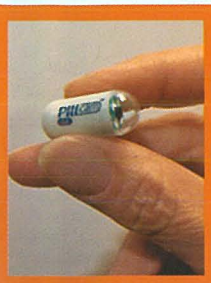
NEWSPAPER POST

Issue 06/09

TheSynapse

The Medical Professionals' Network



Gastro-intestinal Diagnostic Modalities: Capsule Endoscopy

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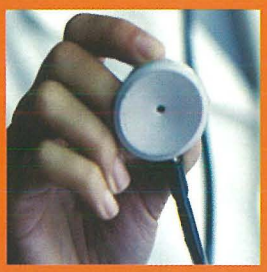

Who is the future general practitioner?

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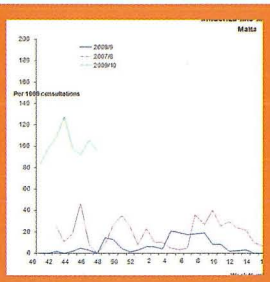

Update on H1N1 virus

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MEDICAL IMAGING

Imaging Diffuse Liver Disease – Part I

by **Pierre Vassallo**
MD PhD FACA Artz für Radiologie
Consultant Radiologist

Diffuse parenchymal hepatic diseases usually represent a failure in a hepatic metabolic pathway and can be categorized as storage, vascular, and inflammatory diseases.

This article discusses the role of computed tomography (CT), in the evaluation of diffuse liver disease. The prominent role of CT is primarily defined by its capability for excellent morphologic visualization. CT evaluation of the liver always includes non-contrast-enhanced and contrast-enhanced scans; iodinated contrast material injected as a bolus via an intravenous route helps demonstrate normal and abnormal vascular anatomy and tissue perfusion of internal organs at CT.

The physiologic attenuation of liver parenchyma at nonenhanced CT varies between individuals between 55 and 65 HU. Usually, the normal liver parenchyma appears homogeneous at CT, and its attenuation exceeds that of the spleen by about 10 HU. The relatively large range variation in hepatic attenuation is due to the varying content of fat and glycogen; increased diffuse deposition of fat leads to a decrease in attenuation (Figure 1), whereas increased glycogen is reflected as increased attenuation. Storage diseases with iron or copper as deposited metabolites also lead to increased attenuation of the hepatic parenchyma (Figure 2).

Besides quantification of segmental or homogeneous liver attenuation, further valid indications for nonenhanced hepatic CT include, the search for calcifications in clinical scenarios such as calcified metastases of mucinous adenocarcinoma or postinflammatory calcifications in cases of alveolar echinococcosis. Furthermore, unenhanced CT can help detect intrahepatic CT–opaque bile duct calculi. Subcapsular or parenchymal hemorrhage can also be identified in cases of trauma.

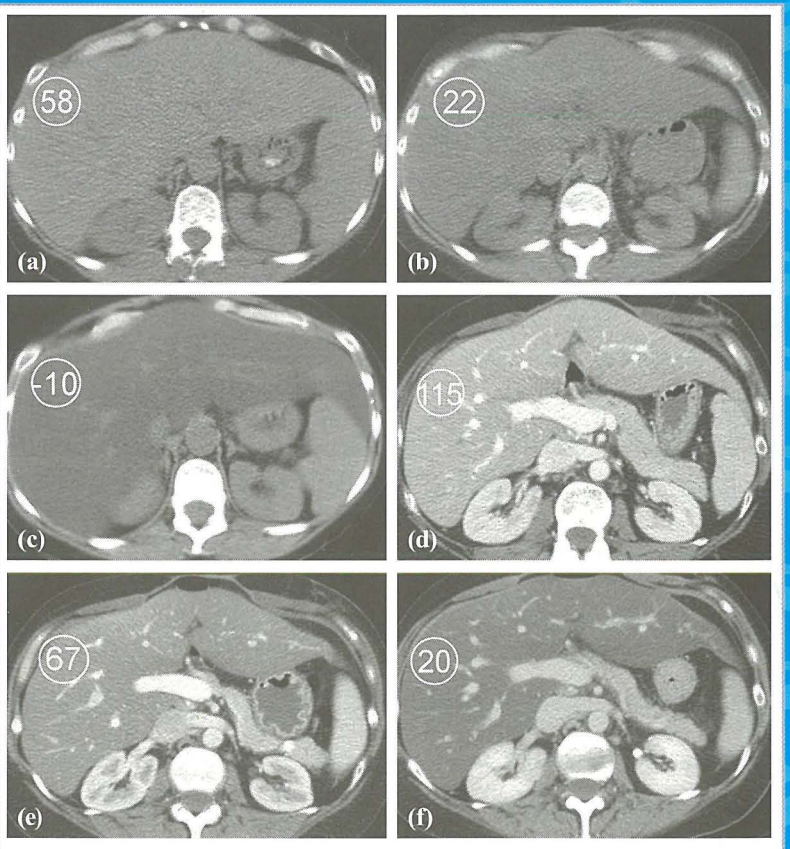


Figure 1. *Fatty infiltration of the liver parenchyma in a 46-year-old woman with ovarian cancer who was undergoing chemotherapy. Sequential nonenhanced* ***(a–c)*** *and portal venous perfusion phase contrast material–enhanced* ***(d–f)*** *CT scans obtained at 3-month intervals show a progressive decrease in hepatic attenuation. Circle = region of density measurement, number = attenuation in Hounsfield units.*

continues on page 22

Editor's Word

Extraordinary Times

As I am writing this editorial I am recovering from an appendicectomy with severe uvulitis as a post anaesthesia complication, which is constantly reminding me of my endotracheal intubation. So reading an article which suggested that influenza vaccinations may be safely administered to patients with egg allergies, was effectively distracting me from my pains. The research, which seeems to apply to both seasonal and H1N1 vaccines, was presented last month at the American College of Allergy, Asthma & Immunology meeting, and apparently concluded that egg-allergic patients can get the vaccination if its egg protein content is 1.2 mcg/mL or less. The vaccinations should, however, be given in graded doses under the evaluation of an allergist.

We are indeed experiencing extraordinary times. One one hand we are seeing Norway gear up for the pandemic by allowing pharmacists, even if for a limited time only, to give the prescription-only Tamiflu and Relenza, to patients in pharmacies, in order to increase access to drugs. On the other hand we are sadly recognising that with all good intentions and efforts most probably next year we will be experiencing simultaneous pandemics / epidemics in many countries. A case in point is Sudan which is currently also struggling with a visceral leishmaniasis epidemic,with cases in the country continuing to rise. And the predicted economic recovery is seriously being undermined by Dubai's current financial meltdown, with many analysts predicting a double-dip recession in 2010.

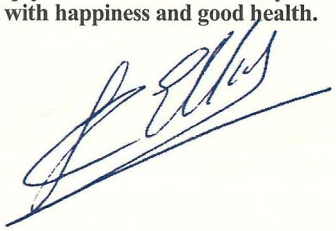
The answer to such challenging times maybe has been found by pharmaceutical companies in their mergers, take-overs and other restructuring strategies. And Sanofi-Aventis is a sterling example of such diverse restructuring, having just completed its $4 billion acquisition of the 50% interest in Merial, a biomedical veterinary research company, acquiring the stake from its joint venture partner Merck & Co. The company is also to acquire the French R&D company Fovea Pharmaceuticals in order to expand its ophthalmology business and has recently signed a exclusive cancer drug development licensing deal with Merrimack Pharmaceuticals. The latter two deals are worth almost $1 billion. Sanofi-Aventis's drug pipeline is also being boosted by an additional $1 billion which are being paid over eight years to Regeneron Pharmaceuticals for the discovery of new monoclonal antibodies. Another strategy which seems to be paying off is the reduced dependency on 'white pill/Western markets' (coined by GSK's CEO Andrew Witty). In fact Sanofi-Aventis has also announced that it has bought a 74% stake in Bioton-Vostok, a Russian manufacturer of insulins, becoming Sanofi-Aventis's first production facility in Russia.

Nearer to us, the long awaited Consultation document - the proposals for the Reform in Primary care in Malta has now been published. This represents a concrete step after more than two decades of presenting the case for a reform by family medicine associations in Malta, innumerable papers and so many conferences.

As with any relationship in life, all stakeholders need to trust, and moreover, prove that they themselves can be trusted. Indeed, trust has to be earned rather than assumed.

Undoubtedly the consultation period and any negotiation period will be filled with debate, mostly because of the intrinsic resistance to change by many. Although change does not necessarily mean improvement ... there can be no improvement without change ...

I sincerely wish you and your loved ones a joyful Christmas and a new year filled with happiness and good health.



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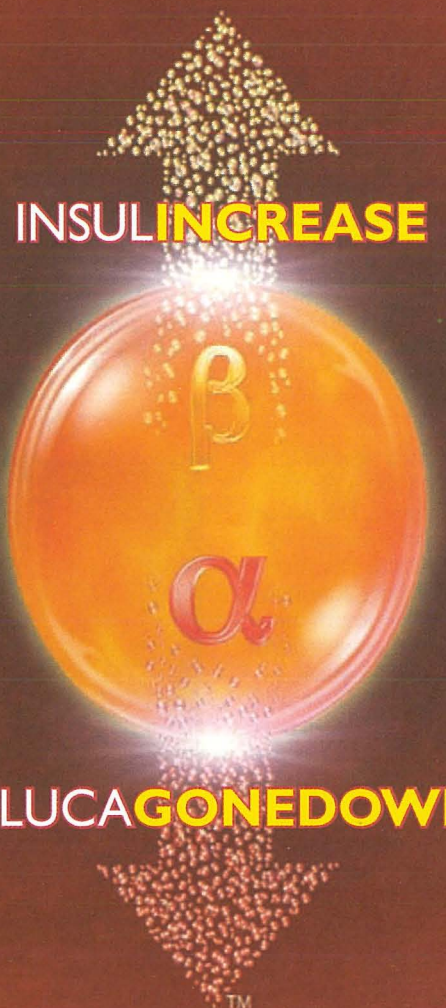
GALVUS and EUCREAS

COMPREHENSIVE POWER TO ADVANCE TYPE 2 DIABETES TREATMENT



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EUCREAS is the combination of a DPP-4 inhibitor, GALVUS, and metformin[2]

