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NEWSPAPER POST

TheSynapse

The Medical Professionals' Network

MEDICAL IMAGING

Imaging Small Bowel Disease

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The small intestine is the most difficult part of the gastrointestinal tract to evaluate due to its length, complex loops and its distance from the mouth and anus. Conventional endoscopic techniques such as push enteroscopy (reaches up to 120cm beyond the ligament of Treitz) and colonoscopy with ileoscopy do not reach most of the small bowel. A complete direct endoscopic evaluation was previously possible only with intraoperative endoscopy.

Non-invasive small bowel evaluation is possible with indirect methods such as barium examination, computed tomography (CT), and magnetic resonance (MR) imaging. Suboptimal bowel distension and overlapping bowel loops make radiologic evaluation challenging. Capsule endoscopy, introduced in 2000, is a new diagnostic tool that makes use of a swallowable video capsule, which, unlike conventional endoscopy, allows visualisation of the entire small bowel and does not require sedation. The endoscopy capsule measures 26 x 11 mm and weighs 4g (Figure1).

It contains a video camera, light source, radio transmitter, and batteries. Eight sensors attached to the patient's abdomen receive the images, which are stored on a portable hard disk recorder strapped around the patient's waist.The capsule acquires two colour images per second with a resolution of 256 x 256 pixels. The sensors also allow a rough approximation of the capsule location inferred from the time of intestinal transit. After 8 hours, the data stored on the recorder is viewed on a computer workstation. The single-use capsule is excreted naturally, usually within 8–72 hours, but sometimes after as along as 2 weeks. The main indication for capsule endoscopy is unexplained intestinal bleeding or blood loss of indeterminate aetiology. Detection of early Crohn's disease may be challenging with radiologic techniques, and more easily achieved with capsule endoscopy. Additional potential indications for capsule endoscopy may include evaluation of patients with hereditary

Figure 1: *The endoscopy capsule measures 26x11mm.*

polyposis syndromes, small bowel damage induced by nonsteroidal anti-inflammatory drugs (NSAIDs), chronic diarrhea, or chronic abdominal pain. The main disadvantage of capsule endoscopy is the inability to definitively localize or treat small bowel lesions. A rough approximation of capsule location is based on time, however this is prone to inaccuracy due to differences in small bowel transit time or variant anatomy. Capsule endoscopy cannot be used in cases of intestinal strictures or obstruction; this includes more advanced cases of Crohn's disease due to intestinal strictures.An initial radiographic study such as a small bowel barium enema, barium follow-through or CT with bowel contrast is recommended for suspected small bowel disease; if negative, and patency of intestinal tract has been confirmed, capsule endoscopy may be performed. The following paragraphs describe the most common small intestinal diseases, in which this investigative approach has been shown to be of value.

continues on page 2

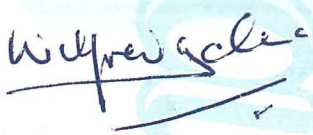
Editor's Word

Welcome to the last issue of TheSYNAPSE Magazine for 2006. In this issue we continue with our focus on Dermatology with articles on the Recent Advances and Treatment of Melanoma Skin Cancer and an interesting review article on Aesthetic Dermatology. Two small articles on Support Groups in Dermatology complement these articles.

We continue with our focus on Medical Ethics with Part 1 of an article on Informed Consent. This issue features the third and final part of the article on Stem Cells – What, Why, Whereabouts and When?

Probably for the first time in local medical magazines, we have an interesting contribution on Medics in Movies and Television. Other articles include Advances in Oral Hormonal Contraception as well as the regular articles on Medical Imaging as well the Update on Avian Influenza.

We would like to thank all contributors who have made TheSYNAPSE a success during 2006 and wish you all a Very Happy Christmas and a Fantastic New Year.



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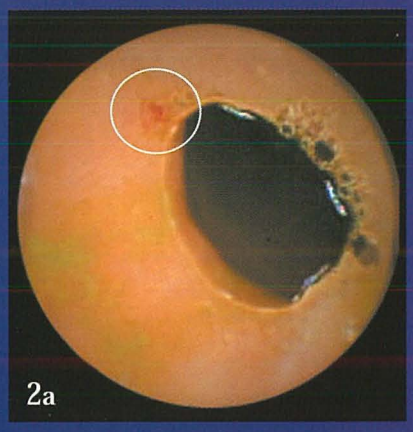
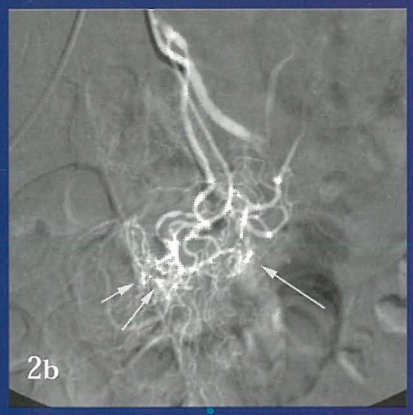
Imaging Small Bowel Disease





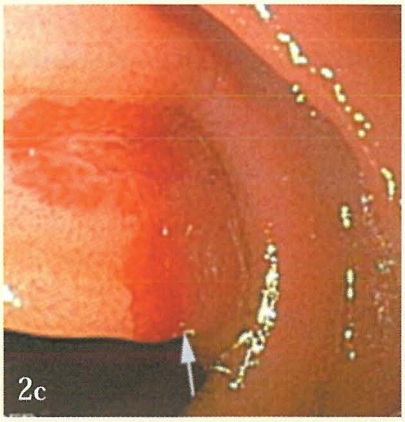


Figure 2: *Bleeding angioectasia in a patient with obscure gastrointestinal bleeding. (a) Capsule endoscopic image shows angioectasia (encircled). (b) Angiogram shows angioectasia (arrows) in the jejunum. (c) Intraoperative endoscopic image helps confirm bleeding angioectasia in the jejunum (arrow).*

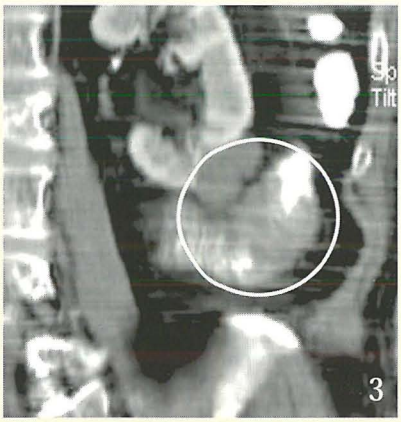
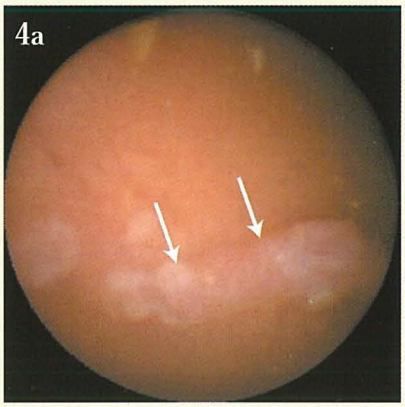


Figure 3: *Gastrointestinal stromal tumour. Coronal CT scan shows a gastrointestinal stromal tumour (encircled), a finding that was confirmed surgically. Capsule endoscopy was non-diagnostic due to retained food.*



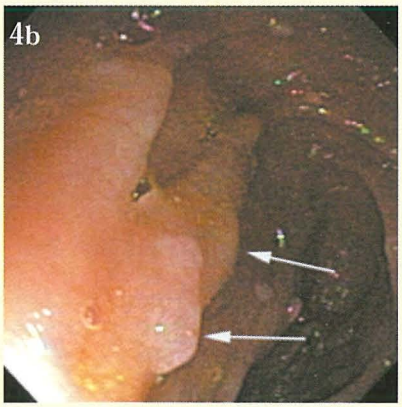


Figure 4: *Familial polyposis in a patient with negative findings at small bowel follow-through examination and CT. Capsule endoscopic (a) and push endoscopy (b) images show multiple small polyps in the proximal small bowel (arrows).*

Arteriovenous malformations, also referred to as angiodysplastic lesions, telangiectasias, or angioectasias, are the most common abnormality accounting for obscure gastrointestinal bleeding.

They occur more frequently with increasing age and are seen at endoscopy as spider-like lesions (Figure 2). They are visible on angiography and CT angiography during a bleeding episode. These lesions can be treated with cauterization or hormone therapy. Small bowel tumours (Figures 3-5) are a less common, accounting for only 1.4% of gastrointestinal cancers.

continues on page 20

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NOVARTIS

Recent advances in treatment

by Joseph L Pace
MD FRCP(Edin) FRCP(Lond) F Coll Phys (Phila) FAAD

1. Introduction

NON MELANOMA SKIN CANCER (NMSC)

1. Actinic (Solar) Keratoses now considered by many authorities to represent a superficial squamous cell carcinoma
2. Bowen's disease
3. Basal cell carcinoma
4. Squamous cell carcinoma

A world wide epidemic of tsunami proportions of NMSC continues, in part due to the:

- *aging of the world's population;*
- *increased frequency of early childhood sunburns;*
- *increased exposure to UV light;*
- *fashion trends (arsenic has made something of a comeback being found repeatedly in some alternative medicine preparations from 3rd world countries but now also available in the West);*
- *increased leisure, sun-holidays;*
- *depletion of ozone layer;*
- *and, more recently, immunosuppression (eg. medication following organ transplant and AIDS).*

Squamous cell carcinoma has increased 30%, whilst Basal cell carcinoma have increased 75% over 10 years in South Wales. It is also likely that similar increases have occurred in other parts throughout the Western world.[1]

Clinical appearance

Actinic keratoses

Multiple scaly pigmented or erythematous patches on exposed areas in middle aged or elderly subjects especially those with an outdoor occupation, where the condition may occur even earlier. *Actinic keratosis* may develop into invasive squamous cell carcinomas.

Bowen's disease

Essentially a *squamous cell carcinoma* in situ, often limited to a single patch of 'eczema' that fails to resolve with treatment.

Squamous cell carcinoma

May follow *Actinic keratosis* or Bowen's Disease or present itself anywhere on skin/mucous membranes with squamous epithelium. An ulcer with an indurated border may occur and causative factors also include scarring from burns, lupus erythematosus and lupus vulgaris. Certain genodermatoses such as xeroderma pigmentosum predispose to *squamous cell carcinoma* as also organ recipients, who have an eighteen fold risk of developing *squamous cell carcinoma*. Metastases from *squamous cell carcinoma* are rare on sun damaged skin but are an important consideration in *squamous cell carcinoma* on scars, mucous membranes, the lip and in organ recipients.

Basal Cell carcinoma

Presents as a pearly nodule or ulcer on hairy skin. It does not occur on mucus membranes or palms and soles except in the rare Gorlin syndrome.

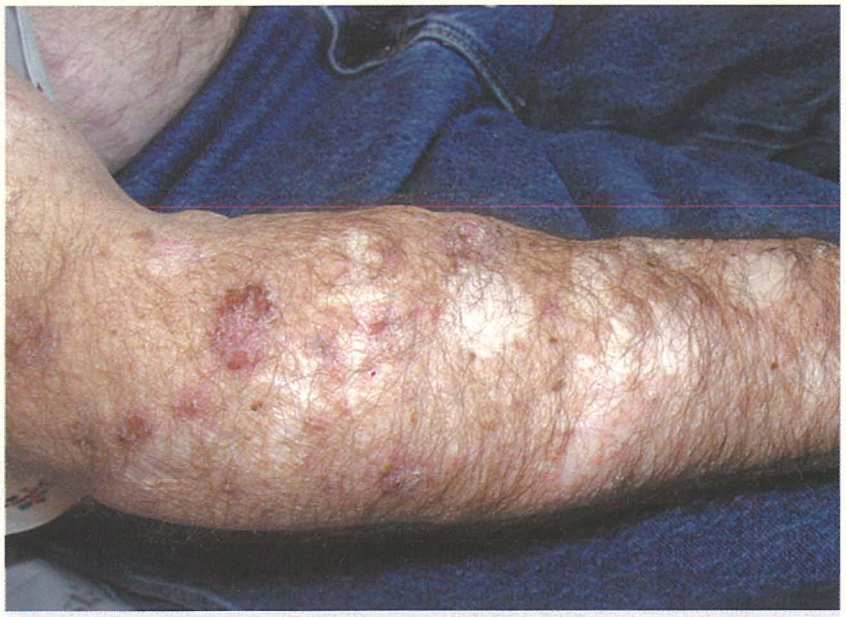

Figure1: *Actinic keratoses and intra epidermal carcinoma*

2. Management

Prevention: sun avoidance from 12pm - 3pm period and protection with sun blocks and sun protective clothing.

Surgical treatment

- Excision.
- Moh's surgery is a highly effective very time consuming method of removing layer after layer and submitting to pathology immediately, with layers of skin being removed until borders are completely clear. Time factor makes it in practical for most centers outside the US.

Non-surgical treatment

- Radiotherapy
- Cryotherapy – liquid nitrogen (-196°C) is useful especially for smaller lesions. Can be painful and requires repeated applications.
- Topical – 5-Fluorouracil cream – works well for small superficial lesions but can cause intense inflammatory reaction for weeks and may be disliked by patients.

What's new

Topical nonsteroidal anti-inflammatory agents for actinic keratoses

Published clinical trials have shown that a topical gel containing 3% diclofenac with 2.5% hyaluronic acid may be used for treating actinic keratoses. The 2.5% hyaluronic acid

# of non melanoma skin cancer

(excipient) delays the transcutaneous uptake of diclofenac, leading to higher concentrations in the epidermis.[2]

Imiquimod

This drug has been recently approved for the treatment of actinic keratoses and superficial basal cell carcinoma. In superficial *Basal Cell carcinoma,* it should be used once daily 5 days each week for 6 weeks. In nodular *Basal Cell carcinoma,* curette lesion first. It also works well on all superficial lesions but can cause marked inflammatory reaction.[3]

Photo dynamic therapy

Following selective accumulation of photoactive porphyrins in neoplastic tissue, red light in presence of oxygen generates reactive oxygen species, which damage cellular membranes, particularly in mitochondria, and lead to cell death. Healthy surrounding tissue that has not accumulated photoactive porphyrins remains undamaged.

