paroxysmal and persistent atrial fibrillation not responding to or intolerant of other anti-arrhythmic drugs</td>
</tr>
<tr>
<td><strong>Rate control drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-blockers</td>
<td>Bradycardia, depression of cardiac pump function, heart block, exacerbation of heart failure and exacerbation of airways disease</td>
<td>Complete heart block or high degree atrioventricular block, asthma or reactive airways disease, decompensated heart failure</td>
<td>Useful for patients with atrial fibrillation associated with heightened sympathetic activity or ischaemia (eg onset of atrial fibrillation with stress or exercise)</td>
</tr>
<tr>
<td>Calcium channel antagonists (non-dihydropyridine)</td>
<td>Hypotension, heart block heart failure, constipation (with verapamil) and drug interactions</td>
<td>Complete heart block or high degree atrioventricular block, decompensated heart failure</td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td>Generally well tolerated when serum levels in therapeutic range. When digoxin levels are excessive may cause gastrointestinal upset, visual disturbance, heart block and ventricular arrhythmias</td>
<td></td>
<td>Not effective for rate control during activity. Can be used (with caution) in combination with either a β-blocker or calcium channel antagonist when single agent is ineffective. Use as a sole agent if the patient has a hypotensive response to other rate controlling drugs. Monitor digoxin levels and digoxin toxicity</td>
</tr>
</tbody>
</table>
The SA Lipid Guideline goal...
...can now be achieved with our affordable treatment

* “The **LDL cholesterol goal** in **very high risk patients** is now **1.8 mmol/L** and in **high risk patients** is **2.5 mmol/L**”

Professor Derrick Raal

Adco-Atorvastatin 10 mg X 30
Adco-Atorvastatin 20 mg X 30
Adco-Atorvastatin 40 mg X 30
Rivaroxaban and apixaban

Rivaroxaban and apixaban are highly selective, direct oral factor Xa inhibitors, which are rapidly absorbed after oral administration (maximum effect within two to four hours). Rivaroxaban is prescribed once daily and apixaban is prescribed twice daily in patients with AF. They must be used with caution in patients with severe renal failure as between one-quarter and one-third of the ingested drug is excreted renally. Apixaban is metabolised in the liver, in part by the cytochrome P450 enzymes; therefore, it is not recommended in patients taking an antifungal drug of theazole class, anti-epileptic drugs (eg, phenytoin, carbamazepine), the antibiotic rifampicin or certain HIV drugs such as protease inhibitors. There are currently no agents capable of reversing the anticoagulant effect of rivaroxaban or apixaban. In phase III trials of rivaroxaban and apixaban, compared with warfarin, in patients with AF, apixaban reduced the risk of stroke, systemic embolism, mortality and major bleeding, and rivaroxaban was found to be non-inferior to warfarin for stroke and systemic embolism with no difference in risk of major bleeding. Both agents reduced the risk of intracranial haemorrhage. Due to their efficacy and ease of use, it is probable that these agents will gradually replace warfarin to a large extent in patients with AF.

Of all newer anticoagulants mentioned, a key point is that compliance is crucial because these drugs have a relatively short half-life, such that patients may be left without anticoagulation if more than one dose is missed.

Pharmacological management

Pharmacological management of patients with AF is directed either at rhythm control or rate control. Rhythm-control drugs act by altering the electrical properties of the atria such that they can no longer sustain the presence of AF. Rate control drugs slow conduction through the atrioventricular (AV) node and therefore reduce ventricular rate response.

Either strategy may be reasonable as no significant difference in mortality or thromboembolic risk has been demonstrated between the two approaches; however, symptomatic patients frequently derive much greater symptom relief from rhythm control. In addition, even in minimally symptomatic patients an initial attempt at rhythm control may be worthwhile, taking into account such issues as patient preference, age and comorbidities. Rhythm control may be achieved either pharmacologically or with electric cardioversion. After cardioversion, anti-arrhythmic drugs may be used to maintain sinus rhythm (Table 4).

Amiodarone is the most effective anti-arrhythmic drug available but should be used as a last resort because of its troublesome side effects. Flecainide should not be used in patients with structural heart disease, particularly coronary artery disease where it may lead to malignant ventricular arrhythmias. It must also be combined with an AV nodal-blocking agent because it may organise AF into atrial flutter, which may lead to conduction down the AV node rapidly leading to haemodynamic compromise.

In patients with no structural heart disease and infrequent episodes of symptomatic AF, a ‘pill-in-the-pocket’ approach with an oral agent such as flecainide may be effective. When the patient becomes aware of an episode of AF they can take a single oral dose of flecainide (50mg to 100mg) with a rate control agent such as a beta blocker. When pharmacological rhythm control fails, catheter ablation is an option in some patients.

The choice to opt for rate control is based both on symptoms and the likelihood of long-term sinus rhythm maintenance (eg, the presence of marked atrial enlargement or other significant structural heart disease reduces this likelihood; see the flowchart on page 21). Rate control is also the default option when rhythm control fails. Commonly used drugs and important caveats are shown in Table 4.

In general, the target in rate control is symptom control rather than a particular heart rate. However, for patients who remain symptomatic the best method for assessing pharmacological response is 24-hour Holter monitoring. Heart rate may appear well controlled when the patient is at rest in the office, but monitoring may show poor control with minor activity. Holter monitoring also allows correlation of the heart rate with symptoms. It is important to be aware that persistently elevated heart rates (even in asymptomatic patients) may result in a decline in left ventricular function. This is termed tachycardia-mediated cardiomyopathy and may occur when the average 24-hour heart rate is above about 100 beats per minute. Tachycardia-mediated cardiomyopathy is usually reversible when better rate control is achieved.

New anti-arrhythmic agents

Two new anti-arrhythmic drugs are under evaluation in some countries. Vernakalant, an atrial selective potassium channel-blocking agent, has been approved in Europe for the conversion of recent-onset AF. In this setting, it has been found to be more effective than amiodarone for conversion to sinus rhythm. However, its use is contraindicated in patients with hypotension, severe heart failure, valvular heart disease, prolonged QT interval or bradycardia.

Dronedarone is similar in structure to amiodarone, but with the iodine moiety removed, and it therefore has a lower side effect profile. Initial studies were encouraging but more recent studies...
Catch the rhythm in a heartbeat...

Choose Tambocor in your Atrial Fibrillation patient with NO structural heart disease

- 30 years young and available in over 50 countries
- Ideal first-line treatment, generally well tolerated, relatively little risk of toxicity
- Found to be more effective in maintaining sinus rhythm than other anti-arrhythmics

Tambocor...

Strike the right chord in AF.


IN757/12.
Choosing a rate control agent for patients with atrial fibrillation

Patient with atrial fibrillation presents for rate control treatment

Does the patient have an inactive lifestyle?

Yes

Prescribe digoxin

No

What associated diseases does the patient have?

None or hypertension

Prescribe one of the following:
- β-blockers
- Diltiazem
- Verapamil
- Combination treatment
- Digoxin

Coronary heart disease

Prescribe one of the following:
- β-blockers
- Diltiazem
- Verapamil

Heart failure

Prescribe one of the following:
- β-blockers
- Digoxin

COPD

Prescribe one of the following:
- Diltiazem
- Verapamil
- Digoxin
- β1-selective blocker

Adapted with permission from Lancet 2012; 379: 648-661.

Non-pharmacological management

Catheter ablation

Catheter ablation is a highly effective strategy for the control of symptomatic AF in patients who do not have advanced structural heart disease and where one or more anti-arrhythmic drugs have failed. The role of ablation in broader AF populations (eg, patients with persistent AF or structural heart disease, or older age groups) remains under investigation and may be appropriate in selected cases.

The aim of ablation in patients with paroxysmal AF is to eliminate the initiating triggers. In patients with paroxysmal AF, these triggers are almost universally located within the pulmonary veins. By electrically isolating the pulmonary veins from the left atrium, these triggers (or foci of rapid electrical activity) can no longer conduct electrical activity to the atrium.

Pulmonary vein isolation can be performed with the use of radiofrequency energy, most commonly, or cryoablation. Randomised controlled trials have reported that the success of pulmonary vein isolation in maintaining sinus rhythm is between 66% and 89% at 12-month follow up.

In a meta-analysis of randomised and non-randomised studies, the single procedure success rate of catheter ablation in patients taking no anti-arrhythmic drugs was 57% (95% confidence interval [CI], 50% to 64%); multiple procedure success rate off anti-arrhythmic drugs was 71% (95% CI, 65% to 77%).

In each trial, catheter ablation was superior to anti-arrhythmic drug use, which had an efficacy of between 9% and 58%. In a meta-analysis, the mean success rate of anti-arrhythmic drug use was 52% (95% CI, 47% to 57%). Furthermore, catheter ablation has been found to be superior to anti-arrhythmic drugs in reducing AF symptoms and resulted in improved quality of life.

It is important to note that about one-
third of patients may require repeat ablation owing to the phenomenon of recovered conduction to the pulmonary veins. With the continued advance in AF ablation technologies, this recurrence rate is gradually decreasing.

The reported efficacy of catheter ablation for patients with persistent AF is less favourable with published mean estimates of about 47% for a single procedure. However, these procedures require more extensive ablation in the atria in addition to targeting pulmonary vein triggers. Although this success rate increases with repeat procedures, there is still uncertainty about the mechanism underlying persistent AF and the best procedure to perform. Over time, it is likely that the success rate, procedural time and risk of complications of AF ablation will continue to improve, meaning that more complex ablation in patients with persistent AF will increase.

Catheter ablation in patients with AF is a complex interventional procedure that requires skilled operators, use of specialised three-dimensional computer mapping systems and dedicated laboratory time (up to four hours per procedure). The procedure is associated with a 1% to 2% risk of major complications, including thromboembolic events (about 0.5%) such as transient ischaemic attack and stroke, and cardiac tamponade (about 1%). Other major complications may occur.

The mortality risk associated with the procedure has been estimated to be about 0.1%. For these reasons, appropriate patient selection and consent is important, taking into account symptom severity, drug response and patient preference. The discussion as to whether to undergo this procedure is necessarily detailed.