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Presentations: Galvus 50 mg tablet Each tablet contains 50 mg of vildagliptin and 47.82 mg of the excipient lactose. **Indications:** For the treatment of type 2 diabetes mellitus: As dual oral therapy in combination with - metformin, in patients with insufficient glycaemic control despite maximal tolerated dose of monotherapy with metformin, - a sulphonylurea, in patients with insufficient glycaemic control despite maximal tolerated dose of a sulphonylurea and for whom metformin is inappropriate due to contraindications or intolerance, - a thiazolidinedione, in patients with insufficient glycaemic control and for whom the use of a thiazolidinedione is appropriate. **Dosage and Administration:** In combination with metformin or thiazolidinedione 100mg daily, administered in two divided doses of one 50 mg in the morning and one 50 mg in the evening. In combination with sulphonylurea, 50 mg once daily in the morning. Galvus can be administered with or without a meal. Doses greater than 100 mg are not recommended. Caution should be exercised when treating patients aged 75 years and over. Galvus is not recommended for use in patients less than 18 years old. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients **Precautions/Warnings:** Galvus should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Galvus is not recommended in patients with moderate or severe renal impairment or in haemodialysis patients with end-stage renal disease. Galvus is not recommended in patients with hepatic impairment, including patients with pre-treatment ALT or AST >3x the ULN. Liver function tests should be performed prior to treatment initiation, at three month intervals during the first year and periodically thereafter. Should an increase in AST or ALT of 3xULN or greater persist, withdrawal of Galvus therapy is recommended. Patients who develop jaundice or other signs suggestive of liver dysfunction should discontinue Galvus. Vildagliptin should be used with caution in patients with congestive heart failure of New York Heart Association (NYHA) functional class I-II and is not recommended in patients with NYHA functional class III-IV. Routine monitoring of diabetic patients for skin disorders such as blistering or ulceration is recommended. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. **Pregnancy and lactation:** Galvus should not be administered during pregnancy or lactation. **Interactions:** Vildagliptin has a low potential for drug interactions. No clinically relevant interactions with other antidiabetics (glyburide, pioglitazone, metformin), amlodipine, digoxin, ramipril, simvastatin, valsartan or warfarin were observed after co-administration with vildagliptin. As with other oral antidiabetic medicines, the hypoglycaemic effect of vildagliptin may be reduced by certain active substances, including thiazides, corticosteroids, thyroid products and sympathomimetics. **Adverse reactions:** Rare cases (>1/10,000 to <1/1,000) angioedema, hepatic dysfunction (including hepatitis). Monotherapy: Common (>1/100, <1/10): dizziness, Uncommon (>1/1,000, <1/100): headache, constipation, arthralgia, hypoglycaemia, oedema peripheral. Very rare (<1/10,000): URTI, nasopharyngitis. Combination with metformin: Common: tremor, headache, dizziness, nausea, hypoglycaemia. Uncommon: fatigue. Combination with sulphonylurea: Common: tremor, headache, dizziness, asthenia, hypoglycaemia. Uncommon: constipation. Very rare: nasopharyngitis. Combination with Thiazolidinedione: Common: weight increase. oedema peripheral, Uncommon: headache, asthenia, hypoglycaemia. **PACK SIZES:** 7, 28 tablets **MARKETING AUTHORISATION NUMBERS:** EU/1/07/414/001, 003. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. Before prescribing please refer to Summary of Product Characteristics (SmPC). Full prescribing information is available on request from Novartis Pharma, P.O. Box 124, Valletta, VLT 1000, Malta. Tel +356 22983217. 2009-MT-03 GAL SEP 2009

Eucreas®

Presentations: Eucreas 50 mg/ 850 mg film-coated tablet. Eucreas 50 mg/1000 mg film-coated tablet. Each 50 mg/850 mg film-coated tablet contains 50 mg of vildagliptin and 850 mg metformin hydrochloride. Each 50 mg/1000 mg film-coated tablet contains 50 mg of vildagliptin and 1000 mg metformin hydrochloride. **Indications:** Eucreas is indicated in the treatment of type 2 diabetes mellitus patients who are unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone or who are already treated with the combination of vildagliptin and metformin as separate tablets. **Dosage and Administration:** The recommended daily dose should be based on the patient's current regimen of vildagliptin and /or metformin hydrochloride. The usual dose is 50 mg/850 mg or 50 mg/1000 mg twice daily one tablet in the morning and the other in the evening. Eucreas should be taken with or just after food. Doses of vildagliptin greater than 100 mg are not recommended. Patients > 65 taking Eucreas should have their renal function monitored regularly, Eucreas is not recommended in patients >75 years. Eucreas is not recommended for use in patients less than 18 years old. For use in renal or hepatic impairment, see contraindications and precautions below or refer to the SmPC for more information. **Contraindications:** Hypersensitivity to vildagliptin or metformin hydrochloride or to any of the excipients. Diabetic ketoacidosis or diabetic pre-coma. Renal failure or renal dysfunction defined as creatinine clearance < 60 ml/min. Acute conditions with the potential to alter renal function e.g. dehydration, severe infection, shock or intravascular administration of iodinated contrast agents. Acute or chronic disease which may cause tissue hypoxia e.g. cardiac or respiratory failure, recent myocardial infarction, shock. Hepatic impairment. Acute alcohol intoxication, alcoholism. Lactation **Precautions/Warnings:** Eucreas should not be used in patients with type 1 diabetes. Due to the risk of lactic acidosis, renal function could be monitored at least once yearly in patients with normal renal function and at least two to four times/year in patients with serum creatinine at the upper limit of normal and in elderly patients. Eucreas is not recommended in patients with hepatic impairment, including patients with pre-treatment ALT or AST >3x the ULN. LFT's should be performed prior to treatment initiation, at three month intervals during the first year and periodically thereafter. Should an increase in AST or ALT of 3x ULN or greater persist, withdrawal of Eucreas therapy is recommended. Patients who develop jaundice or other signs suggestive of liver dysfunction should discontinue Eucreas. Vildagliptin should be used with caution in patients with congestive heart failure of New York Heart Association (NYHA) functional class I-II and is not recommended in patients with NYHA functional class III-IV. Metformin is contraindicated in patients with heart failure, therefore Eucreas is contraindicated in this population. Routine monitoring of diabetic patients for skin disorders such as blistering or ulceration is recommended. As Eucreas contains metformin, treatment should be discontinued 48 hours before elective surgery with general anaesthesia and not usually resumed earlier than 48 hours afterwards. The IV administration of iodinated contrast agents can lead to renal failure. Therefore due to metformin active ingredient, Eucreas should be discontinued prior to or at the time of the test and not reinstituted until 48 hours afterwards and only after renal function has been re-evaluated and found to be normal. **Pregnancy and lactation:** Eucreas should not be administered during pregnancy or lactation. **Interactions:** Vildagliptin has a low potential for drug interactions. No clinically relevant interactions with other antidiabetics (glyburide, pioglitazone, metformin), amlodipine, digoxin, ramipril, simvastatin, valsartan or warfarin were observed after co-administration with vildagliptin. Interactions with metformin hydrochloride that are not recommended include alcohol, cationic active substances e.g. cimetidine and intravascular administration of iodinated contrast media. Combinations requiring caution include metformin hydrochloride with medicines tending to produce hyperglycaemic activity e.g. glucocorticoids, beta agonists and diuretics. The dose of antihyperglycaemic medicinal products may need to be adjusted in combination with ACE inhibitors **Adverse reactions:** Rare cases (>1/10,000 to <1/1,000) angioedema, hepatic dysfunction (including hepatitis) have been reported with vildagliptin. Vildagliptin Monotherapy: Common (>1/100, <1/10): dizziness, Uncommon (>1/1,000, <1/100): headache, constipation, arthralgia, hypoglycaemia, oedema peripheral. Very rare (<1/10,000): URTI, nasopharyngitis. Metformin monotherapy: Very common (>1/10) Nausea, vomiting, diarrhoea, abdominal pain and loss of appetite. Common: metallic taste. Combination vildagliptin with metformin: Common: tremor, headache, dizziness, nausea, hypoglycaemia. Uncommon: fatigue. **PACK SIZES:** 30, 60 film-coated tablets **MARKETING AUTHORISATION NUMBER:** EU/1/07/425/002–3, EU/1/07/425/8-9. **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 2009-MT-03 EUC SEP 09

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Galvus® vildagliptin

Eucreas® vildagliptin/metformin

1. Novartis Europharm Ltd. Galvus® Summary of Product Characteristics 2009
2. Novartis Europharm Ltd. Eucreas® Summary of Product Characteristics 2009

New Gastrointestinal Diagnostic Modalities: Capsule Endoscopy

by **Thomas M. Attard** *MD FAAP FACG*
Consultant Paediatrician, Gastroenterologist
Mater Dei Hospital

With an approximate length of 15 feet, the small intestine presents a daunting challenge to the clinician faced with symptoms referable to this relatively inaccessible area. In the last decade, capsule endoscopy (CE) has established an increasingly broad niche in the diagnostic armamentarium of both paediatric and adult clinicians; it is now the established standard of care in the work up of obscure gastrointestinal hemorrhage, suspected Crohn's Disease, polyposis syndromes and arguably, chronic abdominal pain.

CE usually involves an overnight fast. At the time of the investigation sensors (similar to ECG array) and a Holter-like receiver device are attached to the abdomen. The patient is asked to ingest a small pill-like device about the size of a vitamin pill (measuring 11mm x 26mm) (Figure 1) with a glass of water, and then can resume normal daily activities. After 8 hours the patient returns to the clinic to return the receiver device; the images are then downloaded on a standard PC for viewing. The pill passes naturally with a bowel movement, usually in less than 24 hours. Patients, including children, unable or unwilling to swallow the capsule can have it placed endoscopically; the procedure can be performed in adults and children weighting over 15 kgs.

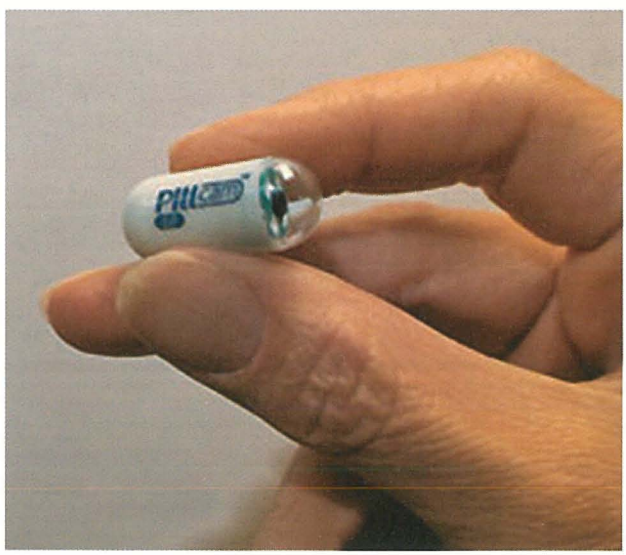

Figure 1: *The miniature device used in capsule endoscopy*

Capsule endoscopic findings include mucosal abnormalities including alterations in color, for example, erythema, surface contour including nodularity, erosions and ulcers, luminal contour abnormalities including extrinsic compression, intramural mass lesions, polyps, and strictures and stenoses (Figure 2). Coeliac disease may be associated with very characteristic scalloping of the intestinal mucosa in the duodenum and jejunum, although the standard of care to diagnose coeliac disease remains endoscopically-obtained biopsies showing villous blunting, crypt hyperplasia and intraepithelial lymphocytes.