Photo dynamic therapy offers may advantages including its non-invasiveness and its ability to treat multiple lesions simultaneously and is, therefore, an interesting alternative for treating certain skin malignancies.

Photo dynamic therapy

Treats both Actinic Keratoses and Basal Cell Carcinomas;

Targets only diseased cells;

Non invasive, minimal scarring;

Fast healing;

Side effects minimal and transient;

High patient preference.

Photo dynamic therapy is simple to perform, is well tolerated, shows excellent clinical results and superior cosmetic outcome, and is therefore preferred by the patients. It has been available in Malta for the past 2 years. Its current use includes:

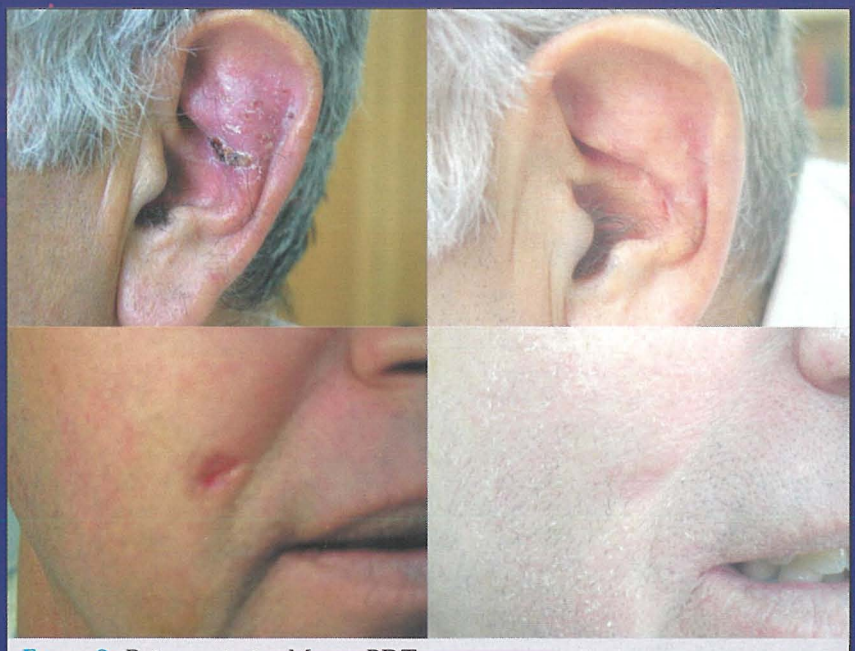

Figure 2: *Before and after Metvix-PDT*

Actinic Keratoses resistant to cryotherapy/5 FU/Imiquimod

Superficial Basal Cell Carcinomas and nodular Basal Cell Carcinomas which are difficult to treat surgically or where surgery is undesirable.

Current practices to follow Photo dynamic therapy with Imiquimod as a 'mopping up operation'.

Oral retinoids

Useful in patients with recurrent or multiple lesions but lipid levels must be checked regularly. Not suitable for use in summer months.

Conclusion

Surgery remains the gold standard of treatment but ... the possible reliable and effective non-surgical alternatives are growing fast and will become increasingly relevant and sought after in view of increasing age of patients and consequent poor anaesthetic risk, desire to avoid surgery and wish to achieve best cosmetic results.

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Malta Eczema Society (MES)

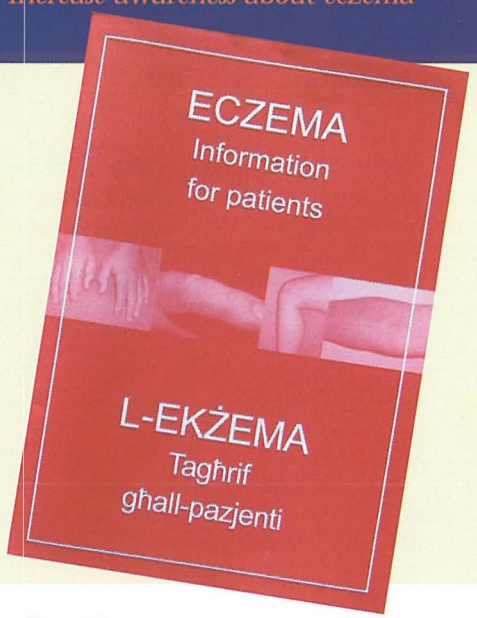
by **Michael Boffa**
Consultant Dermatologist & President, Malta Eczema Society

The MES was set up in 2001 to help patients with eczema and their families. The society aims to help by providing support, information and practical advice via public talks and other activities, to represent the interest of members with government and other authorities and to increase awareness about eczema and the problems it may cause.

A recent survey of schoolteachers in Malta undertaken by the MES confirmed widespread misconceptions about the condition - for instance more than 10% of participating teachers wrongly thought that eczema is contagious and many did not know about its career implications.

The MES has lobbied with the Maltese Health Authorities regarding entitlement for free medication for eczema sufferers. At present eczema sufferers are not eligible for free medication no matter how severe and chronic their condition is because eczema is not included in the Schedule V list of chronic diseases. The MES feels that the present system is unfair and discriminatory and requests that eczema sufferers are given the assistance they deserve.

The MES has recently published a patient information booklet about eczema, in English and Maltese, kindly sponsored by Novartis Pharma Malta. Free copies and information on joining the MES may be obtained from Treasurer Mrs M Bongalais (Tel 21 435649) or other committee members: Mrs A Baldacchino (Tel 21 386 850), Mrs J Borg (Tel 21 436 550), Mr H Debono (Tel 21 335 140) or Mrs J Vella (Tel 21 637 007).



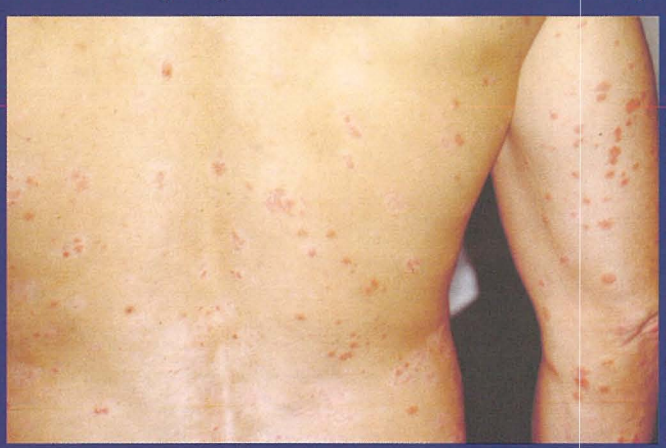
Psoriasis Association Malta

It is a fact that people suffering from Psoriasis face on a daily basis a lot of challenges not only in accepting and treating this condition but also facing people who have never heard of the word Psoriasis let alone know what it is.

With this in mind, the Psoriasis Association Malta has been setup with two main objectives.

1. Increase awareness of this condition among the general public, focusing on informing what Psoriasis is and that it is not contagious.

2. Provide psychological support to psoriasis sufferers through the services of a psychologist and be a main source of information through publications and seminars aimed at Psoriasis patients.



In October 2005, the Association launched a poster awareness campaign titled 'I know what Psoriasis is...do you?'. It has also published a Maltese story book narrating the story of Mark, a child psoriasis sufferer and his trials and tribulations at school. This month, the book will be distributed to all secondary schools in Malta with the aim at increasing awareness on this condition.

The Association has recently launched the 'Psoriasis Association Malta Bulletin', a newsletter which will be distributed on a quarterly basis to all its members. An informational leaflet 'Psorjasi: il-fatti' is also available on request.

Furthermore, the Association is in the process of publishing a handbook on Psoriasis and Psoriatic Arthritis which will include a number of articles of interest and a guide of treatments available in Malta.

The Association's committee is made up of psoriasis sufferers and persons who have direct contact with psoriasis patients. Membership with the Psoriasis Association Malta is Lm 3 a year.

For further information contact Lucienne on 21437606 or Therese on 21416288 or email info@pam.org.mt. The Association also has a website at www.pam.org.mt.

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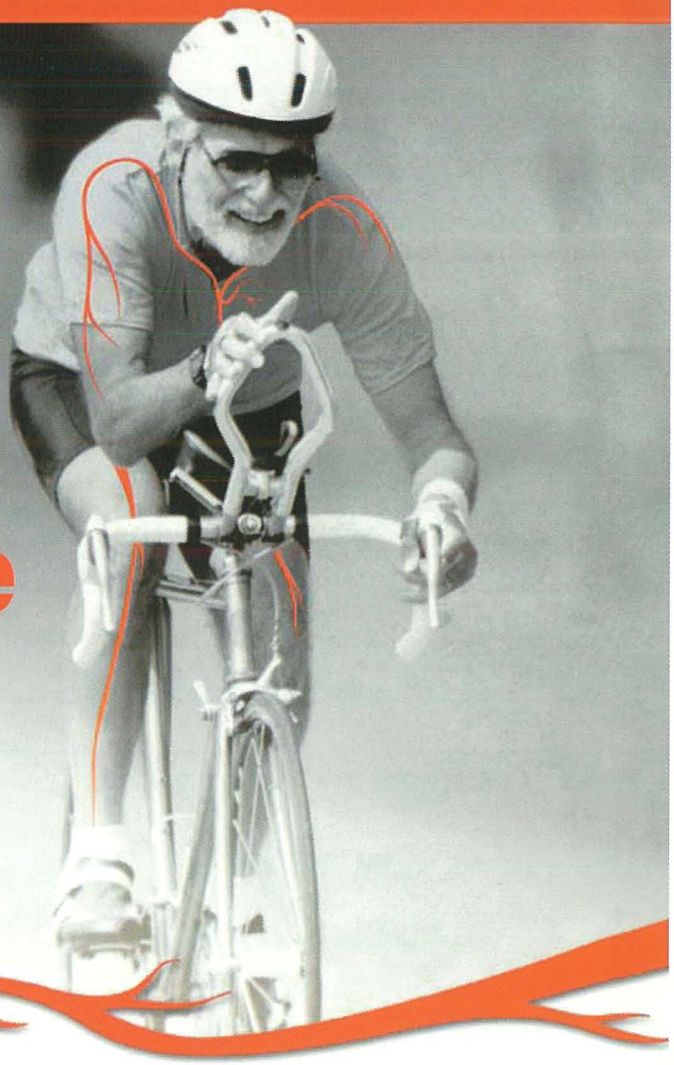

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Contraindications: Known hypersensitivity to the components of this product, pregnancy.
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Adverse reactions: Generally similar in incidence to patients receiving placebo in placebo-controlled clinical trials, e.g. headache, dizziness, fatigue. The observed incidence of cough with valsartan in controlled clinical trials was significantly less than that observed with ACE inhibitors and similar to that seen with placebo. The most common adverse reactions are: viral infections, postural dizziness (reported in heart failure indication), orthostatic hypotension (reported in heart failure indication), neutropenia, upper respiratory tract infection, pharyngitis, sinusitis, hyperkalaemia (reported in post-myocardial infarction and heart failure indications), insomnia, libido decrease, vertigo, hypotension (reported in post-myocardial infarction indication and uncommon in heart failure indication), cough, diarrhoea, abdominal pain, back pain, fatigue, asthenia, oedema, syncope (reported in postmyocardial infarction indication), cardiac failure (reported in post-myocardial infarction indication). Very rare adverse reactions but potentially serious are: thrombocytopenia, hypersensitivity including serum sickness, vasculitis, angioneurotic oedema (uncommon in post-myocardial infarction indication), renal impairment (common in heart failure indication), renal insufficiency, acute renal failure (uncommon in post-myocardial infarction indication).
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Precautions/Warnings: Risk of hypotension in sodium- and/or volume-depleted patients, Caution is advised when administering Co-Diovan to patients with renal artery stenosis, renal and liver disease. Disturbance of serum electrolyte balance. Concomitant treatment with potassium-sparing diuretics or potassium supplements may increase potassium levels. Caution if combined with other antihypertensives or lithium (serum lithium monitoring). Caution in driving or operating machinery. Avoid use while breast-feeding.
Adverse reactions: headache, dizziness, fatigue. For the hydrochlorothiazide component,
other reported adverse reaction s include hypokalaemia, hyperuricemia and other electrolyte disturbances, postural hypotension and rise in blood lipids. Rare: jaundice, cardiac arrhythmias, blood dyscrasias. Very rare: vasculitis, pancreatitis, pneumonitis, pulmonary edema. Post-marketing experience revealed very rare cases of hypersensitivity reactions (e.g. angioedema), and impaired renal function, myalgia and thrombocytopenia.
Laboratory findings: Neutropenia, elevations in creatinine and blood urea nitrogen.
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GOOD FATS vs. BAD FATS

The right fats are a vital part of a healthy diet

Contrary to popular belief, not all fats are bad for us. In fact, certain types of fats are essential to a healthy diet and to maintaining a healthy heart

The dangers of bad fats

It is important to be aware of how diet and lifestyle can help to prevent heart problems which occur when fat builds up in the arteries causing dangerous blockages. An estimated 16.7 million, 29.2% of total global deaths, are a result of the various forms of cardiovascular disease (CVD) http://www.who.int/dietphysicalactivity/publications/facts/cvd/en/. High cholesterol levels are a major risk factor for heart disease and the type of fat you eat affects your cholesterol.

The benefits of good fats

It's hard to shake the image of all fats being unhealthy but 'good' fats, which are monounsaturates and polyunsaturates, including essential (cannot be made by the body and therefore must come from the diet) fatty acids omega 3 and omega 6, help to keep your heart and blood vessels healthy and help to lower cholesterol.

According to a number of nutritional recommendations, total fats should make up no more than 30 per cent of total energy intake. http://www.who.int/hpr/NPH/docs/who_fao_expert_report.pdf Good fats also add nutrients to the foods we eat, help us to absorb vitamins and even provide flavour to foods.

Where to find good fats

Good fats can be found in margarine, sunflower spreads and oils, salad dressings and plant sources such as rapeseed and soya bean oil, walnuts and green vegetables as well as oily fish, such as mackerel and salmon.

