

# The Synapse

The Medical Professionals Network

Exclusive

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How to save a limb p 11**

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No data available for use in patients with severe hepatic impairment. No relevant use in the paediatric population. **CONTRAINDICATIONS:** Hypersensitivity to the active substance, to lactose or to any of the other excipients. **WARNINGS/PRECAUTIONS:** Asthma: \*ONBREZ BREEZHALER SHOULD NOT BE USED IN ASTHMA. **Paradoxical bronchospasm:** \* If paradoxical bronchospasm occurs Onbrez Breezhaler should be discontinued immediately and alternative therapy substituted. **Deterioration of disease:** \* Not indicated for treatment of acute episodes of bronchospasm, i.e. as rescue therapy. **Systemic effects:** \*Indacaterol should be used with caution in patients with cardiovascular disorders (coronary artery disease, acute myocardial infarction, cardiac arrhythmias, hypertension), in patients with convulsive disorders or thyrotoxicosis, and in patients who are unusually responsive to beta2-adrenergic agonists. **Cardiovascular effects:** \* Indacaterol may produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, blood pressure, and/or symptoms, ECG changes. In case such effects occur, treatment may need to be discontinued. **Hypokalaemia:** \* Beta2-adrenergic agonists may produce significant hypokalaemia in some patients, which has the potential to produce cardiovascular effects. In patients with severe COPD, hypokalaemia may be potentiated by hypoxia and concomitant treatment which may increase the susceptibility to cardiac arrhythmias. **Hyperglycaemia:** \*Inhalation of high doses of beta2-adrenergic agonists may produce increases in plasma glucose. Upon initiation of treatment with Onbrez Breezhaler plasma glucose should be monitored more closely in diabetic patients. \*During clinical studies, clinically notable changes in blood glucose were generally more frequent by 1-2% on Onbrez Breezhaler at the recommended doses than on placebo. Onbrez Breezhaler has not been investigated in patients with not well controlled diabetes mellitus. **Pregnancy and Lactation:** \*No data available from the use of indacaterol in pregnant women. Onbrez Breezhaler should only be used during pregnancy if the expected benefits outweigh the potential risks. \*Not known whether indacaterol / metabolites are excreted in human milk. A decision must be made whether to discontinue breast-feeding or discontinue Onbrez Breezhaler therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. **INTERACTIONS:** \*Concomitant administration of other sympathomimetic agents may potentiate the undesirable effects of Onbrez Breezhaler. Onbrez Breezhaler should not be used in conjunction with other long-acting beta2-adrenergic agonists or medicinal products containing long-acting beta2-adrenergic agonists. \*Concomitant treatment with methylxanthine derivatives, steroids, or non-potassium-sparing diuretics may potentiate the possible hypokalaemic effect of beta2-adrenergic agonists, therefore use with caution. \*Indacaterol should not be given together with beta-adrenergic blockers (including eye drops) as these may weaken or antagonise the effect of beta2-adrenergic agonists. Where required, cardioselective beta-adrenergic blockers should be preferred, although they should be administered with caution. \*Inhibition of the key contributors of indacaterol clearance, CYP3A4 and P-gp, does not raise any safety concerns given the safety experience of treatment with Onbrez Breezhaler. \*Indacaterol has not been shown to cause interactions with co-medications. **ADVERSE REACTIONS:** \*The most common adverse reactions with Onbrez Breezhaler are: nasopharyngitis, upper respiratory tract infection, sinusitis, diabetes mellitus and hyperglycaemia, headache, ischaemic heart disease, cough, pharyngolaryngeal pain, rhinorrhoea, respiratory tract congestion, muscle spasm, periorbital oedema. \*Uncommon: paraesthesia, atrial fibrillation and non-cardiac chest pain. \*Please refer to SmPC for a full list of adverse events for Onbrez Breezhaler. **LEGAL CATEGORY: POM PACK SIZES:** Onbrez Breezhaler 150mcg - carton containing 10 or 30 capsules and one Onbrez Breezhaler inhaler. Onbrez Breezhaler 300mcg - carton containing 30 capsules and one Onbrez Breezhaler inhaler. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **MARKETING AUTHORISATION NUMBERS:** EU/1/09/593/001, 002, 007. Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma Services Inc, Representative Office P.O. Box 124, Valletta, VLT 1000 Malta. Tel: +356 22983217 2010-MT-01-ONB-01-Feb-2010

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References:  
1. Gazzola M, Malera MG. Novel long-acting bronchodilators for COPD and asthma. Br J Pharmacol. 2008;155:291-299.  
2. Novartis Europharm Ltd. Onbrez<sup>®</sup> Breezhaler<sup>®</sup> Summary of Product Characteristics

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## Editor's word

Every cloud has a silver lining. Or so they say. However I seriously doubt whether its attributed author (John Milton, most famous for penning *Paradise Lost*) in 1634 had an ash cloud in mind. Or for all that matters the effects that such cloud would herald on the mortality & morbidity of people all over the world. And with predictions telling us that the cloud may persist for months to come, well, the negative effects on the transportation chain of medicines as well as on medical tourism are indeed worrisome.

However on a more positive note, during the past few weeks we have also seen extraordinary advances in healthcare. The J. Craig Venter Institute in Rockville, Maryland, has synthesized the genome of the bacterium *Mycoplasma mycoides*. Having assembled the genome inside a yeast cell, they transplanted it into a cell from a closely related species, *Mycoplasma capricolum*. After the newly made cell had divided, the cells of the bacterial colony that it formed contained only proteins characteristic of *M. mycoides*. The Venter Institute work may thus help to link chemistry to natural history. The new synthetic technology may thus allow the resurrection of ancient bacteria, whose behaviour should inform us about planetary and ecological environments millions of years ago. Following this achievement, it may now be also possible to answer one of the great remaining questions of biology: how did life begin? However many unparalleled risks may arise. New regulations have to be drafted to prevent the release of hazardous life forms. And scientists are having two main concerns, relating to

bioerror and especially bioterrorism. For the latter avoidance, realistic in vitro ecosystems should be standardized to test the ability of new synthetic genomes to persist or exchange genes in the wild. The findings were published online in May in *Science*.

Yet another recent achievement is reminiscent of Almroth Wright's statement that '*The Physician of tomorrow will be the immunisator*'. A preclinical study in mice is suggesting that a preventive breast cancer vaccine might be possible in humans, with clinical trials possibly starting next year. The vaccine targets alpha-lactalbumin, a protein found in the majority of breast cancers, and only present in healthy women when they are lactating. The principal investigator Vincent Tuohy, an immunologist in Cleveland Clinic's Lerner Research Institute, indeed stated that 'If it works in humans the way it works in mice, this will be monumental. We could eliminate breast cancer.' The findings were published online in May in *Nature Medicine*.

Having said all this, I couldn't resist from jotting a couple of points regarding the World Cup! The World cup scenario did not only have to face the ash cloud challenge, but also the fact that FIFA officials are concerned that World Cup players may try to gain an unfair advantage by using traditional African herbal medicines that are not currently banned, some of which have diuretic & stimulant properties. So they are lobbying for the World Anti-Doping Agency to increase its tests. And leaving you with a possible word of advice we could advice to our

Published by Medical Portals Ltd.

The Professional Services Centre  
Guzei Cutajar street  
Dingli, Malta

Email: editor@thesynapse.net

Web: www.thesynapse.net

Editor: Wilfred Galea

Scientific editor: Ian C Ellul

Administration Manager: Carmen Cachia

Graphic Designer: - Jeff Galea

Printer - Europrint Ltd.

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patients ... a study published 4 years ago in the *NEJM* has demonstrated that viewing a stressful soccer match more than doubles the risk of an acute cardiovascular event! (<http://www.thesynapse.net/articles/viewarticle.asp?artid=12184>). So how about advising patients with existing coronary diseases to avoid watching their favourite final game after 4 years waiting? Well, to be honest, I have my doubts about compliance!

*Pan Ellul*  
Ian C Ellul

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The Synapse



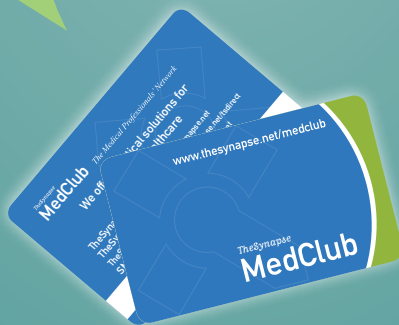
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## Issue Guide

## Contributors



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Dr Charmaine Gauci MD MSc Dip(Fit&Nut) PHD FRSPH is the Director of the Health Promotion and Disease Prevention Directorate. She is a senior lecturer with the University of Malta and delivers lectures in the field of public health with special interest in Epidemiology and Communicable Diseases. She is active in the field of public health and is currently also the President of the Malta Association of Public Health Medicine.



Professor Albert Cilia-Vincenti MD FRCP was Pathology Director to the Winchester & Eastleigh Healthcare Trust and Pathology Chairman, Malta Health Service. He served as London University Lecturer and was Pathology Head, University of Malta. He maintains an interest in nutritional and natural medicine and longevity, and also in wine. He is founding committee member of *il-Qatra*.

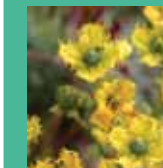


Dr Thomas Attard MD, FAAP, FAGC is a consultant Paediatrician and Gastroenterologist at Mater Dei Hospital; he has trained at The Johns Hopkins and Creighton-UNMC SoM(US) and worked at UNMC-Omaha Children's Hospital since 2001. His research interests are Inflammatory Bowel Disease and Hereditary Polyposis Syndromes.

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## Front Page



*Ruta chalepensis* (Wall rue, wild rue; Fejgel)

*Ruta chalepensis* is a herbaceous, aromatic, perennial shrub native to the Mediterranean and the Balkans. Related to citrus, it grows on rocky, calcareous soils. In Malta, it has a long tradition of use, both in the kitchen, and even more so, as a medicinal herb.

**Medicinal uses:** Fried in olive oil, or as an infusion in vinegar, it has popularly been used as a poultice to treat burns, wounds, bruises, sprains and swollen joints.

Photography: Guido Bonett ARPS AMPS  
Reference: Lanfranco G. Hxejjex medicinali u ohrain fil-gzejjer Maltin. Media Centre Print; Malta. 1993.



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References: 1. Mancia G, Laurent S, et al. *Blood Pressure* 2009;18:308-347. 2. Calhoun DA, Lacourcière Y, Chiang YT, Glazer RD. *Hypertension* 2009;54:32-39. 3. Lacourcière Y, Glazer R, Crikelaire N, Yen J, Calhoun D. Poster presented at: 19th Scientific Meeting of the ESH; 12-16 June 2009; Milan, Italy. 4. Lacourcière Y, Glazer R, Yen J, Calhoun D. Poster presented at: 19th Scientific Meeting of the ESH; 12-16 June 2009; Milan, Italy.

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Avoid use in women planning to become pregnant and while breast-feeding. • Caution when driving or using machinery. **INTERACTIONS:** • Monitoring recommended when used concomitantly with lithium. • Caution when used concomitantly with drugs that may increase potassium levels. • Caution if combined with other antihypertensives, curare derivatives, NSAIDs, corticosteroids, ACTH, amphotericin, carbamazepine, digoxin, CYP3A4 inhibitors and inducers, anti-diabetic agents, allopurinol, probenecid, sulfonpyrazone, pressor amines, amantadine, diazoxide, cytotoxic drugs, anticholinergic agents, methyldopa, cholestyramine, cholestyramine resins, vitamin D, calcium salts, carbamazepine and ciclosporin, alcohol, anaesthetics and sedatives. **ADVERSE REACTIONS:** • Exforge HCT (amlodipine/valsartan/HCT): Common: hypokalaemia, headache, dizziness, hypotension, dyspepsia, pollakiuria, oedema, fatigue. Uncommon: anorexia, hypercalcaemia, hyperlipidaemia, hyperuricaemia, hyponatraemia, insomnia/sleep disturbances, abnormal coordination, postural and exertional dizziness, dysgeusia, lethargy, paraesthesia, peripheral neuropathy, neuropathy, somnolence, syncope, visual disturbance, vertigo, tachycardia, orthostatic hypotension, pleilebils, thrombocytopenia, cough, dyspnoea, throat irritation, abdominal discomfort, upper abdominal pain, breath odour, diarrhoea, dry mouth, nausea, vomiting, hyperhidrosis, pruritus, back pain, joint swelling, muscle spasm, muscular weakness, myalgia, pain in extremity, elevation of serum creatinine, acute renal failure, erectile dysfunction, abasia, gait disturbance, asthenia, discomfort, malaise, non cardiac chest pain, increased blood urea nitrogen, increased blood uric acid, decreased serum potassium, weight increase. • Additional adverse reactions with amlodipine monotherapy: Common: palpitations, flushing. Uncommon: mood swings, tremor, tinnitus, rhinitis, change of bowel habit, alopecia, exanthema, purpura, skin discoloration, arthralgia, micturition disorder, nocturia, gynaecomastia, pain, weight decrease. • Additional adverse reactions with HCT monotherapy: Common: increased lipids. Uncommon: hypomagnesaemia, decreased appetite, urticaria. Rare: thrombocytopenia, hyperglycaemia, depression, arrhythmia (including bradycardia, ventricular tachycardia and atrial fibrillation), constipation, intrahepatic cholestasis, jaundice, photosensitivity reaction, renal failure and impairment, glycosuria. **LEGAL CATEGORY:** POM **PACK SIZES:** Packs of 28 film-coated tablets **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **MARKETING AUTHORISATION NUMBER:** Exforge HCT 10 mg/160 mg/25 mg - EU/1/09/569/038 Exforge HCT 10 mg/320 mg/25 mg - EU/1/09/569/050 Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma Services Inc., Representative Office Malta, P.O. Box 124, Valletta, VLT 1000, Malta. Tel: +356 22983217 2010-MT-01-EXFH-16-OCT-2009

## Social Medicine

# A strategy for the Prevention and Control of Noncommunicable Diseases in Malta

by Charmaine Gauci

One of the Maltese Government's objectives in improving the health status of the population is "To add health to life by increasing years lived free from ill-health, reducing or minimising the adverse effects of illness and disability, promoting healthy lifestyles, healthy physical and social environments and, overall, improving quality of life."<sup>1</sup>

There is a huge burden of illness and death which is preventable. Noncommunicable diseases (NCD) such as coronary heart disease, stroke and diabetes are responsible for about 82% of deaths in Malta<sup>2</sup> compared to 87% of all deaths in the EURO-A region, which includes most of Western Europe, as estimated by the Global Burden of Disease project.<sup>3</sup>

They are also responsible for a similar amount of disability in the form of pain and suffering, reduced mobility and loss of independence. Cardiovascular disease is considered to be the most prevalent of the NCD. In fact, around the Mediterranean basin, a mean of 10.4 DALYs (Disability Adjusted Life Years) per 1000 population are lost due to heart disease, together with another 7.5 DALYs per 1000 population due to cerebrovascular disease. In Malta, these figures were estimated to be 9

DALYs for heart disease and 4 DALYs for cerebrovascular disease. A North-South gradient was observed across the Mediterranean with France, Italy and Spain reporting the lowest rates and North African countries reporting the highest<sup>4</sup> rates.