**Recommendations for catheter ablation**

Current guidelines recommend that catheter ablation should be offered to patients with troublesome symptomatic paroxysmal AF who have either failed or are intolerant to at least one anti-arrhythmic drug (eg, flecainide, sotalol or amiodarone). Referral for catheter ablation of patients with persistent AF of less than 12 months’ duration is considered reasonable if the patient has troublesome symptoms and failure of or intolerance to at least one anti-arrhythmic drug. Catheter ablation is also reasonable in selected patients with heart failure or reduced left ventricular function, especially if the onset of AF precipitates heart failure.

Factors such as advancing age, the presence of structural heart disease, large left atria and long duration of persistent AF reduce the likelihood of success of catheter ablation (Figure 2). In patients undergoing ablation it is important to address associated conditions, including hypertension, obesity and sleep apnoea.

In general, a desire to stop taking anticoagulants is not considered a sole indication for this procedure in the asymptomatic patient in view of the risk of late recurrences of the arrhythmia.

**AV node ablation and pacing**

In patients with AF in whom a rate control strategy is preferred, but who are not responding to or are intolerant of

Continued on page 45
An active and aggressive 14 year old boy presented with episodes of palpitations. These had a sudden onset and gradual offset. During the attacks he felt lightheaded and short of breath. He would be extremely anxious. He often had a heavy feeling in the chest. His maternal aunt and grandmother experienced similar symptoms and were receiving medication. Clinical examination, resting ECG and effort ECG showed no abnormality. He did not respond to treatment with beta-blockers and was referred for psychological assessment which had no immediate benefit although he was assured it would in time. He experienced further episodes and went to an emergency room where the following ECG was taken:

Have you looked beyond the obvious?
Statements for consideration (True or False):
1. The QRS complexes in ECG 1 and 2 are the same. This is therefore a sinus tachycardia and reflects his anxiety state (provided his thyroid gland is normal).
2. The rhythm strip V1 at (at the bottom) shows an alternating size of the QRS complex. This indicates the tachycardia is arising in the ventricles.
3. There are no P-waves seen prior to the QRS indicating that the tachycardia arises in the ventricles i.e. ventricular tachycardia.
4. This is a supraventricular tachycardia that has not responded to betablockers, thus a more powerful antiarrhythmic drug like Amiodarone should be used.
5. The QRS complexes are normal thus this is a supraventricular tachycardia (SVT). The absence of P-waves preceding each QRS is typical of many SVTs.

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

History:
The history is classical of a paroxysmal supraventricular tachycardia. In particular the sudden onset often followed by a sudden offset is a strong diagnostic point. A gradual offset does not argue against an SVT. The blood pressure may fall and be associated with dizziness. The abnormal timing of atrial contraction frequently results in a flushed feeling in the face, pounding in the throat and chest discomfort and often, of course, anxiety.

ECG:
The rhythm is regular and the QRS complexes narrow. This confirms that the rhythm is conducted to the ventricles via normal pathways. Absence of P-waves preceding the ECG is typical of the commonest forms of SVT. V3 shows abnormal P-waves following the QRS and are a clue to the fact that the tachycardia enters (re-enters) the atrium from the ventricle and then back down through the AV node to the ventricles (reciprocates). The observation that each second beat is a different size to the preceding one (rhythm strip V1) is known as electrical alternans and occurs as a result of the rapid rate and does not indicate the site of origin of the tachycardia.

Diagnosis:
This ECG is typical of the commonest form of regular supraventricular tachycardia – AV node re-entrant tachycardia (AVNRT).

Treatment:
Although antiarrhythmic drugs may be effective in the treatment of reciprocating SVT (by far the commonest form of SVT) long-term treatment is usually unsatisfactory with frequent (unpredictable) relapses. Radiofrequency ablation is safe, highly effective offering a greater than 95% cure rate and safe in experienced hands. Referral to a cardiologist/electrophysiologist should be made on diagnosis.

Additional Notes:
Some reciprocating supra-ventricular tachycardias can run in families AV node re-entry & accessory pathway mediated tachycardia.

Have you looked beyond the obvious?
Common Myths and Misunderstandings in Type 1 Diabetes

Although some of the abundant myths in circulation about type 1 diabetes may have been useful in the past, many are misleading now and may lead to inappropriate management. This article discusses some of the more prevalent ones that may mislead doctors.

There are many myths about diabetes in general practice. These easy-to-remember adages have been passed down from generation to generation of doctors and their proponents defend them vigorously. Some may have been applicable and useful in the past, but many are misleading now and may lead to inappropriate management.

**Myth 1**

**GPs should not involve themselves with the management of type 1 diabetes**

In contrast to this view, the following guidelines about shared care are worth noting:

‘The advice of a specialist physician may be valuable for people with complicated problems related to diabetes – especially children, adolescents and adults with type 1 diabetes .... A shared care approach by a general practitioner and specialist will provide the best combination of specialised expertise and continuity of care.’

A specialist may be able to help with some of the special issues related to type 1 diabetes, but many of these can also be dealt with by a GP who knows the patient. Most of the health problems experienced are not related to diabetes or its complications and are the same as problems experienced by a similar person without diabetes. Moreover, the GP usually has a better idea of all the other factors affecting the person and is the first port of call if problems arise – related or unrelated to diabetes. Shared care is the ideal, with prompt communication between the GP and specialist diabetes professionals.

**Myth 2**

**Children get type 1 diabetes, adults get type 2 diabetes**

This adage is superficially true: the median age for developing type 1 diabetes is 11 years and for type 2 is sixty-two. However, it is also true that children who developed type 1 diabetes 30 to 40 years ago are now in their 40s and 50s and still have type 1 diabetes, so not all diabetic patients in their 40s and older have type 2 diabetes.

The most important F word for predisposition to type 2 diabetes is Forty. However, more and more children and adolescents are developing type 2 diabetes, particularly those with the other F words for type 2 diabetes: Family history and Fatness. These children are usually from high risk groups and overweight, and the peak age group for diagnosis of type 2 diabetes in young people is adolescence (see box on high-risk groups).

Also, 5% to 10% of people with type 1 diabetes and autoimmune destruction of pancreatic beta cells are adults when first diagnosed. They may be misdiagnosed as having type 2 diabetes and initially treated with oral hypoglycaemic agents. These people have late onset autoimmune diabetes in adults (LADA) and lack the typical features of type 2 diabetes. They are instead skinny, have rapid progression of hyperglycaemia, are unstable or poorly controlled on oral glycaemic agents early in the course of the disease and have a family or personal history of autoimmune disease (see the box on LADA indicators). It is important to recognise that people with LADA have a form of type 1 diabetes and will require insulin early in the course of their diabetes.

**Myth 3**

**Women who have had gestational diabetes and who develop diabetes later have type 2 diabetes**

It is true that most women who have had gestational diabetes do develop type 2 diabetes, and that the gestational diabetes was an early sign of their rising insulin resistance and falling insulin secretion capacity. The hormonal environment of the pregnancy temporarily increases insulin resistance and precipitates gestational diabetes (Figure 1). Postpartum, the progressive increase in insulin resistance and decrease in insulin secretion capacity continues and the woman develops pre-diabetes (impaired fasting glucose and/or impaired glucose tolerance) and then type 2 diabetes.

However, it is also true that if a woman is in the process of developing type 1 diabetes, with progressive autoimmune destruction of beta cells, the remaining beta cell mass may be enough to control glycaemia before, and in the early stages of, pregnancy but may be insufficient in the last trimester when...
**High risk groups for type 2 diabetes in childhood or adolescence**

- Overweight: (BMI more than 85th percentile for age and gender; weight for height more than 85th percentile, or weight more than 120% of ideal for height)
- Any two of the following: 
  - family history of type 2 diabetes in a first-degree or second-degree relative
  - high risk ethnic group
  - signs or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidaemia, PCOS)
  - maternal history of diabetes or gestational diabetes

Abbreviations: BMI = body mass index; PCOS = polycystic ovarian syndrome.

**Indicators of late-onset autoimmune diabetes in adults (LADA)**

- Skinniness
- Family history of auto-immune disease
- Rapid progression of hyperglycaemia
- Unstable/poor control on oral agents early in the course of the disease

Gestational diabetes is usually diagnosed. Postpartum, the progressive immune beta cell destruction continues and the woman develops pre-diabetes and then diabetes – but in this case, type 1 diabetes. As for people with LADA, it is important to identify these women with type 1 diabetes as they will need insulin therapy much earlier than if they had type 2 diabetes.

**Myth 4**

**Type 1 diabetes is not associated with comorbidities whereas type 2 diabetes is**

It is true that type 1 diabetes, including LADA, is not associated with the type 2 syndrome (the metabolic syndrome) associated with type 2 diabetes: hypertension, dyslipidaemia, prothrombosis and excess cardiovascular risk. However, type 1 diabetes, being an autoimmune disorder, is often associated with other autoimmune disorders, most commonly thyroid disease, vitiligo and coeliac disease (see box on autoimmune disorders). Thyroid disease is particularly common, and the American Diabetes Association recommends screening for thyroid disease with thyroid antibodies (eg thyroid peroxidase) and coeliac disease with anti-transglutaminase antibodies.

One in 10 pregnant women with type 1 diabetes will develop postpartum autoimmune thyroiditis with temporary hyperthyroidism, followed by hypothyroidism and recovery over several months. Many of these women, particularly those with positive thyroid autoantibodies, will become permanently hypothyroid in the medium to long term and should be monitored with thyroid function tests (eg, annually). Family members may be affected with one or more of these autoimmune disorders but not necessarily the same ones as the index case.

**Myth 5**

**Diabetes complications are microvascular in type 1 diabetes and macrovascular in type 2**

There is some truth in this adage because people who develop type 1 diabetes are usually young and have a cardiovascular risk profile similar to their age-matched population peers, whereas those with type 2 are older and have the associated metabolic syndrome with its high cardiovascular risk profile.