Reducing your intake of bad fats

As well as increasing good fats, it is vital to reduce the consumption of bad fats in our diet to maintain a healthy heart. Saturated fats are the bad kind. Fatty meats, cheese, cakes, pastries and butter can raise your cholesterol levels, and high cholesterol levels can lead to heart disease.

A study in Poland demonstrated that a significant reduction in heart disease risk could be seen with a higher consumption of oil based products. In the early 1990s the Polish government cut subsidies for saturated fats from dairy and animal sources, initiating a switch to vegetable based sources.

Between 1991-1999, 7 per cent less saturated fat (bad fat) and 57 per cent more polyunsaturated fats (good fat) were consumed by the Polish population as a result. By 2002, deaths from coronary heart disease had dropped by over a third in the 45-64 age group – a 38 per cent drop for men and a 42 per cent drop for women. This showed a direct improvement in the health of the population, suggesting that the reduced risk of cardiovascular disease could be linked to the reduction in bad fats and thereby lower cholesterol levels.[1]

Speaking about the importance of good fats in the diet, Professor E. Schaefer of the University of Boston, USA, stated, "The replacement of animal fat with vegetable oils has a very profound effect. More effect that you would expect from just the lowering of cholesterol. Some studies, the biggest was a study in a Finnish mental hospital, where just replacing butter with margarine and whole milk with skim milk lowered heart disease mortality by 50%".

Steps to eat more good fats

You can take some simple steps to introduce more good fats into your diet. Natural does not always translate to good for you - replacing 30g of butter per day with margarine such as Flora could reduce the risk of heart disease by 10%.[2]

Flora spreads have been developed especially to fit into a healthy diet as they are low in saturated fat, high in polyunsaturated fats and contain high levels of the important fatty acids omega 3 and omega 6 – all helping to reduce the risk of cardiovascular disease. Try using these spreads in sandwiches, on toast and when baking to help bolster your intake of good fats. Because of the health benefits of Flora spreads in reducing the risk of cardiovascular disease, as part of a healthy balanced diet, it is better to use a Flora spread than not spread at all.

Cholesterol can also be lowered through other dietary approaches which do not rely solely on the replacement of saturated bad fat with good fats. There is strong evidence to show that plant sterols can significantly lower cholesterol, thereby reducing the risk of developing heart disease.

Plant sterols, the active ingredient in Flora pro.activ spread, milk and mini drinks, are clinically proven to significantly lower LDL cholesterol by 10-15%, as part of a healthy diet.

In fact, Flora pro.activ mini-drink contains the same amount of plant sterols as you would get from 50 portions of broccoli, 150 apples or 425 tomatoes!

In addition to switching spreads, try to eat at least two fish meals per week (preferably oily fish which contain high levels of omega 3) and switch to low fat milk and cheeses. World Health Organisation guidelines also encourage you to control your intake of fat and to eat more fruit and vegetables, take more regular exercise and limit your alcohol intake – all of which will contribute to keeping your heart healthy.

References

1. Zatonski A, Willett W. Changes in dietary fat and declining coronary heart disease in Poland: population based study. *BMJ* 2005; 331:187-8.
2. Zock PL, Katan MB. Butter, margarine and serum lipoproteins. *Atherosclerosis* 197; 131(1):7-16.

Just One a Day.
Such a convenient choice for your cholesterol patients.

- *One Becel pro·activ yoghurt mini drink (100 g) contains 2g of plant sterols. Clinical studies have proven that this is the optimal dose to achieve substantial cholesterol-lowering* [1, 2].
- *Plant sterols block the absorption of cholesterol resulting in dramatic lowering of the LDL-cholesterol level* [3, 4].
- *For best results consume with a meal, as part of a healthy diet.*

[1] Law M. BMJ 2000; 320: 861-864.
[2] Katan MB et al. Mayo Clin Proc 2003; 78: 965-978.
[3] Jones PJ et al. J Lipid Res 2000; 41: 697-705.
[4] Pouteau EB et al. Eur J Nutr 2003; 42: 154-164.

In order to reduce cholesterol levels and achieve a healthier heart, World Heart Federation recommend taking regular physical activity and eating a balanced diet rich in fruit and vegetables, low in saturated fats and including foods that contain plant sterols.

WORLD HEART FEDERATION®
Working together with Becel to help improve heart health

To learn more and apply for patient information packs, visit www.becel.de, phone 08000-72 52 35 or send an email to proactivscienceinfo@unilever.com.

NSAIDs and cardiovascular events – frequently asked questions

What caused the concern about non-steroidal anti-inflammatory drugs (NSAIDs) and the risk of serious clinical events related to cardiovascular disease (CVD), such as heart attack or stroke?

In September 2004, Merck voluntarily withdrew Vioxx® (rofecoxib), a cyclooxygenase (COX-2) inhibitor, from the market after findings from clinical trials indicated that the drug increased the risk of CVD events, including heart attack and stroke, compared with placebo. A subsequent combined analysis of rofecoxib studies suggested that the drug increased the risk of heart attack 2.3-fold. Further studies have since emerged suggesting that other COX-2 inhibitors, such as celecoxib, could also increase the risk of CVD events, as could the more traditional types of NSAID, such as ibuprofen.

How might NSAIDs increase the risk of CVD events?

COX enzymes play a range of roles in the body, including influencing the process of pain perception, protecting of the lining of the stomach and digestive tract, and maintaining the function of blood vessels.

In the perception of pain, two main COX enzymes are involved: COX-1 and COX-2. Non-selective NSAIDs, such as ibuprofen, affect both enzymes. However, the COX-1 enzyme also plays a role in protecting the lining of the stomach and digestive tract, which has a direct correlation between COX-1 inhibition and increased risk of gastrointestinal complications. This situation led to the development of selective COX-2 inhibitors, which could block pain signals, but would not affect the digestive tract.

However, both COX-1 and COX-2 also play roles in maintaining the function of blood vessels and in other processes important for the function of the heart, such as effects on the kidney that ultimately increase blood pressure. It is the consequences of blocking the effects of COX enzymes on these important biological pathways that leads to the increase in the risk of CVD events.

What types of CVD events are more likely if NSAIDs are taken?

NSAIDs have been associated with an increased risk of CVD events or with the worsening of the CVD risk profile. NSAIDs are reported to increase the risk of congestive heart failure, especially in people with pre-existing heart disease. NSAIDs also increase the risk of heart attacks, stroke and death from cardiovascular events. Furthermore, NSAIDs can increase blood pressure both through actions on the kidney that lead to the release of hormones that narrow the blood vessels, and through reducing the efficacy of some antihypertensive agents.

Do NSAIDs affect the efficacy of CVD medicines?

There are at least two situations where evidence suggests NSAIDs may reduce the efficacy of CVD medicines. The first is that NSAIDs, in particular ibuprofen, may reduce the protective effect of low-dose aspirin. In an analysis of a subset of individuals involved in the large Physicians Health Study, the long-term use of NSAIDs (>60 consecutive days) negated the protective effects of low-dose aspirin. A further study monitored the effects of taking or not taking NSAIDs in combination with low-dose aspirin in 7,107 patients with known CVD. After 3.3 years of monitoring, those taking ibuprofen were 73% more likely to die from CVD events than those not taking ibuprofen.

NSAIDs can also interfere with the efficacy of some widely-used antihypertensive agents. The effects are greatest when NSAIDs are given in combination with angiotensin-converting enzyme (ACE) inhibitors and -blockers. This is because these agents rely on increasing the production of prostaglandins to decrease blood pressure and NSAIDs act in the opposite way to block production of prostaglandins.

Does paracetamol increase the risk of CVD events?

Paracetamol has a different mode of action to NSAIDs and is unlikely to influence heart function by the same mechanisms as NSAIDs. Therefore, paracetamol may be considered first choice for patients with, or at risk of, cardiovascular disease.

Why does paracetamol not act like the NSAIDs?

While COX-2 inhibitors and non-selective NSAIDs inhibit prostaglandin synthesis in many tissues of the body, paracetamol acts predominantly on the production of prostaglandins in the central nervous system. Therefore, there is little potential for paracetamol to affect the kidney, blood vessel and heart systems that are detrimentally affected by NSAIDs.

Guidance on analgesic use in cardiovascular conditions

Patient characteristics	Recommendations
Hypertension	Recommend paracetamol, unless contraindicated [12, 17]
Cardiovascular disease	Recommend paracetamol, unless contraindicated [12, 18]
Receiving low dose aspirin	Paracetamol or NSAIDs, however consider potential additive gastrointestinal effects of the latter [11]
Elderly	Risk of cardiorenal effects of NSAIDs increases with age, therefore monitoring for early onset of oedema, de-stabilisation of blood pressure control and/or onset of congestive heart failure should be undertaken [12]
	Consider also potential drug-drug interactions with NSAIDs and anti-hypertensive and anticoagulant medication
	Recommend paracetamol, unless contraindicated [12]

Why is this issue important now?

The latest paper showing up to a 63% increase in the risk of serious CVD events with NSAIDs, authored by Kearney et al, has been released by a highly eminent group with vast experience in the analysis of data relating to analgesics.

continues on page 22

I need an effective pain reliever, not potential GI complications

- Over the counter (OTC) non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and aspirin, are contra-indicated in people with Gastrointestinal (GI) bleeding and ulceration. [1]
- When used regularly at OTC doses, ibuprofen and aspirin have the potential to cause serious GI problems. [2-8]
- The risk is exacerbated by factors such as age, smoking, alcohol consumption, or use of corticosteroids or anticoagulants. [4-6, 9]
- The active ingredients in Panadol (paracetamol) does not increase the risk of serious GI adverse events[4-6], is not associated with upper GI bleeding regardless of dose[10] and remains drug of first choice for patients with mild to moderate pain. [2-4, 8, 10]

The next time they need pain relief, be sure to recommend Panadol.

Panadol tablets are for the relief of mild to moderate pain.

It's my choice.

References: 1. British National Formulary. Edition 51, March 2006. Chapter 10. Musculoskeletal and joint diseases: Non-steroidal anti-inflammatory drugs. 2 Singh G. Am J Ther 2000; 7:115-121. 3. Wilcox CM et al. Arch Intern Med 1994; 154:42-46. 4. Garnett WR. J Am Pharm Assoc. 1996; NS36:565-72. 5. Blot WJ, McLaughlin JK. J Epidemiol Biostat 2000; 5 137-142. 6. Peura DA et al. Am J Gastroenteral 1997; 92:924-928. 7. Biskupiak J et al. Abstract presented at the American College of Gastroenterology 70th Annual Meeting, 2005. 8. Scheiman JM et al. Clin Gastroenterol Hepatol 2004; 2: 290-295. 9. Stiel D. Am J ther 2000; 7: 91-98. 10 Lewis SC et al Br J Clin Pharmacol 2002: 54 (3): 320-326.

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Informed Consent – Part I

by **Pierre Mallia** *MD MPhil PhD FRCGP*
Lecturer in Biomedical and Clinical Ethics

The use of the phrase 'informed consent' has become much of a cliché. People perhaps use it without appreciating the meaning. I was recently at a meeting in Brussels, and the document we were reviewing spoke about 'withdrawing informed consent'. You do not, of course *withdraw* informed consent; you withdraw consent. *Informed consent* is a process. Conversely, at a meeting with the Data Protection commissioner, an insurance company, argued that they obtained 'consent' from a lady in order to look into her hospital file. She was subsequently refused settlement. Was the process of consent a truly informed process? Given the fact it was not explained to her that in the event that she suffered from a related condition she would not get the settlement, one cannot argue that a legal consent was obtained. I will refrain from commenting on how the hospital actually gave them the records of the patient.

There are five stages to the informed consent process. Although it seems complicated, doctors will usually go through them in their minds and it will only take a few moments to consider the stages. Informed consent presumes however the autonomy of the person giving the consent.

Autonomy is derived from the Greek *auto* (self), and *nomos* (control). It therefore speaks of self control. Just as a country exercises control over its territory, a person exercises control over his body. Nowadays, taking decisions 'for the good of the patient' without actually allowing the patient to participate in the process is not respecting the autonomy of the individual. A person who acts autonomously, acts according to his or her own free will (voluntariness); thus understanding what he or she is doing; and acts without any controlling influences. There are many examples one could bring to illustrate these, but of course it is obvious from the start that many categories of people cannot act autonomously (children, elderly with dementia, people who may be under the influence of drugs, those suffering from illness, or even stress). It is the responsibility of the physician to empower the person to see that he/she makes an autonomous choice. One must ask, 'Is this person making a voluntary choice? Has he understood what we are explaining? And are there any controlling influences?'. Controlling influences can be pressure from relatives or friends or perhaps the fear of the physician (people may fear that if they do not do what the doctor is saying, they will not get the full attention of the doctor, which may then abandon their cause).