Affordable solutions exist to prevent 40 to 50% of premature deaths from NCD. We need to move NCDs from important and not urgent to important AND urgent. Hence the Public Health Regulation Department embarked on formulating a strategy for the prevention and control of NCD. The concept of an integrated approach borrowed from the experience gained by the WHO Countrywide Integrated Noncommunicable Disease Intervention (CINDI) Programme as well as from international research on how to cope with major chronic diseases throughout a person's entire life span has served as a solid base for the formulation of this national strategy. The CINDI approach<sup>5</sup> is based on evidence that a small number of risk factors and conditions are common to major chronic diseases. This commonality means that integrated action against selected risk factors implemented within the social context can lead to a reduction of major NCD as well as an improvement in public health.

Presently NCD preventive efforts are targeted at specific risk factors and social and environmental determinants, through health promotion initiatives and primary health care services via an effective information system. The strategy aspires to reduce NCD by implementing population strategies which encourage healthy lifestyles and the creation of a social environment that supports health, as well as targeting high-risk behaviours aimed at improving risk profile through preventive measures at an individual level.

There are a number of factors which contribute to the development of NCD. There are the non-modifiable risk factors such as age, gender and genetics. Other factors which are directly related to NCD are the four main behavioural lifestyle risk factors of diet, physical activity, tobacco and alcohol and the four biological risk factors of obesity, hypertension, hyperlipidaemia and carbohydrate abnormalities.

All these factors are directly contributing to the development of NCDs. For the non-modifiable risk factors we cannot do much but for – in fact a national strategy which was launched in April 2010.<sup>6</sup> There are various examples where preventive actions have worked. Finland has embarked on a 25 year project in North Karelia and has obtained an 80% reduction in coronary heart disease mortality by a decline in the major risk factors.<sup>7</sup> Ireland has obtained a 48.1% reduction in coronary heart disease mortality in 25 to 84 year olds, attributable to favourable trends in population risk factors.<sup>8</sup>

There are various effective interventions which include:

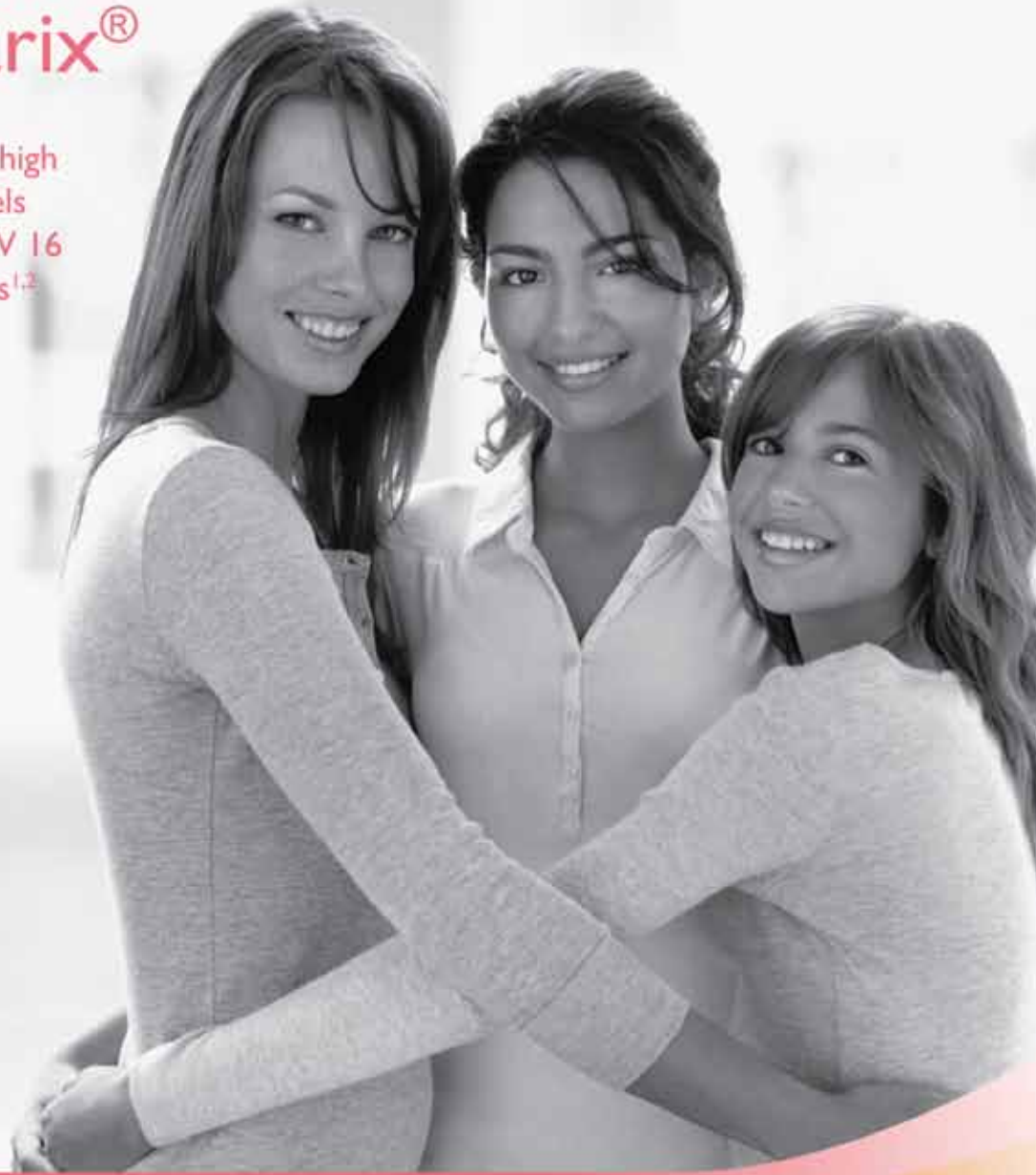
- Laws and regulations – environment, tobacco;
- Tax and price interventions – increase tax on tobacco, subsidies for healthy choices;
- Lowering the fat, salt and sugar content of processed foods;
- Advocacy – web sites, mass media, lobbying;
- Enhancing the health-enhancing environments in schools, the workplace and the community – promoting exercise facilities, improved nutrition, legislation on sales of alcohol;

Continued on page 9



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**TRADE NAME:** CERVARIX. **ACTIVE INGREDIENT:** 1 dose (0.5 ml) contains: Human Papillomavirus type 16 L1 protein 20 micrograms, Human Papillomavirus type 18 L1 protein 20 micrograms, (recombinant, adjuvanted, adsorbed). **PHARMACEUTICAL FORM:** Suspension for injection in pre-filled syringe. **THERAPEUTIC INDICATIONS:** CERVARIX is a vaccine for the prevention of pre-malignant cervical lesions and cervical cancer causally related to Human Papillomavirus (HPV) types 16 and 18. **POSODOLOGY AND METHOD OF ADMINISTRATION:** The recommended vaccination schedule is 0, 1, 6 months. Not recommended for use in girls below 10 years of age. Cervarix is for intramuscular injection in the deltoid region. **CONTRAINDICATIONS:** Hypersensitivity to the active substances or to any of the excipients; acute severe febrile illness. **PRECAUTIONS:** Anaphylactic reaction; Caution in individuals with thrombocytopenia or any coagulation disorder. Cervarix protects against disease caused by HPV types 16 and 18. Other oncogenic HPV types can also cause cervical cancer and therefore routine cervical screening remains critically important and should follow local recommendations. Not indicated for treatment of cervical cancer, cervical intraepithelial neoplasia (CIN) or any other established HPV-related lesions. Cervarix does not prevent HPV-related lesions in women who are infected with HPV-16 or HPV-18 at the time of vaccination.

**DRUG INTERACTIONS:** Data have not been generated on the concomitant administration of Cervarix and other vaccines. There is no evidence that the use of hormonal contraceptives has an impact on the efficacy of Cervarix. In patients receiving immunosuppressive treatment, an adequate response may not be elicited. **PREGNANCY AND LACTATION:** Vaccination should be postponed until after completion of pregnancy. Cervarix should only be used during breast-feeding when the possible advantages outweigh the possible risks. **ADVERSE EVENTS:** Common and very common: headache; gastrointestinal symptoms including nausea, vomiting, diarrhoea and abdominal pain; itching/pruritus, rash, urticaria; myalgia and arthralgia; injection site reactions including pain, redness, swelling, fatigue; fever (≥38°C); Uncommon: dizziness, upper respiratory tract infection, other injection site reactions such as induration, local paraesthesia. **PRESENTATION:** Pack of 1 pre-filled syringe

with a plunger stopper containing 0.5ml of suspension + 1 needle (refer to full SPC for information on disposal). **LEGAL CATEGORY:** POM. **M.A. HOLDER:** GlaxoSmithKline Biologicals S.A. Belgium. **M.A. NUMBER:** EU/1/07/419/004. For further information and full prescribing information contact GlaxoSmithKline (Malta) Ltd, Tel: 21 238 131. Date of preparation: September 2008.

1. Harper D, Gall S, Naud P, Quint W, Dubin G, Jenkins D, et al. Sustained immunogenicity and high efficacy against HPV-16/18 related to cervical neoplasia: long-term follow up through 6.4 years in women vaccinated with Cervarix™ (GSK's HPV 16/18 AS04 candidate vaccine). Society for Gynecologic Oncologists (SGO), Tampa, Florida, USA, 2008, March 9-12.
2. Wheeler C, Teixeira J, Romanowski B, De Carvalho NS, Dubin G, Schuind A. High and sustained HPV-16 and 18 antibody levels through 6.4 years in women vaccinated with Cervarix™ (GSK HPV-16/18 AS04 vaccine). 26th Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), Graz, Austria, 2008, May 13-16.

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## Social Medicine

Continues from page 7

- Enhancing social support for the elderly;
- Training programmes to equip people with problem-solving skills;
- Screening programmes if feasible and effective eg. breast screening;
- Encourage health professionals to promote preventive measures;
- Disease management – evidence-based management, effective information systems, multidisciplinary healthcare teams, patient self-management;
- Clinical prevention – the correct choice of medicines including antihypertensives, lipid lowering medicines etc;
- Rehabilitation and palliative care.

The overall goal of the NCD strategy is to develop a multifactorial approach to NCD prevention by tackling common risk factors targeting both at a population level, and also high-risk groups. In developing such a strategy the main focus is on the prevention of various aspects including the onset of disease, preventing late diagnosis, preventing recurrence and preventing progression. Ultimately if disease has set in, we aim to prevent complications and also prevent disability or premature death. Hence the focus is not only on the prevention of disease but the

strategy also looks at the quality of life.

For example, a high-risk intervention for reducing high blood pressure would target the members of the population whose systolic blood pressure lies above 140 mmHg, which is considered hypertensive. However, a large proportion of the population are not considered to be hypertensive, but still have higher than ideal blood pressure levels and thus also face a raised health risk.<sup>5</sup> Although the risks for this group are lower than for those classified as hypertensive, there may be more deaths due to high blood pressure in this group because of the larger numbers of people it contains. Considering only the effect of hypertension on population health, as is often done, gives decision-makers an incomplete picture of the importance of the risk factor for the population because it underestimates the full effect of raised blood pressure on population health. Population-based strategies seek to change the social norm by encouraging an increase in healthy behaviour and a reduction in health risk. They target risks via legislation, tax, financial incentives, health promotion campaigns or engineering



solutions. However, although the potential gains are substantial, the challenges in changing these risks are great. Population-wide strategies involve shifting the responsibility of tackling big risks from individuals to governments and health ministries, thereby acknowledging that social and economic factors strongly contribute to disease.

This strategy when performed collectively by all stakeholders, will tackle the growing public health burden imposed by NCD.<sup>9</sup> In order for the strategy to be implemented successfully, high-level political commitment and the concerted involvement of government, communities and health-care providers are required; in addition, public health policies will need to be reoriented and allocation of resources improved.

## European Immunization Week

The European Immunization Week (EIW) is a regional initiative, led and coordinated by WHO/Europe and implemented by Member States to address country-specific issues related to immunization. In 2010, the fifth European Immunization Week held between 24th April and 1st May continued to promote the message that immunization of every child is vital in order to prevent diseases and protect life. EIW 2010 also emphasized national immunization efforts towards meeting the regional goal to eliminate measles and rubella by the end of the year.

More than a decade ago, Member States adopted a regional goal of eliminating measles and rubella by 2010. However the goal has stalled in recent years. Measles coverage in many western European countries has fallen below the recommended 95% and measles has made a comeback, with ongoing outbreaks in the western part of Europe.

The 2010 measles elimination goal is vital and attainable, but it will only be met if individual countries, and Europe as a whole, make a focused and concerted effort to achieve it. Malta has participated in this enhanced awareness by encouraging parents to immunise their children, and with the help of health care professionals to spread the word to 'Prevent. Protect. Immunize.'

The Health Promotion and Disease Prevention Directorate has published a booklet of information on this subject which is currently being given to the mothers of all newborn babies - <http://www.thesynapse.net/articles/viewarticle.asp?artid=12084>





# The Diabetic Foot

## How to save a limb – Part I

by Kevin Cassar

The high prevalence of diabetes mellitus in our country is well recognized and it is estimated that there are around 40,000 diabetics in Malta. This is steadily increasing, as it is in the rest of the world, as a result of longer life expectancy, sedentary lifestyles, and dietary choices. Diabetic foot problems are the most serious and costly complications of diabetes. The World Health Organisation estimates that in the high income countries treatment of diabetic foot complications accounts for 15-25% of all healthcare resources for diabetes. Over 1 million major lower limb amputations are performed each year in diabetics amounting to a leg being lost to diabetes every 30 seconds. In Malta 120 major amputations are performed per year and this figure has remained relatively static for at least the last 6 years. The sad thing is that a lot of these complications can be prevented using low cost and low technology solutions. The International Working Group on the diabetic Foot (IWGDF) states that by implementing a care strategy that combines prevention, the multidisciplinary treatment of foot ulcers, appropriate organization, and close monitoring and education of people with diabetes and healthcare professionals, it is possible to reduce major amputations by a staggering 85%!