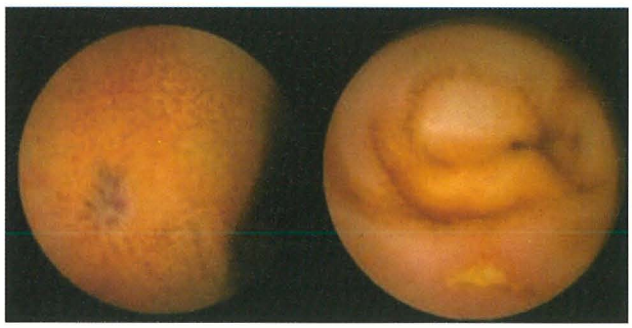

Figure 2: *Venous malformation (L) and jejunal ulceration (R) on Capsule Endoscopy*

Indications for Capsule Endoscopy

CE may disclose a variety of small intestinal causes for gastrointestinal bleeding, including tumors, telangiectasia, ulcers and erosions including NSAID enteropathy. With recent advances in CE software that is available, including locally, images showing possible bleeding lesions are automatically identified, with further refinements rendering the detection of vascular pattern abnormalities easier.

Obscure gastrointestinal bleeding, defined as suspected chronic gastrointestinal hemorrhage in the context of negative upper endoscopy and colonoscopy, may be caused by a variety of lesions including small intestinal malignancy. CE is a safe, non-invasive, easily performed procedure that allows visualization of the entire small bowel. Two meta-analyses support the value of CE over push-enteroscopy in clinical practice, with an incremental yield of CE of 0.30.[1,2] In addition, both push and double balloon enteroscopy depend on operator experience and are more invasive. A strategy employing CE and endoscopic enteroscopy in tandem appears to give best diagnostic yield and risk-benefit ratio.[3,4] Negative CE findings in obscure gastrointestinal hemorrhage are reassuring in that the incidence of rebleeding is exceedingly lower in negative compared to positive studies (5.6 cf 48% p=0.03).[5] The International Conference on Capsule Endoscopy (ICCE) has published a widely supported management algorithm on obscure gastrointestinal hemorrhage (Figure 3).[6]

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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, irbesartan, 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, carbenoxolone, penicillin G, laxatives, salicylic acid derivatives, other kaliuretic diuretics), ♦ Caution if combined with other antihypertensives, curare derivatives, NSAIDs (especially in the elderly), digoxin, antidiabetic agents, allopurinol, amantadine, diazoxide, cytotoxic drugs, anticholergenic agents, cholestyramine and colestipol resins, vitamin D, calcium salts, pressor amines, antigout medicine, and ciclosporin. ♦ Caution should be excercised on concomintant use with ketoconazole or other moderate P-gp inhibitors (ketoconazole, itraconazole, clarithromycin, erythromycin, amiodarone, telithromycin). ♦ Grapefruit juice ♦ Alcohol **Adverse reactions:** Common: Diarrhoea **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/agranulocytosis, haemolytic anaemia, leucopenia, thrombocytopenia, depression, sleep disturbances, restlessness, light-headedness, vertigo, paraesthesia, dizziness, transient blurred vision, xanthopsia, cardiac arrhythmias, postural hypotension, respiratory distress (including pneumonitis and pulmonary oedema), pancreatitis, anorexia, diarrhoea, constipation, gastric irritation, sialadenitis, loss of appetite, jaundice (intrahepatic cholestatic jaundice), anaphylactic reactions, toxic epidermal necrolysis, necrotising angiitis, (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 hypokalaemia and hyponatraemia, hyperuricaemia, glycosuria, hyperglycaemia, increases in cholesterol and triglycerides **Legal Category:** POM **Pack sizes:** 7, 28 film-coated tablets **Marketing Authorisation Holder:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **Marketing Authorisation Numbers:** Rasilez HCT 300/12.5 mg - EU/1/08/491/041-060. Rasilez HCT 300/25 mg - EU/1/08/491/061/080 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 22983217. (vsn 2009-MT- RASHCT April 2009)

References : 1. Palatini P, Jung W, Shlyakhto E, et al. *J Hum Hypertens.* 2009: 1-11 online publication, 21 May 2009 **2.** Villamil A, Chrysant SG, Calhoun D, et al. *J Hypertens.* 2007; 25:217-226.

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Counterfeit Medicines

by **Anthia Zammit**
LL.B Dip.N.P.

The counterfeiting of medicinal products is a growing concern for patients, the pharmaceutical industry and national policy-makers worldwide. EU internal market rules for medicinal products for human use coupled by wide-ranging International cooperation, and proposed European legislative reforms are hoped to have a positive impact against the problem of counterfeit medicines – one of the greatest current threats to public health and safety.

The WHO defines counterfeit medicines as "medicines that are deliberately and fraudulently mislabelled with respect to identity and/or source".[1] Since the first international initiative that addressed the problem of counterfeit medicines at the Conference of Experts on the Rational Use of Drugs in Nairobi in 1985, the worldwide import and export of counterfeit medicines has become a highly sophisticated criminal enterprise and a major public health concern. The astronomical 118% increase in the number of medicinal products detained by customs authorities in 2008 makes medicines the third largest specific product category in terms of quantities of intercepted counterfeit articles.[2] This increase in customs discovery was largely due to the EU coordinated 'MEDI-FAKE' action which targeted customs control of counterfeit medicines over a two-month period in 2008 and led to the seizure of 34 million tablets, including antibiotics, antineoplastic, anti-malaria and lipid-regulating medicines, as well as painkillers,and drug precursors. This by far exceeded any previous results.[3]

This growing global problem is being counteracted by international endeavours of the WHO and the pharmaceutical industry, and through European legislative reforms. In 2006 the WHO launched the International Medical Products Anti-Counterfeiting Taskforce (IMPACT) which is a partnership comprising several stakeholders including international non-governmental organizations, regulatory authorities, enforcement agencies and pharmaceutical manufacturers associations. Furthermore, the European Directorate for the Quality of Medicines and Health care of The Council of Europe has set up a Committee of Experts aimed at minimizing the public health risk posed by counterfeit medicinal products and related crimes; whilst the US Food and Drug Administration (FDA) launched its Counterfeit Drug Task Force in July 2003 to receive proposals from security experts, Federal and State law enforcement officials, technology developers, manufacturers, wholesalers, retailers, consumer groups, and the general public, in order to help deter counterfeit medicines. The European Medicines Agency (EMEA) also collaborates with member states in combating counterfeit medicinal products and has recently issued a warning about counterfeit medicines for the treatment of H1N1 influenza being sold over theinternet.[4]

Directive 2001/83/EC on medicinal products for human use, as amended[5] includes provisions for manufacturing, importation, placing on the market, and wholesale distribution of medicinal products in the Community, as well as rules relating to active pharmaceutical ingredients used as starting materials. The Commission's proposal to amend this Directive[6] aims to further optimise the functioning of the internal market for medicinal products while ensuring a high level of protection of public health in the EU.

The proposed amendments include:

- Obligations for stakeholders, acting in the distribution chain and involved in the transactions but who do not actually handle the products;
- A legal basis for the Commission to introduce obligatory safety-features (such as a serialisation number or a seal) on the packaging of prescription medicines;
- Prohibition of manipulating (i.e. removing and tampering with the packaging, or over-labelling) safety features on the packaging by intermediaries between the original manufacturer and the last stakeholder in the distribution chain (pharmacist/doctor/patient);
- Obligatory audits of supplying wholesale distributors in order to ensure reliability of business partners;
- Strengthened requirements for the importation of active pharmaceutical ingredients from third countries, if the regulatory framework in the respective third country does not ensure a sufficient level of protection of human health for products imported into the EU;
- Audits of manufacturers of API;
- Strengthened mandate for inspections including increased transparency of inspection results through publication in the EudraGMP database managed by the EMEA.

The European Patients' Forum has published a Position Paper[7] supporting the Commission's legislative proposal, focusing principally on patient-centred health care and patient involvement in counteracting the public health threat of counterfeit medicinal products. The European Federation of Pharmaceutical Industries and Associations (EFPIA) has however expressed concern that the patient safety would not be fully secured through the Commission's current proposals.[8] EFPIA has recommended a technological anti-counterfeiting strategy based on the integrity of the product packaging through the use of tamper-evident packaging or tamper-resistant closures for all medicines, the use of overt, covert and forensic authentication features, and better product identification through one harmonized European coding of each individual pack. EFPIA has advocated the prohibition of repackaging in order to guarantee the integrity of the product throughout the entire supply chain. The latter proposal is highly controversial as it would severely limit parallel importation. Parallel importation of a medicinal product is a lawful form of trade within the Internal Market based on article 28 of the EC Treaty and subject to the derogations provided by article 30 of the EC Treaty.[9]

Increasing product safety is also a key priority in the US, with the focus being on the physical-chemical identifiers (PCIDs) in medicinal products. The FDA issued a Draft Guidance for Industry on Drug Anti-counterfeiting[10] in July 2009 on the use of inks, pigments, flavours, and other PCIDs by manufacturers to make medicinal products more difficult to duplicate by counterfeiters, and to make it easier to identify the genuine version of the medicinal product. This is an important collaborative step between the FDA and drug manufacturers in making medicinal products more difficult to counterfeit.

It is clear that the eradication of counterfeit medicines is a challenging undertaking which requires multi-disciplinary collaboration between national governments, the pharmaceutical industry and international bodies; structured cooperation between regulatory authorities and national law enforcement agencies such as the police and customs officials; as well as rigorous information campaigns directed at consumers.