You do not, withdraw informed consent; you withdraw consent

1. Information

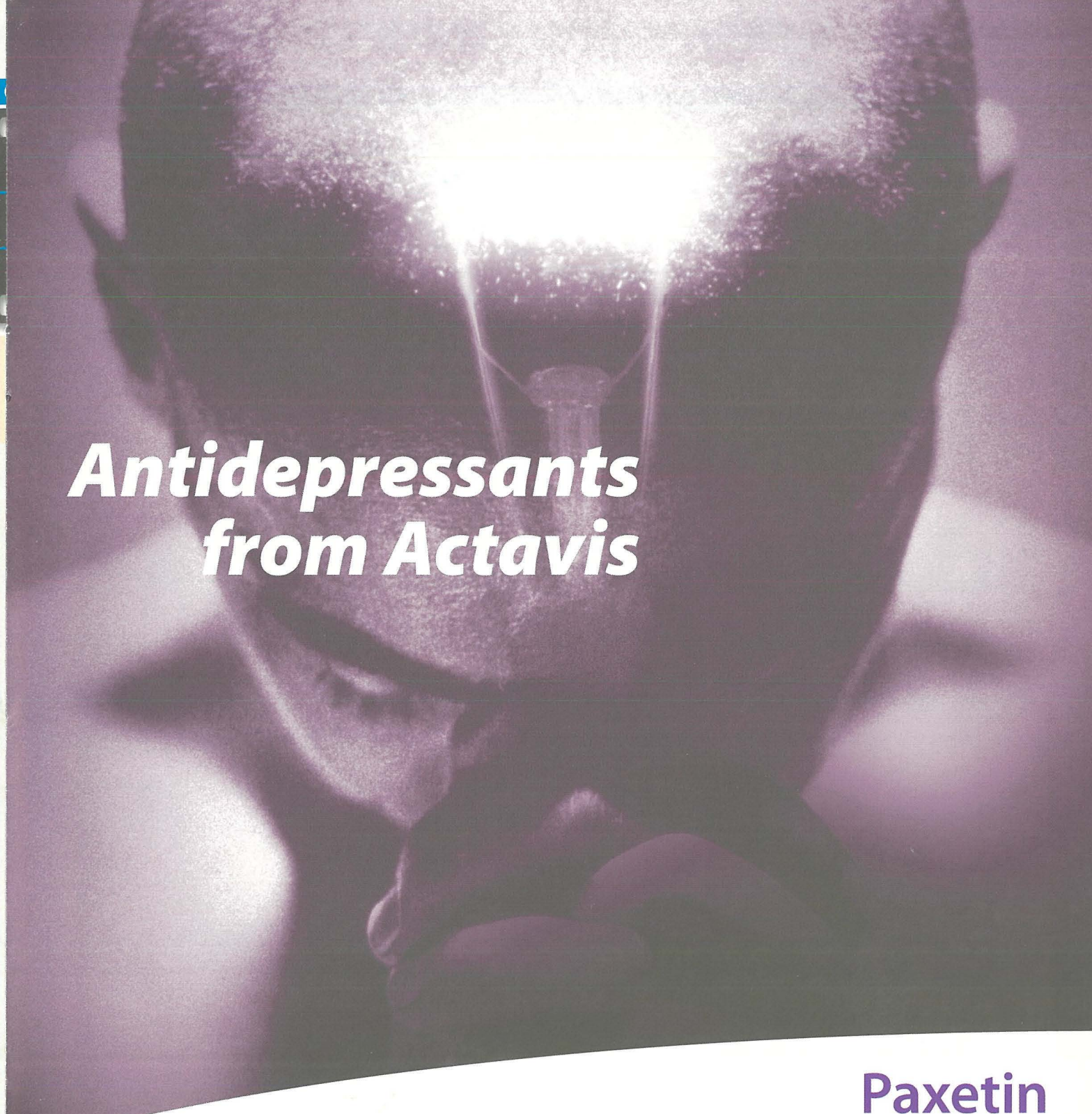
Having said that, we turn briefly to the five conditions. Information. What amount of information do I actually tell or give the patient? When prescribing an antibiotic, do I really have to explain all that is on the package leaflet? It is quite acceptable to follow two basic rules. The first is to tell what a reasonable person would want to know. This is basically a transposition of the Golden Rule: *Do to others…..* Therefore if I am going in for a thyroidectomy, I would want to know that there is a moderate risk of hoarseness as a complication. Someone going in for a prostatectomy has given his consent for that procedure and not for sterilization – which may be a complication. We cannot take for granted that because the gentleman is beyond his reproductive years, then he automatically does not need to function. I once saw a patient being told when waiting outside the operating room that it would be better to remove his testicle in order that his inguinal hernia repair has less chance of recurrence. That is definitely not the ideal circumstance to concede, no matter how much faith the patient has in the doctor.

The second rule is to follow a personalized standard. Some patients merely let the doctor do the decisions. In this case the doctor would still be wise to explain what he or she feels the patient should know. Conversely, some people, perhaps out of anxiety or perhaps because they find it difficult to decide, find that they need a lot of detail, which may even tax on the doctor's patience. Time spent here may make the difference between a fully satisfied patient and one who is not.

2. Understanding

Obvious as it may seem, do we actually make sure the patient has understood? Are we explaining what we have to say under the right conditions? Do we give news or explain outcomes in the hospital corridors; do we give advice on treatment when we have just imparted bad news? Do we allow moments for people to digest what we have said? In a busy outpatient's department this is not all that easy. Only prudent doctors would put all else aside and focus on the being in front of them. Thankfully most are (prudent). Sometimes the environment we work in does not help people understand. Interruptions (telephone calls, nurses coming in and out of the office, etc) distract doctors, let alone patients. Patients may not yet be ready to take the news and may need time. Understanding really is a process studied considerably in social sciences and perhaps from the ethical point of view all we can ask is 'Have you actually ever read, and made an effort to understand and implement, a chapter from a psychology book, on understanding?'. How often have you seen colleagues on committees who make you wonder what effort they put in to understand patients – they seem to understand only after they would have taken up half the discussion time talking themselves, only to finally say what you or someone else has been saying all along. If only they make the effort to be quiet – and when they do so, actually *think* about what the person is saying rather than what they are going to say themselves. *Understanding…*Hmmm!

In the second part we will deal what constitutes a voluntary choice and competence.



Antidepressants from Actavis

Paxetin

– More affordable SSRI treatment

Paroxetine 20mg tablets

Compositon: Paroxetine HCl equivalent to Paroxetine 20 mg. **Therapeutic indications:** Treatment of symptoms of depression, obsessive-compulsive neurosis, panic/panic attacks, social phobia/social apprehension, general anxiety disorder and post-traumatic stress disorder. **Posology and method of administration:** Paxetin should be administered once a day, in the morning, with or without food. The maximum effects of the drug may be achieved in 3-4 weeks. *Dosage for adults:* The initial dose of Paxetin is 20 mg per day. For patients who do not respond to a dose of 20 mg per day, it should be considered to increase the dose gradually to 40mg per day. The recommended maximum dose for depression, social phobia/social apprehension, general anxiety disorder, post-traumatic stress disorder is 50mg per day. The recommended maximum dose for obsessive-compulsive neurosis and Panic/panic attacks is 60mg per day. *Elderly:* A lower initial dose should be considered for elderly and weak patients. The dose may be increased, if required, up to 40 mg per day. *Children:* Paxetin is not recommended for individuals under 18 years of age. *Impaired renal and/or hepatic function:* Paxetin should be used with caution in patients with impaired renal or hepatic function. The maximum dose is 40 mg per day. **Contra-indications:** Paxetin is not intended for patients who are hypersensitive to the drug or to any of its excipients. Paxetin should not be used concurrently with MAO inhibitors, and not within two weeks from the time, treatment with MAO inhibitors was discontinued. Subsequently, treatment with Paxetin should be started with caution, and the doses should be raised progressively until maximum response is achieved. Treatment with MAO inhibitors should not be initiated within two weeks from the time treatment with Paxetin has been discontinued. **Special warnings and special precautions for use:** Patients considered to be at risk of suicide should be kept under close observation during the entire time of treatment. It is recommended that caution should be observed in patients who have previously had convulsions and been subject to mania. Patients who have recently suffered from myocardial infarct or heart disease should be kept under appropriate observation. **Interaction with other medicaments and other forms of interaction:** As is the case with other serotonin reuptake inhibitors, paroxetine inhibits the specific hepatic enzyme cytochrome P450 isoenzyme (2D6). Drugs that are metabolised by cytochrome P450 (2D6) include specific tricyclic antidepressants (e.g. nortryptiline, amitryptiline, imipramine and dexipramine), specific serotonin reuptake inhibitors (e.g. fluoxetine), sedative phenothiazine drugs (e.g. perphenazine and thioridazine) and drugs for arrhythmia (e.g. propaphenone and flecainide). Caution should be observed with the administration of Paxetin concurrently with sedatives (neuroleptics) and oral anticoagulants. Drugs that inhibit (e.g. cimetidine) or activate (e.g. phenytoin) microsomal enzymes that are necessary for the metabolism of paroxetine can affect its metabolism and pharmacokinetic properties. The adaptation of doses at the start of the treatment is not considered necessary when the drug is to be administered together with a drug that activates enzymes necessary for the metabolism of drugs. If doses are adapted later, this should be done on the basis of the clinical effects. Patients should be advised to avoid taking alcohol during Paxetin treatment. The use of Paxetin together with tryptophan is not recommended as it can lead to side effects, mainly headache, nausea, increased perspiration and dizziness. The use of paroxetine together with anticonvulsive drugs (e.g. phenobarbitol) can lead to an increased frequency of side effects. Paroxetine can interact with drugs that are mostly bound to plasma proteins thus leading to increased side effects. Utmost caution should be observed when administering Paxetin together with lithium as the experience with such patients is limited. Following repeated doses, a study of the interaction between paroxetine and diazepam showed no changes in the pharmacokinetic properties of paroxetine which would recommend changes in the dosage for patients taking both drugs. **Pregnancy and lactation:** Paxetin should not be used during pregnancy and lactation. **Effects on ability to drive and use machines:** Patients should be advised not to drive a car or operate dangerous machinery until they are sure that Paxetin does not affect them. **Side effects:** The most common: Malaise, pains. Hypertension, syncope, tachycardia. Pruritus. Nausea and vomiting. Weight gain, weight loss. Stimulation of the nervous system, impaired concentration, depression, emotional instability, vertigo. Increased coughing, rhinorrhea. **Overdose:** A wide margin of safety is evident from available data. Experience of paroxetine in overdose has indicated that, in addition to those symptoms mentioned under Side Effects, vomiting, dilated pupils, fever, blood pressure changes, headache, involuntary muscle contractions, agitation, anxiety and tachycardia have been reported. Treatment should consist of general measures employed in the management of overdose with any antidepressant. Early administration of activated charcoal may delay the absorption of Paxetin.

For full prescribing information please contact the local representative of the Marketing Authoristion Holder.

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Thank you

TheSynapse Magazine is currently celebrating its fifth anniversary. The aim of the magazine is to bring at the tips of healthcare professionals, different aspects of recent advances in healthcare, written by distinguished colleagues.

We would like to thank the various sponsors for their steady support throughout the current year. Their trust clearly demonstrates their ability to recognize the various achievements of the magazine amongst healthcare professionals.

Needless to say, sponsors play an important part in sustaining the quality of the magazine throughout the year.

Special thanks also goes to the various contributors who have submitted articles during 2006 (around 50 articles in 6 issues). This clearly reflects their commitment towards delivering continuing medical education to fellow colleagues. This also means that contributors are increasingly acknowledging our allegiance to increase teamwork approach amongst healthcare professionals.

However this also means that we have to shoulder the increased responsibility towards all stakeholders. In fact during the past months, TheSynapse Magazine has experienced a qualitative and quantitative upgrade. This has been nurtured by better scientific coordination and enhanced product planning.

The Editorial Board also gratefully acknowledges the invaluable contributions of the following reviewers:

Professor Albert Fenech
Dr Paul Vassallo-Agius
Dr Bridget Ellul
Dr Pierre Schembri-Wismayer

E-Learning Modules for Continuing Medical Education

During this year, the Association of Surgeons of Malta has launched a series of three online interactive medical modules. Supported by the European Social Fund, this initial group of modules aims at improving local continuing medical education. They seek to cover common medical and surgical topics in a way that is clinically oriented and of practical use to surgeons and physicians.

The three modules are:

- Vertigo – written by Mr Adrian Agius
- The Acute Abdomen – written by Mr Arthur Felice
- Prevention of Postoperative Pulmonary Complications – written by Professor Joseph Cacciottolo

The modules are endorsed by the Departments of Medicine, Surgery, Family Medicine and Community Pharmacy at the University of Malta.

Certificates issued

eCME
electronic continuing medical education
the Synapse

There is no registration fee until the end of December 2006. One may save, exit and log in at other subsequent sessions to continue the module at one's convenience.

The modules are open to basic medical and surgical trainees, medical practitioners, medical students, pharmacists and professionals in allied specialties.

Certificates of completion of modules have recently started to be awarded to participants. 3 CME credits will be awarded on successful completion of each module.

Registration takes place by logging on at http://cme.thesynapse.net

Winning with TheSYNAPSE

Over the last few months members of TheSYNAPSE were able to have some fun and win great prizes with TheSYNAPSE.

Dr Marvic Masini is the Winner of the PLAVIX eQuiz by Sanofi Aventis and won a book token.

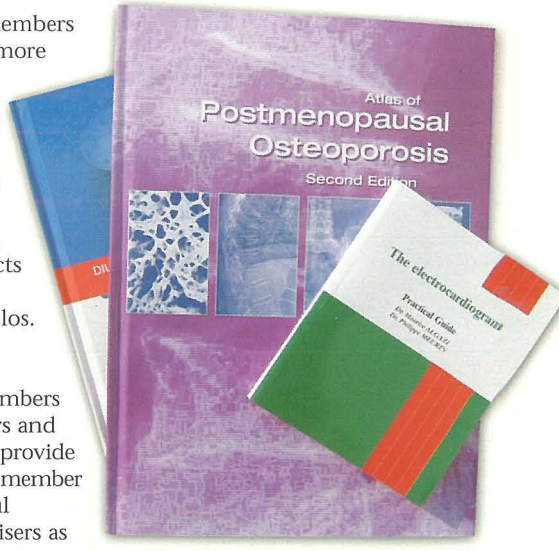
Plavix® (Clopidogrel) is an antiplatelet agent licensed for the reduction of atherosclerotic events in patients with a history of symptomatic atherosclerotic disease such as myocardial infarction (MI), stroke or established peripheral vascular disease (PAD).

Plavix® is an advanced, specific adenosine diphosphate (ADP) receptor antagonist that selectively inhibits platelet aggregation induced by ADP resulting in an antithrombotic effect. Plavix® 75mg/day has a rapid onset of action that is maintained during long term therapy. Initiation of treatment by a loading dose of 300mg of Clopidogrel significantly increases the pharmacodynamic activity observed during the first days of treatment. Plavix® is significantly more effective than aspirin at reducing the incidence of MI, stroke and vascular death.