### What causes diabetic foot problems?

Foot problems arise mainly because of one or both of the following conditions: peripheral neuropathy and/or peripheral vascular disease. Peripheral neuropathy causes loss of sensation, autonomic dysfunction and alteration of the shape of the foot which predisposes to the development of ulceration, diabetic foot infection, and Charcot's osteoarthropathy. The prevalence of polyneuropathy in diabetics is estimated to be around 24% in Type II diabetics.<sup>1</sup>

Diabetes is a major risk factor for atherosclerosis and as a result many diabetics suffer from peripheral vascular disease affecting any part of the vascular tree including the aortoiliac segments, the femoropopliteal segment and the crural vessels. Based on UK population surveys peripheral vascular disease occurs in up to 23% of diabetics.<sup>2</sup> Although diabetics also suffer from microangiopathy, the major problem with diabetics who have arterial disease lies in the major arteries. It is a commonly held misconception that there is nothing to do for diabetics with arterial disease because the problem lies in the small vessels. Nothing could be further from the truth. Most diabetics with arterial disease are amenable to revascularisation either using endovascular or open surgical techniques. There is clear evidence that with increasing numbers of revascularisation there is a drop in the number of major amputations performed.<sup>3-5</sup>

In the vast majority of diabetic patients who end up requiring a major amputation, there is a repetitive causal sequence of minor trauma, ulceration and wound healing failure which often goes on for several weeks if not months.<sup>6</sup> Based on the recognition of the sequence of events, various guidelines have been drawn up for Diabetic Foot Care including SIGN (Scottish Intercollegiate Guidelines Network guideline 55), NICE guidance (National Institute of Clinical Excellence), and the Consensus statement of the International Working Group for the Diabetic Foot. All of these guidelines have a common theme - that a significant proportion of major amputations can be prevented if adequate measures are in place.

*"It is a commonly held misconception that there is nothing to do for diabetics with arterial disease because the problem lies in the small vessels"*

*Continues on page 20*



OTHER INDICATIONS:

- Treatment of GIO
- Male osteoporosis

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\*\*Nonvertebral fracture includes wrist, rib, arm, shoulder, or hip fracture; excludes finger, toe, or craniofacial fracture.

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**PRESENTATION:** Zoledronic acid. 100 mL solution bottle contains 5 mg zoledronic acid (anhydrous), corresponding to 5.330 mg zoledronic acid monohydrate.

**INDICATIONS:** Treatment of osteoporosis in post-menopausal women and men at increased risk of fracture, including those with a recent low-trauma hip fracture. Treatment of osteoporosis associated with long-term systemic glucocorticoid therapy in post-menopausal women and in men at increased risk of fracture. Treatment of Paget's disease of the bone.

**DOSAGE AND ADMINISTRATION:** Osteoporosis: A single intravenous infusion of 5 mg Aclasta administered once a year. In patients with a recent low-trauma hip fracture, it is recommended to give the Aclasta infusion two or more weeks after hip fracture repair. Paget's Disease: A single intravenous infusion of 5 mg Aclasta. Specific re-treatment data are not available for Paget's disease. Aclasta is administered via a vented infusion line and given at a constant infusion rate. The infusion time must not be less than 15 minutes. Adequate calcium and vitamin D are recommended in association with Aclasta administration. In patients with recent low-trauma hip fracture a loading dose of 50,000 to 125,000 IU of Vitamin D is recommended prior to the first Aclasta infusion. No dose adjustment in patients with creatinine clearance  $\geq 35$  mL/min, or in patients with hepatic impairment, or in elderly patients. The safety and efficacy of Aclasta in children and adolescents below 18 years of age has not been established.

**CONTRAINDICATIONS:** Hypersensitivity to zoledronic acid or to any of the excipients or to any bisphosphonate; hypocalcaemia; pregnancy; lactation.

**PRECAUTIONS AND WARNINGS:** Serum creatinine should be measured before each Aclasta dose. Aclasta should not be used in patients with creatinine clearance  $< 35$  mL/min. Transient increase in serum creatinine may be greater in patients with underlying impaired renal function. Monitoring of serum creatinine should be considered in at-risk patients. Patients must be appropriately hydrated prior to administration of Aclasta, especially important for the elderly and for patients receiving diuretic therapy. Use with caution in conjunction with medicinal products that can impact renal function. A single dose of Aclasta should not exceed 5mg and the duration of infusion should be at least 15 minutes. Pre-existing hypocalcaemia and other disturbances of mineral metabolism must be treated by adequate intake of calcium and vitamin D before initiating therapy with Aclasta. It is strongly advised that patients with Paget's disease receive supplemental calcium and vitamin D. Measurement of serum calcium before infusion is recommended for patients with Paget's disease. Severe and occasionally incapacitating bone, joint and/or muscle pain have been infrequently reported with bisphosphonate therapy. A patient being treated with Zometa should not be treated with Aclasta. As a precaution against osteonecrosis of the jaw (ONJ) a dental examination with appropriate preventive dentistry should be considered prior to treatment in patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids, poor oral hygiene). While on treatment, these patients should avoid invasive dental procedures if possible. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk of osteonecrosis of the jaw. Aclasta is not recommended in women of childbearing potential.

**INTERACTIONS:** Specific drug-drug interaction studies have not been conducted with zoledronic acid. Caution is recommended when Aclasta is used concomitantly with drugs that can significantly impact renal function, such as aminoglycosides and diuretics that can cause dehydration. In patients with renal impairment, the systemic exposure to concomitant medicinal products that are primarily excreted via the kidney may increase.

**ADVERSE REACTIONS:** The incidence of adverse reactions (e.g. fever, myalgia, flu-like symptoms, arthralgia and headache) are greatest with the first infusion and decrease markedly with subsequent infusions. The majority of these reactions occur within the first three days and were mild to moderate and resolved within three days of the event onset. The incidence of these adverse reactions can be reduced with the administration of paracetamol or ibuprofen shortly following Aclasta administration. Very common: Fever. Common: Flu-like symptoms, chills, fatigue, pain, asthenia, malaise, arthralgia, myalgia, bone pain, back pain, pain in extremity, vomiting, nausea, headache, dizziness, atrial fibrillation, hypocalcaemia†, ocular hyperaemia, diarrhoea, increased C-reactive protein, infusion site reactions. Uncommon: Hypertension, flushing, palpitations and others. Not known: Scleritis, orbital inflammation, hypotension, renal impairment, osteonecrosis of the jaw, dehydration secondary to post dose symptoms, hypersensitivity reactions.

† Common in Paget's disease only. Please refer to SmPC for a full list of adverse events.

**PACK SIZE:** Aclasta is supplied in packs containing one 100ml bottle

**LEGAL CATEGORY:** POM.

**MARKETING AUTHORISATION NUMBER:** EU/1/05/308/001.

**MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom.

Consult full Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available upon request from: Novartis Pharma, P.O. Box 124, Valletta VLT 1000, Malta. Tel +356 22983217. (vsn 2010-MT-001 ACL 18-05-2010)

References: 1. Aclasta SmPC. Novartis Europharm Ltd. 2. Black DM, Delmas PD, Eastell R, et al; for the HORIZON Pivotal Fracture Trial. Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis. N Engl J Med. 2007;356:1809-1822. 3. Saag K, Lindsay R, Kriegman A, Beamer E, Zhou W. A single zoledronic acid infusion reduces bone resorption markers more rapidly than weekly oral alendronate in postmenopausal women with low bone mineral density. Bone. 2007;40:1238-1243. 4. McClung M, Recker R, Miller P, et al. Intravenous zoledronic acid 5mg in the treatment of postmenopausal women with low bone density previously treated with alendronate. Bone. 2007;41:122-126.

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Indicated as substitution therapy in patients adequately controlled with aliskiren and hydrochlorothiazide, given concurrently, at the same dose levels as in the combination. **Dosage:** One tablet of Rasilez HCT 300/12.5 mg or 300/25 mg daily. **Contraindications:** \*Known hypersensitivity to the components of this product or to sulfonamides. \*History of angioedema with aliskiren \*pregnancy and breast-feeding \*severe hepatic impairment \*severe renal impairment (creatinine clearance < 30 mL/min) \*refractory hypokalaemia \*hypercalcaemia \*concomitant use with ciclosporin and other potent P-gp inhibitors. **Warnings/Precautions:** \*Avoid use in women planning to become pregnant \*Caution in patients with heart failure \*Symptomatic hypotension in sodium- and/or volume-depleted patients which should be corrected prior to initiation of therapy. \*Treatment should be discontinued if angioedema occurs and appropriate therapy and monitoring provided until resolution of signs and symptoms. \*Caution is advised when administering Rasilez HCT to patients with renal artery stenosis, renal and liver impairment, renovascular hypertension or systemic lupus erythematosus. \*Disturbance of serum electrolyte balance including hypokalaemia, hypochloreaemic alkalosis, hyponatraemia and hypercalcaemia (monitoring recommended), glucose tolerance and serum levels of cholesterol, triglycerides and uric acid. \*Use with caution in patients with aortic and mitral valve stenosis. \*Caution with moderate P-gp inhibitors such as telocicazole. \*Caution with concomitant potassium-sparing diuretics, potassium supplements or potassium-containing salts. \*Stop treatment in the event of severe and persistent diarrhoea. \*Caution in excessive reduction of blood pressure in patients with ischaemic cardiopathy of ischaemic cardiovascular disease. \*Caution in driving or operating machinery. \*Caution with patients with history of allergy and asthma. \*Not recommended in patients below 18 years of age. \*Cyclosporin. Contains lactose and wheat starch. **Interactions:** \*Monitoring when used concomitantly with furosemide, lithium, products affected by serum potassium disturbances (eg digitalis glycosides, antiarrhythmics), calcium supplements or calcium sparing medicinal products. \*Possible interaction with digoxin, ibuprofen, St. John's wort, and rifampicin. \*Meals with high fat content substantially reduce absorption. \*Caution when used concomitantly with drugs that may increase potassium levels (eg potassium supplements, heparin sodium) and drugs that decrease potassium levels (eg corticosteroids, ACTH, amphotericin, carbamazepine, penicillin G, laxatives, salicylic acid derivatives, other kaliuretic diuretics). \*Caution if combined with other antihypertensives, curane derivatives, NSAIDs (especially in the elderly), digoxin, antidiabetic agents, allopurinol, amantadine, diazoxide, cytotoxic drugs, anticholinergic agents, cholestyramine and colestipol resins, vitamin D, calcium salts, pressor amines, antitussive, and ciclosporin. \*Caution should be exercised on concomitant use with ketoconazole or other moderate P-gp inhibitors (telocicazole, itraconazole, clarithromycin, erythromycin, amiodarone, leflunomide). \*Grapefruit juice. \*Alcohol. **Adverse reactions:** Common: Dizziness. For the aliskiren component, other reported adverse reactions include: Uncommon: Rash. Rare: Angioedema. Laboratory values: decrease in haemoglobin and haematocrit, increase in serum potassium. For the hydrochlorothiazide component, other reported adverse reactions include: Aplastic anaemia, bone marrow depression, neutropenia/leucopenia, haemolytic anaemia, leucopenia, thrombocytopenia, depression, sleep disturbances, restlessness, light-headedness, vertigo, paraesthesia, dizziness, transient blurred vision, xanthopsia, cardiac arrhythmias, postural hypotension, respiratory distress (including pneumonia and pulmonary oedema), pancreatitis, anorexia, diarrhoea, constipation, gastric irritation, sialadenitis, loss of appetite, jaundice (intrahepatic cholestatic jaundice), anaphylactic reactions, toxic epidermal necrolysis, necrotising angitis, (vasculitis, cutaneous vasculitis), cutaneous lupus erythematosus-like reactions, reactivation of cutaneous lupus erythematosus, photosensitivity reactions, rash, urticaria, weakness, muscle spasm, interstitial nephritis, renal dysfunction, fever. Laboratory values: electrolyte imbalance, including hyponatraemia and hypocalcaemia, hypernatraemia, glycaemia, hyperglycaemia, increases in cholesterol and triglycerides. **Legal Category:** POM. **Pack sizes:** 7, 28 film-coated tablets. **Marketing Authorisation Holder:** Novartis European Limited, Wellesbourne Road, Herts, West Sussex, RH12 5AB, United Kingdom. **Marketing Authorisation Numbers:** Rasilez HCT 300/12.5 mg - EU/1/06/491/041-060. Rasilez HCT 300/25 mg - EU/1/06/491/061-080. Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma, P.O. Box 124, Valletta, VLT 1000, Malta. Tel: +356 25983217. (2010-MF-RASHCT March 2010)

References: 1. Palatini P, Jung W, Shykoff E, et al. *J Hum Hypertens* 2010; 24:93-103; published online 21 May 2009. 2. Vilami A, Chrysant SG, Calhoun D, et al. *J Hypertens* 2007; 25:217-226

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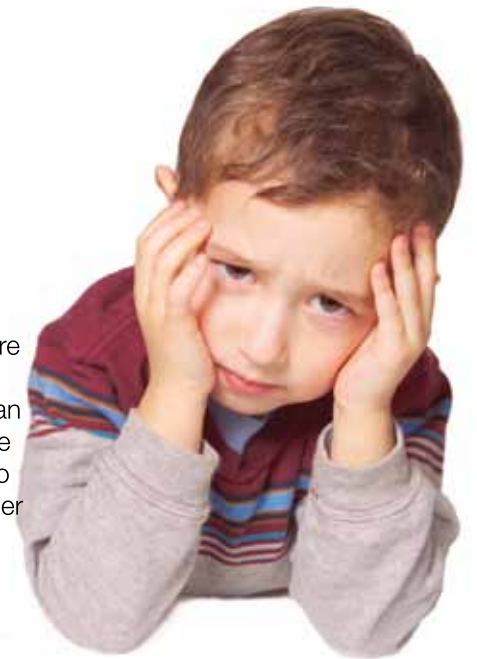
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Pediatrics

# Chronic Abdominal Pain in Children

by Thomas Attard

Recurrent abdominal pain in childhood, is classically defined as three or more episodes of pain severe enough to interfere with daily activities over the span of more than three months.<sup>1</sup> It is a common presenting complaint to both general practice and paediatricians with a prevalence of 10–15 % of school age children. However, an organic underlying disorder is rare; most studies suggest in the order of 5–10%. The clinical characteristics that facilitate the recognition of children who are more likely to harbor organic disease are therefore important to the practicing primary care provider and paediatricians in order to avoid unnecessary, costly and invasive investigations.