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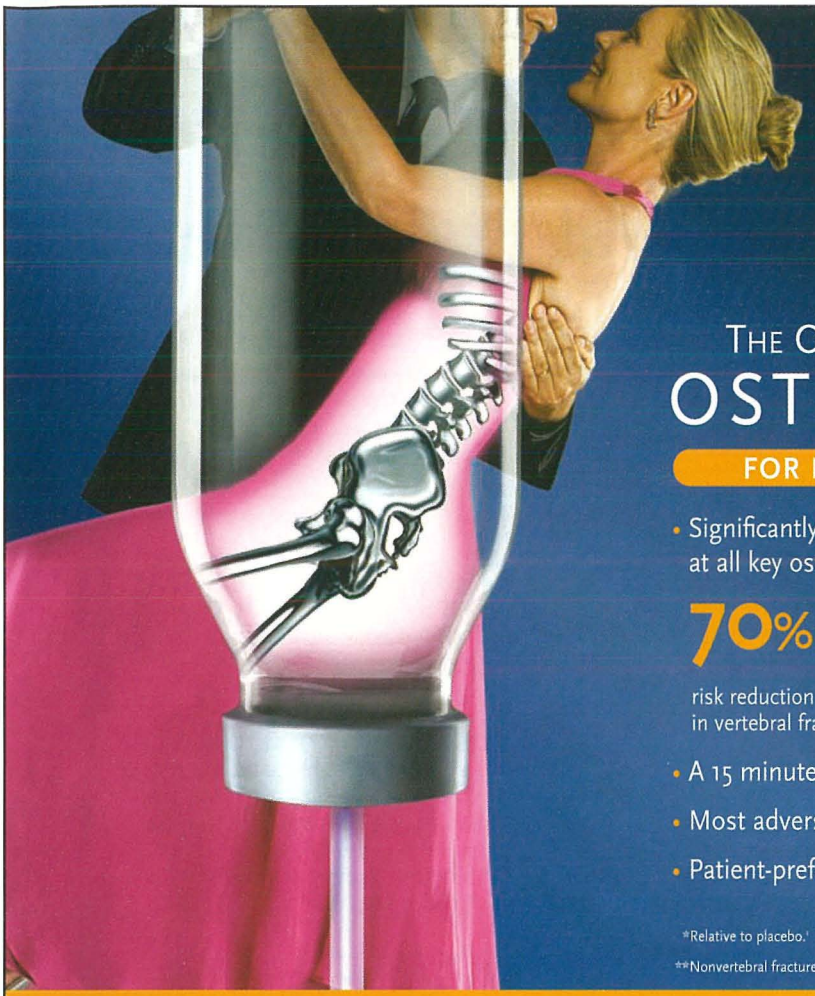

NEW INDICATION: TREATMENT OF GIO

ACLASTA®

THE ONCE-YEARLY INFUSION OF POWERFUL OSTEOPROTECTION

FOR POSTMENOPAUSAL OSTEOPOROSIS

- Significantly reduced 3-year risk of fractures at all key osteoporotic sites[1]*

70% risk reduction in vertebral fracture[1]

41% risk reduction in hip fracture[1]

25% risk reduction in nonvertebral fracture[1]**

- A 15 minute, once-yearly infusion ensures yearlong compliance[1]
- Most adverse events were transient and mild to moderate[1,2]
- Patient-preferred over weekly oral alendronate[3,4]

*Relative to placebo.[1]

**Nonvertebral fracture includes wrist, rib, arm, shoulder, or hip fracture; excludes finger, toe, or craniofacial fracture.[1]

Aclasta® 5 mg
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. Patients must be appropriately hydrated prior to administration of Aclasta, especially important for the elderly and for patients receiving diuretic therapy. 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. Not recommended for use in patients with severe renal impairment (creatinine clearance <35 ml/min). No dose adjustment in patients with creatinine clearance ≥35 mL/min, or in patients with hepatic impairment, or in elderly patients. Aclasta should not be given to children or adolescents.

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 giving Aclasta. Not recommended in patients with creatinine clearance <35 ml/min. Appropriate hydration prior to treatment, especially in the elderly and in combination with diuretics. Use with caution in conjunction with medicinal products that can significantly impact renal function (e.g. aminoglycosides or diuretics that may cause dehydration); 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.

ADVERSE REACTIONS: The incidence of post-dose symptoms (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 symptoms occur within the first three days and were mild to moderate and resolved within three days of the event onset. The incidence of post-dose symptoms 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†, rigors†, ocular hyperaemia, atrial fibrillation, diarrhea, increased C-reactive protein. Local reactions: redness, swelling and/or pain. Others: renal dysfunction and osteonecrosis of the jaw. † 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. (JUL 09 2009-MT-01)

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;41:122-128.

NOVARTIS

Aclasta®
zoledronic acid 5 mg
solution for infusion
One Infusion. Yearlong Osteoprotection.

ACL Ad1 11/09 MT

Who is the future General Practitioner?

by **Francesco Carelli**

We are currently experiencing a shift in general practice. Our patients are becoming increasingly knowledgeable with more access to expert information, which together with a longer life expectancy characterised by better quality of life has increased their expectations of health care professionals.

According to Bibi Holge-Hazelton, the concept of the traditional doctor has evolved too. The doctor 'should' meet the patient's expected demands and at the same time keep pace with the introduction of technological tools which are being requested by patients as part of diagnostic tests and treatments.[1]

Until now, we have essentially ignored the limited capacity of general practice. Certainly, doctors complain when new obligations are introduced, but after a while they accept and adapt. It is however hardly a surprise to anyone that this means squeezing more work with a consequential extension of the work hours.

Like other people, doctors value leisure and closer relations with the family but have also to face other challenges … quality of care given, career progression, working hours with the fewest possible shifts and flexible working conditions... but are these attributes compatible with the work of general practitioners?

In this context, the consequences of the fact that currently a greater proportion of junior doctors is female, are yet unknown. Reasons for this may be due to complex and therefore less visible factors. In debates regarding the future for doctors, the positive significance that in times to come the medical profession will be evenly divided between men and women is accepted, but at the same time concerns exist whether general practice is becoming a female-dominated profession.[2] This concern has its roots in the assumption that this will possibly result in a glass ceiling, for female doctors, and more requests for reduced working hours which may affect the continuity of the healthcare provision in general practice. The most efficient scenario in the medical profession entails a balance between genders

A recent survey[3] on medical students' attitudes toward a career in general practice revealed that such a career is not popular amongst medical students (13.8%), however it increased significantly when students had teaching in general practice. The results also showed that overall, a career in general practice is more popular in the female population.

Now, among general practitioners, prevails a sense of uncertainty regarding the content of their work and its lack of direction. We feel like a social worker, priest, marriage counsellor, educator, substitute mother or substitute daughter or brother … leaving us to wonder why we have acquired all these roles. But the social worker has interminably long waiting lists, psychologists and therapists are expensive and the real pedagogues are increasingly giving the parents a bad conscience, whilst the close family bonds are not that close any more. Parents of small children are insecure and many old people are lonely. Much too often it is said "*Go to your GP, he/she always has time.*"

The General Practitioners are also feeling frustrated for the current reward mechanisms … being rewarded for the quantity and not for the quality of their work. In Italy, till now, the concept is … the more patients, the higher the salary. All these people knocking on our offices with their expectations and demands are at the same time our work, but at which price?

The questions: '*Who are we?*' or '*Who is the doctor?*' are relevant and actual because the all these vague tasks demand that the individual doctor interprets them in a complex relationship with his/ her professional background and experiences and combines them with the respective myths in the field, as well as with his/her subjective background consisting of the past experiences, social background, gender, ethnicity, etc.

In other words, it is not enough to assume that a doctor is a doctor and that his or her actions therefore are visible and predictable. In order to understand who the doctor is, it is necessary to include many complicated perspectives.[4] These may vary depending on the interplay between politics and welfare structures, patient and professional interests, knowledge-development, democratisation, and technological development towards a more holistic healthcare provision keeping the patient at the centre of pharmaceutical care … ◻

References

1. Holge-Hazelton B. Is a doctor a doctor? Feminization of General Practice. Oral presentation, WONCAannual meeting. 2004.

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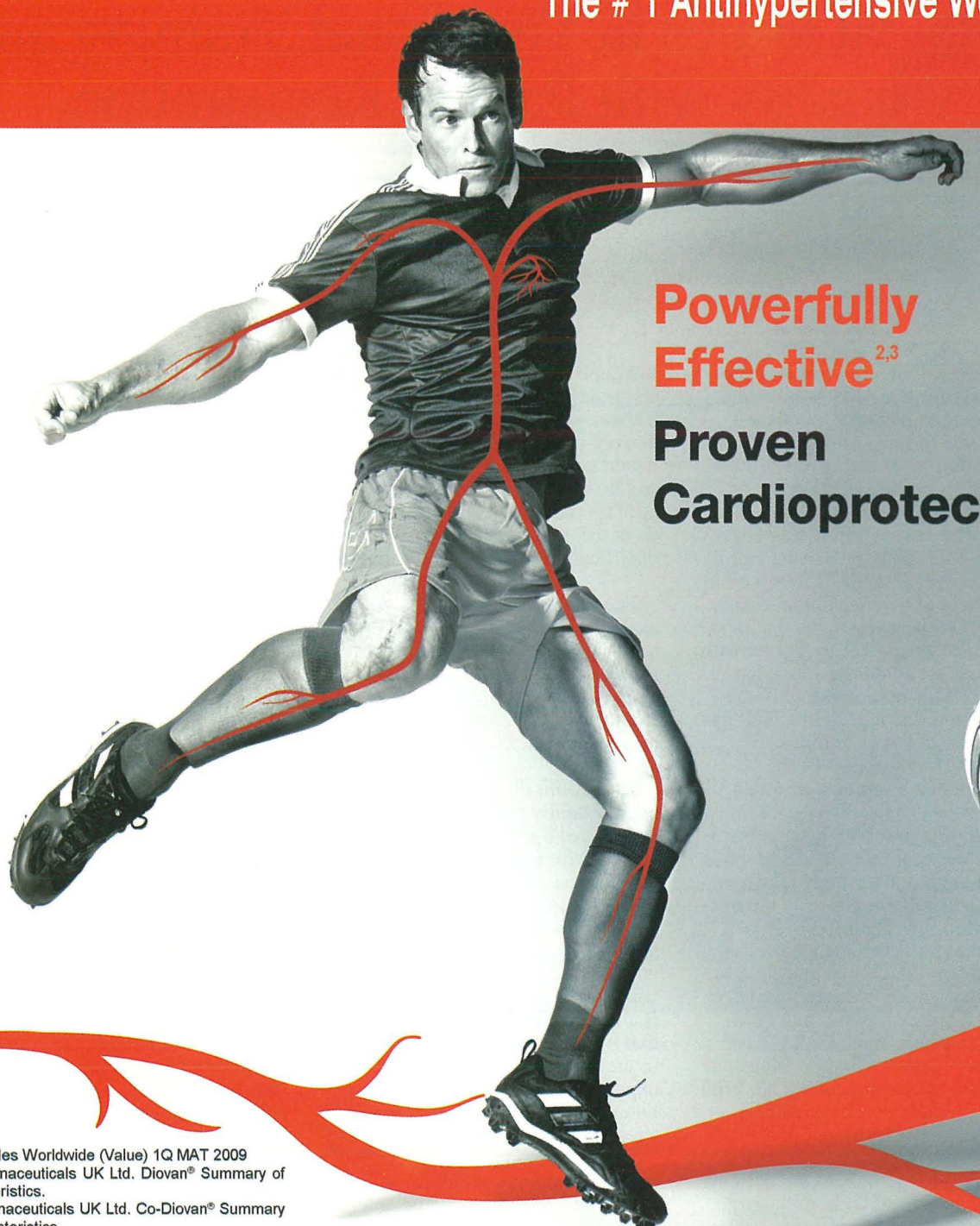
3. Ali B, Jones M. Do medical students want to become GPs? *Br J Gen Pract* 2003; 53:241.