With type 1 diabetes, there will be plenty of time after diagnosis to develop microvascular complications (these take five to 15 years to occur). With type 2 diabetes, there has been plenty of time for cardiovascular disease to develop before diagnosis. However, cardiovascular risk increases dramatically once nephropathy occurs in type 1 diabetes.5

A series of vicious cycles is initiated, as shown in Figure 2 and listed below.

- **Glycaemic vicious cycle.**
  - Hyperglycaemia (with or without

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**Figure 1. Insulin resistance and secretion capacity**

In a person developing type 2 diabetes, insulin resistance progressively increases with time and insulin secretion capacity progressively decreases. Pregnancy temporarily increases insulin resistance to above the insulin secretion capacity and precipitating gestational diabetes, which resolves as insulin resistance decreases back to below the insulin secretion capacity (B). After the pregnancy, insulin resistance and secretion capacity continue to change and the blood glucose level progressively rises as insulin resistance and secretion capacity become equal (the point of intersection) and then insulin resistance exceeds secretion. Diagnosis of diabetes usually follows shortly after the point of equivalence.

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**Common Myths and Misunderstandings in Type 1 Diabetes (continued)**
**Myth 6**

In type 1 diabetes, treatment focuses on glycaemic control, whereas in type 2 diabetes, the ABCss are targeted

Cardiovascular risk in people with type 1 diabetes is similar to the risk in the general population – until renal impairment initiates the vicious cycles, accelerating further renal impairment and cardiovascular disease. However, some of those with type 1 diabetes, like some people from the general population, will have or develop hypertension and/or dyslipidaemia, or will develop a lifestyle behaviour (especially smoking) that increases cardiovascular risk.

In all people with diabetes, the five major goals of diabetes care – the ABCss – should be targeted. The ABCss are listed below, and the treatment targets are shown in the Table.

- **A =** controlling HbA1c (glycosylated haemoglobin)
- **B =** controlling Blood pressure
- **C =** Controlling cholesterol
- **s =** quitting Smoking
- **s =** taking Salicylates

The risk factors associated with cardiovascular disease, especially hypertension, are also associated with renal impairment. The ‘double whammy’ of hyperglycaemia and hypertension more than doubles the risk of renal damage. It is important to maintain blood pressure below 130/80mmHg or as close as possible to values at diagnosis. A ‘healthy’ blood pressure of 125/75mmHg is not ideal for someone who previously had a blood pressure of 95/60mmHg, and represents a considerable increase of 30/15mmHg. Blood pressure control is particularly important once renal impairment occurs, and a lower target (below 125/75mmHg) is recommended if there is proteinuria.

**Myth 7**

In people with type 1 diabetes, glycaemia should be tightly controlled

With the caveat, ‘…..if this can be achieved safely’, this is generally true. There are two reasons why glycaemic targets cannot be met: patient capacity and willingness, and medical caution mainly related to hypoglycaemic risk.

The everyday burden of glycaemic control is considerable. Some people may not have the mental capacity to juggle the current blood glucose reading, the mealtime glycaemic load and the corrective and prandial bolus insulin doses, or the physical capacity to perform multiple blood glucose measurements and insulin injections. For others, it is just too hard. They may understand that they are risking future complications but they do not want the ‘hassle’ of the complex diabetes routines.

As thirty-two year old Tim, a patient who has had type 1 diabetes since he was 14, put it: ‘I often get sick of it. All
I hate it. ‘I just want to forget it and get on with my life without all that hassle. I hate it.’

Hypoglycaemia is the main reason for medical caution. Minor hypoglycaemia disrupts life with its unpleasant symptoms and the need to interrupt whatever is happening, eat carbohydrates and check that the blood glucose value increases to a safe level. Severe hypoglycaemia can be life-threatening if it is very profound or if it causes loss of control in a dangerous situation (such as when driving). On average, a person with type 1 diabetes has a minor hypoglycaemic episode weekly and a severe hypoglycaemic episode (requiring help from a third party to recover) once a year. Within that average, however, there is a wide range. A few unlucky people have most of the hypoglycaemia (minor and severe), while the lucky few rarely have it.

There are several ‘red flags’ to identify those who are more likely to develop severe hypoglycaemia (see the box on red flags).³

The glycaemic targets for people lacking the capacity or will to handle the hassle of the necessary diabetes routines will be determined by how much they are able and/or willing to tolerate. For those at high risk of severe hypoglycaemia, targets will be determined by how low they can go without an unacceptable risk of severe hypoglycaemia. This may be an A1c of 8% to 9%, or even higher. Circumstances do, however, change with time and people may become more able and/or willing to try to control their glycaemia, or become less prone to hypoglycaemia and able to achieve tighter targets.

### Summary

**Myths and misunderstandings demystified**

- **Myth 1:** GPs should not get involved with the management of type 1 diabetes.
  **Reality:** A specialist may be able to help with some of the special issues related to type 1 diabetes but most issues can be dealt with by a GP who knows the patient and is aware of their other health problems.

- **Myth 2:** Children get type 1 diabetes, adults get type 2.
  **Reality:** Many children who are overweight and have a family history of type 2 diabetes, a maternal history of diabetes or gestational diabetes, or signs and conditions associated with insulin resistance, develop type 2 diabetes that is diagnosed mostly in adolescence. About 5% to 10% of those with type 1 diabetes are adults who have late onset autoimmune diabetes in adults (LADA).

- **Myth 3:** Women who have had gestational diabetes and develop diabetes later have type 2 diabetes.
  **Reality:** Some women who are developing type 1 diabetes first present during gestation.

- **Myth 4:** Type 1 diabetes is not associated with comorbidities whereas type 2 diabetes is.
  **Reality:** Type 1 diabetes, including LADA, is an autoimmune disorder and is often associated with other autoimmune disorders (most commonly thyroid disease). One in 10 pregnant women with type 1 diabetes will develop postpartum autoimmune thyroiditis.

- **Myth 5:** Diabetes complications are microvascular in type 1 and macrovascular in type 2.
  **Reality:** This is largely true, but once nephropathy develops in type 1 diabetes several vicious cycles are initiated (glycaemic, hypertensive, dyslipidaemic) that accelerate renal impairment and cardiovascular disease.

- **Myth 6:** In type 1 diabetes, the treatment focuses on glycaemic control, whereas in type 2 diabetes the ABCss are targeted.
  **Reality:** People with type 1 diabetes have similar cardiovascular risks to the general population, and some will have or will develop cardiovascular risk factors or renal impairment. Cardiovascular risk factors, the ABCss, should be sought and treated actively in all people with diabetes.

- **Myth 7:** In people with type 1 diabetes, glycaemia should be tightly controlled.
  **Reality:** This is true if it can be achieved safely. Patient capacity and willingness, and medical caution related to hypoglycaemic risk, may mean that tight glycaemic control cannot be achieved. ‘Red flags’ to identify people most likely to develop severe hypoglycaemia include a history of hypoglycaemic episodes, hypoglycaemic unawareness, an erratic lifestyle and sleeping alone. In these situations, glycaemic targets depend on the level of glycaemia achievable without an unacceptable risk of severe hypoglycaemia.

### Hypoglycaemic red flags in order of importance

- History of hypoglycaemic episode
- Hypoglycaemic unawareness (autonomic neuropathy)
- Erratic lifestyle
- Tight glycaemic targets
- Sleeping alone

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**TABLE**

<table>
<thead>
<tr>
<th>The ABCss of diabetes care and treatment targets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ABCss</strong></td>
</tr>
<tr>
<td>A1c (glycosylated haemoglobin)</td>
</tr>
<tr>
<td>Blood pressure</td>
</tr>
<tr>
<td>Cholesterol</td>
</tr>
<tr>
<td>smoking</td>
</tr>
<tr>
<td>salicylates</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Hypoglycaemic red flags</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypoglycaemic red flags</strong></td>
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<tr>
<td>* History of hypoglycaemic episode</td>
</tr>
<tr>
<td>* Hypoglycaemic unawareness (autonomic neuropathy)</td>
</tr>
<tr>
<td>* Erratic lifestyle</td>
</tr>
<tr>
<td>* Tight glycaemic targets</td>
</tr>
<tr>
<td>* Sleeping alone</td>
</tr>
</tbody>
</table>

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3. Hypoglycaemia red flags: A few unlucky people have most of the hypoglycaemia (minor and severe), while the lucky few rarely have it.
Improvements in Glycaemic Control for Patients with Diabetes on PD
The Role of Extraneal® as a Non-Glucose PD Solution

As an initial modality PD can effectively maintain diabetics on their chosen therapy, whilst preserving their vascular access. Therefore further dialysis modalities can be introduced at a later point in the patient’s management.

Reducing glucose load with Extraneal® may preserve peritoneal membrane function and improves glycaemic control for Diabetic patients on PD.

- Extraneal® significantly reduces glucose load.
- A reduction in glucose load reduces hyperglycaemia and results in smoother glycaemic control.
- Substitution of one glucose exchange per day with Extraneal® results in a significant fall in HbA1c.

Lightening the Load for PD Patients with Diabetes.

References:
2. Johnson DW et al. Iodoestin as salvage therapy in peritoneal dialysis patients with seleter fluid overload BMC Nephrology 2001;22

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Cardiovascular diseases are the main cause of morbidity and mortality among dialysis patients, in both haemodialysis (HD) and peritoneal dialysis (PD). Fluid overload and hypertension underlie these disturbances.

Control of extracellular fluid volume (ECFv), and therefore hypertension, retards the loss of residual renal function and decreases morbidity and mortality.8–10 Nevertheless, control of ECFv is not an easy goal for dialysis patients to achieve.

One of the most important issues in PD therapy today is how to minimise the use of glucose as osmotic agent in PD solutions in order to avoid its metabolic side effects.

Use of hypertonic glucose has been associated with hyperglycaemia, hyperinsulinaemia, and obesity.11–13 Other disadvantages include bio-incompatibility, advanced glycated end-product generation, peritoneal damage, and in the long term, loss of ultrafiltration (UF).