Functional Gastrointestinal Diseases (FGID) is an allied concept, and a more modern definition that includes recurrent abdominal pain (RAP). This includes paediatric patients with a presentation and course very similar to adult-onset irritable bowel syndrome (IBS).

## Biomedical and Biopsychosocial Models of Disease

There is an increasingly compelling body of evidence that undermines the classic biomedical model of illness. This defines the impact of the disease, or the illness, solely in terms of the organic impact of the underlying pathology. Indeed, a recent, prospective study from general practice reported a very low eventual detection of a specific etiology in patients in general (15%) which was even lower in patients presenting with abdominal pain (10%). This has spawned interest in a biopsychosocial model of disease that attempts to define the illness in terms of the underlying pathology, which may be minimal, undetectable or insignificant but modulated by psychologic, personal and societal factors that ultimately define the experience of illness by the patient and the family.<sup>2</sup> It therefore becomes paramount to recognize, treat or refer for management, factors that determine the psychosocial component of the illness.

A history of *longstanding pain*, including constant pain and pain as the sole presenting symptom despite careful history-taking, are more consistent with a diagnosis of FGID. *Normal appetite*, the *absence of nocturnal symptoms*, and pain that diminishes with distraction or redirection are all similarly reassuring. The presence and pattern of abdominal tenderness is usually unhelpful and inconsistent. A past medical history of atopy may signal a child with milk protein or other food allergy. It is similarly important to understand the symptom in the context of the family involved: parents with a history of IBS, migraine-headaches and fibromyalgia are far more likely to report similar symptoms in the offspring. This 'enabling' behavior has long been recognized as a cardinal clinical feature of functional abdominal pain in children and also a

negative prognostic factor in the resolution of functional abdominal pain in childhood.

**Inflammatory Bowel Disease (IBD)** can present acutely or insidiously including as chronic abdominal pain. Typical 'red flags' would include poor longitudinal growth, change in bowel habit, blood in the stool, or evidence of an inflammatory process including fever, and nonspecific abnormalities on screening laboratory testing including increased platelet count, raised ESR or CRP. Inflammatory markers may however be entirely normal in active IBD. Upper and lower endoscopy with ileoscopy and biopsy is indicated if there is sufficient clinical suspicion although, even then, it is important to bear in mind that isolated small intestinal involvement in IBD is more prevalent in childhood and adolescence and may warrant capsule enteroscopy or small intestinal imaging.

Depending on the population being studied, **Celiac Disease** merits consideration as a potential cause of isolated, chronic abdominal pain. This of course is rendered more pertinent in the context of poor growth, chronic diarrhea but also constipation. It appears justified to screen most patients presenting with chronic abdominal pain for celiac disease with the appropriate serologic testing (anti tTG IgA and IgG). Abdominal pain in the context of celiac disease tends to remit rapidly with the implementation of a gluten-free diet.

An additional (stool) laboratory screening tool that is both non-invasive, relatively cheap and that is increasingly being used to distinguish between FGID and inflammatory enteropathies is *stool calprotectin*. This marker tends to correlate with colonic, and to lesser degree small bowel inflammation better than either of the other hematologic markers.

Although a recognized cause of chronic abdominal pain, **chronic pancreatitis** is rare in childhood; a history of significant trauma to the abdomen or evidence of an underlying metabolic disorder or cystic fibrosis should

Continues on page 19

The Synapse





# The H1N1 post-mortem

by Tanya Melillo Fenech

The H1N1 pandemic started more than a year ago at the end of March in Mexico with Malta having its first positive cases on the first of July. Since July 2009, we had 913 persons who were positive to H1N1 with 261 cases hospitalised (207 with H1N1 and 54 with Influenza A) and from these 8 cases needed intensive care. In all, 5 died as a result of this pandemic locally. Over 91,471 residents took the vaccine and 2,700 antiviral courses have been dispensed through the government pharmacies. In retrospect one would easily conclude that a massive amount of money has been spent on a minor threat but judgment using hindsight is not appropriate when dealing with the potential risk of a public health threat. The real question that needs to be asked is what are the aims and objectives for this country if the threat of a novel influenza virus emerged and was spreading all over the world? And where the objectives for the H1N1 strategy achieved or not?

The main objectives to be achieved in Malta's response to a pandemic threat are:

1. To reduce the severity and spread of illness by judicious use of antivirals and by containment measures as far as is humanly possible;
2. To treat those severely effected with all necessary modalities of management;
3. To maintain essential services;
4. To vaccinate the population as soon as a vaccine becomes available.

All decisions taken by the Health Authorities were specifically aimed to achieve these objectives. It is the opinion of the author that they were achieved. By the time the virus hit our shores we were able to obtain first hand experience from other countries hit by the virus before us and it was evident that this virus was affecting younger age groups especially children, adolescents and pregnant women which usually are not affected by seasonal influenza and worse of all, some deaths were occurring in these age groups.

Which country would not do its utmost to save every child and pregnant woman from dieng from influenza? And through the hard work of all the staff at IDCU, pharmacies, virology department, as well as MMNDA nurses and the valuable cooperation of general practitioners, paediatricians and casualty officers we succeeded in preventing any deaths in these categories. Just imagine what would have happened if a Maltese

child or pregnant woman died of H1N1. The media and the general public would obviously have hounded us for not preventing such deaths.

One has to remember that decisions had to be taken rapidly based on the limited scientific information available and political challenges posed by H1N1. Could we have reacted differently in that situation? I doubt it especially if our main priority was to limit morbidity and mortality in the Maltese population.

This time round, the Maltese Health Authorities had a plan - a pandemic preparedness plan which had been prepared way back in 2005 and revisited over the years with amendments done to reflect the changes that occurred in our health system during the past 4 years. The plan was implemented quite efficiently thanks to the cooperation and hard work of many health care workers who prioritised the health needs of the population during the pandemic.

But what would have happened if we did not have a plan? If we were not prepared for it? Probably total chaos!

Public Health officials all over the world are getting the flack for the fuss they made over the H1N1 pandemic because the media and general public argue that it did not kill many people but then, it is our job to plan and prepare for potential threats and minimize destruction and death.

What if we did not have any plans in place and had not stocked up with antivirals or ordered the vaccines and instead we had 100, 1000 or 5,000 deaths caused by H1N1, would it have been acceptable by all? I think not. We would have been greatly criticized for not preparing for such a threat and avoiding so many deaths. The next step is for us to evaluate what went right and what went wrong and redraft our plans accordingly. We have to continue preparing and planning for new threats.

One of the biggest challenges that public health officials faced during this pandemic and which we need to address is Communication - Communication with health care professionals, the media and with the general public. It is extremely challenging and difficult to alleviate people's fears and misconceptions. We need to start from now, by educating everyone.

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Deep venous thrombosis or pulmonary embolism present or in history; arterial thrombosis present or in history (e.g. myocardial infarction) or predoctoral conditions (e.g. angina pectoris and transient ischaemic attacks, cerebrovascular accident present or in history, presence of a severe or multiple risk factors) for venous or arterial thrombosis; diabetes mellitus with vascular symptoms; severe hypertension; severe dyslipoproteinemia; hereditary or acquired predisposition for venous or arterial thrombosis, such as APC-resistance, antithrombin III-deficiency, protein C deficiency, protein S deficiency, hyperhomocysteinemia and anti-phospholipid antibodies (anticardiolipin antibodies, lupus anticoagulant); Pancreatitis or a history thereof if associated with severe hypertriglyceridemia; Presence in history of severe hepatic disease as long as liver function values have not returned to normal; Presence or history of liver tumours (benign or malignant); Known or suspected sex-steroid influenced malignancies (e.g. of the genital organs or the breasts); Undiagnosed vaginal bleeding; History of migraine with focal neurological symptoms; Hypersensitivity to the active substances or to any of the excipients. Side effects: Common side effects reported in clinical trials include headache, abdominal pain, acne, breast discomfort, amenorrhoea, dysmenorrhoea, metrorrhagia, weight increase. For uncommon side effects and details see package insert leaflet. Dosage and regimen: one tablet is to be taken daily at about the same time on a continuous basis, following the order shown on the blister pack. Each sub-sequent pack is started the day after the last tablet of the previous blister. Interactions with other medicinal products: contraceptive failure and breakthrough bleeding have been described for the concomitant use of hydantoines, barbiturates, primidone, carbamazepine and rifampicin. Such interactions are also suspected for oxcarbazepin, topiramate, felbamate, HIV- medication (e.g. ritonavir), griseofulvin and preparations containing St. John's wort extracts. Contraceptive failure has also been described for concomitant use of antibiotics, such as penicillins and tetracyclines. 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Kindly contact 79060903

**Dermatologists required**

Dermatologists required to work in established pharmacies in the South and North of Malta. Kindly contact Andrew on: 99682115 or 99451632

**Wanted - Xray Box for clinic**

Should be in good condition. Contact by sms on 79060903

**Wanted: Authors for eLearning modules**

Opportunities exist for persons interested in developing eLearning modules for publication on TheSynapse. The target audience will include all or a mix of the following professions at postgraduate level: Medical Doctors, Pharmacists or Dentists. Modules will be accepted subject to peer review and evaluation of academic content. Authors will be suitably remunerated. Those interested should send a proposal to editor@thesynapse.net

**Annual board meeting of the European Union of Medical Specialists in Otolaryngology**

Malta is happy to welcome the annual board meeting of the European Union of Medical Specialists in Otolaryngology between the 7th and 10th October 2010. Representatives from 37 countries shall be meeting at the Mediterranean conference centre in Valletta.

The European Union of Medical Specialists represents the national associations of medical specialists in the European Union and other associated countries. The UEMS promotes the movement of European medical specialists while ensuring the highest quality of medical care for European citizens.

For this purpose the UEMS has developed standards and policies in the key areas of postgraduate training, continuing medical education, professional development; and quality assurance in specialist practice. Mr Adrian M Agius, current President of the Malta Association of ENT and Head and Neck Surgeons has represented Malta on the UEMS-ORL Board for several years and is organizing this visit.

For more information access <http://www.thesynapse.net/events/view.asp?eventID=100> [www.orluems.com](http://www.orluems.com)



**1st Maltese Gastroenterology Conference**

The Gastroenterology Department, supported by the European Social Fund, has the honour to welcome you to the first Maltese Gastroenterology Conference. This conference shall be held on the 8th & 9th October 2010 at the Mater Dei Central Auditorium and is free of charge. We will surely promise you a professional, highly stimulating, interactive, guidelines-based gastroenterology knowledge 2010 update. The main target audience are doctors from all specialties especially general practitioners, consultants in internal medicine, resident specialists, HSTs, BSTs, as well as 5th year medical students. A limited number of places are available to nurses, pharmacists and other medical professionals with an interest in gastroenterology.

Topics to be discussed include GORD, H.pylori, coeliac disease, inflammatory bowel disease, irritable bowel syndrome, colorectal cancer screening, iron deficiency anaemia, hepatitis B and many more. Speakers from USA, UK and Italy will enrich us with their experience. There will also be an interactive session with the use of keypads for the participants.

Registration is a must. This will be in the form of an 'Online Registration' through the MAM website. Certificate of attendance including CPD points will be distributed to each person attending. We hope to see you all in this conference, and keep watching this space for more updates.

For further details access <http://www.thesynapse.net/events/view.asp?eventID=107> or <http://sites.google.com/site/gastroenterologydepartment/home>

**COMPETITION ANSWERS – ISSUE 2/10**

A 54 year old farmer developed high fever, chills, aches and pains, severe headache and photophobia, followed 4 days later by a rash. On examination, she looked unwell, was febrile, and had a maculopapular rash (Figure 1) which involved the palms. Closer inspection revealed a healing necrotic ulcer on the skin of her back (Figure 2)



Figure 1



Figure 2

What is the name of her disease? *Mediterranean spotted fever*  
By what other name is it called? *Boutonneuse fever*  
What name is given to the ulcerated lesion on her skin? *Eschar, tache noir*  
What is the name of the causative micro-organism? *Rickettsia conorii*  
How is it transmitted? *By the bite of the infected dog tick Rhipicephalus sanguineus*

The Rickettsiosis are a group of vector borne diseases caused by species of Rickettsia, which are gram-negative, obligate intracellular parasites. They can be broadly divided into two groups: a spotted fever group (SFG) and a typhus group (TG). Different species of Rickettsia are transmitted by different vectors depending on geographical location.

In Malta, two distinct diseases are endemic: murine typhus (MT) from the TG, and Mediterranean spotted fever (MSF) also known as Boutonneuse fever from the SFG. Both are febrile illnesses which may exhibit a cutaneous eruption during their course. Flea borne spotted fever, caused by *R. felis* and transmitted by the bite of the cat flea is a recently recognised rickettsial illness which in Europe is known from Germany, although infected cat fleas have also been found in France<sup>1</sup>. Infected rats constitute the reservoir for murine typhus. The causative Rickettsia (*R. typhi*) is transferred to humans by the inoculation of infected flea faeces into the skin following the bite of an infected rat flea. Mediterranean spotted fever, on the other hand, is caused by *R. conorii* and is transmitted by the bite of an infected dog tick, Rhipicephalus sanguineus. The maculopapular rash of MSF, unlike that of MT, tends to involve the palms and soles. A necrotic ulcer, or eschar (tache noir) can be found in most patients infected with MSF if carefully sought. It represents the site of the tick bite, and does not occur in MT.

Other diseases which may manifest an eschar include ulcero-glandular tularaemia and cutaneous anthrax. Maculopapular rashes may occur in a small percentage of those infected with tularaemia. Both diseases (and especially tularaemia), however, are associated with prominent regional lymphadenopathy, and are potentially very much more serious.  
Reference

1.Gilles J, Just FT, Silaghi C, Pradel I, Lengauer H, Hellmann K, et al. Rickettsia felis in fleas, France [letter]. Emerg Infect Dis [serial on the Internet]. 2008 Apr [Accessed 7th June 2010]. Available from <http://www.cdc.gov/EID/content/14/4/684.htm>

**WINNERS ISSUE 2/10**

The winners are:  
1st prize - **Dominic Agius** (EUR 60 book voucher from BDL)  
2nd prize - **Angelique Pace** (EUR 40 book voucher from BDL)  
TheSynapse team would like to congratulate the winners and thank the sponsors of this competition.