4. Carelli F. Flexibility for special clinical and non-clinical interests. *Br J Gen Pract* 2004; 54(509):947-8.

Francesco Carelli is a General Practitioner and Professor of Family Medicine at the University of Milan. He is the Italian representative on EURACT's Council and Director of Communications and Chairman of the Basic Medical Education Committee within EURACT. EURACT is the European Academyof Teachers in General Practice. He is member of the RCGP and the General Medical Council (London), Trustee for International Academy of Educational Services and International Ambassador for the Association of Health Care Professionals. He is also a member of the Italian Journalists Council as well as Editorial Board member of scientific journals for General Practice including EJGP, IJM, NWLJP and LJPC. He is also author of numerous papers published internationally.

The # 1 Antihypertensive Worldwide[1]



Powerfully Effective[2,3]

Proven Cardioprotective[2]

1. IMS MIDAS Sales Worldwide (Value) 1Q MAT 2009
2. Novartis Pharmaceuticals UK Ltd. Diovan® Summary of Product Characteristics.
3. Novartis Pharmaceuticals UK Ltd. Co-Diovan® Summary of Product Characteristics.

Diovan®

Diovan® (valsartan) film-coated tablets

PRESENTATION: Valsartan. Film-coated tablets of 40 mg, 80 mg, 160 mg and 320 mg. **INDICATIONS:** Treatment of essential hypertension, recent myocardial infarction, symptomatic heart failure. **DOSAGE: Hypertension:** Recommended dose is 80 mg once daily. The dose can be increased to 160 mg and to a maximum of 320 mg if necessary. The addition of a diuretic such as hydrochlorothiazide will decrease blood pressure even further. **Recent-myocardial infarction:** Initial dose is 20 mg twice daily. Uptitration to a maximum of 160 mg twice daily as tolerated by patient. **Heart failure:** Starting dose is 40 mg twice daily. Uptitration to 80 mg and 160 mg twice daily as tolerated by patient. **CONTRAINDICATIONS:** Hypersensitivity to the components of this product, Severe hepatic impairment, biliary cirrhosis and cholestasis, Pregnancy. **PRECAUTIONS/WARNINGS/INTERACTIONS:** In severely sodium-depleted and/or volume-depleted patients, symptomatic hypotension may occur in rare cases after initiation of therapy with Diovan. Sodium and/or volume depletion should be corrected before starting treatment with Diovan. Caution is advised when administering Diovan to patients with renal artery stenosis, hepatic impairment, aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy or those who have undergone kidney transplantation. Caution should be observed when initiating therapy in patients with heart failure or post-myocardial infarction. The combination of Diovan with an ACE inhibitor and the triple combination of an ACE-inhibitor, beta-blocker and Diovan are not recommended. In patients with severe congestive heart failure, treatment with Diovan may cause impairment of renal function. Avoid treatment in patients with primary hyperaldosteronism. Alternative treatments to be sought in patients planning pregnancy and alternative treatment should be sought in patients in whom pregnancy is diagnosed. Concomitant use with potassium supplements, potassium-sparing diuretics and salt substitutes containing potassium that may increase serum potassium levels is not recommended. Concomitant use with lithium is not recommended. Caution when used with NSAIDs. Caution is advised when driving or operating machines. Avoid use in women planning to become pregnant and whilst breast-feeding. **UNDESIRABLE EFFECTS:** In clinical trials where valsartan was compared with an ACE inhibitor, the incidence of dry cough was significantly less in patients treated with valsartan than in those treated with an ACE inhibitor. The most common adverse reactions reported in post-myocardial infarction and/or heart failure indications are: dizziness, postural dizziness, hypotension, orthostatic hypotension, renal failure and impairment. Uncommon adverse reactions are: vertigo, cough, abdominal pain and fatigue reported in hypertension and hyperkalaemia, syncope, headache, vertigo, cardiac failure, cough, nausea, diarrhoea, angioedema, acute renal failure, elevation of serum creatinine, asthenia and fatigue reported in post-myocardial infarction and/or heart failure. Other adverse reactions were the frequency is not known: decrease in haemoglobin, decrease in haematocrit, neutropenia, thrombocytopenia, hypersensitivity including serum sickness, increase of serum potassium, vasculitis, elevation of liver function values including increase of serum bilirubin, angioedema, rash, pruritis, myalgia, renal failure and impairment, elevation of serum creatinine reported in hypertension and thrombocytopenia, hypersensitivity including serum sickness, increase of serum potassium, vasculitis, elevation of liver function values, rash, pruritis, myalgia, increase in blood urea nitrogen reported in post-myocardial infarction and/or heart failure. **MARKETING AUTHORISATION NUMBER:** 089/00601 - 4. **MARKETING AUTHORISATION HOLDER:** Novartis Pharmaceuticals UK Ltd., Frimley Business Park, Frimley, Camberely, Surrey GU16 7 SR, UK. **PACK SIZES:** 7 or 28 film-coated tablets **LEGAL CATEGORY:** POM Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma Services Inc., P.O. Box 124, Valletta, VLT 1000, Malta. Tel +356 22983217. 2009-MT-02-DIO-26-Mar-2009

Co-Diovan®

Co-Diovan® (valsartan, hydrochlorothiazide) film-coated tablets

PRESENTATION: Film-coated tablets containing 80 mg valsartan (an angiotensin II receptor antagonist) and 12.5 mg hydrochlorothiazide (a thiazide diuretic) or 160 mg valsartan and 12.5 mg hydrochlorothiazide or 160 mg valsartan and 25 mg hydrochlorothiazide or 320 mg valsartan and 12.5 mg hydrochlorothiazide or 320 mg valsartan and 25 mg hydrochlorothiazide. **INDICATION:** Treatment of essential hypertension in adults. **DOSAGE:** One tablet of Co-Diovan 80/12.5 mg or 160/12.5 mg or 160/25 mg or 320/12.5 mg daily or 320/25 mg daily. **CONTRAINDICATIONS:** Hypersensitivity to the components of this product or to sulfonamides, Pregnancy, Severe hepatic impairment, biliary cirrhosis and cholestasis, Severe renal impairment (creatinine clearance < 30 ml/min), anuria, Refractory hypokalaemia, hyponatraemia, hypercalcaemia and symptomatic hyperuricaemia. **PRECAUTIONS/WARNINGS:** In severely sodium-depleted and/or volume-depleted patients, symptomatic hypotension may occur in rare cases after initiation of therapy with Co-Diovan. Sodium and/or volume depletion should be corrected before starting treatment with Co-Diovan Caution is advised when administering Co-Diovan to patients with renal artery stenosis, renal and hepatic impairment, systemic lupus erythematosus, aortic and mitral valve stenosis, hypertrophic obstructive cardiomyopathy or those who have undergone kidney transplantation. Disturbance of serum electrolyte balance, glucose tolerance and serum levels of cholesterol, triglycerides and uric acid have been experienced. Co-Diovan should not be used in patients with severe chronic heart failure or other conditions with stimulation of the renin-angiotensin-aldosterone-system and patients suffering from primary hyperaldosteronism. It is recommended to stop treatment in patients who experience photosensitivity reactions. Caution in patients who have shown prior hypersensitivity to other angiotensin II receptor antagonists. Caution is advised when driving or operating machines. Avoid use in women planning to become pregnant and while breast-feeding. **INTERACTIONS:** Concomitant use with potassium supplements or potassium-sparing diuretics and salt substitutes containing potassium that may increase potassium levels is not recommended. Caution if combined with other antihypertensives or lithium (careful monitoring of serum lithium levels is recommended), curare derivatives, NSAIDs, digoxin, antidiabetic agents, medicinal products used in the treatment of gout (e.g. allopurinol), amantadine, cytotoxic agents, anticholinergic agents, cholestyramine and cholestipol resins, vitamin D, calcium salts, ciclosporin and carbamazepine (blood sodium monitoring). Caution is recommended during concomitant use with kaliuretic diuretics, corticosteroids, laxatives, ACTH, amphotericin, carbenoxolone, penicillin G, salicylic acid and derivatives, medicinal products that could induce torsades de pointes, digitalis glycosides, beta-blockers and diazoxide, alcohol, anaesthetics and sedatives, methyldopa, iodine contrast media. **UNDESIRABLE EFFECTS:** Uncommon: dehydration, paraesthesia, blurred vision, tinnitus, hypotension, cough, myalgia, fatigue. Very rare: dizziness, diarrhoea, arthralgia. Not known: syncope, non cardiogenic pulmonary oedema, impaired renal function. Investigations: serum uric acid increased, serum bilirubin and serum creatinine increased, hypokalaemia, hyponatraemia, elevation of blood urea nitrogen, neutropenia. For the valsartan component: Uncommon: vertigo, abdominal pain. Not known: decrease in haemoglobin, decrease in haematocrit, thrombocytopenia, other hypersensitivity/allergic reactions including serum sickness, increase of serum potassium, vasculitis, elevation of liver function values, angioedema, rash, pruritus, renal failure. For the hydrochlorothiazide component: Common: postural hypotension, loss of appetite, mild nausea and vomiting, urticaria and other forms of rash, impotence. Rare: thrombocytopenia sometimes with purpura, depression, sleep disturbances, headache, cardiac arrhythmias, constipation, gastrointestinal discomfort, intrahepatic cholestasis or jaundice, photosensitisation. Very rare: agranulocytosis, leucopenia, haemolytic anaemia, bone marrow depression, hypersensitivity reactions, respiratory distress including pneumonitis and pulmonary oedema, pancreatitis, necrotising vasculitis and toxic epidermal necrolysis, cutaneous lupus erythematosus-like reactions, reactivation of cutaneous lupus erythematosus. **MARKETING AUTHORISATION NUMBERS:** 088/00401- 5. **MARKETING AUTHORISATION HOLDER:** Novartis Pharmaceuticals UK Ltd., Frimley Business Park, Frimley, Camberely, Surrey GU16 7 SR, UK. **PACK SIZES:** 7 or 28 film-coated tablets. **LEGAL CATEGORY:** POM. Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma Services Inc., P.O. Box 124, Valletta VLT 1000, Malta. Tel +356 22983217. 2009-MT-02-CODIO-3-Jul-2009.