In a significant number of patients classified as high transporters, glucose use as osmotic agent has its limitations due to rapid peritoneal glucose absorption into the circulation with dissipation of the osmotic gradient. It is common practice when facing such a situation to use solutions with higher glucose content, resulting in increases in the adverse metabolic effects of glucose exposure. The disadvantages of hypertonic glucose are even greater in diabetic patients, many of whom are high transporters.14–17

**Mexican trial with diabetes proves icodextrin superior in fluid and metabolic control**

In the 1990s, icodextrin, a glucose polymer, began to be used in Europe as a replacement for the traditional glucose in PD solutions for the long dwell in both continuous ambulatory PD (CAPD) and automated PD.20–22

The 2009 report of a trial conducted in Mexico City (where diabetes is prevalent) demonstrated the effectiveness of of icodextrin as an oncotic agent. The gradient can be maintained at adequate UF values for 8–12 hours and both fluid and metabolic control improved.

**Trial information**

Fifty nine diabetic patients using CAPD were recruited from four general hospitals in the metropolis area of Mexico City. A 12-month multicentre, open label, randomised, controlled trial was conducted to compare ICO (n=30) versus GLU (n=29) in diabetic CAPD patients with high-average and high peritoneal transport characteristics.

The basic daily schedule was 3×2 L GLU (1.5%) and either 1×2 L ICO (7.5%) or 1×2 L GLU (2.5%) for the long-dwell exchange, with substitution of 2.5% or 4.25% for 1.5% GLU being allowed when clinically necessary. Variables related to metabolic and fluid control were measured each month.

**Results**

**Body weight**

Body weight remained stable in the ICO group throughout the study; in contrast, it increased progressively in the GLU group.

**Extra-cellular fluid volume**

ECFv decreased significantly in the ICO group from the first week of treatment, whereas it remained unchanged in the control group (GLU).

Reductions in TBW were more pronounced than those observed in ECFv, probably due to the reduction in intracellular water. It is known that end-stage renal disease patients show increments in intracellular water and in intracellular concentrations of sodium. In this condition, we attributed the difference between TBW and ECFv to a reduction in intracellular oedema.

**Blood pressure**

Systolic and diastolic BP decreased in the ICO group from soon after beginning treatment to the ninth month, after which BP differences from baseline were less pronounced. In the GLU group, systolic and diastolic BP remained essentially unchanged from the beginning of the study.
Peritoneal clearance
Soon after the beginning of the treatment, peritoneal clearances of small-size molecules increased in the ICO group. After month 6, both Kt/V and creatinine clearance returned to baseline. In the control group, Kt/V and creatinine clearance decreased significantly over time.

Metabolic control
At baseline, values of metabolic control parameters were similar in both groups; two thirds of patients were using insulin. During the follow-up, insulin medication was individually reconsidered and adjusted according to fasting serum glucose values. Metabolic control was better in the ICO group, which presented lower glucose exposure and glucose absorption, than in the GLU group. Insulin requirements decreased significantly and progressively in the ICO group, whereas an inverse pattern was observed for the control group.

Statistical evaluation
The numbers of dropouts was 11 in the GLU group and 12 in the ICO group; the remaining patients completed the scheduled follow-up and were available for statistical evaluation. Adverse events related to fluid overload and metabolic control were more frequent in the GLU group compared to the ICO group.

Conclusion
Icodextrin represents a significant advantage in the management of high transport diabetic patients on PD, improving peritoneal UF and fluid control and reducing the burden of glucose overexposure, thereby facilitating metabolic control.

References on request.

Similar Outcomes with Haemodialysis and Peritoneal Dialysis in Patients with End-Stage Renal Disease

There are well over 500 000 Americans living with end-stage renal disease (ESRD). Even though patients with ESRD constitute less than 1% of the government health-funded (Medicaid) programme, they account for 5.8% of the programme’s total expenses.

In 2007, the annual, per-person cost for peritoneal dialysis (PD) patients was almost $20 000 (R180 000) lower than that for haemodialysis (HD) patients.

Worldwide there has been considerable interest in a large group study to determine if there is any difference in the mortality outcomes of HD and PD patients.

Large US study findings
This US study examined data made available by the US Renal Data System for secular trends in survival among patients treated with HD and PD on day 90 of end-stage renal disease with 620 020 patients on HD and 64 406 patients on PD. The examination of data was divided into three periods of three years each with up to five years of follow-up.

Adjustments
For all statistical analyses, the models were adjusted for demographics (age, sex, race, and current employment status), facility characteristics (period-prevalent patient census, and for profit or not-for-profit status), cause of ESRD, 10 different comorbid conditions (cardiac arrest or dysrhythmia, cerebrovascular disease, congestive heart failure, ischaemic heart disease or myocardial infarction, peripheral vascular disease, limited activities of daily living, chronic obstructive pulmonary disease, current smokers, diabetes primary or contributing, and malignant neoplasm), baseline estimated glomerular filtration rate, body mass index, and selected laboratory variables (serum albumin, blood urea nitrogen, and haemoglobin).

Conclusion
The findings demonstrate that, even though there was a progressive attenuation in the higher risk for death seen in patients treated with PD in the earlier time periods of the study, the 2002-2004 group, showed no difference in the risk of death for HD and PD patients through five years of follow-up. The median life expectancy of HD and PD patients was 38.4 months and 36.6 months, respectively.

Since 1996 there has been no change in the first year mortality rates of patients on haemodialysis, whereas both short- and long-term mortality outcomes of PD patients have improved.

Excerpted from “Similar outcomes with haemodialysis and peritoneal dialysis in patients with end-stage renal disease.” Rajnish Mehrotra et al, Published online: September 27, 2010 /archinternmed.2010.352.
References on request.
Smoking is a significant cause of preventable illness and death. About half of all lifelong smokers die prematurely from their habit and smokers live ten years less on average than non-smokers.1 Many smokers want to quit2 and most who do want to quit make repeated attempts to do so. About 40% try to stop smoking at least once each year.3 However, long-term quitting is an elusive goal for many smokers. Only 3% to 5% of unaided quit attempts are successful six to 12 months later.4 Even with professional counselling and pharmacotherapy, only 28% of smokers are abstinent at six to 12 months.5 Even among those who do quit, there is a steady attrition over time. After 12 months, about half of all quitters will subsequently relapse.7

Most smokers repeatedly fail to quit because they are addicted to nicotine and have lost control of their smoking behaviour. This article examines why it is so hard to break the habit in the long term, suggesting strategies GPs can use to optimise their interventions. Smokers need to be re-engaged and helped through repeated attempts to quit over the long term.

Nicotine Dependence: Why is it so Hard to Quit?

Most smokers repeatedly fail to quit because they are addicted to nicotine and have lost control of their smoking behaviour. This article examines why it is so hard to break the habit in the long term, suggesting strategies GPs can use to optimise their interventions. Smokers need to be re-engaged and helped through repeated attempts to quit over the long term.

## Key points

- Nicotine dependence is a substance abuse disorder involving compulsive drug use in spite of known health risks.
- Most smokers continue to smoke because they are addicted to nicotine. Today’s smokers may be more addicted than in the past.
- The psychoactive effect of nicotine is mediated by activation of the powerful reward pathway in the brain and the release of dopamine.
- Other mechanisms underlying nicotine addiction are environmental cues, nicotine cravings and withdrawal symptoms.
- Successful treatment is based on optimising pharmacotherapy and behavioural strategies to counter smoking cues.

### Adolescent uptake

Eighty percent of adult smokers start smoking before they’re 18 years old.11 Adolescents are more sensitive than adults to nicotine and develop dependence more quickly and from lower levels of nicotine intake.13 Among teenagers who lose control over their tobacco use, 10% do so within two days of inhaling from a cigarette for the first time and 25% within 30 days.13 Symptoms of nicotine dependence develop in 70% of adolescents before they are smoking daily.15 Children whose mothers smoked during pregnancy are also more likely to become dependent on tobacco if they start smoking.14

### Role of genetics

Twin studies have indicated that genetic factors account for 60% to 70% of the chance of becoming nicotine dependent after starting to smoke.15-16 The cytochrome P450 CYP2A6 gene is responsible for the metabolism of about 90% of nicotine. Variations in the gene determine the rate of nicotine breakdown, which can vary by up to fourfold. Slower metabolisers have lower nicotine dependence, smoke fewer cigarettes, respond better to nicotine replacement therapies and are able to quit more easily.17-18 Rates of nicotine breakdown also vary considerably across gender and race. For example, men metabolise nicotine more slowly than women.17 Genes affecting the sensitivity of nicotine receptors and the reward pathway have also been identified.

### About the author

Colin Mendelsohn MB BS (Hons) is a general practitioner in Sydney, Australia, with a special interest in smoking cessation. He is also the editor of Your Health Newsletter and a member of the Executive Committee, Australian Association of Smoking Cessation Professionals.
Reward pathway

Similar to other drugs of abuse, such as cocaine and heroin, nicotine activates the mesolimbic reward pathway, releasing dopamine. Dopamine creates the pleasurable sensations associated with smoking that are central to its addictive properties and lead to further drug-seeking (nicotine) behaviour (Figure 1).

Dependence on nicotine is reinforced further by repeated and very rapid exposure to the drug. The 20 cigarette-a-day smoker gets 200 hits of nicotine every day and each bolus of nicotine reaches the brain within 10 to 19 seconds of inhalation. Chronic nicotine exposure up-regulates nicotinic receptors. Over time, more receptors release dopamine, making quitting even more difficult.

Within a few hours of the last cigarette, the smoker experiences nicotine withdrawal symptoms due to reduced dopamine levels. The unpleasant psychological and physical symptoms of the nicotine withdrawal syndrome can be relieved by smoking and are a powerful trigger for early relapse (see the box on this page).

A reduction in nicotine levels in the brain leads to background cravings for nicotine, which are also an important cause of relapse in the first week of quitting. Smokers regulate their smoking behaviour to maintain their blood nicotine level within a comfortable range to avoid cravings and withdrawal symptoms.