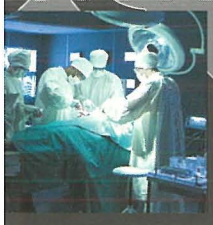
Dr Julian Mamo is the winner of the SERTRAL eQUIZ by Actavis

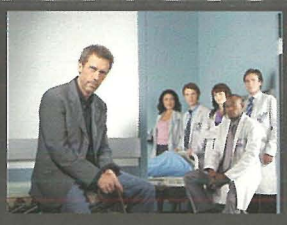
Sertral 50mg (Sertraline) is the new antidepressant treatment from Actavis. Sertraline is a selective serotonin re-uptake inhibitor. As a result of its selective inhibition of serotonin reuptake, Sertraline does not influence catecholamine activity. In addition, Sertraline has no affinity for muscarinergic, serotonergic, dopaminergic, histaminergic, benzodiazepine, GABA or adrenergic receptors.

More than 70 members have won one or more interesting books as they participated in a series of surveys by Les Laboratoire Servier – the surveys dealt with the Servier products Diamicron MR, Vastarel and Protelos.



We are greatly encouraged by members response to surveys and eQUIZES – these provide an opportunity for member interactions, useful feedback to organisers as well as an opportunity to have some fun. More of this is planned in the coming months.





"Doctor, Doctor – Medics in Movies ar

by **Justin Camilleri**

Without a doubt the 20th century will be remembered for the birth of cinema and television. They played an important role in shaping our lives and cultures due to their growing popularity and now easy accessibility forever instilling in us a passion for screen entertainment.

Over the years countless stories told by celluloid images, projected onto the big screen and television, has led audiences to build perceptions on different fields e.g.: music, sport, commerce, politics and science.

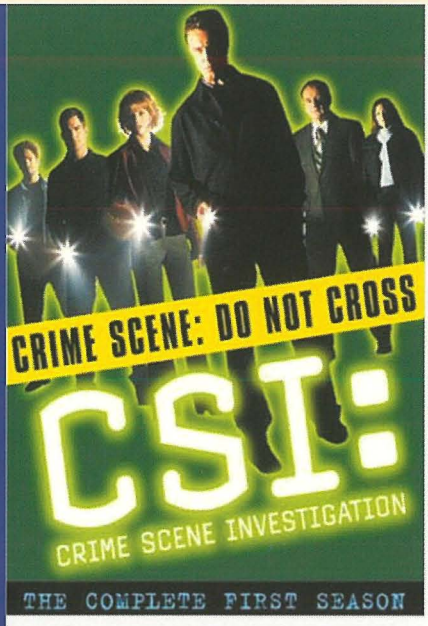
The Medical Profession is no exception, from the 1930s till now doctors have been portrayed in films and TV series, very often influencing the public's perception, inspiring a lot of young students to become doctors and most importantly having a tremendous effect on doctor – patient relationships.

From the humble Dr Watson (*Sherlock Holmes*) to *Star Trek's* Dr 'Bones' McCoy, from William Hurt in *The Doctor* to TV's hit series' *ER, C.S.I* and *House*, doctors can be found in any film and television programme.

Maybe its time that these films and television programmes are added to the medical school curriculum, providing a comprehensive sociological reflection on the way medics are portrayed in the Media and their place in society?

Doctors and medical students may be pleased to know that according to Glenn Flores' research paper *Doctors in the Movies*, where he reviewed 131 doctor films excluding television, from nine countries, spanning eight decades, the medical specialisation favoured by doctors is surgery (33%), psychiatry, (26%) family or general practice (18%) whilst paediatrics accounts for only 2%.

Despite Glenn Flores' extensive research on the medical specialisation favoured by television producers for doctor's onscreen, one should hope that doctors and medical students are intelligent enough to decipher the fact that producers give prominence to surgery only because it is more dramatic and glamorous onscreen e.g. ER and Nip/Tuck. The fact is, any person going into health care whether they want to become a surgeon, a general practitioner , a specialist, nurse or midwife, they all



hold equal importance in the real medical profession and rightly so.

Over the years cinematic portrayals of doctors have been mixed; a positive and negative presentation of medics onscreen has appeared in every decade. For every fictitious Mad doctor (*The Cabinet of Dr Caligari*) or scientist (*Dr Frankenstein*) the 1930's gave us very positive insights in the medical profession, with the classic memorable *Arrowsmith* (1932) and *The Citadel* (1938).

Arrowsmith is based on the Pulitzer Prize winning novel written by American author Sinclair Lewis. Nominated for four Academy Awards and directed by the influential John Ford (*The Searchers*), the film is set during the 1920s depression era. It chronicles the life of Dr. Martin Arrowsmith (*Ronald Colman*) as he makes his way through medical school, marries and considers the lure of high-paying industrial research taking a post within a research institute. The young medical researcher's job takes him to a Caribbean island, where he must prevent a plague while prioritising who has the right to take the vaccine. This film was considered avant garde for the time in which it was released, as it explores a doctor's internal conflicts between choosing to help patients or career status rewards.

Despite Arrowsmith being a story on a lone doctor's pursuit against a death plague, it is a social commentary on the state and prospects of medicine in the United States in the 1920s depression era.

Based on the Novel by Scottish author Archibald Joseph Cronin and directed by King Vidor *The Citadel* takes place in England where a young, idealistic Dr. Manson (*Robert Donat*) becomes disillusioned after practicing in a Welsh mining town. Manson is then influenced by a friend to make a lucrative practice from rich hypochondriacs, where he finally realises what the truth of being a doctor really is.

Show me the Money!!!

Both *Arrowsmith* and *The Citadel* portrayals of doctor's onscreen are a fine example of humanity and compassion that bring out the best in doctors. One may beg to differ, according to Glenn Flores' research paper *Doctors in the Movies*: "Materialism and a love of money have pervaded cinematic portrayals of doctors dating back to the 1920s and continue to be prominent in recent movies."[1]

This maybe shocking to many, but Flores substantiates his claim of cinematic doctor's materialistic approaches, by citing various film anecdotes, that funnily enough all give common reference to Harley Street in London, which is synonymous with private medical care in the United Kingdom. For example in *Doctor at Sea* (1956), Dr Simon Sparrow played by Dirk Bogarde states: "A Roll Royce is the ambition of almost every newly qualified doctor and preferably a I Iarley Street Address to go with it." 1 In *Carry on Again Doctor* (1969), Dr Jim Nookey (Kenneth Williams) confides to a colleague. "Specialise, that's what I'd like to do! The whole Harley Street bit with bags of lovely filthy rich women patients."[1]

- Where are thou?"
nd Television – Part I

Another example is in *Doctor at Large* (1957), where the doctor in charge of a Harley Street practice gives advice to a fellow colleague: "You know, it's a chastening thought, but good clothes are more important to a GP than a good stethoscope."[1]

Flores in his debate goes to the point to even mention cinematic American slang anecdotes taken from *Not as a Stranger* (1955), where 1950's American Medical Students discuss their career options:

"Personally, I'm for surgery. I just got a look at Dr Dietrich's car. You know what he drives? A Bentley. $17,000 bucks."
"That guy doesn't take out a splinter for less than £1,000."
"I'll still take ear, nose, and throat. The common cold is still the doctor's best friend."
"Call it a virus. You make more dough that way."
"Look, if you kiddies are all through, your old man here will really wise you up. It's not what you practice, its where."
"What do you mean?"
"I've done a little research on this problem. The average doctor's income is 11 Gs. In the Southwest, west and more…."
"Pebble Beach, Colorado Springs, Beverly Hills, that's where the rich are cracking up fast."[1]

The Swinging Sixties

The 60's were catalyst to bringing doctors to the masses through the medium of television. Viewers were introduced to the charming, benevolent, morale *Dr Kildare* (1961) played by Richard Chamberlain. This was the pioneering medical television drama that started it all!! Kildare told the story of a young intern, Dr. James Kildare (Chamberlain), working in a fictional large metropolitan hospital (Blair General), who dealt with patient's problems, and wins the respect of his mentor, Dr. Leonard Gillespie (Raymond Massey).

The series became part of popular culture including Malta and was largely responsible for making Chamberlain, who beat out 35 other actors for the role, a teen poster boy idol of the 1960s.

In fact, it is said that so many students wanted to become doctors in order to emulate Chamberlain. While young male doctors wanted to mimic Chamberlain and female medics were being wooed by his charms, out of nowhere came in British slapstick comedy, that proved it was ok to laugh a little at the seriousness of doctor's prescriptions.

One of the faces of British slapstick comedy namely, Peter Sellers humorously gave us the realities of medical multiculturalism, in *The Millionaires* and exposed how doctors can also have tantrums in *What's new Pussycat?*

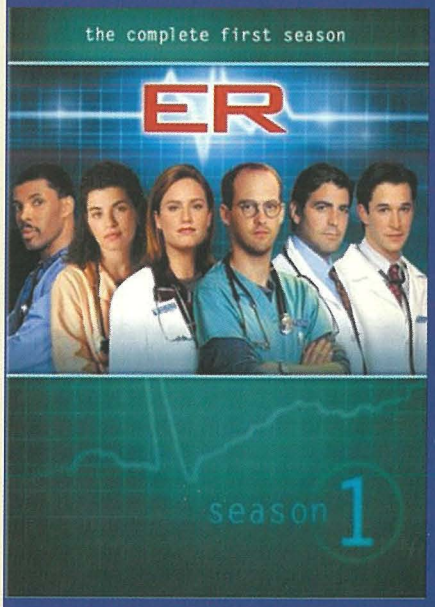
The Millionaires introduced us to the first cinematic Asian medic, in the form of Indian doctor Dr. Ahmed el Kabir played by Sellers. Co – Starring Sophia Loren the plot centres on the world's richest woman who falls in love with a humble, Indian physician. Despite her advances he ignores her flirtations, leading to hilarious consequences for both.

Despite the fact that nowadays *The Millionaires* may be criticised for not being "politically correct", the message behind Sellers comical one-liner: "Goodness Gracious Me" is relevant till this day that despite the post WWII setup of a multicultural Britain, there is still a lot to be done.

Sellers followed his Indian medic persona with another comical take on the medical profession in *What's New Pussycat?* This time, an engaged womaniser (Peter O'Toole) seeks aid of a psychiatrist who has extra – marital problems of his own.

Satire was the order of the day, with the "Carry On!" series injecting sardonic farce, parody and humour in the medical profession. Even by today's standards the Carry On! scripts found in Carry *On Doctor*, *Carry On Again Doctor* and *Carry On Matron* are still considered a healthy dose of laughing medicine for audiences. Without a doubt they ingeniously managed to bring to the fore countless real-life hospital problems in the British National Health Service, that were never discussed or regarded simply as taboo.

Many thought that the hospital



comical setting was over once the "Carry On!" team dissolved in 1978, little did anyone know that it would be mimicked yet again in 1983's *Monty Phyton's The Meaning of Life* and revived on the UK Channel 4's sketch comedy show *Green Wing*.

The sixties will be infinitely remembered as the era in which one doctor went boldly where no man has gone before….

Fans of the medical genre were left in awe, as we were introduced to a new breed of doctor namely, Dr. Leonard "Bones" McCoy, the Chief Medical Officer aboard the U.S.S star ship, *The Enterprise*, in the hit science fiction TV series, *Star Trek*.
Star Trek's Dr "Bones" McCoy would present a captivating vision of what medicine might one day achieve. Four decades later patients in hospitals now rest on tables similar to the Enterprise's sickbay bed, while an automated computer scanner delivers diagnostic images of the bodies' interior.

Back in the 1960's, imaging techniques could only outline basic internal anatomy example: detecting a broken bone, nowadays technology has advanced so much that it can also detect tissues with an abnormal concentration of blood vessels or a faster metabolic system.[4]

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Stem Cells – What, Why, Whereabouts and When? – Part III

by **Pierre Schembri-Wismayer** *MD PhD MMCPath*
Lecturer, Department of Anatomy & Cell Biology
Faculty of Medicine, University of Malta

Ethical and Safety issues

I will not be discussing the ethical issues with embryonic stem cells and personhood in detail here. However other ethical issues relating to stem cell therapy should be noted.

A possible cause for concern with stem cell therapy involves the risk of cancer.[1] Whilst this was hardly considered till a few years ago, nowadays, the literature teems with papers about tumour stem cells.

Mouse experiments involving the injection of stem cells or their progenitors clearly show the link with teratomas.[2]

In the case of embryonic stem cells, prolonged *in vitro* culture can be associated with genetic changes making embryonal stem cells similar to embryonal carcinomas.[3] This raises important questions about safely using embryonic stem cell lines propagated for a long time in vitro as a source of donor stem cells.

Although the amount of therapeutic studies using embryonic stem cells is presently very small, and no such statistics can be calculated, there is theoretically an increased risk of cancer developing from stem cells.

The increased plasticity of adult stem cells and the possibility of creating patient-specific stem cells through processes similar to therapeutic cloning may make this a mute point in the near future.

Regarding tumour stem cells, the author's personal opinion is that tumour cells, upon becoming immortal obtain much of the properties of stem-ness. However, many papers now specifically describe a specific sub-population of tumour stem cells.[4,5] Whichever of these positions is the more accurate, there is little doubt that the more primitive a cell, the more propensity it has for malignant transformation. Due to this, detailed and extensive studies following transplantation of early stem cells (autologous or heterologous) will be required before the procedure will be accepted as one with minimal associated risk.

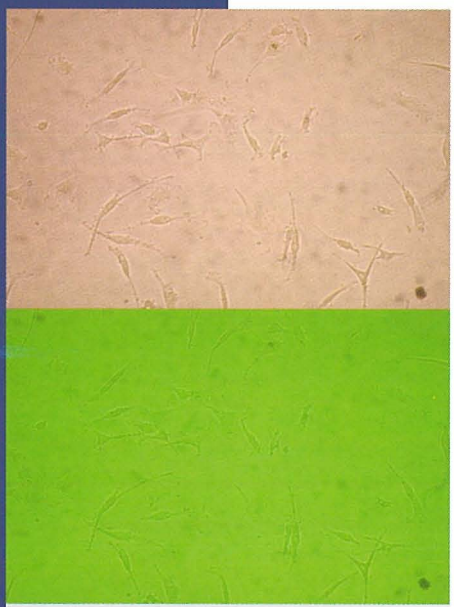

Figure 1: *Cord blood mesenchymal cells cultured in University of Malta Laboratories*

Stem cell collection and banking

With all this stem cell-related research ongoing throughout the world, are there any measures worth taking up locally?