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DIO Ad1 11/09 MT

Ethical issues in Vocational Training and quality with Patient Registration

by **Pierre Mallia** *MD MPhil PhD MRCP FRCGP*
Bioethics Research Programme
Medical School, University of Malta

Vocational Training is an obligation in all specialties under the EU Health laws. This means that if a specialty is listed on the specialist register of a country, it is not only an exam which is required to work, but specific Vocational Training (VT). The EU obliges governments to guarantee for patients that anyone working with the National Health Services should have VT.

The consultation document on the proposals for the Reform in Primary care in Malta has been published earlier this month. And patient registration is on the agenda of the primary care reform. What is suggested here is however solely my responsibility and ideas. It is good that the Association of Private Family Doctors (APFD) will be involved in this. It would be wise however that the APFD asserts its rights that those who can accept people to register with doctors must be on the specialist register. This asserts not only their right to practice in a field which has now been shown to require specialization but it gives the government a guarantee of quality.

Tied to this however must come a strong proposal that those who hold an MD alone, unless they qualified for the specialist register by the one-off grandfather clause, will not be allowed to practice. There are varying opinions on this. Some continue to assert that an MD degree should be an exit degree allowing one to practice; others consider it a basic 'entrance' degree which enables one to specialize in a particular field. With family medicine considered as a specialty at EU level and in the rest of the Western World, one has to question the legitimacy of practicing in the community without having completed specialist training (unless one qualified for a grandfather clause). If one obliges VT, then it will only be an entrance degree. One cannot not argue for other areas, but certainly, if we feel that VT is not only a guarantee, but it is worth something extra, then it is about patient rights, and as patient advocates, doctors must uphold this principle.

It is a question of who is competent to work in the community as happens in other specialties. Although I may take the risk and remove an appendix, I would be in a very tight position if I were to defend myself in front of a medical council. I cannot see how someone can escape negligence and malpractice. Although there are instances where countries require GPs to work in areas of specialization, they would not be on the specialist register and there is a limit to what they can do. This means in effect that what they do is still regulated and the MD qualification would not be enough.

We must also consider that we are in the EU and that by giving registration to private family doctors, *the government has in effect acknowledged that private Family Doctors are now part of the NHS and ties itself with this directive.*

Actually this directive binds countries even if family medicine is not considered a specialty. In Italy the government has taken to control primary care and employs a fixed quantity of doctors calculated on a thousand patients per doctor. VT is imposed, even though family medicine is still not on their specialist register. It is not merely about the register. It is about quality, and about asserting that before we send doctors working in the community, they have been exposed to the local situations and know how to deal with non-manifest agendas, which often are not seen in the hospital setting. One must be astute to detect domestic violence, and offer treatment to substance abuse and help the family to cope. Being versant with all the available services does not come that quick. If one is to be registered with a doctor, this doctor must cover a comprehensive care – from children to elderly and from palliative care to offering some minor procedure and investigations. All WONCA core competencies must be satisfied.

The key therefore, for a successful implementation of patient registration, is to make sure that the doctors are adequately qualified and uniformly distributed according to population density. This does not mean that someone who works in a government health department may not form part of a group or network, so long as he or she is on the specialist register. But it does mean that doctors should not be allowed to be following one specialty and be allowed to sit in a pharmacy seeing patients which they will abandon as soon as they pass their membership exams. Having Vocation Training is about patients' rights. It is not about the right to chose to do VT or not. The government has now taken in and acknowledged the important role private doctors play for our NHS. With this come moral responsibilities to our patients.

It will also mean making a jump in quality assurance, pharmacovigilance, infectious disease surveillance etc. If we have doctors who do not have patients registered with them practicing in parallel, this may mean that these quality improvements will not occur. For example, patients who hold a Schedule V card often have drugs which have been prescribed by specialists within the secondary setting. They go to primary care for prescriptions. Although hospital specialists and primary care specialists may be held to a different standard of care for certain drugs, the primary care physician writing the prescription still has responsibility of pharmacovigilance and other monitoring and examination duties.

When patients do not have one doctor, one finds that several may be writing out a prescription within a period of time. This may lead to decisions by different people to change a dose or to a related drug without proper communication and records. Patient registration will put more responsibility on the doctor to ascertain any necessary changes and to monitor their conditions; it is often the case that a patient comes for a prescription and refuses examination or testing because he claims to have had them recently at another doctor or the health centre. If one is taking responsibility for prescribing drugs, it would make medico-legal and ethical sense to monitor the patient as well.

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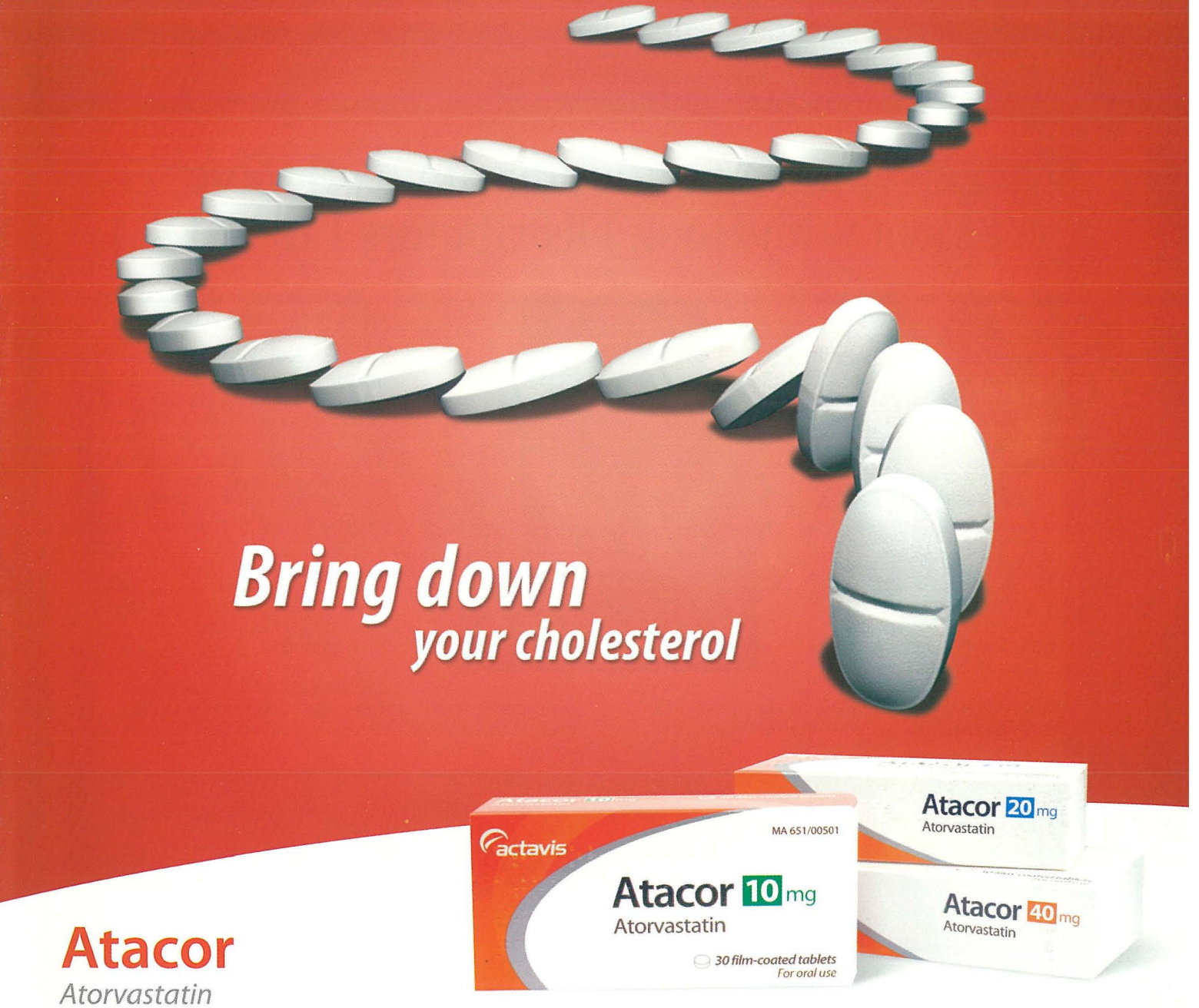