As well as dopamine, nicotine triggers the release of a range of other neurotransmitters that play a role in nicotine addiction (Figure 1).

Other mechanisms underlying nicotine dependence

Cue-induced cravings

Specific behaviours and situations, such as drinking a cup of coffee or the smell of smoke, are associated with smoking and its pleasurable effects. This creates a conditioned or learned response so that exposure to the smoking cue can trigger a strong urge to smoke, especially in women.

Desire for the positive effects of nicotine

As well as pleasure, nicotine can generate arousal, heightened alertness, relief of anxiety or depression, reduced hunger and control of body weight. Smokers use it for these effects (Figure 2).

Light and non-daily smokers

Light (10 or less cigarettes per day) and non-daily smokers are a growing proportion of smokers. These smokers tend to smoke more for the positive effects of nicotine and in response to smoking cues, such as in social situations.

However, numerous studies have shown that many low-level smokers experience nicotine withdrawal and other indicators of nicotine dependence. This is important because even the presence of a single symptom can affect quitting.

Low-level smoking is not harmless. Significant health risks are associated with light smoking. Smokers of one to four cigarettes a day almost triple their risk of dying from ischaemic heart disease compared with never smokers (odds ratio, 2.84) and have a 50% increased mortality from all causes (odds ratio, 1.52).

Is nicotine harmful?

Although nicotine is the main cause of tobacco dependence, it is not in itself carcinogenic, does not cause respiratory disease and has only minor haemodynamic effects. However, it can delay wound healing and increase insulin resistance and it is associated with harmful effects on the fetal brain and lungs.

The ‘hardening hypothesis’

Some evidence supports the ‘hardening’ hypothesis that proposes that smokers who have found it easy to quit have already done so, leaving a more resistant group for whom quitting is more difficult. Although this seems logical, a recent review suggests that more research is needed to verify it.

People with mental health disorders now form an increasing core of the remaining smokers. They are twice as likely to smoke as other people; they also smoke more heavily. This group is more dependent on nicotine than other smokers, has lower quit rates and is often neglected by health professionals.

Countries with low smoking rates have higher nicotine dependence levels and smokers find it harder to quit.
A first line treatment option for smoking cessation

- The first smoking cessation treatment specifically designed to target the neurobiological mechanism of nicotine dependence
- A unique, dual mechanism of action
- Significant effectiveness in long-term relapse prevention

Assessing nicotine dependence

Assessing nicotine dependence helps predict whether the smoker will experience nicotine withdrawal symptoms and is a guide to the intensity of treatment required. In the clinical setting, the single most reliable indicator is the time to first cigarette. As most nicotine is cleared overnight (the half-life of nicotine is two hours), smokers wake in a state of nicotine deprivation. Acting quickly to replenish nicotine levels is a sign of dependence.

Cravings and withdrawal symptoms experienced in previous quit attempts are also a useful guide to nicotine dependence. The number of daily cigarettes is less useful because self-reports are often unreliable, cigarette brands differ in strength and smoking behaviour and nicotine metabolism vary from one smoker to the next.

Nevertheless, the risk of nicotine dependence rises with higher levels of use. Smoking more than 15 cigarettes a day is generally associated with a greater likelihood of dependence.

Clinical implications

Continuing smokers are not weak-willed or simply making a bad lifestyle choice. Rather, they are victims of a potent drug addiction mediated by powerful neurochemical processes, often with an underlying genetic predisposition. In nearly all cases, the addiction has already developed in adolescence. Smokers deserve an empathic, non-judgemental and supportive approach.

Although some smokers can quit without help, many individuals need assistance, especially those with higher levels of nicotine dependence. Similar to addicts to other substances, smokers have lost control of their behaviour. Medical treatment is often essential and appropriate.

However, many light and non-daily smokers are also nicotine dependent and at risk of smoking-related diseases. Non-daily smokers are more likely to want to quit than daily smokers but their doctors are less likely to advise them to quit. This group should be informed that no level of smoking is safe. They should be advised to stop smoking and offered assistance, including help with smoking cues. Pharmacotherapy may sometimes have a role.

Reducing the number of cigarettes or changing to lighter cigarettes are not effective strategies in dependent smokers because the smokers typically compensate by varying their puff frequency and depth to keep the nicotine level within a certain range.

Smoking (nicotine dependence) is now classified as a chronic medical disease, with multiple cycles of relapse and remission. Similar to patients with poorly controlled diabetes, relapsed smokers need to be re-engaged and assisted through repeated attempts to quit over the long term.

Effective intervention is based on the smoker’s readiness to quit. Different strategies are required for smokers who are not ready or unsure, and those who are ready to quit.

TABLE 1

### Fagerström test for nicotine dependence

<table>
<thead>
<tr>
<th>Questions</th>
<th>Answers</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How soon after you wake up do you smoke your first cigarette?</td>
<td>Within 5 minutes</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>6 to 30 minutes</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>31 to 60 minutes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>After 60 minutes</td>
<td>0</td>
</tr>
<tr>
<td>2. Do you find it difficult to refrain from smoking in places where it is forbidden (e.g. in church, at the library, in cinemas, etc)?</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>3. Which cigarette would you hate most to give up?</td>
<td>The first one in the morning</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>All others</td>
<td>0</td>
</tr>
<tr>
<td>4. How many cigarettes do you smoke each day?</td>
<td>10 or less</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>11 to 20</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>21 to 30</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>31 or more</td>
<td>3</td>
</tr>
<tr>
<td>5. Do you smoke more frequently during the first hours after waking than during the rest of the day?</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>6. Do you smoke if you are so ill that you are in bed most of the day?</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>0</td>
</tr>
</tbody>
</table>

A score of 0 to 2=very low dependence; 3 to 4=low dependence; 5=medium dependence; 6 to 7=high dependence; 8 to 10=very high dependence.

Pharmacotherapy

Guidelines recommend using pharmacotherapy for all nicotine-dependent smokers. First-line medications (nicotine replacement therapy, varenicline and bupropion) increase success rates by two to three times those of placebo. In view of the potency of nicotine addiction, it is important to optimise the use of pharmacotherapy (Table 2). Background nicotine cravings and withdrawal symptoms are relieved by all forms of smoking pharmacotherapy and settle within a few weeks of cessation. Cue-induced cravings, however, can persist for many years after quitting and are a common cause of early and late relapse. They are alleviated by fast-acting forms of nicotine replacement therapy such as gum or lozenge but not by the nicotine patch.
Some smokers who are highly addicted and cannot choose to stop smoking, may benefit from harm reduction with long-term nicotine replacement therapy to reduce the risk of smoking-related disease, although this is controversial.

**Counselling**

The best results are achieved when pharmacotherapy is combined with counselling. Even minimal interventions are effective in increasing cessation rates. However, more intensive interventions with multiple sessions are most effective and longer counselling sessions are more successful than shorter ones. In view of the high risk of early relapse, smokers need most support in the first week or two after quitting.

It is advisable to help smokers develop coping strategies to overcome the risk of smoking-related disease, and to deal with high-risk situations and specific smoking cues after quitting. For example, a smoker could plan to drink tea instead of coffee if the latter triggers an urge to smoke. Avoiding other smokers for the first week or two after quitting is also sensible.

In addition, it is important to assess the individual smoker’s barriers to quitting and develop strategies to overcome them. Common barriers are withdrawal symptoms, stress, fear of failure, social pressure and weight gain. Support from family and friends increases success rates and should be encouraged.

**Conclusion**

Smoking is now viewed as a powerful substance abuse disorder. Most smokers continue smoking because they are addicted to nicotine and have lost control of their smoking behaviour.

Nicotine dependence is mediated by powerful neurochemical processes and an underlying genetic predisposition that makes it extremely difficult for many smokers to quit, especially as smokers today may be more nicotine dependent than in the past.

Similar to other victims of serious, chronic disease, smokers need empathy and support over the long term. Intervention is a vital and appropriate function for GPs, and effective treatment begins with assessing the level of nicotine dependence. Optimal therapy includes maximising the use of medication for all nicotine-dependent patients, intensive support and behavioural change to counter the conditioned response to smoking cues.
Doctors have a number of investigations available to them to help diagnose suspected injuries in sports medicine. Many involve ionising radiation (conventional radiography, CT scanning, bone scanning), others do not (MRI, ultrasound). One of the dictums of medical practice is Primum non nocere (First, do no harm). Exposure to diagnostic ionising radiation, like other medical tests and procedures, is associated with a risk to the patient. In this case, there is a potential risk, albeit small, of a radiation-induced cancer and/or a genetic disorder in one’s offspring.

The use of ionising radiation in medicine is the single largest man-made source of population radiation exposure. Exposure to diagnostic ionising radiation, like other medical tests and procedures, is associated with a risk to the patient. In this case, there is a potential risk, albeit small, of a radiation-induced cancer and/or a genetic disorder in one’s offspring.

The effective dose associated with most diagnostic imaging modalities is in the range of 0.03 to 20 mSv. This dose range may be compared with the annual dose of background radiation, or with the doses received by the survivors of the two atomic bombs of 1945, which were in the range of 5 mSv to more than 2000 mSv.

The box on page 39 shows the effective dose for various common investigations performed in sports medicine, which have been estimated for a theoretical patient: Athlete X. Athlete X is an 80 kg male athlete, aged 20 to 29, who plays a contact sport. Such a patient is common in sports medicine practice. Effective dose estimates are shown for conventional radiography (Table 1), CT scans (Table 2) and bone scanning.

Analysis of the effective doses received by Athlete X in Tables 1 and 2 demonstrates some important points:

- CT scanning (particularly in the trunk region) and bone scanning have a significantly higher effective dose than conventional radiography. Although CT scans account for only 11% of the radiological examinations in the USA, CT delivers about 67% of the medical effective dose.
- CT scanning and conventional radiography of the extremities (distant from radiosensitive tissues) are associated with significantly lower effective dose values than investigations in the trunk region.