**THIS MONTH'S CHALLENGE**



In contrast to the previous issues, this months' challenge is of a more general nature and the answers to all questions can be found in issue 2/10. Those who get a correct answer will participate in a draw where we are offering the following prizes – first prize: TWO tickets to the Winter Moods concert to be held the 28th of July and the two runner-ups will win a one-day membership to the Corinthia Athenaeum Spa Attard.

1. *Arum Italicum* (the plant featured in the front cover) has been used in the past to remove freckles? True or False \_\_\_\_\_
2. Mention the name of the contributor from Turkey? \_\_\_\_\_
3. Where are the Grape Expectations Wine Events planned to be held? \_\_\_\_\_

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Kindly submit the answers by mail by filling the form on this page addressed to The Professional Services Centre, 3 Guzi Cutajar Street, Dingli, DGL 1201 or submit your answers on-line on [www.thesynapse.net/quizz](http://www.thesynapse.net/quizz). All submissions will participate in a draw. You have up to the 20 July 2010 to submit your answers.





More effective acid control compared to all existing PPIs<sup>1</sup>

Release the power...

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esomeprazole

AstraZeneca

**Nexium Tablets**  
**Abridged Prescribing Information** (See full Summary of Product Characteristics before prescribing.) **USE:** Nexium is a proton-pump inhibitor. **NEXIUM® Tablets:** Gastro-Oesophageal Reflux Disease (GORD), *Helicobacter pylori* eradication in combination treatment with antibiotics. Healing of gastric ulcers and prevention of gastric and duodenal ulcers associated with NSAID therapy. Zollinger-Ellison Syndrome. **Presentation:** Gastro-resistant tablets containing 20mg or 40mg esomeprazole. **Dosage and administration:** **Adults (including the elderly) and adolescents:** NEXIUM® 20mg/40mg Tablets **GORD:** Adults and adolescents from the age of 12; treatment of Reflux Oesophagitis: 40mg once daily (od) for 4 weeks. An additional 4 weeks treatment is recommended for patients in whom oesophagitis has not healed or who have persistent symptoms. Long-term management of patients with healed oesophagitis to prevent relapse: 20mg od. Symptomatic treatment of GORD: 20mg od (in patients without oesophagitis). If symptoms have not been controlled after 4 weeks, the patient should be further investigated. Once symptoms have resolved, subsequent symptom control can be achieved in adult patients using on-demand Nexium 20mg od, when needed. **Helicobacter pylori eradication (in combination with appropriate antibiotics):** Adults only, healing of *H. pylori* associated duodenal ulcers and prevention of relapse of peptic ulcers in patients with *H. pylori* associated ulcers. Nexium 20mg, amoxicillin 50, clarithromycin 50mg, all twice daily for 7 days. **Patients requiring continued NSAID therapy:** Adults only, healing of gastric ulcers associated with NSAID therapy. The usual dose is 20mg once daily. The treatment duration is 4-8 weeks. Prevention of gastric and duodenal ulcers associated with NSAID therapy in patients at risk: 20mg once daily. In NSAID treated patients at risk of developing gastric and duodenal ulcers, subsequent symptom control using an on-demand regimen is not recommended. **Treatment of Zollinger-Ellison Syndrome:** Adults only, initial dose 40mg bid, then to be individualised, treatment to continue for as long as needed. Patients usually controlled on 80 to 120mg daily doses. Doses above 120mg to be taken bid. **Renal Impairment:** No dose adjustment needed. Patients with severe renal insufficiency should be treated with caution. **Hepatic Impairment:** No dose adjustment needed except in patients with severe liver impairment where a maximum daily dose of 20mg should not be exceeded. **Adolescents:** Nexium Tablets may be used for GORD in adolescents from the age of 12. **Children below the age of 12 years:** Nexium should not be used in children since no data is available. **Elderly:** No dose adjustment needed. **Contraindications:** Known hypersensitivity to esomeprazole, substituted benzimidazoles or any other constituents of Nexium. Esomeprazole, like other PPIs, should not be administered with atazanavir. **Precautions:** In the presence of any alarm symptoms and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment may alleviate symptoms and delay diagnosis. Patients on long-term treatment should be kept under regular surveillance. Patients on on-demand treatment should contact their physician if their symptoms change in character. When prescribing Nexium for on-demand therapy, the implications for interactions with other pharmaceuticals should be considered. When prescribing Nexium for *H. pylori* eradication, possible drug interactions for all components in the triple therapy, particularly clarithromycin, should be considered. Nexium Tablets contain sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose maldigestion or sucrose-isomaltase insufficiency should not take Nexium Tablets. Treatment with proton pump inhibitors may lead to slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter. **Interactions:** (See SPC for full information). Risperidone or itraconazole absorption may be reduced. When Nexium is combined with drugs metabolised by CYP2C9, such as diazepam, citalopram, imipramine, domperidone, phenytoin, voriconazole etc., a dose reduction should be needed. This should be considered especially when prescribing Nexium for on-demand therapy. Plasma concentrations of phenytoin should be monitored when treatment with Nexium is introduced or withdrawn. In warfarin, or other coumatin derivative treated patients, monitoring is recommended when initiating and ending concomitant treatment. AUC and half-life of ciprofloxacin increased/prolonged. CYP 3A4 and CYP2C9 inhibitors e.g. clarithromycin & voriconazole may increase exposure to Nexium. Atazanavir use is contraindicated. **Pregnancy & Lactation:** (See SPC for full information) Exercise caution when prescribing Nexium to pregnant women. It is not known whether esomeprazole is excreted in breast milk. Do not use Nexium during breast-feeding. **Undesirable effects:** Common: Nausea/vomiting, headache, abdominal pain, diarrhoea, flatulence, and constipation. Uncommon: dermatitis, pruritus, urticaria, rash, dizziness, dry mouth, peripheral oedema, insomnia, increased liver enzymes, paraesthesia, somnolence and vertigo. For less common side effects refer to SPC. **Package quantities:** Nexium 20mg - blister packs in wallets or cartons of all tablets. Nexium 40mg - blister packs in wallets or cartons of all tablets. **Storage precautions:** Do not store above 30°C. **Marketing Authorisation numbers:** MA 0400701-Nexium Tablets 20mg; MA0400702-Nexium Tablets 40mg. **Legal classifications:** Prescription only medicine (POM) **Marketing Authorisation holders:** AstraZeneca AB Sweden, S-151 85, Sodertalje, Sweden. **Further information available from:** AstraZeneca Pharmaceuticals (Ireland) Ltd., College Park House, 20 Nassau Street, Dublin 2. Tel: (01) 609 2900; Fax: (01) 609 6650. **Abridged Prescribing Information prepared:** 01/09. **Date of preparation:** February 2009. Nexium<sup>®</sup> is a trademark of the AstraZeneca Group of companies.

References: 1) Miner P et al. Am J Gastroenterol 2003;98:2966-20.

Further information may be obtained from AstraZeneca, Triq I-Esportatur, Mriehel, BKR3000

## Pediatrics

Continued from page 13

be sought. Even here though, abdominal pain as an isolated symptom is rare but care needs to be taken insofar as amylase and lipase levels may be normal in this disease.

Rarely chronic, or rather recurrent severe abdominal pain may be the sole presenting complaint of **Familial Mediterranean Fever** in patients of Mediterranean or Middle-Eastern extraction. Naturally, the presence of periodic fever should heighten the clinical suspicion of this disorder.<sup>3</sup> In some cases severe, peritonitic pain will be accompanied by leucocytosis or raised ESR. The condition is hereditary, with most patients harboring mutation in the pyrin gene (MEFV).

Although ubiquitous in the textbook differential diagnosis for obscure causes of severe chronic or recurrent abdominal pain, porphyria is rarely encountered in this clinical context (although the exasperated clinician might be forgiven for testing in otherwise atypical clinical scenarios for fear of missing yet another King George III).<sup>4</sup>

Given the heterogeneity of the population with FGID it is little wonder there are very few evidence-based effective therapies for childhood IBS. When the pooled experience is formally studied through meta-analysis some options appear to have therapeutic advantage over placebo. These include both pharmacologic and non-pharmacologic measures.

There is evidence that **peppermint oil**, probably through its spasmolytic properties is efficacious in childhood FGID, and side effects are rare which include perianal pruritus.<sup>5</sup> The role of other spasmolytics, including hyoscine butylbromide, and ortolinium bromide is, as yet unproven although the latter has

### References

1. Apley J, Naish N. Recurrent abdominal pains: a field survey of 1,000 school children. Arch Dis Child 1958; ;33(168):165-70.
2. Engel GL. The clinical application of the biopsychosocial model. Am J Psychiatry. 1980;137(5):535-44
3. Tunca M, Akar S, Onen F, et al. Familial Mediterranean fever (FMF) in Turkey: results of a nationwide multicenter study. Medicine (Baltimore) 2005; 84(1):1-11.
4. Cox TM, Jack N, Lofthouse S, Watling J, Haines J, Warren MJ. King George III and porphyria: an elemental hypothesis and investigation. Lancet 2005;366(9482):332-5.
5. Kline RM, Kline JJ, Di Palma J et al. Enteric-coated, pH-dependent peppermint oil capsules for the treatment of irritable bowel syndrome in children. J Pediatr 2001; 138(1):125-8.
6. Saps M, Di Lorenzo C. Pharmacotherapy for functional gastrointestinal disorders in children. J Pediatr Gastroenterol Nutr 2009; 48(Suppl 2):S101-3.

poor systemic absorption and therefore less likely to have adverse effects.

Several studies have addressed the impact of **pre- and probiotics** in FGID; although they may be of benefit in some populations there is insufficient data, at this stage to recommend routine use. Both **amityrptiline**, a tricyclic antidepressant (TCA) and **citalopram**, a selective serotonin reuptake inhibitor (SSRI) are useful and have proven efficacy in chronic abdominal pain in children.<sup>6</sup> Given the need for slow dosage escalation and the spectrum of adverse effects, use of these agents is usually reserved to specialist care and with close monitoring in refractory or especially severe cases.

**Cognitive-behavioral therapy**, guided imagery and deep relaxation as well as **hypnotherapy** have been shown to improve, even beyond the period of therapy, the functional outcome of abdominal pain in children. Liaison with a child psychologist is central to the management of FGID in children and the concept should be discussed early in the management of at-risk cases, well in advance of a barrage of tests that do little but exacerbate the parent's anxiety that 'something is definitely wrong but nobody can pin it down'. In summary therefore, functional abdominal pain in children is common, the vast majority of patients have an illness best understood in the context of a biopsychosocial model of disease rather than through often fruitless over-investigation. The experienced clinician needs to have a clear appreciation of historic 'red flags' and may opt to pursue limited laboratory investigation. Liaison with a child-psychologist is critical and a therapeutic partnership with the family aimed at minimizing morbidity needs to be emphasized.



## Malta Association of Crohn's and Colitis

The Inflammatory Bowel Diseases (IBD) mainly consist of Ulcerative colitis and Crohn's disease. A less common form is known as microscopic colitis. Although the names and symptoms may be similar to Irritable Bowel Syndrome (IBS) it is extremely important to distinguish between them as both the pathophysiology and management differ. Genetic and environmental factors are both involved in IBD. While Ulcerative colitis mainly affects the large intestine, Crohn's disease can affect any part of the gastrointestinal tract. Smoking makes the latter disease worse. Diagnosis can be done with the aid of endoscopy. This can take the form of oesophagogastroduodenoscopy (OGD), colonoscopy and/or capsule endoscopy. Capsule endoscopy is extremely useful in investigating the small bowel as unlike radiological studies no radiation is involved while more pathology is diagnosed. Medical treatment with 5-ASA drugs (e.g. mesalazine), immunosuppressant's (e.g. azathioprine) and biological agents (e.g. Infliximab) form the mainstay of treatment. Corticosteroids

are ideally used only during flare-ups. Surgery may be required in certain instances. The aim of the management is to keep patients in both clinical and endoscopic remission.

Since the identification of IBD as a recognisable chronic illness, self-help patient associations began to appear across Europe so that now, the European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) currently has 24 member associations. Locally, the Malta Association of Crohn's and Colitis (MACC) was set up last January with the aims of offering support to persons and relatives of persons suffering from IBD, to help them improve their quality of life and to promote public awareness about these chronic conditions. It also intends to promote patients' needs and rights and to encourage and promote research. Medical and paramedical professionals who are interested in the association, or would like to join can send an email to [info@macc.org.mt](mailto:info@macc.org.mt) for more information.



Continued from page 11

**How can amputations be prevented?**

*Education*

Footcare education is a fundamental part of the strategy to save limbs in this group of patients. There is evidence that programmes which include education with podiatry show a positive effect on minor foot problems within a relatively short space of time.<sup>7-9</sup> A randomized controlled trial showed that by showing diabetic patients the potential complications of diabetic foot disease, amputations and recurrent ulceration were prevented.<sup>9</sup>

*Foot Screening*

Because of the high prevalence of neuropathy in this group of patients a lot of them are asymptomatic even when they have severe ischaemia or ulceration. As a result pain cannot be relied upon as a symptom in this cohort. It is therefore recommended that all diabetics undergo foot screening.



is that in this situation the damage sustained by the foot can progress very rapidly. Any delay in appropriate referral of these patients will inevitably lead to limb loss.

*Structured foot care*

There is level I evidence that access to podiatry reduces the number and size of foot calluses and improves self care.<sup>7</sup> A multidisciplinary foot team has been shown to allow rapid access to vascular surgery and intensive treatment, including control of infection and revascularisation which leads to wound healing and foot saving amputations which ultimately leads to a reduction in the number of major amputations.<sup>10</sup> All patients with diabetes should have access to structured foot care.