Atacor

Atorvastatin

10mg, 20mg, 40mg tablets

Lipid Reducing Agent

Composition: Each tablet contains Atorvastatin calcium equivalent to Atorvastatin. **Therapeutic indications:** Atacor is used as a supplement to a change in diet for reduction of elevated total cholesterol, LDL - cholesterol, apolipoprotein B, or triglycerides in patients with primary hypercholesterolaemia, heterozygous familial hypercholesterolaemia or combined (mixed) hyperlipidaemia (such as Frederickson's types IIa and IIb), when satisfactory results have not been obtained by a special diet or measures other than medication. In combination therapy with e.g. other LDL-cholesterol reducing medicinal products or if satisfactory results have not been obtained by other measures of reducing total cholesterol and LDL - cholesterol in patients with homozygous familial hypercholesterolaemia. **Posology and method of administration:** The patient should be placed on a standard cholesterol-lowering diet before receiving Atacor and should continue following this diet during treatment with Atacor. Doses should be determined individually according to the baseline LDL - cholesterol value, treatment objective and patient response. The usual starting dose is 10 mg once a day. Adjustment of dosage should be made at intervals of 4 weeks or more. The maximum dose is 80 mg once a day. The daily dose should be administered all at once and can be taken at any time of the day, with or without food. Treatment objectives for patients with a confirmed coronary disease or other patients at increased risk of ischemia are LDL - cholesterol <3 mmoles/l (or <115 mg/dl) and total cholesterol <5 mmoles/l (or <190 mg/dl). *Primary hypercholesterolaemia and combined (mixed) hyperlipidaemia:* An appropriate dose for most patients is 10 mg Atacor a day. A response is evident within 2 weeks and maximum response is usually achieved within 4 weeks. The response is maintained during long term treatment. *Heterozygous familial hypercholesterolaemia:* The initial dose is 10 mg Atacor a day. Doses should be determined for each patient and adjusted at 4 week intervals up to 40 mg a day. Then the dose can be increased to either a maximum of 80 mg a day or else, 40 mg of atorvastatin once a day can be administered in combination with a bile acid sequestrant. *Homozygous familial hypercholesterolaemia:* In a clinical study of 64 patients, 46 of whom had homozygous familial hypercholesterolaemia, atorvastatin was administered in up to 80 mg doses. For these 46 patients the mean reduction of LDL - cholesterol was 21%. Patients with homozygous familial hypercholesterolaemia who had not been responsive to alternative treatments received atorvastatin of 10-80 mg doses a day concurrently with other blood lipid lowering-treatment (e.g. other LDL-cholesterol reducing medicinal products). *Patients with impaired renal function:* Renal diseases influence neither plasma concentration nor the effects of atorvastatin on blood lipids and therefore no dose adjustment is required. *Elderly:* Efficacy and safety of the use of recommended doses for patients over 70 years old are similar as for other adults. *Children and adolescents:* The use in children should be supervised by a specialist. Experience of the use of the medicinal product in children is limited and restricted to a small group of patients (aged 4 - 17 years) with serious hyperlipidaemia such as homozygous familial hypercholesterolaemia. The recommended initial dose for this group is 10 mg atorvastatin a day. Based on response and tolerance the dose can be increased to 80 mg a day. Information regarding safety with respect to maturation for this group has not been evaluated. **Contraindications:** Atacor is contraindicated in patients with a history of hypersensitivity to the active substance or to any of the excipients, in patients with an active liver disease or unexplained persistent elevation of serum transaminase levels where the elevation exceeds three times the mean upper limits, in patients with myopathy, pregnant and breast feeding women and women of child bearing potential not using contraceptives. **Special warnings and precautions for use:** *Liver effects:* Liver function tests should be performed before the initiation of treatment and periodically during treatment. Liver function tests should be performed if signs or symptoms of possible liver damage are observed. Patients who develop increased transaminase levels should be monitored until the abnormality(ies) resolve. In case of an elevation of transaminase levels exceeding three times the mean upper limit, dose reduction or discontinuation of treatment with Atacor is recommended. Atacor should be used with caution in patients who consume substantial amounts of alcohol and/or have a history of liver disease. *Skeletal muscle effects:* Like other HMG-CoA reductase inhibitors, atorvastatin can very rarely influence skeletal muscles and cause myalgia, myositis and myopathy which can evolve into rhabdomyolysis, which is a potentially fatal condition and is characterized by an elevated CPK value (exceeding ten times measured upper limits), myoglobinaemia and myoglobinuria, which can cause renal insufficiency. **Interaction with other medicinal products and other forms of interaction:** *Cytochrome P450 3A4 inhibitors:* Atorvastatin is metabolised by cytochrome P450 3A4. Interactions can occur during concurrent administration of atorvastatin and a cytochrome P450 3A4 inhibitor (e.g. cyclosporin, macrolide antibiotics including erythromycin and clarithromycin, nefazodone, azole antifungals including itraconazole and HIV protease inhibitors). Special precaution is required during concurrent administration of atorvastatin and these products because it can result in elevated plasma concentration of Atorvastatin. *Erythromycin, clarithromycin:* Concurrent administration of atorvastatin, 10 mg once a day and erythromycin (500 mg four times a day) or clarithromycin (500 mg twice a day), known cytochrome P450 3A4 inhibitors, resulted in a higher plasma concentration of atorvastatin. *P-glycoprotein inhibitors:* Atorvastatin and its metabolites are substrates of P-glycoprotein. P-glycoprotein inhibitors (e.g. cyclosporin) can increase the bioavailability of atorvastatin. *Itraconazole:* Concurrent administration of atorvastatin 40 mg and itraconazole 200 mg a day resulted in a threefold increase in the AUC of atorvastatin. *Protease inhibitors:* Concurrent use of atorvastatin and protease inhibitors which are known CYP3A4 inhibitors resulted in an increased plasma concentration of atorvastatin. *Grapefruit juice:* Contains one or more CYP3A4 inhibitors and can cause elevation in plasma concentration of medicinal products metabolised by CYP3A4. Drinking large amounts of grapefruit juice is therefore not recommended during atorvastatin treatment. *Cytochrome P450 3A4 inducers:* The effects of cytochrome P450 3A4 inducers (e.g. rifampicine or phenytoin) on atorvastatin are not known. Possible interactions with other substrates of this isoenzyme are not known, but should be considered in case of medicinal products with a narrow therapeutical index, e.g. class III antiarrhythmics, including amiodarone. *Gemfibrozil / fibrates:* The risk of atorvastatin induced myopathy can increase during concurrent administration of fibrates. *Digoxin:* Repeated administration of digoxin and atorvastatin 10 mg at the same time did not influence the steady state plasma concentration of digoxin. Digoxin concentration however increased by 20% during concurrent use of digoxin and atorvastatin 80 mg a day. Patients treated with digoxin should be monitored carefully. *Oral contraceptives:* Concurrent use of atorvastatin and oral contraceptives increased the concentration of norethisterone and ethinyl oestradiol. These increased concentrations should be considered when selecting oral contraceptive doses. *Colestipol:* Plasma concentration of atorvastatin and its active metabolites decreased (approx. 25%) when colestipol was administered with atorvastatin. However, lipidaemic effects were greater when atorvastatin and colestipol were administered together than when either drug was administered alone. *Antacids:* Concurrent administration of atorvastatin and oral antacid liquid formulations containing magnesium and aluminium hydroxides decreased atorvastatin plasma concentrations by approx. 35%; reduction of LDL-cholesterol was however not altered. *Warfarin:* Concurrent use of atorvastatin and warfarin caused a minor decrease in prothrombin time during the first days of treatment, but returned to normal within 15 days. Nevertheless patients receiving warfarin should be closely monitored when atorvastatin is added to their treatment. *Phenazone:* Concurrent use of atorvastatin and phenazone for some time resulted in little or no visible effect on the clearance of phenazone. **Pregnancy and lactation:** Atacor is contraindicated in pregnancy and while breast feeding. Women of child bearing potential have to use effective contraceptive measures during treatment. Safety of atorvastatin use during pregnancy and lactation has not been established. **Effects on ability to drive and use machines:** Atorvastatin has no known influence on the ability to drive and use machines. **Undesirable effects:** The most frequent adverse effects that can be expected are symptoms of the gastrointestinal system, including constipation, flatulence, dyspepsia, abdominal pain, usually resolving during continued treatment. Less than 2% of patients had to discontinue clinical trials due to side effects related to atorvastatin. **Gastrointestinal disorders:** *Common:* Constipation, flatulence, dyspepsia, nausea, diarrhoea, *Uncommon:* Anorexia, vomiting. **Blood and lymphatic system disorders:** *Uncommon:* Thrombocytopenia. **Immune system disorders:** *Common:* Hypersensitivity, *Very rare:* Anaphylaxis. **Endocrine disorders:** *Uncommon:* Alopecia, hyper- or hypoglycaemia, pancreatitis. **Psychiatric disorders:** *Common:* Insomnia, *Uncommon:* Amnesia. **Nervous system disorders:** *Common:* Headache, dizziness, paraesthesia, hypoesthesia, *Uncommon:* Peripheral neuropathy. **Hepatobilary disorders:** *Rare:* Hepatitis, cholestatic jaundice. **Ear and labyrinth disorders:** *Uncommon:* Tinnitus. **Skin and subcutaneous tissue disorders:** *Common:* Rash, pruritus. *Uncommon:* Urticaria. *Very rare:* Angiodema, bullous eruptions (including erythema multiforme, Steven-Johnsons syndrome and toxic epidermal necrolysis). **Musculoskeletal disorders:** *Common:* Myalgia, arthralgia, *Uncommon:* Myopathy, *Rare:* Myositis, rhabdomyolysis. **Reproductive system:** *Uncommon:* Impotence. **General disorders:** *Common:* Fatigue, chest pain, back pain, peripheral oedema, *Uncommon:* Malaise, weight gain. **Overdose:** No specific treatment for Atacor overdose is available. In case of an overdose the patient should be treated symptomatically and supportive measures should be instituted if required. Liver function should be monitored and serum CPK values also. Due to its extensive binding to plasma proteins haemodialysis is not expected to increase atorvastatin clearance significantly.

Marketing Authorisation Holder: Actavis Group hf, Reykjavikurvegi 76-78, 220 Hafnarfjörður, Iceland. **Date of first authorisation or renewal of authorisation:** 27th March 2007.

This medicinal product is subject to a medical prescription.

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

actavis

creating value in pharmaceuticals

TheSynapse announces an exclusive agreement with Book Distributors Ltd (BDL)

TheSynapse and Book Distributors Ltd (BDL) have recently reached an agreement whereby members of TheSynapse portal and magazine will now be able to enjoy a wealth of literary treasures in addition to the valued medical content that is published regularly through TheSynapse services.

Book reviews will now be available in the issues of TheSynapse magazine and a section of TheSynapse portal designated as a book store is also available. Members will also be receiving updates by mail through eINFOs whichTheSynapse sends periodically, as well as through eNEWS updates, circulated during weekends.

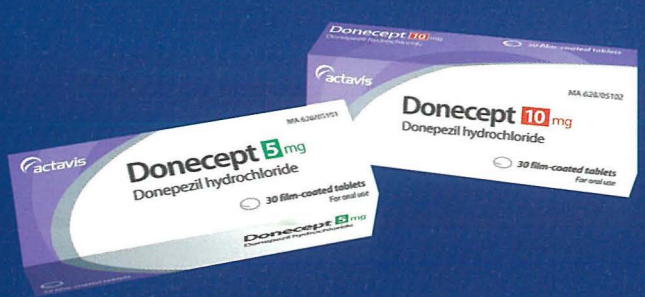
Another interesting feature will be the introduction of E-quizzes. Winners will receive book vouchers redeemable at BDL.