For a bone scan, the effective dose depends on the activity of the radiophar-
Effective doses and risk estimates for some common investigations in sports medicine*

The effective doses and risk estimates shown in the tables below were calculated for a theoretical male patient (20 to 29 years of age, 80 kg), and are based on the machines and imaging protocols in use at a particular radiology practice in Sydney, Australia in 2003. It should be appreciated that the effective dose can vary significantly between radiological practices because of differences in machinery and imaging protocols. Effective doses and risk estimates were estimated using mathematical modelling developed by the National Radiological Protection Board (NRPB) and International Commission on Radiological Protection (ICRP).

The risk estimate is defined as the risk incurred by this theoretical patient that he will develop a fatal cancer earlier in life than he would otherwise have developed had he not been exposed to a particular effective dose of ionising radiation.

**TABLE 1**

<table>
<thead>
<tr>
<th>Examination</th>
<th>Effective dose per examination series (mSv)</th>
<th>Risk estimate (fatal cancer)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest</td>
<td>0.067</td>
<td>1 in 250 000</td>
</tr>
<tr>
<td>Ribs</td>
<td>0.720</td>
<td>1 in 23 000</td>
</tr>
<tr>
<td>Sternum</td>
<td>1.270</td>
<td>1 in 13 000</td>
</tr>
<tr>
<td>Face/nose/orbit</td>
<td>0.030</td>
<td>1 in 550 000</td>
</tr>
<tr>
<td>Cervical spine</td>
<td>0.034</td>
<td>1 in 480 000</td>
</tr>
<tr>
<td>0.060 (with oblique views)</td>
<td></td>
<td>1 in 260 000</td>
</tr>
<tr>
<td>Thoracic spine</td>
<td>0.730</td>
<td>1 in 22 000</td>
</tr>
<tr>
<td>Lumbar spine</td>
<td>1.630</td>
<td>1 in 10 000</td>
</tr>
<tr>
<td>1.960 (with oblique views)</td>
<td></td>
<td>1 in 8 000</td>
</tr>
<tr>
<td>Pelvis</td>
<td>0.860</td>
<td>1 in 19 000</td>
</tr>
<tr>
<td>Shoulder</td>
<td>0.040</td>
<td>1 in 410 000</td>
</tr>
<tr>
<td>Elbow/forearm</td>
<td>0.003</td>
<td>1 in 5 460 000</td>
</tr>
<tr>
<td>Hand/wrist</td>
<td>0.003</td>
<td>1 in 5 460 000</td>
</tr>
<tr>
<td>Knee</td>
<td>0.020</td>
<td>1 in 820 000</td>
</tr>
<tr>
<td>Leg</td>
<td>0.040</td>
<td>1 in 410 000</td>
</tr>
<tr>
<td>Foot and ankle</td>
<td>0.040</td>
<td>1 in 410 000</td>
</tr>
</tbody>
</table>

**TABLE 2**

<table>
<thead>
<tr>
<th>Examination</th>
<th>Effective dose per examination series (mSv)</th>
<th>Risk estimate (fatal cancer)</th>
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</thead>
<tbody>
<tr>
<td>Brain</td>
<td>2.3</td>
<td>1 in 7 000</td>
</tr>
<tr>
<td>Facial bones</td>
<td>1.0</td>
<td>1 in 16 000</td>
</tr>
<tr>
<td>Chest</td>
<td>4.1</td>
<td>1 in 4 000</td>
</tr>
<tr>
<td>Abdomen</td>
<td>7.6</td>
<td>1 in 2 200</td>
</tr>
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<td>Pelvis</td>
<td>4.5</td>
<td>1 in 3 600</td>
</tr>
<tr>
<td>Cervical spine</td>
<td>4.4</td>
<td>1 in 3 700</td>
</tr>
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<td>Thoracolumbar spine</td>
<td>11.7</td>
<td>1 in 1 400</td>
</tr>
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<td>Lumbar spine</td>
<td>5.2</td>
<td>1 in 3 200</td>
</tr>
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<td>Leg length</td>
<td>1.0</td>
<td>1 in 16 000</td>
</tr>
<tr>
<td>Shoulder</td>
<td>2.0</td>
<td>1 in 8 200</td>
</tr>
<tr>
<td>Elbow</td>
<td>0.5</td>
<td>1 in 33 000</td>
</tr>
<tr>
<td>Wrist</td>
<td>0.5</td>
<td>1 in 33 000</td>
</tr>
<tr>
<td>Knee</td>
<td>0.5</td>
<td>1 in 33 000</td>
</tr>
<tr>
<td>Foot and ankle</td>
<td>0.5</td>
<td>1 in 33 000</td>
</tr>
</tbody>
</table>

**Bone scanning**

For a bone scan, the effective dose for the same theoretical patient was calculated to be 4.6mSv (based on 800 MBq of 99mTc radioisotope injected intravenously). This effective dose confers a risk estimate of inducing a fatal cancer of one in 3500.

* Effective doses and risk estimates are based on the methodology briefly described above. For a more thorough explanation, the reader is referred to reference 10. Methodology is based on practice in 2003 – the transferability of data to 2012 is discussed in the text (see page 74).

The company that revolutionised business technology with bizhub now brings that experience, technology and innovation to the medical market with bizmed™.

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What is the risk of radiation-induced injury?

At the very low levels of radiation used in diagnostic procedures, radiation-induced injury is expressed as the probability of biological and/or genetic effects. Since the first excess cancers were observed following the atomic bombs of 1945, scientists have worked to establish the relation between dose of radiation and the risk of that exposure. The ICRP has reviewed the research and concluded that all radiation exposure, even at an extremely low level, carries a risk.

Using accepted mathematical modelling, risk estimates for Athlete X have been calculated for common sports medicine investigations (see the box on page 39). The term ‘risk estimate’ is defined as the risk incurred by the theoretical patient (Athlete X) that he will develop a fatal cancer earlier in life than he would otherwise have developed had he not been exposed to that particular dose of ionising radiation.

These risk estimates are roughly transferable to adult female patients. However, for paediatric patients, the risk estimates are higher than for adults. This is because young people’s tissues are more radiosensitive and their longer expected life ahead means they carry the risk for a longer time. The ICRP estimates the relative risk to be 1.8 times higher for a child exposed to a particular effective dose of ionising radiation than for a 30-year-old adult.

Uncertainties in the estimation of risk

Risk estimates are derived from epidemiological studies of survivors of the two atomic bombs of 1945. Complex mathematical modelling by the ICRP has estimated and extrapolated the risk estimates to the very low levels of ionising radiation associated with the diagnostic tests stated above, but some uncertainties remain in this process. Indeed, a number of scientists argue that many of the DNA breakages caused by very low levels of radiation are repairable and therefore a ‘threshold’ level of ionising radiation exists, below which there is no risk.

There are no convincing studies in the medical literature which have proven or disproven that individuals exposed to diagnostic radiation from conventional radiography, CT scans or bone scans have developed early fatal cancers or have an increased incidence of birth defects in their offspring. No statistically significant increase in genetic effects have been observed in the children of the atomic bomb survivors of 1945.

It is extremely difficult to demonstrate accurately the causality between low-dose radiation and the risk of inheritable disease. This is because the natural incidence of genetic anomalies in children is high (one in 44 births). The ICRP estimates that 1mSv of radiation exposure may confer an increased risk of a genetic anomaly in one in 77,000 births.

Cumulative effective dose and cumulative risk

It should be appreciated that radiation-induced effects are believed by the ICRP to be cumulative – that is, the dose and risk associated with each new exposure can be added to the dose and risk from any previous exposure(s). The cumulative effective dose and cumulative risk for an individual may become quite significant. Such an individual may be an elite athlete who has a long career and suffers many injuries over a period of years, or a patient with a chronic disease such as rheumatoid arthritis or a chronic respiratory disease.

Dose reduction strategies

The ICRP promotes two important dose reduction strategies for minimising patients’ exposure to ionising radiation:

- Justification
- Optimisation.

It is ethically right to restrict the use of
diagnostic tests that involve ionising radiation to those who will benefit from them. It is incumbent on the treating doctor to balance expected benefits and possible risks for every investigation that is ordered in each patient’s particular case. It should be stated clearly that if the result of performing an investigation on a patient will benefit his or her overall health (in the short and longer term), despite the possible theoretical risk of the radiation exposure discussed, then the investigation is justified.6,11 For example, a whole body bone scan is justified to investigate a patient presenting with multiple joint symptoms suggestive of an inflammatory polyarthropathy or spondyloarthropathy. A CT scan of the lumbar spine is not justified to investigate non-specific mechanical low back pain.

When a patient presents to a radiology practice for an x-ray, CT scan or bone scan, the aim should be to minimise the radiation exposure (as much as is reasonably achievable) without compromising the quality of the diagnostic images. This is the principal of optimisation.6,11 Closer communication, either written or spoken, between the referring doctor and the radiologist/radiographer may result in more limited imaging protocols being adopted and a reduction in the effective dose.1,2,11,20

The principles of justification and optimisation are particularly relevant to paediatric patients.1-4,9-17,21 Whenever possible, diagnostic imaging procedures that do not use diagnostic radiation (MRI and ultrasound) should be used if they can yield the same or even superior information. MRI is decreasing in cost and becoming increasingly available to many patients.

Conclusion

The significant overall health benefits to patients from advances in medical imaging cannot be overstated. However, the small and theoretical risk of a detriment to their health from single or multiple exposures to diagnostic ionising radiation should also be appreciated. Doctors who care for patients who require sports medicine diagnostic procedures involving ionising radiation (and indeed other interventions that involve exposure to such radiation) should have a working knowledge of the effective doses and risk estimates associated with the more common tests. The concepts of justification and optimisation should be appreciated, particularly when caring for paediatric patients. Investigations that do not involve ionising radiation should be considered whenever possible and affordable.

Acknowledgement

The author acknowledges the collaboration of Dr Richard Smart and Dr Julian Thomson, co-authors in earlier published research on this topic.

References are available on request.
A Pain-free, Nature-based Answer to Warts

While the effective treatment of warts remains contentious in parts of the medical fraternity, a new, nature-based, pain-free product is notching up huge successes in Europe.