*Footwear, Orthoses and Total contact casting*

Ordinary shoes should be avoided in diabetics as plantar pressures generated using normal footwear is equivalent to walking barefoot. These patients should be advised at least to wear high quality cushioned-soled trainers.<sup>11-12</sup> These however are not as effective as custom built shoes in reducing plantar pressures and therefore the risk of ulceration.<sup>13-14</sup> Access to total contact casting is important both for the treatment of acute Charcot's osteoarthropathy and in the treatment of neuropathic ulceration.<sup>15</sup>

*Arterial reconstruction*

The identification of an ulcer in a diabetic does not constitute a diagnosis. An ulcer is simply a clinical sign of an underlying problem which in diabetics is either neuropathy or arterial disease or both. In the case of arterial disease, in the majority of cases this can be treated. It is therefore crucial that patients with ulceration are referred as early as possible. There is little point in treating these patients with repeated applications of the local favourite topical antibiotic or oral antibiotics in increasing doses and combinations or prescribing increasingly expensive and fancy local dressings. Identification of arterial disease requires initiation of treatment to control risk factors – diabetes control, treatment of hypertension, initiation of antiplatelet treatment and statins, and smoking cessation. If the patient's foot is ischaemic the solution is to refer quickly for revascularisation. Indeed failure to feel bounding and easily palpable pulses in these patients should instigate an immediate referral for vascular assessment. If no pulses are felt one should assume that the ulcer is ischaemic until proven otherwise through a full vascular assessment. Rates of limb salvage after distal bypass surgery are relatively high with salvage rates of over 80% reported in the initial presence of tissue loss or gangrene.<sup>5</sup>

**EXAMPLE PROTOCOL FOR THE ASSESSMENT OF RISK OF THE DIABETIC FOOT ADAPTED FROM THE TAYSIDE FOOT RISK ASSESSMENT PROTOCOL**

Patients with diabetes should be assessed annually by a diabetologist, GP, chiropodist, diabetes nurse specialist, or practice nurse with training in diabetes to look for presence of neuropathy, ischaemia or deformity.

Patients should be categorized according to the presence of the following signs or symptoms

Normal Sensation AND good pulses AND no previous ulcer AND no foot deformity AND normal vision	Loss of Sensation OR Absent pulses (or previous vascular surgery) OR Significant visual impairment OR Physical disability (e.g. gross obesity, stroke)	Previous ulcer due to neuropathy/ischaemia OR Absent pulses and neuropathy OR Callus with risk factor (neuropathy/absent pulse/foot deformity) OR Previous amputation	Active foot ulceration, painful neuropathy which is difficult to control
<b>LOW RISK</b>	<b>MODERATE RISK</b>	<b>HIGH RISK</b>	<b>ACTIVE FOOT DISEASE</b>
-No specific regular chiropody input needed (except in exceptional circumstances) - patients can undertake their own nail care after appropriate education - annual foot check	- regular (4-12 weekly) general chiropody input advised. For patients with visual impairment or physical disability, who would otherwise fit into the low risk category, input from trained foot care assistants can be substituted (where available)	- chiropodist with interest and expertise in diabetes either at diabetes unit or in community centre - chiropodist may want to consider orthotic referral	- suggest making contact with local specialist diabetes foot team (hospital based)

In addition, patients with any of the following signs of ischaemia or infection should be considered for emergency referral to the hospital surgical/vascular receiving service or diabetic foot clinic, where appropriate

<b>CRITICAL ISCHAEMIA</b> Rest or night pain Pale/mottled feet Dependent rubor Ischaemic ulceration Gangrene	<b>INFECTION</b> Abscess Cellulitis
---	---

Foot screening should involve:

- i. assessment of sensation by using clinical neuropathy scores or 10g microfilaments or vibration sensation perception threshold;
- ii. examination of pulses;
- iii. inspection of the feet for deformity, ulceration, callus, and inspection of footwear.

There is no agreed frequency for foot screening but NICE guidance recommends that annual review should be arranged at which, based on the observations made, patients are stratified into risk groups for foot ulceration: low, medium and high risk or in those who have already developed ulceration or tissue loss as 'ulcerated foot'.

Classification into these groups is based on standard criteria and action is initiated based on the classification group (Figure 1). This screening ensures that those at high risk in particular are seen regularly and active measures are taken to reduce the risk of development of ulceration to the minimum possible. More importantly, those who have ulcers or gangrene should be referred immediately to hospital. Patients with new ulceration, swelling and discoloration should be seen in hospital within 24 hours. The reason

**References**

1. Young MJ, Boulton AJM, McLeod AF et al. A multicenter study of the prevalence of diabetic peripheral neuropathy in the United Kingdom hospital clinic population. *Diabetologia* 1993; 36:150-4. 2. Williams DRR and Airey CM. The size of the problem: epidemiological and economic aspects of foot problems in diabetes. In: *The foot in diabetes*. 3rd ed. Boulton AJM, Connor H, and Cavanagh PR (eds). Chichester: John Wiley & Sons 2000; 3-18. 3. Conte MS, Belkin M, Upchurch GR et al. Impact of increasing comorbidity on infrainguinal reconstruction: a 20-year perspective. *Ann Surg* 2001; 233:445-52. 4. Shah DM, Darling RC 3rd, Chang BB et al. Long-term results of in situ saphenous vein bypass. Analysis of 2058 cases. *Ann Surg* 1995; 222:438-46. 5. LoGerfo FW, Gibbons GW, Pomposelli FB, et al. Trends in the care of the diabetic foot. Expanded role of arterial reconstruction. *Arch Surg* 1992; 127:617-21. 6. Pecoraro RE, Geber GE, Burgess EM. Pathways to diabetic limb amputation: basis for prevention. *Diabetes Care* 1990; 13:513. 7. Rönemaa T, Hamalainen H, Tokka T, Liukkonen I. Evaluation of the impact of podiatrist care in the primary prevention of foot problems in diabetic subjects. *Diabetes Care* 1997; 20:1833-7. 8. Dargis V, Pantelejeva O, Jonushaitė A, Viliškys L, Boulton AJ. Benefits of a multidisciplinary approach in the management of recurrent diabetic foot ulceration in Lithuania: a prospective study. *Diabetes Care* 1999; 22:1428-31. 9. Malone JM, Snyder M, Anderson G, Bernhard VM, Holloway GA Jr, Bunt TJ. Prevention of amputation by diabetic education. *Am J Surg* 1989; 158:520-3. 10. Faglia E, Favales F, Aldegheri A et al. Change in major amputation rate in a center dedicated to diabetic foot care during the 1980s: prognostic determinants for major amputation. *J Diabetes Complications* 1998; 12:96-102. 11. Kastenbauer T, Sokol G, Aunger M, Irsliger K. Running shoes for relief of plantar pressure in diabetic patients. *Diab Med* 1998; 15:518-22. 12. Perry JE, Ulbrecht JS, Derr JA, Cavanagh PR. The use of running shoes to reduce plantar pressures in patients who have diabetes. *J Bone Joint Surg Am* 1995; 77(12):1819-28. 13. Uccioli LE, Faglia, Monticone G et al. Manufactured shoes in the prevention of diabetic foot ulcers. *Diabetes Care* 1995; 18:1376-8. 14. Colagiuri S, Marsden LL, Naidu V, Taylor L. The use of orthotic devices to correct plantar callus in people with diabetes. *Diabetes Res Clin Pract* 1995; 28:29-34. 15. McGill M, Molyneux L, Bolton T et al. Response of Charcot's arthropathy to contact casting: assessment by quantitative techniques. *Diabetologia* 2000; 43:481-4.

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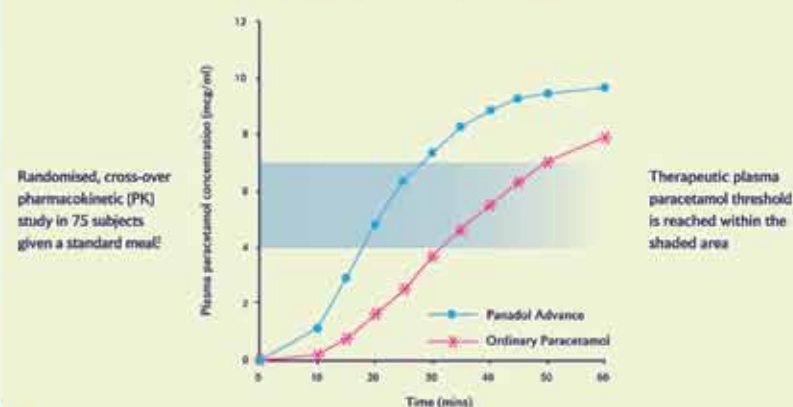
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domperidone, metoclopramide, colestyramine. Refer to doctor if persistent headache or non-serious arthritis requiring daily analgesia. **Pregnancy/breastfeeding:** Pregnancy: Refer to doctor. Breastfeeding: not contraindicated. **Side effects:** Hypersensitivity including skin rash, blood dyscrasias. **Overdosage:** Immediate medical advice due to risk of delayed, serious liver damage. **Legal category:** OTC. **Product licence number:** AA460/00701 **Product licence holder:** GlaxoSmithKline Consumer Healthcare, Brentford, TWB 9GS, U.K. **Package quantity:** Compact 12's. Date of last revision: November 2008. Panadol is a trade mark of the GlaxoSmithKline group of companies.



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Members' Corner

# Grape Expectations

by Albert Cilia-Vincenti

*"Lazarus, you are more indebted to wine than to your father, for he gave you life but once, while wine has given it back to you a thousand times"*  
Spanish Source (16th century)

In spite of long tradition, classifications and regulations, the world of wine never stands still. Every vintage is different, the wine keeps changing at an unpredictable pace, in barrel and in bottle with every year of maturity. But also in constant flux are vineyard and winery ownership, regulations, winemakers' techniques and philosophies, and so also the resultant wine quality.

The terroir is, however, constant. This is not just the soil, but the whole environment in which the vines grow, produce their grapes and in which the wine is made and cellared. Terroir has a major impact on both character and quality. The market, however, is anything but constant, and the tastes, perceptions and demands of wine drinkers play a major role in the ever-changing fashions of the wine scene.

Modern wine is the result of technology, or rather scientific philosophy, in vineyard and winery that evolved in the late 20th and early 21st century. The modern wine era started with discovery of the effects of different temperatures on grape skin and juice fermentation. The chemistry of fermentation was worked out by Pasteur in the 1860s, but slowing down fermentation by lowering the temperature was the first big breakthrough, enabling New World wines from hot Mediterranean type climates in the New World to challenge the Old.

The New World challenge, however, has made the Old World re-examine its entrenched ideas, and change, adapt and abandon old dogma to such an extent that Old and New have now met in what is evolving into a global wine village. It carries potential risks, the first of which is a tendency to make the same wine style as everyone else, starting with the near-universal planting of Chardonnay and Cabernet Sauvignon. Another negative result is the fashion of using oak, not as originally intended (to condition wine before bottling), but to flavour it, like adding sauce to food. Because use of new oak barrels is expensive, the push for oak flavour degenerated to adding cheap oak chips or

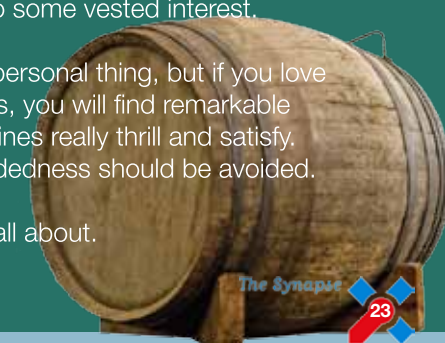
even oak essence to the wine. The result is a whole generation of wine drinkers deluded into believing that the Chardonnay grape makes vanilla-flavoured wine while, in reality, if it does, it is either badly made or not ready for drinking.

There is also the relatively recently emerged fundamental differences in taste, initially sparked off by influential American critics who have been judging wine more on the immediate impact they have on your senses, than on those traits that make them good companions – the power to tempt with subtle nuances. My own personal feeling about this apparent gulf in opposing wine style opinions is that both sides are perhaps too entrenched in their views of what a pleasure-giving wine should smell and taste like. The more traditional view is that wine should be food-friendly and, to be so, its aromas and flavours should not be so powerful as to mask those of the food. The traditionalists tend to regard modern-style wines as little more than powerful fruit-juices with added alcohol that clash with food flavours. Those who prefer modern style wines tend to denigrate traditional style wines as being often rather feeble on flavour, acidic, tannic and overall odour.

One needs to stand back a bit from these opposing opinions and accept that peoples' tastes vary. Speaking for myself, there are many wines of both traditional and modern style that I enjoy. Modern winemaking has improved wine quality beyond recognition these last few decades, and perhaps the claim of traditionalists that modern wines are only fit for wine bars, and not to accompany dinner, borders on unrealistic exaggeration, sometimes possibly due to some vested interest.

Wine enjoyment is a very personal thing, but if you love it, and mix with wine-lovers, you will find remarkable consensus about which wines really thrill and satisfy. Prejudice and narrow-mindedness should be avoided.

Preferences are what it is all about.





# An individual story of Art

by Marika Azzopardi

Acts 27



John Martin Borg recently made the news when one of his paintings became part of the Vatican collection after it was donated to Pope Benedict XVI by the President of Malta during the pope's visit in April 2010. It is not the first John Martin Borg's paintings to make it into a prominent collection. Another forms part of the Royal Collection in London and was presented to the Queen and her consort in 1992. Borg's works have graced the walls of varied international exhibition halls such as the UNESCO Head Quarters in Paris, the Mall Gallery in London, and then varied locations in Munich, Cologne, Stuttgart, Heidelberg, San Tropez, Paris, Tunisia, Dubai and Florida (USA). Apart of course, from the very many local exhibitions held in our Islands through the years.

Appreciated for his maritime scenes, landscapes and religious works alike, John Martin Borg is one of Malta's most exponential contemporary artists. He was the student of a handful of Malta's best artists, the likes of Harry Alden, Esprit Barhet and Vincent Apap. But what has Borg the artist got to do with this medical journal? John Martin Borg's first profession was actually that of a pharmacist and medical representative. And in between all the innuendos of his career, he had, unbeknown even to himself, one very problematic condition to deal with. "It was only two years ago, and I am now 57 years old,

that I discovered I am dyslexic. I have always been, and that is the amazing thing – that nobody recognised this problem. In hindsight I am now working on revising and re-organising my thoughts about my past sufferings in this regard and it is an eye-opening experience which is helping me deal with all that I've been through."

John Martin Borg speaks passionately about his life's difficulties surrounding dyslexia and of how he recognised the condition in himself, thanks to his daughter's daily reporting on the problems she encountered in her work as a facilitator working with children. "As she spoke I often recognised some of my own problems and voiced this openly. Of course my comments were quickly dismissed, but the doubts lingered on. Then I chanced upon meeting Ruth Falzon who lectures on dyslexia, and posed her the question – could I be dyslexic? She quickly fired some questions away and told me there and then. I was, I am and always have been."