In the author's opinion, the obvious and relatively easy option is to start up public cord blood banking. In fact a proposal document had been submitted to the health authorities by the author on behalf of a private charity a number of years ago.

Cord blood banking has been developed over the last decade or so in a number of countries around the world, including Italy, the Netherlands and the UK. Recognition of the usefulness of this resource were heralded by titles such as 'turning garbage into clinical gold' in some of the world's most prestigious scientific journals.[6]

Cord blood banking can be separated into private and public banking. Private/individual banking normally involves the preservation of the cord blood from a child's placenta at birth and keeping those blood cells for the child in question. This involves an initial payment and sometimes a recurrent payment to cover cryopreservation. Since the blood is only tested for infective organisms and does not need to be cross-matched against other individuals, it is relatively cheap to bank such blood.

In 1999, the American pediatric association issued a recommendation stating 'Families may be vulnerable to emotional marketing at the time of birth of a child and may look to their physicians for advice. No accurate estimates exist of the likelihood of children to need their own stored cells. The range of available estimates is from 1:1000 to 1:200 000. Empirical evidence that children will need their own cord blood for future use is lacking. There also is no evidence of the safety or effectiveness of autologous cord blood transplantation for the treatment of malignant neoplasms. For these reasons, it is difficult to recommend that parents store their children's cord blood for future use'.[7]

recognition of the different types of stem cells found in cord blood and their much greater plasticity potential. However even much more recently, the Canadian Society of Obstetricians and Gynaecologists issued the following amongst a long list of recommendations'.[5] Altruistic donation of cord blood for public banking and subsequent allogeneic transplantation should be encouraged when umbilical cord blood banking is being considered by childbearing women, prenatal care providers, and(or) obstetric facilities.[6] Collection and long-term storage of umbilical cord blood for autologous donation is not recommended because of the limited indications and lack of scientific evidence to support the practice'.[8]

Public banking is much more expensive on a per unit basis but provides a resource for the whole health service. Due to the relative immunological naivety of cord blood, a perfect 6/6 major HLA match is not required for successful transplantation. 4/6 matches are often successful.

Studies by the Turin cord blood bank have in fact found that with just 500 units (1/10th of the amount of cord units which could be collected in a year in Malta) one would be able to successfully cross match about 90% of the Italian population, ie more than 50 million people.[9]

Until recently, cord blood was only found adequate for transplant into children and small adults of less than 50kg body mass, due to a need for more stem cells to adequately replace bone marrow in a larger individual.[10]

Recent studies however are suggesting a wider range of potential recipients due to a number of modifications including the simultaneous transfusion of more than one cord blood unit into the same patient[11] as well as ex-vivo expansion of the stem cell population.[12,13]

Mesenchymal stem cells (MSCs), presently being used in numerous clinical trials (in heart, bone and cartilage regeneration amongst others) are also found in cord blood. These cells, require culturing in the lab however before cord blood freezing, something already being done on a research basis on donated cord blood samples at the University of Malta (Figure 1).

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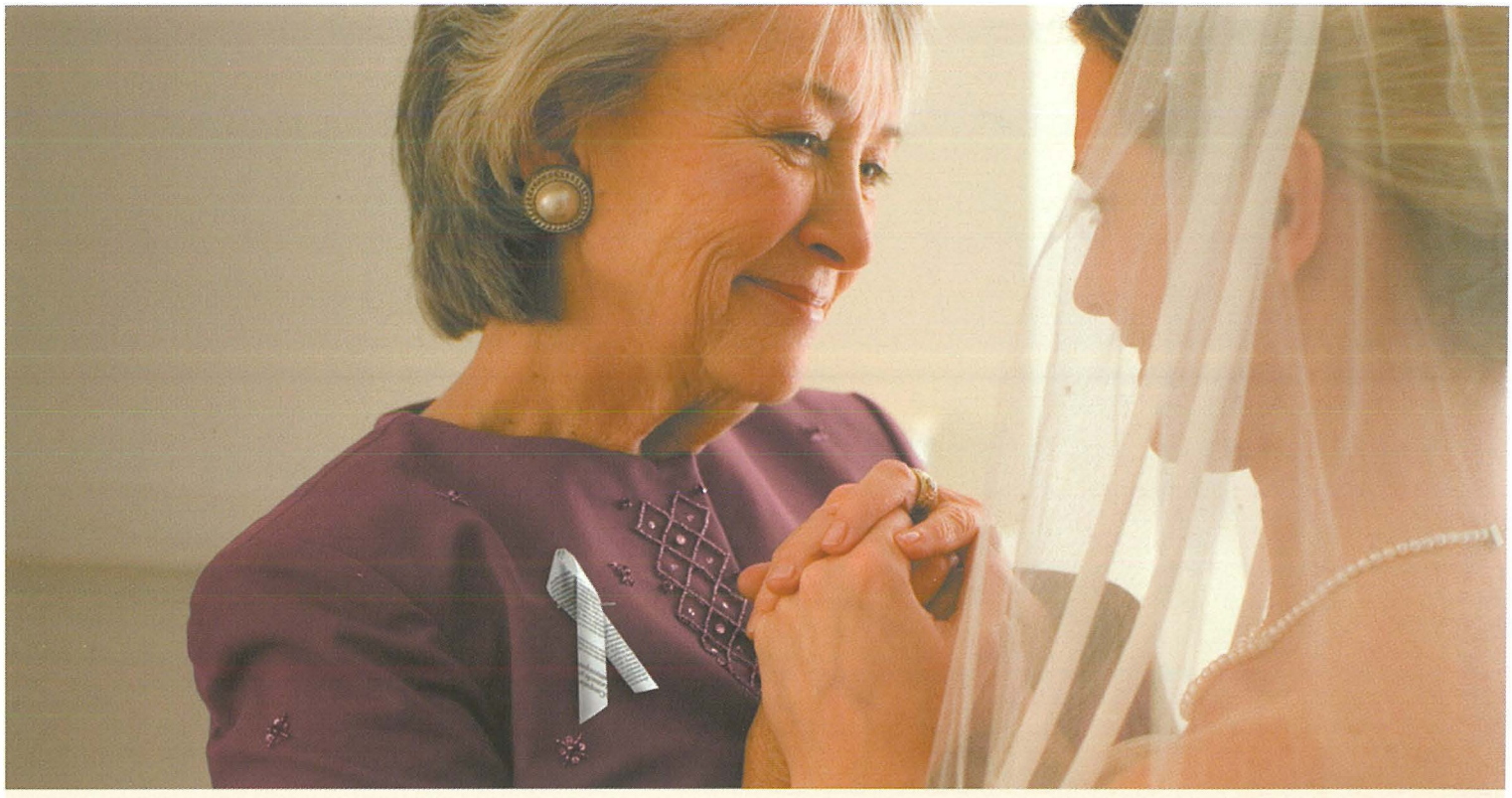

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- FEMARA significantly reduced risk of recurrence by 28% versus tamoxifen in patients who required chemotherapy. [1]
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References:
1. The Breast Interntional Group (BIG) 1-98 Collaborative Group. A comparison of letrozole and tamoxifen in postmenopausal women with early breast cancer. *N Engl J Med.2005;353:2747-2757.*

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Imaging Small Bowel Disease

continued from page 2

Nonetheless these lesions are an important cause of obscure gastrointestinal bleeding and account for 75% of the symptomatic small bowel lesions that require surgery. Small bowel ulcers (Figures 6-7) are another common abnormality detected at capsule endoscopy. Although the majority of small bowel ulcers detected at capsule endoscopy are due to Crohn's disease or NSAIDs, other causes include infection, ischemia, trauma, or vasculitis.

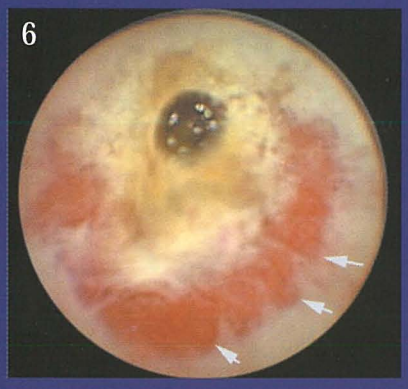
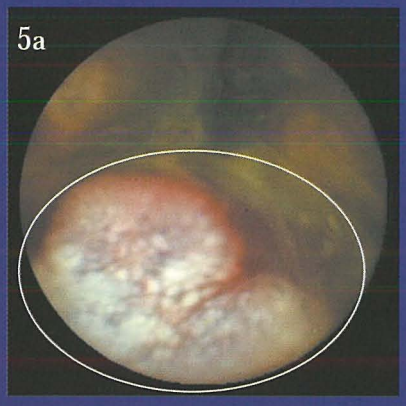
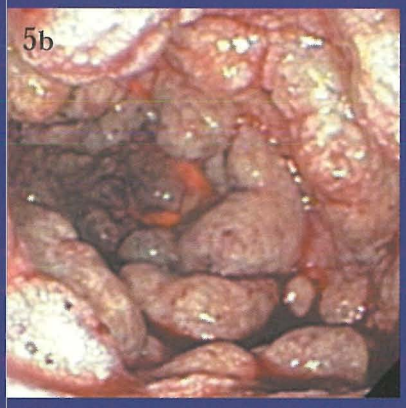
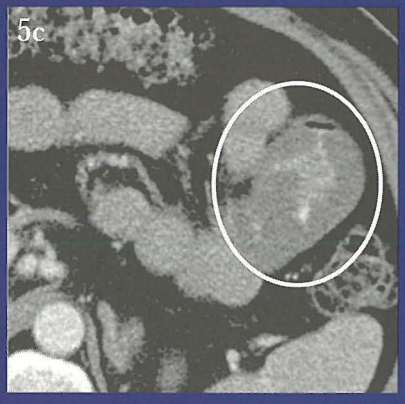


Figure 6: *Small bowel ulcers. Capsule endoscopic image shows small bowel ulcers that were not seen at enteroclysis or CT.*







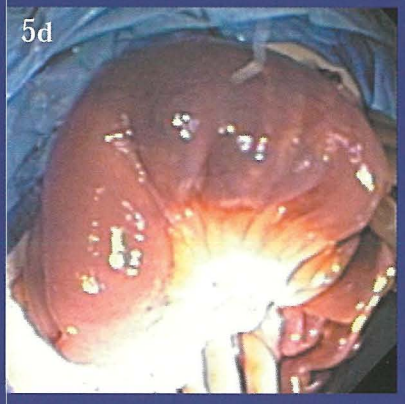
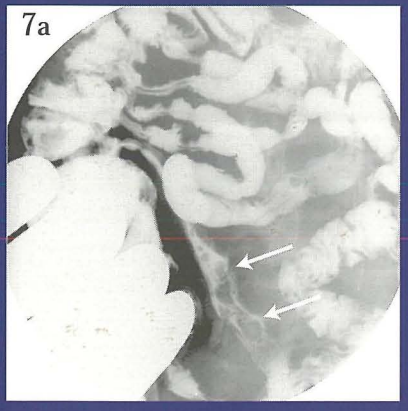
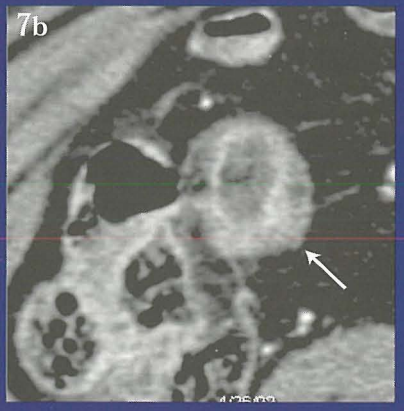


Figure 5: *Lymphangioma. (a) Capsule endoscopic image shows multiple punctate white lesions (encircled) in the proximal small bowel. (b) Intraoperative endoscopic image shows markedly thickened small bowel folds. (c) CT scan shows circumferential low-attenuation wall thickening in a jejunal segment (encircled) causing narrowing of the lumen and enlargement of the small bowel loop. (d) Intraoperative photograph shows marked distension of a jejunal loop, a finding that corresponds to the abnormality seen at CT.*





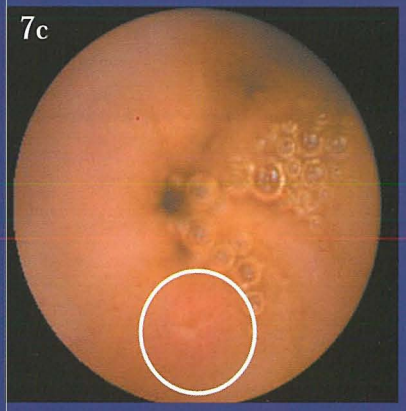


Figure 7: *Early Crohn's disease. (a) Image from a small bowel follow-through study shows mild nodularity in the terminal ileum (arrows). (b) CT scan shows mild diffuse wall thickening and mucosal enhancement of the terminal ileum (arrow). (c) Capsule endoscopic image shows a small apthous ulcer in the terminal ileum (circled).*

Dr Pierre Vassallo can be reached at the Medical Imaging Centre on 21 491 200 or by email on pvassallo@mic.com.mt

Stem Cells – What, Why, Whereabouts and When? – Part III

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At the recent meeting in Rotterdam of the Tissue Engineering and Regenerative Medicine International Society, F. P Barry from Galway's National Centre for Biomedical Engineering Science, showed very interesting (presently unpublished) data which indicates that in rat experiments, MSCs transplanted 10 minutes post myocardial infarction engrafted strongly into the heart whilst those given 2 weeks post-MI were much less actively taken up.

This may possibly explain why so many of the present clinical trials on humans with MSCs have been so disappointing so far. What I take this to mean is that, in future, having donor stem cells readily available on your doorstep might well be the most important therapeutic option. Growing your own bone marrow stem cells, or bringing your own stem cells over from abroad may not be much of an option.

So cord blood banking might just be the most useful stem cell-related health investment for the local health authorities. Private public partnerships may also provide a useful option, especially to allay costs. Here, public health authorities could take over cord blood units banked privately for individuals after a fixed time period or after private individuals decide to stop paying cryopreservation costs, thus forfeiting ownership. By performing HLA typing and by recording these units in a database, they will slowly build a local stem cell therapeutic resource, with the private sector having initially footed the start-up cost.