Researchers at Austin Hospital in Melbourne, Australia, report that amyloid beta deposits accumulate slowly, in fact over decades. These deposits are fragments of protein and the brains of Alzheimer’s patients always contain amyloid beta deposits. On the other hand, not all people who have amyloid beta in their brains will develop AD.

Protracted development
Large quantities of amyloid beta accumulated in the brain over time appear to be key elements for developing AD, although the exact process is not yet fully understood. However, the process is protracted and, it now appears, can take more than twenty years.

In the Austin Hospital study, researchers calculated the rates of amyloid beta build-up, cerebral atrophy and cognitive decline in a control group, in patients with mild cognitive impairment, and in patients with confirmed AD. All 200 participants were assessed at regular intervals by means of neuropsychological examinations, MRI and a Positron Emission Tomography (PET) scan able to detect the brain’s amyloid burden. Although the patients with confirmed AD had higher baseline accumulations of amyloid beta than other participants at the start of the study, 82% of all the participants showed increased accumulation of plaques over the course of the study. Projected rates of accumulation indicated that AD has a prolonged preclinical phase. Deposit build up is a protracted process, without symptoms, apparently reaching a threshold of positivity at about 17 years. Atrophy appeared at a little over four years and memory impairment at approximately three years before dementia’s onset. It may, therefore, take over twenty years for AD to develop.

Time offers hope for intervention
These findings are important because they will help to guide the development of therapeutic interventions. Targeting treatment of amyloid beta deposits early in the process of accumulation might give researchers greater insight into the efficacy of drugs designed to halt the cascade of effects which amyloid beta seems to trigger. A longer period in which to intervene may yield further important findings about how to modify, or even reverse, the progress of AD.

A Pain-free, Nature-based Answer to Warts

While the effective treatment of warts remains contentious in parts of the medical fraternity, a new, nature-based, pain-free product is notching up huge successes in Europe.

A discussion document on general practitioners and warts from the University of Maastricht notes that there is a “lack of clarity” on the best treatment of warts among GPs and that a more uniform approach is required. “A wait-and-see attitude in the treatment of warts is a good first option,” noted the document, authored by Dr Frank Guldermond.

Treatments containing salicylic acid cured around 75% in a review of 52 clinical trials, but warts may often regrow after removal. Treatment with salicylic acid is also reportedly painful and may lead to scarring. Other treatment methods include cryotherapy but this is also reportedly painful, may lead to blistering and has a low success rate.

Bye Wart! comprises only natural active ingredients for the external treatment of warts and has proven to be effective and painless. The cream penetrates the root, weakening the virus and ultimately eliminating the wart – all the while creating a protective layer over the skin and stimulating healing.

Active ingredients include essential oils that disinfect and have a bactericidal effect, red pepper to stimulate blood circulation, urea to regulate the moisture level and promote skin feeding and dimethicone, which casts a protective yet breakable layer on the wart, soothing and elasticising the skin while repelling water.

“Now, there’s no need for anxiety over invasive treatments like laser or other painful surgery. Bye Wart! is quite simply the best, easiest and most importantly, pain-free solution to eradicating warts permanently, and more and more people are discovering this not only in Europe but now in South Africa too,” says Maria Ascencao, spokesperson for suppliers, OTC Pharma.
Seeking Wings, Energy Drinkers Temporarily Raise Their QT Intervals and BP

Energy drinks, which have been linked to deaths and hospitalisations, may boost blood pressure and lead to an erratic heartbeat, a study found.

An analysis of seven previous studies showed the beverages appeared to disturb the heart’s natural rhythm, which over time may lead to an irregular heartbeat, raise blood pressure, and death. The findings were presented at a recent American Heart Association meeting in New Orleans.

The FDA and other regulators have been investigating the drinks made by companies including Germany’s Red Bull after they were linked to hospitalisations and death. The findings mean people, particularly those with pre-existing heart conditions, should be cautious when consuming the drinks, said Sachin Shah, the lead study author.

“We need to look at the effects of long-term energy drinks consumption and see what the consequences are,” said Shah, an assistant professor of pharmacy practice at the University of the Pacific, California. “Everything is good in moderation. Drink them within the limits that have been provided and be vigilant of what else you’re consuming with it.”

No guidelines

The high caffeine content may be causing these heart changes or it could be another ingredient in the drinks, Shah said. The heart changes don’t appear to be permanent, he said.

Energy drinks aren’t bound by FDA guidelines for caffeine in soft drinks because they are often sold as dietary supplements. Regular soft drinks typically can have as much as 71mg of caffeine per can, while caffeine in energy drinks often ranges from 160mg to 500mg the FDA found.

Last month 18 doctors from centres that included Johns Hopkins University recommended that energy drinks should have no more caffeine than regular soft drinks and companies should be required to list caffeine content on labels.

Study findings

Researchers evaluated 93 people from three studies after they consumed one to three energy drinks. They found that the QT interval was 10 milliseconds longer after they consumed the drinks than before.

Shah said doctors become concerned if patients have an extra 30 milliseconds in their QT interval. Prolonging QT over the long term could lead to life-threatening arrhythmias, or irregular heartbeats.

QT Interval

Prof Gordon Tomaselli from Johns Hopkins University explained a typical QT interval is about 400 milliseconds. People who have had a heart attack or heart failure may already have a prolonged QT interval so adding another 10 milliseconds could worsen their health. He suggests that patients with heart problems or who have a family history of heart disease might want to avoid these drinks.

“These energy drinks should be considered like we consider a medication,” he said. “They have a series of pharmacologically active ingredients, natural or not. They need to be treated with that level of respect.”

In another analysis of six trials and 132 patients, the researchers found that systolic BP increased about 3.5 points on average. The findings are particularly concerning for people who consume these drinks frequently and those who have high blood pressure, Shah said.

Zemax has a New Name – Cipla Lisinopril

The name of Zemax 5 and 10 has been changed to Cipla Lisinopril 5 and 10. The new name now appears on the packaging which has the same look as before. The new product is identical, manufactured in the same facility by the same company. However the name change of Zemax 20mg strength is not effective as yet, says Cipla.
Controlled-release Tambocor Now Available in SA

iNova Pharmaceuticals has introduced Tambocor CR, a controlled-release version of the anti-arrhythmic drug Tambocor (flecainide acetate). Indicated for the treatment of atrial fibrillation (AF) in the patient with no structural heart disease, Tambocor has achieved international support as an anti-arrhythmic drug with a heritage spanning 30 years.1-3 Tambocor is the anti-arrhythmic market leader in France, Italy, Germany and Spain.4

New Tambocor CR’s controlled-release formulation offers the potential for improved patient compliance thanks to once-daily dosage.1,5,6 Steady-state plasma concentrations over a 24-hour period ensure better drug coverage and therapeutic success. Furthermore, Tambocor CR helps reduce QRS variation compared with normal Tambocor immediate release tablets.5 With proven efficacy in the prevention of paroxysmal AF recurrences, Tambocor CR is a noteworthy therapeutic choice, said researchers.8

The only flecainide on the SA market, Tambocor is available in four convenient dosage forms:
• Tambocor injection,
• Tambocor 100mg tablets,
• Tambocor CR 100 mg, and
• Tambocor CR 200 mg.

References on request.

Adcock Ingram Receives FDA Accreditation for Its Wadeville Factory

Adcock Ingram says the Center for Drug Evaluation and Research of the US Food and Drug Administration (FDA) has accredited the company’s Wadeville manufacturing facility, located in Germiston. Adcock’s Wadeville pharmaceutical facility is also certified by SA’s Medicines Control Council as a current Good Manufacturing Practice facility.

The FDA accredited Adcock’s Wadeville facility following an inspection of the plant’s manufacturing and testing activities. It has the capacity to produce 6 million litres of syrups and liquids, 500 000 kg creams, 2 billion tablets and capsules. Last August the FDA accepted the company’s research & development establishment.

Adcock’s Wadeville facility is responsible for the manufacture and testing of critical medication, such as anti-retrovirals (ARVs), creams and effervescent. The Wadeville plant will be used in the manufacturing the Department of Health’s ARV tender awarded to Adcock in December 2012.

“The FDA’s acceptance of the Wadeville facility is evidence of the quality of systems and processes at Adcock Ingram’s manufacturing plants – we strive to provide products and services that consistently exceed customer expectations. Accreditation is key to our strategy of building our business outside SA because FDA approval is a pre-requisite to accessing donor funding and so fulfill tenders in the rest of Africa. It’s also a stepping stone to ensuring global best practices across all our production sites” said Adcock Ingram Medical Executive, Dr Abofele Khoele.

Recent Advances in the Treatment of Atrial Fibrillation

Continued from page 23

AV nodal-blocking agents, insertion of a permanent pacemaker followed by AV node ablation has been shown to improve symptoms and quality of life.23 Although this represents a relatively small group, the improvement in symptoms and quality of life can be dramatic. This is particularly the case in the elderly who tend to tolerate pharmacological agents poorly. In patients with heart failure, biventricular pacing may be preferable to right ventricular pacing to prevent further deterioration of left ventricular function.

AF is the most frequent cardiac arrhythmia encountered in clinical practice, occurring in paroxysmal, persistent or permanent forms. Recognition and treatment of underlying risk factors or associated conditions is important in the overall management strategy of these patients. Treatment is directed primarily at symptom control and reduction in stroke risk.

Catheter ablation is an excellent strategy for AF management in patients with paroxysmal AF and limited structural heart disease. It may also play a role in some patients with persistent AF. The development of newer anticoagulant agents may greatly simplify management of stroke risk in at-risk patients.

References are available on request.
MODERN MEDICINE’S CPD JOURNAL PROGRAMME

ANSWER FORM

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

<table>
<thead>
<tr>
<th>SURNAME</th>
<th>INITIALS</th>
<th>YOUR HPCSA REG. NO. MP</th>
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<tbody>
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</tr>
</tbody>
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Postal Address: ________________________________________________________________ Postcode: ________________

Tel: __________________ Fax: __________________

E-mail: ________________________________________________________________

INSTRUCTIONS
1. Use a blue or black pen only.
2. Fill in the appropriate circle completely, i.e. – 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.