He explains how as a boy, he just hated school with a passion, and how he fought his problems of confusing and trying to memorise numbers, even whilst having an alarmingly good memory for things he really liked. His reading was painstakingly slow and reading English was a nightmare – he needed to read word by word and recalls being always last in class to finish copying off the blackboard. Skimming through his reading was never an option. He was marked as being lazy, ignorant, unable to concentrate and needless to say, he started to develop a very evident inferiority complex. "All through my fatherhood I could never bring myself to attend a parents' day at my children's school – not because I couldn't care less, but because the day in itself brought back too many bad memories of my own experiences. I could never live up to my father's expectations, although he was always a positive influence throughout my life."

The end result was that John Martin emerged from school with only one O'level, surprisingly enough, in physics. But then in the short space of two years, spurred on by friends and a personal enthusiasm that, typical of dyslexic people, saw him going about training in a completely roundabout fashion, he achieved 14 O'levels and proceeded to obtain an A'level in physics. He learnt biology in one summer and got a straight A grade in that. He suddenly shone as he forced himself to love English by writing one essay a day. This transformed into one poem a day and to this day he owns a healthy collection of his own private poetry. At University he chose pharmacy. He recounts how

he didn't really want to do chemistry albeit his father's (a pharmacist) proddings. But in the end he loved it all so much that he was ready to do a post-graduate degree, which aspiration fell short when the 1977 dispute between government and UOM saw his tutoring professor leave university. "I was dismayed of course but I still had the momentum to do something tangible and so I decided to resume painting. Painting and running free in the fields around our house in Ta' Xbiex had been childhood joys which I cherish to this day, because they were the moments in life which kept me sane. I started watercolours and thanks to Censu Apap, who recognised my penchant and natural aptitude for the medium, I quickly grasped its multi-faceted complications."

*"It was only two years ago, and I am now 57 years old, that I discovered I am dyslexic. I have always been, and that is the amazing thing – that nobody recognised this problem."*

At the time, only one other Maltese artist did watercolours successfully and this was Giuseppi Archidiacono whom Borg would become well acquainted with later on in life. The discovery of the wet-in-wet technique was a marvel to him even though the way to success was an arduous one. "Something strange happened in the meantime – I fell in love with painting on location and again rediscovered a childhood dream world – that of the open country. I was enjoying the best of both worlds."

When the German pharmaceutical company he represented eventually was closed down internationally,



he was encouraged by his wife Doris to take a sabbatical and concentrate on painting. By then he was already well-known locally and highly appreciated for his art which had been made public in 1979. Somewhere in the late 1980s his painting became more ethereal. He represented local landscape in a manner no other local artist had attempted before. He became a Romantic in his escapism from reality, striving not to depict any hard edges even when his mood was sombre and morose. "I was never after trying to come up with something new. I'm not that type of person. My work is all about transmitting emotions. I do not paint to a formula. Then again, my religious work is highly influenced by my own spirituality which has accompanied me through life. It is thanks to this that I have achieved that much more in inspiration and eked a niche so particular to myself and my work. I am still beaming from the meeting with the Pope, which memory I cherish with joy."

Afternoon light over Senglea creek



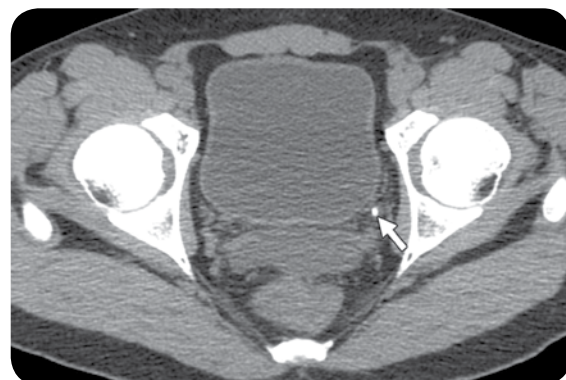


# Imaging Urinary Stone Disease: New Concepts

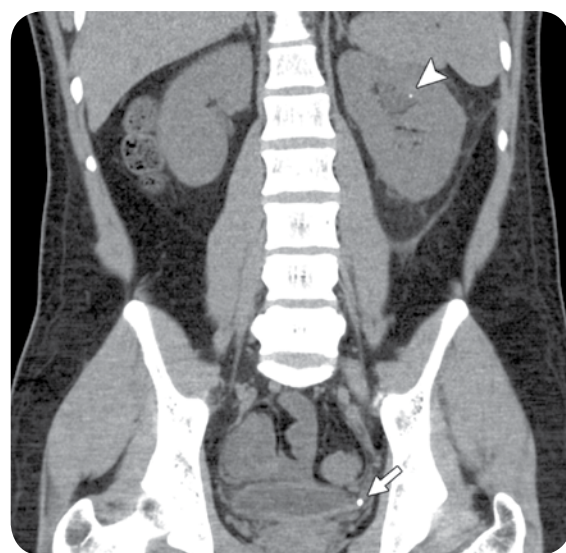
by Pierre Vassallo

Urinary stone disease is a universal problem that is particularly common in countries with warm climates like Malta and even more so during the hot summer months. It has been estimated that 14% of men and 6% of women suffer from urinary stone disease within their lifetime. In addition, many individuals will have recurrence of stone disease with stones recurring in 50% of cases within 5-10 years and 70% within 20 years. Over the last decade, an increase in stone disease in women has been reported.

Imaging urolithiasis (i.e. urinary tract stones) has evolved over the years due to technologic advances and a better understanding of the disease process. Baseline tests such as X-ray intravenous urography (IVU) have been replaced by computed tomography (CT), which resulted in improved diagnostic accuracy and speed and has avoided the need for bowel preparation and intravenous injection of contrast material (Figures 1 & 2).



**Figure 1** - Axial CT scan showing a 4-mm stone in the left distal ureter (arrow).



**Figure 2** - Coronal reformatted CT image shows the left distal ureteric stone (arrow) and a 2-mm stone in the left upper pole (arrowhead).

The efficiency of CT in detecting stones and monitoring treatment and follow-up has further improved with the development of spiral and multidetector technology and may offer further advantages with the introduction of Dual-Energy CT scanners. Sensitivity of CT for urinary tract stone detection is 95-98% with a specificity of 96-100%. CT also provides information regarding stone burden, composition, and fragility, all of which may aid in the selection of treatment strategies and may help in predicting success of treatment. In addition, CT detects extraurinary disease (that may mimic stone disease) such as appendicitis, diverticulitis, pancreatitis and gynaecological disorders. Other possible concurrent urinary tract diseases are also detectable with CT including renal abscesses, congenital anomalies and neoplasms, which could potentially alter the therapeutic approach.

As indicated earlier, the incidence of stone disease is strongly influenced by environmental factors, but dietary and genetic factors and certain chronic systemic diseases also play a role. Most stones (70-80%) are calcium-containing and include calcium oxalate monohydrate, calcium oxalate dehydrate and calcium phosphate. Stuvite stones account for 5-15% and are composed of magnesium ammonium phosphate. 5-10% of stones are uric acid stones, which occur in acid urine (pH <4.8) and may be treated by urinary alkalinisation. Cystine, xanthine and protein-matrix stones are usually due to hereditary factors, while drug stones are due to concentration of medication within the urine - such medications include Indavir, an antiretroviral agent used for HIV/AIDS treatment and Triamterene, a potassium-sparing diuretic. Indavir stones are not visualized by CT due to their low density, but clinical history should point towards this diagnosis. Hereditary and drug stones account for <5% of all stone disease.

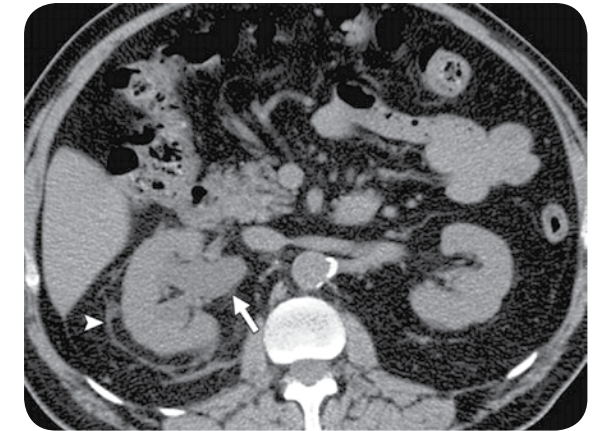
Treatment of urinary tract stones depends on the patient's symptoms and stone location, size and composition. Asymptomatic stones measuring <1cm in diameter are usually observed, as they are likely to pass spontaneously. Symptomatic stones of this size are treated with ureteronephroscopy or extracorporeal shockwave lithotripsy (ESWL), the former is particularly useful for low lying stones and the latter for stones in the renal pelvis or calyces. If fever occurs (i.e. secondary infection), a ureteric stent is inserted to relieve the kidney, and the stone may pass spontaneously or be extracted at a later date. Stones measuring 1-2cm in diameter may be treated with ESWL or percutaneous nephrolithotomy (PCNL). PCNL is an imaging-guided

procedure that uses ultrasound or X-ray fluoroscopy to locate the stone and to guide puncture followed by dilatation of the tract through which the stone can be fragmented and extracted. While larger stones such as staghorn calculi may be treated by PCNL or laparoscopic or open nephrolithotomy.

Success of ESWL is related to a number of factors that may be evaluated with CT, including stone location (i.e. lower renal pole calyces versus other calyces), size, and composition, as well as stone-to-skin distance. Ureteronephroscopy is an endoscopic procedure in which thin endoscopes (7-9 French in calibre) are inserted via the urethra and bladder into the ureter and renal pelvis. This procedure may be combined with laser and electrohydraulic or pneumatic lithotrites to shatter the stone and therefore ease its passage down the ureter.

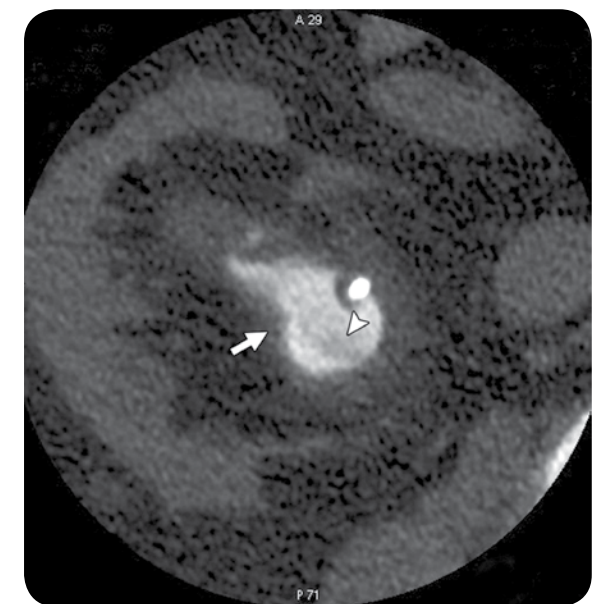
Stone size and location are therefore the key factors that influence therapeutic planning of upper urinary tract stones. Stone composition also influences the choice of treatment. Cystine stones do not respond to ESWL and will require treatment with ureteronephroscopy or PCNL. Based on stone density, CT can distinguish three types of stone; Stones with a density < 400HU (Hounsfield Units) are likely to be uric acid stones and may be treated by oral dissolution therapy if asymptomatic. If symptomatic or causing obstruction, ESWL or ureteronephroscopy will be required. Stone with densities >400HU are classified as non-uric acid stones and are divided into two groups, those with densities <1000HU and those with readings > 1000HU. Those stones with densities 400-1000HU that are not cystine stones may be treated with ESWL and if refractory to that treatment with ureteronephroscopy or PCNL is administered depending on stone location. Those stones with densities >1000HU or cystine stones will require ureteronephroscopy or PCNL depending on location.

The most obvious CT sign of a urinary tract stone is naturally seeing the stone itself, however there are secondary signs that would improve detection rate particularly for matrix stones such as Indavir stones that have density readings similar to soft tissue (15-30HU). Secondary signs include perinephric and periureteric fat stranding, pelvic ureteric dilatation, periureteric oedema and unilateral renal enlargement (Figure 3). Stones <1cm in diameter that are accompanied by the presence of secondary signs are more likely to eventually require intervention with ureteronephroscopic extraction or lithotripsy. Intravenous contrast material may be used to identify the location of a non-CT-opaque stone,



**Figure 3.** Axial CT scan reveals secondary signs of ureterolithiasis, including right renal enlargement, hydronephrosis (arrow), and perinephric stranding (arrowhead).

which would appear a filling defect in the contrast filled uretero-pelvi-calyceal system. Stone burden influences the success of treatment and various ways of estimating stone size and volume on CT have been devised including linear and volumetric measurements as well as automated electronic volume estimation. It has been shown that a stone burden of more than 700 mm<sup>3</sup> as determined from the product of the three spatial dimensions is a significant predictor of failure for ESWL.



**Figure 4** - Axial CT scan in bone window settings shows internal inhomogeneities (arrowhead) within a stone (arrow) located in the right kidney.





Bupropion XR Tablet (Wellbutrin XR) is a once daily medication for the treatment of depression. It should be distinguished from bupropion sustained-release tablets which are also available in Europe as:

- Wellbutrin SR - a twice daily medication for the treatment of depression.
- Zyban - a twice daily medication used as an aid to smoking cessation.

Wellbutrin XR, Wellbutrin SR and Zyban all contain the same active ingredient (bupropion hydrochloride) and should not be used together. Bupropion XR tablet should be swallowed whole and not crushed or chewed. The maximum dose of bupropion extended-release tablet should not be exceeded.