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The entire article will also be shortly available on http://www.thesynapse.net/.

NSAIDs and cardiovascular events – frequently asked questions

continued from page 10

The study showed that high doses of non-selective NSAIDS, such as ibuprofen, were associated with a similar increase in the risk of vascular events to COX-2 inhibitors. This meta-analysis included data from 138 trials among 145,373 patients, providing a much more reliable estimate of the cardiovascular risk of these drugs, as individual trials were too small to study this question.

The production of this paper by such a well recognised group will carry much influence within the clinical community. Therefore, this paper is likely to influence healthcare recommendation and prescribing patterns.

What does the data mean for healthcare professionals?

Combined with the vast amount of previously published material linking NSAIDs with increased cardiovascular risk, the Kearney paper reinforces the need for a rational approach to the recommending and prescribing of analgesics. These data show that those with CHF, a history of hypertension, those being treated for hypertension and the elderly are at particular risk of NSAID-related CVD events. This information is likely lead to recommendations on which analgesics should be recommended for certain patient types. Indeed, as summarised in the table below, experts are already starting to release such recommendations into the medical press.

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"Doctor, Doctor – Where are thou?" Medics in Movies and Television – Part I

continued from page 17

Today we have scanning technologies such as ultrasounds, CAT scans and PET scans that give out three dimensional images of bodily organs, to give a fully diagnostic picture. However according to Dr. Sanjiv Sam Gambhir we still don't have anything like the universal scanning device that allowed Dr "Bones" McCoy to diagnose practically anything in seconds.[4]

The medicine presented in *Star Trek* was so much ahead of its time, that even though today's scanning technologies have improved so much and so drastically, they still have a long way to go to emulate anything that is hailed as science fiction.

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Justin Camilleri graduated with a Bachelor in Communications in 2004 and has just completed a Masters in Magazine Journalism from the University of Central Lancashire. He regularly contributes to local newspapers and international magazines.

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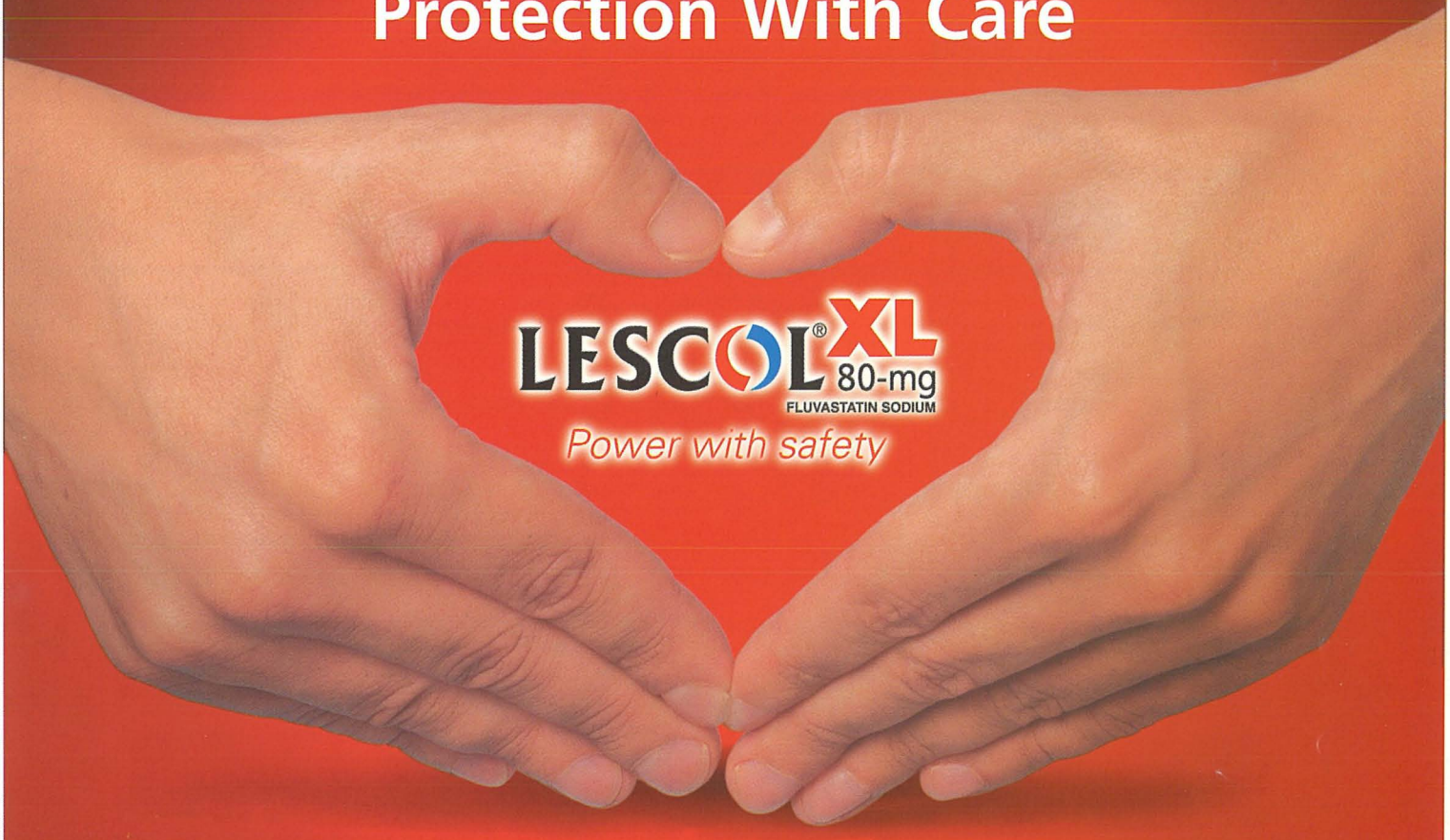

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(1) Corsini A, et al. The Use of Statins in Optimising Reduction of Cardiovascular Risk : Focus on Fluvastatin. Int J Clin Pract 2004; 58(5) : 494-503

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Presentation: Fluvastatin sodium. Lescol capsules containing the equivalent of 20 mg or 40 mg fluvastatin free acid. Lescol XL prolonged release tablets containing the equivalent of 80 mg fluvastatin free acid. Indications: For the reduction of TC, LDL-C, apoB, and TG, and the increase in HDL-C in patients with primary hypercholesterolemia and mixed dyslipidemia (Fredrickson Types IIa/IIb) as an adjunct to diet. Slowing of the progression of coronary atherosclerosis in patients with primary hypercholesterolemia, including mild forms, and coronary heart disease. Secondary prevention of major adverse cardiac events in patients with CHD after coronary transcatheter therapy. Dosage: Prior to initiating Lescol, the patient should be placed on a standard cholesterol lowering diet; dietary therapy should be continued during treatment. The recommended starting dose is 40 mg (1 capsule Lescol 40 mg) or 80 mg (2 capsules Lescol 40 mg once daily in the evening or 1 tablet Lescol XL 80 mg at any time of day). 20 mg (1 capsule Lescol 20 mg) may be adequate in mild cases. Contraindications: Hypersensitivity to the drug or excipients. Active liver disease or unexplained, persistent elevations in serum transaminases. Pregnancy, lactation, women of childbearing potential unless they are taking adequate contraceptive precautions. Precautions/Warnings: Caution is required in patients with a history of liver disease or heavy alcohol consumption, with unexplained diffuse myalgias, muscle pain/tenderness/weakness, and marked elevation of creatine kinase (CK) values. In patients with pre-disposing factors for rhabdomyolysis, the CK-level should be measured prior to treatment initiation. Caution with co-administration of fibrates, nicotinic acid and ciclosporin. Interactions: Fibrates; nicotinic acid; fluconazole; ciclosporin; bile acid-sequestrants; rifampicin; phenytoin; oral anticoagulants. Adverse reactions: Dyspepsia, abdominal pain, nausea, headache, insomnia. Rare cases of hypersensitivity reactions (mainly rash and urticaria), myalgia, muscle tenderness/weakness, myopathy. Very rare cases of thrombocytopenia, paraesthesia, dysaesthesia, hypo-aesthesia, vasculitis, hepatitis, other skin reactions (e.g. eczema, dermatitis, bullous exanthema), face oedema, angioedema, rhabdomyolysis, myositis, lupus erythematosus-like reactions. Elevation of transaminase and CK levels. Packs: Country specific

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Advances In Oral Hor

by **Charles Savona-Ventura** *MD DScMed FRCOG AccrCOG MRCPI CLJ OMLJ*
Consultant Obstetrician-Gynaecologist & Medical Historian

Down through the centuries, efforts to understand and to control fertility have been documented in almost every society. These efforts were two-edged: on one hand improving fertility to increase family size; on the other taking measures to prevent conception.

Various Egyptian medical papyra describe methods for increasing fertility and for decreasing the likelihood of conception. The Industrial Revolution, beginning in the middle of the eighteenth century, resulted in dramatic changes in world economy. The resulting urbanisation brought on major problems of poverty, crowding and over-population with the attendant health hazards. By the beginning of the nineteenth century, the birth control movement had got under way first in Britain and subsequently in the United States. The methods of birth control available at the time included natural methods [prolonged lactation, the safe period and coitus interruptus]; barrier techniques [condom, cervical cap and diaphragm]; and surgical interventions [intrauterine device, abortion and sterilization]. Pre-twentieth century contraceptive methods known to have been used in Malta included prolonged lactation, coitus interruptus and abortion. These were generally frowned upon by the clergy and medical community alike.

These methods obviously had their limitations. The post-Second World War social movement created a pressing need for an effective reversible contraceptive method that would allow women to delay their fertility while responding to the sexual revolution of the mid-twentieth century. The first orally active progestational agent, 17alpha-ethyltestosterone, had been synthesized by a Schering scientist, Hans Inhoffen, just before the beginning of World War II. This was to initiate the development of the first oral contraceptive pill and an ongoing programme to develop safer formulations. Dr Gregory Pincus, known as the 'father of the pill', together with John Rock and Celso Ramon Garcia tested the principle of hormonal inhibition of ovulation in 1951-1958. Their work led to the development of the effective hormonal contraceptive pill – Enovid in 1960. The scientists at Schering AG developed Anovlar using a highly effective progestogen and high dose oestrogen – 4 mg norethisterone acetate plus 0.05 mg ethinylestradiol – synthesised in Berlin and launched in 1961. The hormonal oral contraceptives were quickly introduced in Malta but were by 1967 being advertised as menstrual cycle regulators in the local medical press. However in spite of their availability on the local market, only 2% of the female population interviewed in 1971 were using hormonal contraception. By 1993, the usage rate had increased to 15.8%. The increasing use of contraception resulted in a definite drop in fertility rates over the second half of the twentieth century

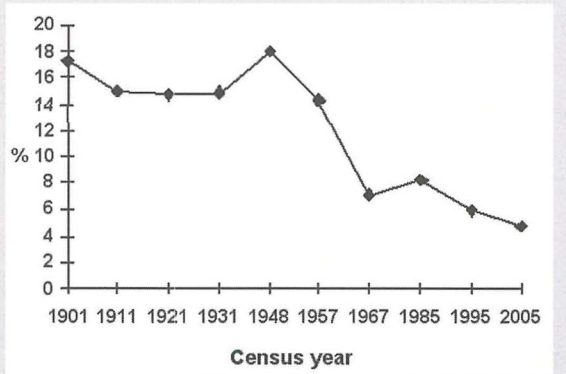

Table 1: *Fertility rates per 100 births in the Maltese Islands during the twentieth century [2005 approximate value]*

The increasing acceptance rate of the combined oral hormonal contraceptive pill was a multifaceted process linked partly to changing socio-religious norms on the Islands, but also the result of Schering's ongoing quest to develop and market safer formulations with minimal side-effects. The first oral hormonal contraceptives were plagued with adverse media coverage because of the observed risks of increased incidence of thrombo-embolism and cardiovascular events. These effects were found to be oestrogen dose-dependant which resulted in a move to progressively reduce the dose of the ethinylestradiol component of the formulation from the original 0.05 mg. The traditional progestins, generally derived from either 19-norestosterone or 17alpha-hydroxyprogesterone, were associated with significant androgenic and anabolic side-effects that caused marked side-effects in susceptible individuals. Irrespective of the measures taken to reduce the dose in the various formulations, these medications continued to be associated with adverse effects and tolerability issues such as bleeding irregularities, nausea, acne, headaches and fluid retention-related symptoms such as bloating, breast tenderness and weight gain.

In view of these toleratibility issues, Schering continued its investigations to search for new progestagens with favourable clinical profiles. The result of this work was the novel progestin – drospirenone – a 17alpha-spirolactone derivative which has a unique pharmacological profile that, in addition to its potent progestogenic activity, has both antiandrogenic and antimineralocorticoid activities. Clinical studies with the oral contraceptive formulation containing 0.03 mg ethinylestradiol and 3 mg drospirenone (Yasmin) have demonstrated an excellent contraceptive efficacy and a good safety profile with an additional favourable impact on fluid retention-related symptoms, particularly fluid-related weight gain, wellbeing and acne and other skin-related problems. Yasmin was a success story, but its developers continued in their efforts towards making the formulation even safer by reducing the oestrogenic dose from 0.03 mg to 0.02 mg. To achieve this while retaining optimal contraceptive efficacy, the ethinylestradiol compound was bound within two molecules of betadex in order to improve the stability of ethinylestradiol at a lower dosage. In general, the pharmacokinetics and relative bioavailability of ethinylestradiol are unaffected by its inclusion within a betadex complex. This formulation

rmonal Contraception

	Progestogenic	Glucocorticoid	Androgenic	Antiandrogenic	Antimineralocorticoid
Progesterone	+	-	-	(+)	+
Drospirenone	+	-	-	+	+
Levonorgestrel	+	-	(+)	-	-
Gestodene	+	-	(+)	-	(+)
Norgestimate	+	-	(+)	-	-
Desogestrel	+	-	(+)	-	-
Dienogest	+	-	-	+	-
Cyproterone acetate	+	(+)	-	+	-

Table 2: *Pharmacological profiles of various progestins.*

containing 0.02 mg ethinylestradiol and 3 mg drospirenone has been recently launched under the tradename Yasminelle.