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

<table>
<thead>
<tr>
<th>ATRIAL FIBRILLATION</th>
<th>ECG OF THE MONTH</th>
<th>MYTHS IN TYPE 1 DIABETES</th>
<th>NICOTINE DEPENDENCE</th>
<th>RADIATION EXPOSURE</th>
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<td>5 T F</td>
</tr>
</tbody>
</table>

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: ________________________________________________________________

Month of issue APRIL 2013

Please return by July 31, 2013

NAVIGATING CONFLICTS OF INTEREST (2pts)

| 1 T F |
| 2 T F |
| 3 T F |
| 4 T F |
| 5 T F |
QUESTIONS FOR CPD ARTICLES: APRIL 2013
CPD: 5 Regular points; 2 Ethics points

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 April 2013 issue must reach Modern Medicine, PO Box 84622, Greenside 2034 by July 31, 2013.
4. You must score at least 80% 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.

ATRIAL FIBRILLATION (AF) (Pg 12)
1. Atrial fibrillation produces a regular irregular pulse.
2. Most patients newly diagnosed with AF have no discernible risk factors.
3. Patients with a high-risk CHADS2 score (+2) should be treated on prophylactic aspirin.
4. Amiodarone is the most effective anti-arrhythmic drug but has many side-effects.
5. Catheter ablation is offered to those where anti-arrhythmic drug treatment has failed.

ECG OF THE MONTH (Pg 24)
1. The QRS complexes in ECG 1 and 2 are the same. This is therefore a sinus tachycardia and reflects his anxiety state (provided his thyroid gland is normal).
2. The rhythm strip V1 at (at the bottom) shows an alternating size of the QRS complex. This indicates the tachycardia is arising in the ventricles.
3. There are no P-waves seen prior to the QRS indicating that the tachycardia arises in the ventricles i.e. ventricular tachycardia.
4. This is a supraventricular tachycardia that has not responded to betablockers, thus a more powerful anti-arrhythmic drug like Amiodarone should be used.
5. The QRS complexes are normal thus this is a supraventricular tachycardia (SVT). The absence of P-waves preceding each QRS is typical of many SVTs.

MYTHS IN TYPE 1 DIABETES (Pg 26)
1. Type 2 diabetes in childhood usually co-exists with obesity.
2. First-line treatment for LADA is an oral glycaemic agent.
3. Type 1 diabetics with nephropathy usually die from end-stage renal failure.
4. The glycaemic target should be independent of the individual diabetic’s lifestyle.
5. Most of the medical problems occurring in diabetics can be handled by GPs.

NICOTINE DEPENDENCE (Pg 34)
1. Nicotine dependence is gradually acquired of years of smoking.
2. Rapid metabolisers of nicotine are more easily addicted.
3. Smoking activates the mesolimbic pathway causing release of dopamine.
4. Low-level smoking (1-4/day) carries minimal health risks.
5. Cue-induced cravings are alleviated by the nicotine patch.

RADIATION EXPOSURE (Pg 39)
1. Diagnostic radiation of bone marrow in the extremities is more dangerous than the trunk.
2. The ‘Effective Dose’ of radiation integrates radiation absorbed with organ sensitivity.
3. Children carry about twice the relative risk of radiation damage compared to adults.
4. There is strong statistical evidence that diagnostic radiation causes premature cancer.
5. CT scan of lumbar spine is justified to investigate non-specific, mechanical low back pain.

ETHICS (Pg 10)
1. Trivial gifts from the pharmaceutical industry have minimal effect on prescribing patterns.
2. Referrals between specialists are an important source of conflicts of interest.
3. The major promotional expense of the pharmaceutical industry is advertisements in medical journals.
4. Concerted efforts to avoid COIs are usually in place when developing Clinical Practice Guidelines.
5. Clinicians should not accept medical samples under any conditions.

See answer form opposite

JANUARY WINNER: CONGRATULATIONS TO DR AG STONER OF WOODBRIDGE ISLAND WHO WINS THE OTC PHARMA HAMPER!
<table>
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<th>Date</th>
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<th>Venue</th>
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<td>7 - 9 May</td>
<td>Africa Health Exhibition and Congress</td>
<td>Gallagher Convention Centre, Midrand, JOHANNESBURG</td>
<td>Informa Exhibitions • +97-14-336-5161 <a href="mailto:jenny.watson@informa.com">jenny.watson@informa.com</a></td>
<td><a href="http://www.africahealthexhibition.com">www.africahealthexhibition.com</a></td>
<td>CPD (13), EXHIBITION, 10-50 Speakers</td>
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<td>7 - 11 May</td>
<td>CDE - Centre for Diabetes and Endocrinology: 5-Day Advanced Course in Diabetes Care</td>
<td>81 Central Street, Houghton, JOHANNESBURG</td>
<td>Centre for Diabetes and Endocrinology • 011-712-6000 <a href="mailto:john@cdecentre.co.za">john@cdecentre.co.za</a> or <a href="mailto:michael@cdecentre.co.za">michael@cdecentre.co.za</a></td>
<td><a href="http://www.cdecentr.co.za">www.cdecentr.co.za</a></td>
<td>CPD (30), EXHIBITION, 10-50 Speakers</td>
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<td>10 - 11 May</td>
<td>SAFSA - Foot Surgeons Association Biennial Foot Surgery Congress</td>
<td>Southern Sun - Oliver Tambo International Hotel, Airport Grounds, Kempton Park, JOHANNESBURG</td>
<td>Hendrika van der Merwe • 021-919-4227 <a href="mailto:footcongress@iafrica.com">footcongress@iafrica.com</a></td>
<td><a href="http://www.footcongress.co.za">www.footcongress.co.za</a></td>
<td>CPD, EXHIBITION, 50-100 Speakers</td>
</tr>
<tr>
<td>10 - 12 May</td>
<td>SASDA/VSSA - 6th Annual National Congress of Society for Dermatological Surgery and Vitiligo Society</td>
<td>The Boardwalk Hotel &amp; Convention Centre, PORT ELIZABETH</td>
<td>Eastern Sun Events • 041-374-5654 • <a href="mailto:sasds@easternsun.co.za">sasds@easternsun.co.za</a></td>
<td><a href="http://www.sasdscongress.co.za">www.sasdscongress.co.za</a></td>
<td>CPD, EXHIBITION, 50-100 Speakers</td>
</tr>
<tr>
<td>14 - 16 May</td>
<td>CMASA - Case Manager Association - Third Annual National conference</td>
<td>Lagoon Beach Hotel, CAPE TOWN</td>
<td>NC Connect • 082-927-1442 • <a href="mailto:sharon@ncconnect.co.za">sharon@ncconnect.co.za</a></td>
<td><a href="http://www.casemanagement.co.za">www.casemanagement.co.za</a></td>
<td>EXHIBITION, 10-50 Speakers</td>
</tr>
<tr>
<td>16 - 18 May</td>
<td>O&amp;G - Obstetrics and Gynaecology Update</td>
<td>CSIR Convention Centre, PRETORIA</td>
<td>Yvonne Fernandes • 011-768-4355 • <a href="mailto:yvonne@londocor.co.za">yvonne@londocor.co.za</a></td>
<td><a href="http://www.sasog.co.za">www.sasog.co.za</a></td>
<td>CPD, EXHIBITION, 10-50 Speakers</td>
</tr>
<tr>
<td>18 May</td>
<td>SASLHA - Speech-Language-Hearing Association AGM Seminar</td>
<td>Senate Chamber, Westville Campus, University of kwazulu Natal, DURBAN</td>
<td>SASHLA • 086-111-3297 • <a href="mailto:admin@sashla.co.za">admin@sashla.co.za</a></td>
<td><a href="http://www.sashla.co.za">www.sashla.co.za</a></td>
<td>CPD (6), 10 Speakers</td>
</tr>
<tr>
<td>16 - 19 May</td>
<td>SATS - Theatre Sister Congress</td>
<td>NH The Lord Charles Hotel, SOMERSET WEST</td>
<td>Lalique Smit • 051-436-8145 • <a href="mailto:congress@internext.co.za">congress@internext.co.za</a></td>
<td><a href="http://www.theatrenurse.co.za">www.theatrenurse.co.za</a></td>
<td>EXHIBITION, 10-50 Speakers</td>
</tr>
<tr>
<td>20 - 21 May</td>
<td>Professional Beauty Durban</td>
<td>Sibaya Casino &amp; Entertainment Kingdom, DURBAN</td>
<td>Professional Beauty • 011-781-5970 • <a href="mailto:belinda@probeauty.co.za">belinda@probeauty.co.za</a></td>
<td><a href="http://www.probeauty.co.za">www.probeauty.co.za</a></td>
<td>EXHIBITION, No Speakers</td>
</tr>
<tr>
<td>23 - 26 May</td>
<td>CMT (Continuing Medical Training) Dental Conference 2013 No. 1</td>
<td>Kopusong Hotel, Benoni, JOHANNESBURG</td>
<td>Continuing Medical Training • 011-849-8966 • <a href="mailto:cmt@iburst.co.za">cmt@iburst.co.za</a></td>
<td><a href="http://www.cmtcc.co.za">www.cmtcc.co.za</a></td>
<td>CPD, 10-50 Speakers</td>
</tr>
<tr>
<td>24 - 26 May</td>
<td>FCPSA - 2nd Annual Congress of the Faculty of Consulting Physicians</td>
<td>Wild Coast Sun, SOUTH CAPE</td>
<td>Stacey Coetzee / Dine Poulton • 011-768-4355 <a href="mailto:stacey@londocor.co.za">stacey@londocor.co.za</a> / <a href="mailto:dine@londocor.co.za">dine@londocor.co.za</a></td>
<td><a href="http://www.physician.co.za">www.physician.co.za</a></td>
<td>CPD, EXHIBITION, 10-50 Speakers</td>
</tr>
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