**WELLBUTRIN XR ABridged Prescribing Information:** Please refer to full Summary of Product Characteristics (SPC) before prescribing. **TRADE NAME:** WELLBUTRIN XR. **ACTIVE INGREDIENT:** Bupropion Hydrochloride (50mg and 300mg). **PHARMACEUTICAL FORM:** Modified release tablet. **MAJOR INDICATIONS FOR USE:** WELLBUTRIN XR is indicated for the treatment of major depressive episodes. **DOSE AND METHOD OF USE:** WELLBUTRIN XR tablets should be swallowed whole and not crushed or chewed as this may lead to an increased risk of adverse events including seizures. can be taken with or without food. Use in Adults: The recommended starting dose is 150mg once daily. If no improvement is seen after 4 weeks the dose may be increased to 300mg once daily. There should be an interval of at least 24 hours between successive doses. As with all antidepressants the full effect of WELLBUTRIN XR may not be evident until after several weeks of treatment; patients should be treated for a period of at least 6 months to ensure that they are free of symptoms. Insomnia is a very common but transient adverse event which may be reduced by avoiding sleeping at bedtime. Use in Children and Adolescents: WELLBUTRIN XR is not indicated for use in children or adolescents aged less than 18 years. Use in Elderly Patients: Same as adults but with greater sensitivity in some elderly individuals. Use in hepatic and renal impairment: The recommended dose in these patients is 150mg once a day. Discontinuing therapy: Although no discontinuation reactions were observed during clinical trials with WELLBUTRIN XR, they cannot be excluded and a tapering off period may be considered. Overdose: In addition to these events reported as Undesirable Effects, overdose has resulted in symptoms including drowsiness, loss of consciousness and/or ECG changes such as conduction disturbances, arrhythmias and tachycardia; deaths have been reported rarely even with large overdoses. **CONTRAINDICATIONS:** Hypersensitivity to bupropion or any of the excipients; co-administration with other medicinal products containing bupropion as the incidence of seizures is dose-dependent; current seizure disorder or history of seizures; known CNS tumor; withdrawal from alcohol or any medicinal product known to be associated with the risk of seizures on withdrawal; severe hepatic cirrhosis; current or previous diagnosis of bulimia or anorexia nervosa; concurrent use with MAOIs. **PRECAUTIONS:** Do not exceed the recommended dose of WELLBUTRIN XR especially in patients who have predisposing factors for seizures since the risk of seizures is dose-related. WELLBUTRIN XR is not recommended and should be discontinued in patients who experience a seizure during treatment. Careful monitoring should be carried out during the first weeks of treatment, during dose changes and in patients who have history of suicide-related events prior to treatment. Close supervision should accompany drug therapy in particular those at high risk especially in early treatment and following dose changes. Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medicinal product, in patients who experience the emergence of suicidal ideation/behaviour especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. There is limited data on the use of bupropion in combination with mood stabilisers and ECT. WELLBUTRIN XR should be discontinued promptly if patients experience hypersensitivity reactions during treatment. Even though bupropion was well tolerated in studies for smoking cessation in patients with ischaemic heart disease there is limited clinical experience of its use in frail such patients with depression; therefore care should be exercised if it is used in these patients. Monitor blood pressure especially in patients with pre-existing hypertension; consider discontinuation if a clinically significant increase in blood pressure is observed. Use with caution in patients with hepatic and renal impairment. **DRUG INTERACTIONS:** Concurrent use with MAOIs is contraindicated; the dose of medicinal products which are metabolized by the CYP2D6 pathway like certain antidepressants, anti-psychotics, beta-blockers, SSRIs and Type 1C antiarrhythmics should be reduced when given concurrently with WELLBUTRIN XR; caution should be exercised when using medicinal products that may affect the CYP2D6 isoenzyme like cyclophosphamide and scopolamine, those known to induce metabolism e.g. carbamazepine, phenytoin, rifampin or inhibit metabolism e.g. valproic acid; caution also advised when Wellbutrin XR is administered to patients on levodopa or amantadine, alcohol and nicotine transdermal system. **ADVERSE EVENTS:** Very Common: Insomnia, headache, dry mouth, gastrointestinal disturbance including nausea and vomiting. Common: Hypersensitivity reactions such as urticaria, anorexia, agitation, anxiety, tremor, dizziness, taste disorders, visual disturbance, irritability, increased blood pressure (sometimes severe), flushing, abdominal pain, constipation, rash, pruritus, sweating, fever, chest pain and asthma. Not known: suicidal ideation and suicidal behaviour (see Precautions). Refer to the SPC for a full list of adverse events. **PREGNANCY AND LACTATION:** Pregnancy: The safety of WELLBUTRIN XR for use in human pregnancy has not been established. 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#### References

1. Nutt DJ, Demjensere K, Janika Z, Kauer T, Bourin M, Cameron PL, et al. The other face of depression; reduced positive affect: the role of catecholamines in causation and cure. *J Psychopharmacol* 2007; 21: 461-471.
2. Stahl SM, Pradko JF, Haight BR et al (2004) A review of the neuropharmacology of bupropion a dual Norepinephrine and dopamine reuptake inhibitor. *Prim Care Companion J Clin Psychiatry*; 6, 158-168.
3. Fava M, Rush AJ, Thase ME, Clayton A, Stahl SM, Pradko JF, et al. 15 years of clinical experience with bupropion HCl: from bupropion to bupropion SR to bupropion XL. *Prim Care Companion J Clin Psychiatry* 2005; 7: 106-113.



### A different treatment approach for major depressive episodes

Symptoms of low motivation and energy in patients with major depression have been associated with noradrenaline and dopamine dysfunction<sup>1</sup>. Now there is an alternative: Wellbutrin XR, a dual acting antidepressant, providing both Noradrenaline and Dopamine Re-uptake Inhibition (NDRi)<sup>2,3</sup>

Stone fragility can also be assessed by CT; a stone with heterogenous internal structure is likely to require less sessions and is more likely to respond to ESWL than stones with a homogeneous internal structure (Figure 4).

Stone composition has been shown to be reliably identified by CT in vitro. The attenuation values of urinary calculi usually fall within certain ranges: uric acid, 200–450 HU; struvite, 600–900 HU; cystine, 600–1100 HU; calcium phosphate, 1200–1600 HU; and calcium oxalate monohydrate, 1700–2800 HU. However measurement in vivo is not as reliable, and by general consensus CT density measurement is limited to the distinction of uric acid (<400HU) from non-uric acid (>400HU) stones and in the latter group, ESWL treatable (<1000HU) from less likely ESWL treatable (>1000HU) stones.

Dual-energy CT utilizes two X-ray beam energies (80 and 120kVp) to acquire tissue density information and through X-ray beam absorption of urinary tract stones is able to reliably distinguish calcium-containing from uric

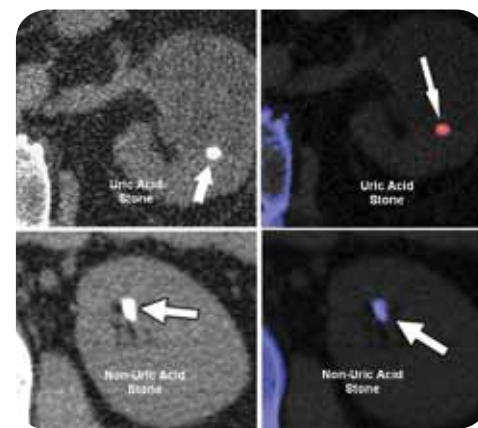


Figure 5 - Dual-energy CT can reliably distinguish uric acid (coded red) from calcium-containing (coded blue) stones based on tissue attenuation characteristics.

acid stones with a colour-coding for ease of diagnosis (Figure 5)

Location of a renal stone is also very important in planning therapy. A skin-to-stone distance (SSD) of >10cm indicates an increased likelihood of failure of potential treatment with ESWL. In addition, localization of the stone in the upper, mid or lower calyces will influence the percutaneous approach for PCNL.

CT analysis is finally useful for post-therapeutic assessment and important factors include, confirmation of stone-free status, assessment of residual stones and detection of residual renal obstruction, perirenal haematomas or urinomas. For dense stones larger

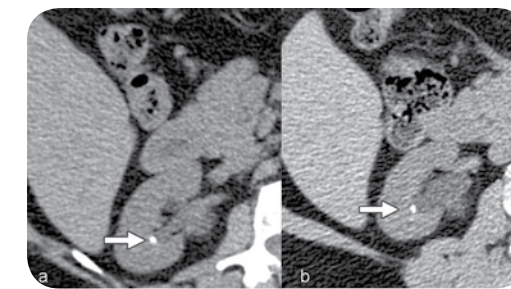


Figure 6 - CT scans taken with normal (120kVp, 240mAs) (a) and with low-dose (100kVp, 100mAs) (b) settings, both allow confident diagnosis of the renal stone (arrow) in spite of graininess in the low dose image.

than 10mm, plain X-rays may suffice to monitor stone position and state of fragmentation. After urologic intervention, identification of residual stones is important because the recurrence rates are higher with persistent stone fragments (50%–80%) than under stone-free conditions (10%–15%).

Despite the immense benefits of CT, there is some concern regarding its use in stone disease due to the risk of radiation exposure. This is particularly true in young individuals who undergo repeated CT examinations for stone disease and are consequently likely to be at risk for greater cumulative lifetime exposure. Rough estimates of radiation exposure in relation to the older and less sensitive IVU show a 2-5 fold increase. However careful selection of imaging parameters, limitation of scanned levels to the area-of-interest and new image processing algorithms have resulted in a much reduced radiation exposure requirement for urologic CT (Figure 6).

In summary, CT currently plays an important management role in patients with urolithiasis, from the initial diagnosis to treatment planning and post-treatment follow-up. Keeping abreast of recent technologic developments helps to meet the growing expectations in this field. In addition, we must be aware of the radiation risk and to take appropriate measures to minimize this risk and optimize the diagnostic value of the technique.

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Nutritional Medicine

# Healing & Disease Reversal

The Series

by Albert Cilia-Vincenti

*This series explores Dean Ornish's 30-year research experience into healing & disease reversal by dietary and lifestyle changes. He is a California University Professor of Medicine in San Francisco. This instalment continues to explain his claims why his programme works, whilst others prove unsustainable.*



Joy of living is a much better motivator than fear of dying. Trying to scare people into changing doesn't work very well. Efforts to motivate people to change based on fear of getting sick or dying prematurely are generally unsuccessful. Similarly, talking about "prevention" or "risk factor reduction" is boring to most people. Who wants to live longer if they're not enjoying life? People may say, "I don't care if I die early - I want to enjoy life". Whether good or fun is a false choice - why not both? It's both good and fun to look good, feel good, have more energy, think more clearly and perform better.

Behaviours that many people think are fun and sexy (like smoking, overeating, abusing alcohol, being super-busy and stressed out) are the ones that leave them lethargic and depressed - how fun is that? Recent studies show how much more dynamic our bodies are than previously believed. What you eat and what you do can increase blood flow in different body parts very quickly with powerful effects - for better or worse. A meal high in fat, sugar and calories, coffee, chronic stress, nicotine, cocaine, amphetamines and a lack of exercise constrict your arteries, reducing blood flow. How do you feel after a big meal? Sleepy? Why? Because your brain is receiving less blood flow and oxygen.

When you eat healthier, quit smoking, and exercise, your brain receives more blood and oxygen, so you think clearer, have more energy and need less sleep. Your face gets increased blood flow, so your skin glows more and wrinkles less. Your heart also gets more blood flow, so you have more stamina and can even begin to reverse heart disease. For many people, these are choices worth making - not just to live longer, but to live better.

Life comes round only once and is to be fully enjoyed. One of the most effective anti-smoking campaigns, conducted in California, dressed up an actor like the Marlboro Man in full cowboy regalia, and put his photograph on billboards and magazines with a limp cigarette hanging out of his mouth. The large headline was IMPOTENCE, not a warning about lung cancer, heart disease or emphysema. Studies show that half of men who smoke are impotent - how sexy is that? This approach was brilliant because it went to the heart of how smoking is marketed - smoking is sexy.

The deeper issues that underlie our behaviours need to be addressed. Information is important but not usually sufficient to motivate lasting dietary and lifestyle changes - if it were, nobody would smoke. We need to work at a deeper level. Loneliness, anxiety and depression are epidemic. If these deeper issues are addressed, it becomes easier for people to make lasting behavioural changes.

Change isn't easy, but if you're in enough pain, the idea of changing habits may start to seem more attractive. Awareness is the first step in healing. Part of the benefit of pain is to get our attention, to help us make the connection between when we suffer, and why, so we can make choices that are a lot more fun and healthy. Emotional pain and unhappiness are powerful catalysts for transforming not only behaviour (e.g., diet and exercise), but also for dealing with deeper motivating issues. We are most successful when we address the emotional and spiritual dimensions that most influence our choices. It's hard to motivate depressed, lonely or fearful people to make even simple behavioural changes in diet and exercise. It's only when deeper issues of pain, self-esteem, apathy and purposelessness are addressed that people become willing to make lifestyle choices that are life-enhancing rather than self-destructive ones.

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\*The Natural Way to Beat Depression, 2004, by Professor Bessert K.Puri, Hobler & Staughton

\*Chronic Fatigue Syndrome - a natural way to beat ME, 2005, by Professor Bessert K.Puri, Hammersmith Press Ltd.

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CYP1A2 inhibitors (e.g. fluvoxamine, ciprofloxacin). **Dosage:** The recommended dose is 25 mg once daily taken orally at bedtime. After 2 weeks, the dose may be increased to two 25 mg tablets. **Interactions:** Combination of Valdoxan and alcohol is not advisable. **Side effects:** Common: headache, dizziness, somnolence, insomnia, migraine, nausea, diarrhea, constipation, upper abdominal pain, hyperhidrosis, back pain, fatigue, anxiety, increases serum transaminases. **Precautions:** Not recommended in patients under 18 years old, pregnant woman and during breast-feeding. Not for use in elderly patients with dementia. Use with caution in patients with a history of mania or hypomania and discontinue therapy if manic symptoms appear. Possible effects on the ability to drive a car or operate machinery. Perform liver function tests when initiating treatment, periodically after around 6, 12, and 24 weeks, and thereafter when clinically indicated. Perform liver function tests in patients with symptoms suggesting hepatic dysfunction. Do not use in patients with galactose intolerance or glucose-galactose malabsorption. As prescribing information may vary from country to country, please refer to the complete data sheet supplied in your country. **LES LABORATOIRES SERVIER France.** Correspondent: **SERVIER INTERNATIONAL**: 35 rue de Verdun, 92284 Suresnes Cedex - France. [www.servier.com](http://www.servier.com) [www.valdoxan.com](http://www.valdoxan.com)

1. Lemoine et al. Efficacy of Valdoxan on symptoms relief at week 1 in a comparative study versus venlafaxine (n=332). *J Clin Psychiatry*. 2007. 2. Lemoine et al. Efficacy of Valdoxan on remission at week 6 in a comparative study versus venlafaxine (n=328). *J Clin Psychiatry*. 2007. 3. Kennedy et al. Efficacy of Valdoxan on remission at week 12 in a comparative study versus venlafaxine (n=276). *J Clin Psychopharmacol*. 2008. 4. Goodwin et al. Efficacy of Valdoxan on relapse prevention at week 24 in a placebo-controlled study versus venlafaxine (n=339). *Eur Neuropsychopharmacol*. 2007.

  
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