Clinical trials with Yasminelle have demostrated excellent contraceptive reliability with a pearl index of 0.23; improved emotional and physical well-being; stable body weight; reduction of acne lesions; good overall tolerance and non-significant changes in metabolic parameters. Patient satisfaction for Yasminelle reached 86.6%. Its main disadvantage over the higher dose ethinylestradiol formulations is that of an increased rate of intracycle bleeding – estimated at 20.8% for the first cycle and 5.1-11.3% in subsequent ones. This is mainly dependant on the overall patient weight and individual pharmacokinetics. Yasminelle therefore appears to be the best first-line oral contraceptive pill on the market today ensuring the delivery of a minimum dose of hormone to achieve the desired effect. Its progestogenic and antimineralocorticoid properties also make it highly tolerable with positive effects on weight, skin and PMS. If intracycle spotting persists or in women with a high BMI, then the patient can be upgraded to the 0.03 mg formulation – Yasmin.

Cosmetic Dermatology: or an aestheti

by **Adrian Micallef**
MD, Dip IMC RCS (Ed.), Dip Ther (ICGP), Dip Prev (ICGP), MMCFD

Throughout the ages, the human race has been preoccupied with the quest for preserving and enhancing the aesthetic appearance of the human form

Disfigurement of face and body through disease or trauma has inspired the development of various ingenious surgical and non-invasive techniques which, aided by advances in research and technology, have evolved into the speciality of plastic and reconstructive surgery. In tandem with these developments, society has imposed an increasing desire to retain and enhance aesthetic features, so it is not surprising that the application of these techniques would eventually evolve into the fascinating art and science of aesthetic dermatology. The boundary between correcting and enhancing desirable features or changing unflattering ones has thus been blurred, and in the following article, we shall be reviewing some examples of these applications.

Botilinum toxin (BTX)

Botilinum toxin is the exotoxin of the spore-forming anaerobe *Clostridium botilinum*. BTX works on the neuromuscular endplate and other cholinergic synapses, causing irreversible synaptic blockade. BTX has been used since the 1980s in suitably modified form to treat dystonias such as blepharospasm, spasmodic torcicollis, limb dystonias and dysphonias.[1-3] The cosmetic properties of BTX were discovered quite by chance when a patient being treated for blepharospasm by a pioneering ophthalmologist commented that her perorbital wrinkles had greatly improved over the course of therapy. Subsequent trials on facial wrinkles led to widespread acceptance of this technique as a very effective treatment for hyperfunctional facial expression lines such as frown lines or those around the eyes[4] (Figure 1). BTX is even used to effectively treat axillary and palmar hyperhydrosis.[5] Since the body breaks down this substance, the effects described above are not permanent and top-up treatment is needed for continued efficacy.

Dermal fillers

Tissue augmentation, the filling-in of dermal or subdermal defects, is a technique which has found clinical applications in reconstructive surgery, ophthalmic and ENT fields and orthopaedics. In cosmetic dermatology worldwide, dermal fillers occupy fourth place in the list of most performed procedures. The earliest tissue expander was autologous fat which today is undergoing a revival with improved extraction and injection methods. Intensive research and innovative pharmacology have provided a variety of natural or synthetic fillers.

Hyaluronic acid is an avian-derivative of the connective tissue matrix of the skin, and is used to till in wrinkles, enhance lips and contour chin and cheeks[6] (Figure 2).

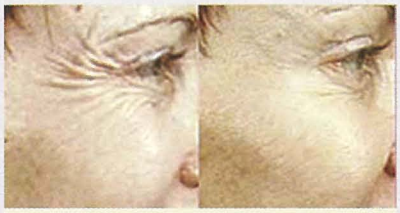

Figure 1: *Before and after BTX treatment of crow's feet around eyes.*

Figure 2: *Lip augmentation with Hyaluronic acid.*

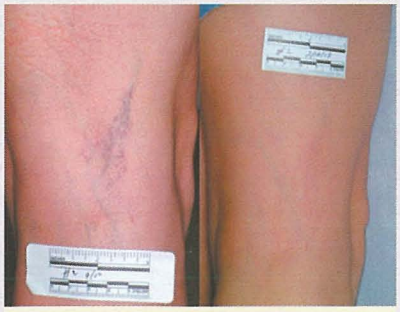

Figure 3: *Thread vein removal with sclerotherapy.*

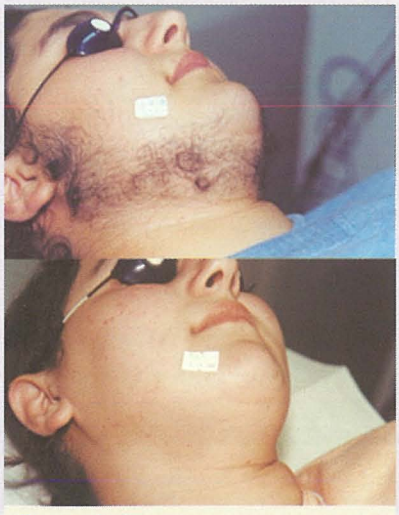

Figure 4: *Laser hair removal of facial hair – before and after.*

Unlike many other fillers, it is immunologically inert and does not need test-patching on the patient, but, being organic, it is broken down eventually and requires a top-up after about 6 months for continued effect. Collagen is one of the longest established fillers and can be either naturally extracted from bovine tissue,[7] again requiring top-ups after a few months; or a semi-synthetic development with a longer life span of 3 to 5 years.[8] These products are used to correct acne and other scars, frown lines, deep wrinkles and nasolabial folds. They do require a test-patch since some people are immunologically sensitive; the most recent development in this field has been human collagen (cadaveric or bioengineered) which has entered clinical use this year after FDA approval.

There are also synthetic fillers such as gore-tex and silicone which have much longer persistence but carry attendant risks of complications notably rejection, granuloma formation and scarring.

Non-surgical facelifts

Toning up the facial and neck muscles by using micro-current stimulation has become an established and effective alternative to the scalpel. The technique is the legacy of technology developed to treat patients suffering from facial paralysis as a result of stroke or Bell's palsy by delivering electric pulses to stimulate muscles. In aesthetic dermatology, the technique is suitable for the whole face including lips and eyes as well as neck and throat.

Microexfoliation

Microexfoliation is a highly effective form of treatment for several types of skin conditions such as acne, facial scarring and post-surgical scars, but cosmetically has been applied to improve pigmentation, stretch marks and the effects of skin aging. The principle of the technique is that by removing the most superficial skin layers, skin turnover is encouraged with production of a healthier skin and subdermal matrix. Traditionally, exfoliation has been carried out by controlled application of à-hydroxyacids (eg. glycolic and lactic acid) but a more recent development is microdermabrasion which is a mechanical exfoliation where tiny granules of sterile aluminium oxide are directed at high speed onto the skin surface to produce a 'sandblasting' effect. In both these techniques, the depth of the exfoliation can be precisely controlled for the respective outcome, and the procedures are carried out without need for anaesthesia.

Sclerotherapy

The selective destruction of unwanted veins by injecting chemicals into them is a procedure that has been applied to a

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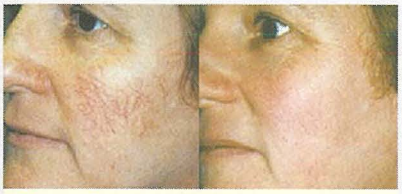

Figure 5: *Intense pulsed light treatment of facial veins – before and after.*

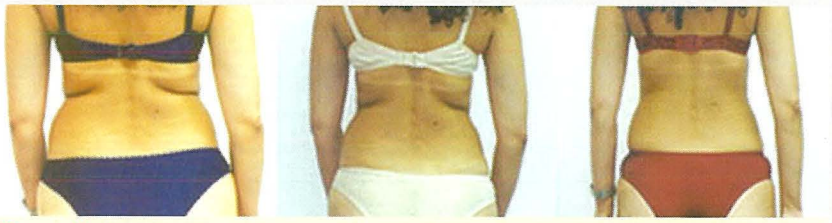

Figure 6: *Mesotherapy of bra strap folds – patient before and after a series of treatments.*

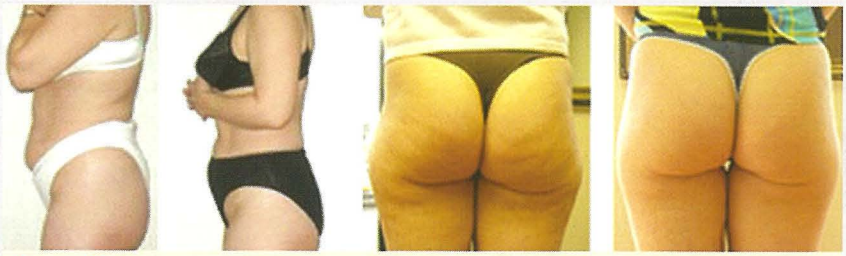

Figure 7: *Mesotherapy of abdominal fat and cellulite – before and after.*

variety of vascular conditions ranging from non-surgical removal of varicose veins, down to ablation of the minute spider or thread veins mostly on the lower limbs which may be the cause of symptoms such as cramps, leg pain or heaviness. Many patients however seek this treatment for cosmetic removal of unsightly thread veins (Figure 3). Various chemicals have been used,[9] including hypertonic saline, mannitol, polydocanol and tetradecylsulfate. The procedure involves multiple injections of the chemical into the length of the vessels using a very fine needle, following which the veins closes up and is absorbed by the body over a period of a few weeks. There is usually no need for anaesthesia and the patient is ambulant and can remain active immediately after the procedure.

Laser treatments and intense pulsed light

Light-based therapy has been one of the greatest technological success stories of recent times and its rapid evolution continues to push this modality to the forefront of therapeutic and cosmetic applications. Laser uses a focused beam of light of one specific wavelength, whereas intense pulsed light sources give out a broad wavelength spectrum but uses a selection of filters to cut off successive wavelengths depending on the indication of the treatment. Both systems operate on the principle of *selective photothermolysis* which means that individual wavelengths can selectively target and destroy specific structures in the skin by thermal energy, with minimal effect on surrounding less sensitive tissue. Light-based therapy has thus been used to selectively destroy pigmented lesions, thread veins and unwanted vessels, birth marks as well as excess facial and body hair[10, 11] (Figures 4, 5).

The latest cosmetic application which has gained worldwide popularity is photorejuvenation[12] whereby intense pulsed light is used to reverse the harmful effects of sun exposure and stimulate the natural production of collagen by the skin, with improvement of texture and elimination of blemishes such as age spots, thread veins, open pores and facial wrinkles.

Mesotherapy

Developed in 1952 by a French doctor, mesotherapy is a fascinating technique whereby medication is injected into the mesoderm, which is the layer of fat and connective tissue between the dermis and subcutaneous tissue. Clearance of any injected substance from this area is slow, leading to a controlled release and persistence of the substance into the vicinity of the application thus enabling a localised desired effect. The principle has been a development of prolotherapy where various medications are infiltrated in the vicinity of joints, tendons and soft tissues to treat a variety of orthopaedic and sport-related conditions.[13] Although mesotherapy has not yet been universally endorsed on account of approval of the concoction of substances used, its undeniably successful results have made it popular worldwide in treating a myriad of cosmetic conditions including overall weight loss, spot weight reduction (non-surgical liposculpture) and cellulite reduction, as well as for hair loss, scar revision and wrinkle elimination[14, 15] (Figures 6, 7).

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Update on Avian Influenza

by **Tanya Melillo Fenech** *MD MSc*
Principal Medical Officer at Disease Surveillance Unit, Department of Public Health

As of mid October, the number of cases in Indonesia were 72 and the number of deaths were 55 with a case fatality rate of 76%. The avian virus is endemic now in almost all provinces in the Indonesian archipelago of 17,000 islands It clearly shows how vulnerable humans are when they are in direct contact with their backyard poultry who become infected with the avian virus. If not treated immediately, the condition is fatal. This week the first human victim to suffer from brain inflammation (encephalitis) due to the avian virus is an adult woman and this has occurred in Indonesia.

Data collected from human cases in Vietnam and Thailand since 2003 show that disease and mortality from H5N1 avian influenza tends to be more severe among children than adults. This is complicated by the fact that severe and fatal H5N1 infections in children and adolescents have been shown to occur in the absence of respiratory presentations or marked respiratory involvement. This represents an apparent change in the epidemiology of the H5N1 virus in humans subsequent to the 1997 outbreak in Hong Kong, where severe disease symptoms were seen less frequently among children than adults.

The apparent higher frequency of non-respiratory disease syndromes and symptoms among children and adolescents reported in recent literature on human H5N1 cases suggests that H5N1 infections in children are more likely to be confused with other more common diseases. Children are therefore more likely to be overlooked as possible bird flu cases when they are not associated with infected adults exhibiting classical severe acute respiratory collapse or 'cytokine storm' syndromes.

Latest on antivirals

Instances of oseltamivir resistance in patients have been reported previously, but there has been no unequivocal confirmation of transmission of resistant virus from person to person.

Oseltamivir (Tamiflu®) and Zanamivir (Relenza®) inhibit the activity of the viral neuraminidase, an enzyme that enables influenza virus to escape from an infected cell and spread to other cells. Several studies suggest that viral resistance to oseltamivir may be a greater problem than previously believed. For example, in epidemics of H3N2 influenza in Japan in 2002 and 2003 about 1/5 of children developed resistance by day 4 or later during treatment with oseltamivir, and about 1/4 of children who shed virus for 3 days or more had drug-resistant influenza viruses. The neuraminidase-resistant mutations isolated were found to be from 300 to 100 000 times more resistant to oseltamivir than oseltamivir-susceptible virus. These reports of the emergence of drug resistance make the development of new anti-influenza molecules a priority.

Latest in animal infection caused by avian influenza virus

The Team of Veterinary Faculty at Udayana University has found evidence that the avian influenza virus has infected pigs in Bali.

Recent studies have revealed that cats can contract the avian influenza virus and that there is no evidence that migratory birds are responsible for the spread of the disease.

A study conducted by the Indonesian Environment Information Center in Yogyakarta found that stray cats had caught the H5N1 virus through contact with infected poultry at traditional markets.