BDL is the leading publication distributor in Malta. In the span of eight years, it has published over sixty successful titles. These include a range of children's readers, flashcards and a first dictionary for kids. Also, a Maltese thesaurus, a dictionary of Maltese family surnames and a CD course on learning Maltese. Not to mention a variety of multilingual guidebooks and postcards. BDL is the leader in the publication of books on crime and punishment. They are also the publishers of the award-winning masterpiece 'The Photography Collection' by Richard Ellis.

This agreement was only natural considering the fact that TheSynapse, now in its thirteenth year, is always endeavoring to give better added value to its users.

TheSynapse eQuiz Winner

The overall prize winner for The Synapse Donecept/Remirta eQuiz was Dr. Lucienne Attard.



Donecept contains donepezil hydrochloride which is a specific and reversible inhibitor of acetylcholinesterase, the predominant cholinesterase in the brain. It is indicated for the symptomatic treatment of mild to moderately severe Alzheimer's dementia.
Donecept is available in two doses: 5mg and 10mg. Each dose is available in packs of 30 film-coated tablets.

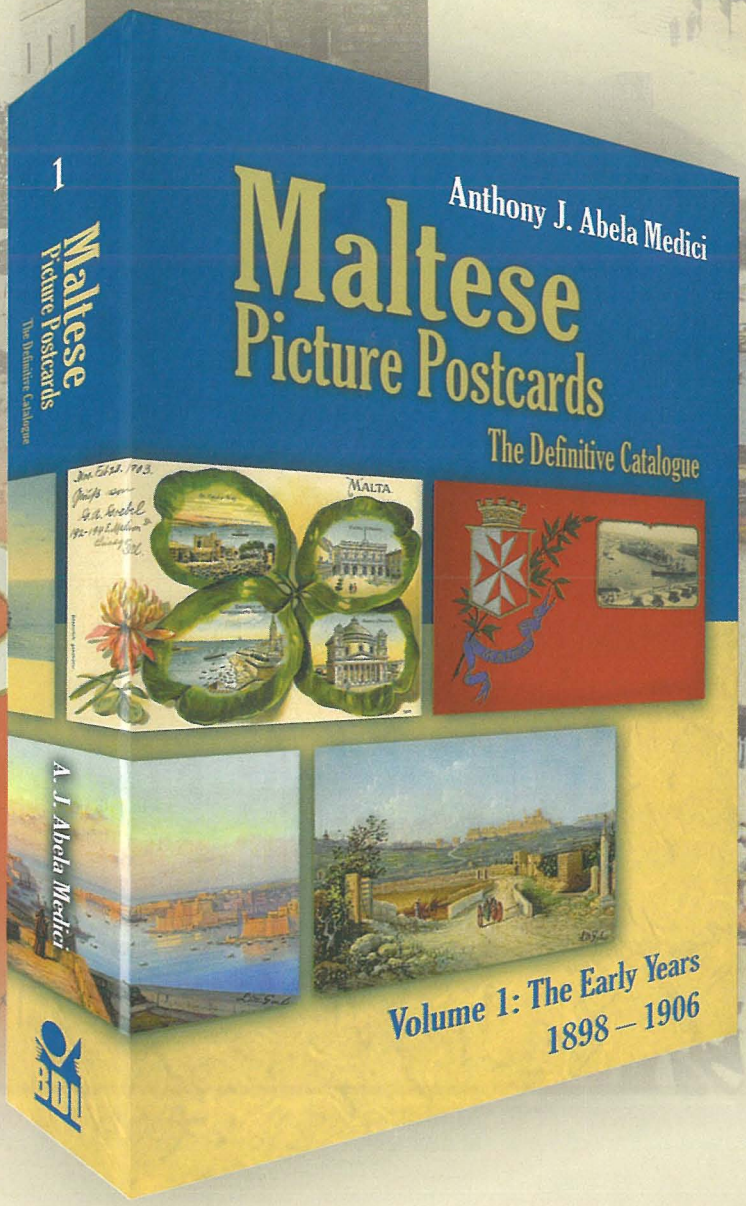
Treatment is initiated at 5 mg/day. Donecept should be taken orally, in the evening, just prior to retiring. The 5 mg/day dose should be maintained for at least one month in order to allow the earliest clinical responses to treatment to be assessed and to allow steady-state concentrations of donepezil hydrochloride to be achieved. Following a one-month clinical assessment of treatment at 5 mg/day, the dose of Donecept can be increased to 10 mg/day. The maximum recommended daily dose is 10 mg.

Remirta contains mirtazapine, a presynaptic α_2 αntagonist, which increases noradrenergic and serotonergic neurotransmission in the central nervous system. Mirtazapine is used to treat Major depressive episodes.

Remirta is available as 15mg and 30mg **orodispersible** tablets. Each dose is available in packs of 30. Orodispersible tablets should be placed on the tongue with dry hands where the tablet will be rapidly dissolved. The tablets should be taken with water and with or without food.

The initial dose is preferably 15 mg or 30 mg, taken in the evening. The maintenance dose is usually between 15 mg and 45 mg per day. Remirta tablets can be taken once daily, since the half-life is 20 to 40 hours. The tablets should be taken preferably as a single dose immediately before bedtime. The daily dose can also be divided into two doses taken in the morning and at bedtime. The larger dose should be taken in the evening.

The antidepressive effect of mirtazapine usually becomes evident after 1 to 2 weeks' use. Treatment with an adequate dose should result in a positive response within 2 to 4 weeks. If the response is inadequate, the dose can be increased up to the maximum dose. After having obtained an optimal clinical effect and after the patient is free of symptoms, the treatment should be continued for 4 to 6 months, until a gradual discontinuation can be considered.



The Defintive Catalogue is a detailed study of the earliest postcards published in Malta incorporating over 1,590 images of postcards published between 1898 and 1906 and over 1,000 other images incorporating details of postcards. Each card has been catalogued in great detail and practically all known postcards have been reproduced in full colour in this study.

The memory of a country in the late nineteenth and early twentieth century can be seen from the postcards published in that period. Maltese picture postcards were introduced in late 1898, and by 1906 hundreds of postcards were issued and re-issued. It is this imprint of our Maltese nation which is being captured in this first detailed definitive catalogue of early Maltese postcards.

This work should not only be of special interest to the postcard collector but should also interest the Melitensia collector and the public in general who now have the opportunity to see an illustrated history of Malta, with its people and its customs, as it was a hundred and more years ago.

* Hard bound
* 608 pages
* A4
* Full colour

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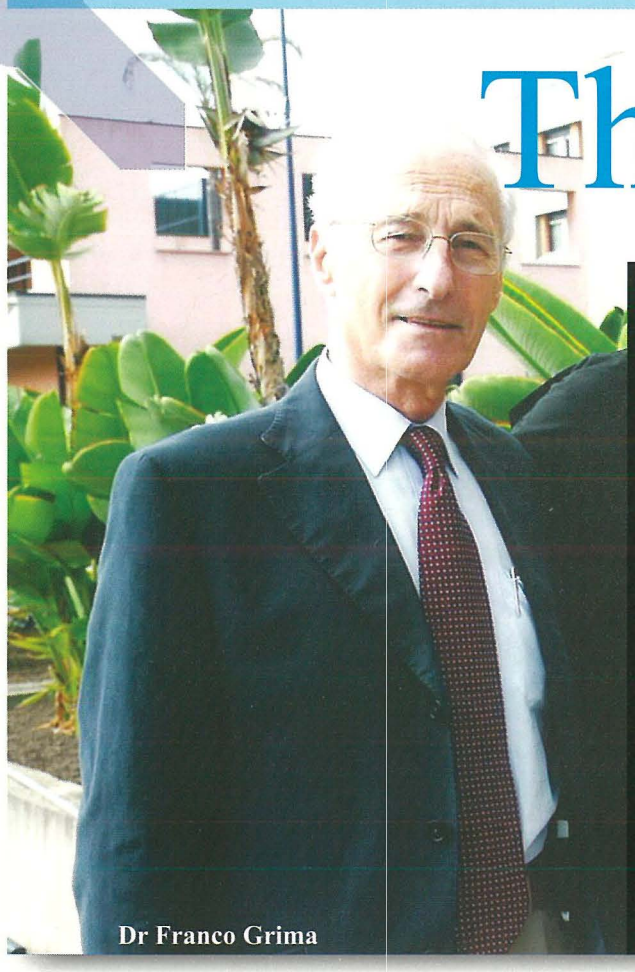
The RAF and



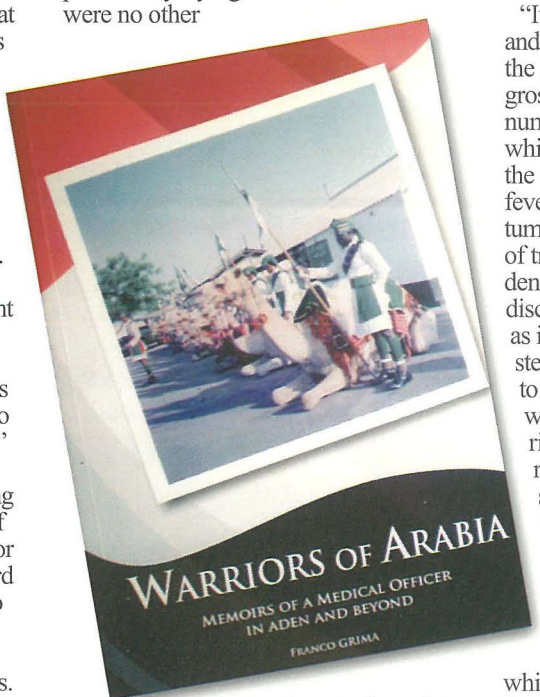
Dr Franco Grima

Dr Franco Grima's comfortable home in Naxxar is a far cry from the outposts which saw him embarking on his journey in military medicine as an RAF medical officer. He sits calmly across the study and asks what I would like to know. There is much to be told and part of his story which was penned in diaries over several years has been merged into a book of memoirs that was published last June. Franco Grima's story harks back to the 1960s when as a young doctor who graduated in 1958, he joined the Royal Air Force and trained as flight surgeon at No 4 Flying Training School in North Wales. He soon volunteered to be seconded to the Arab Army of the Federation of South Arabia, now part of Yemen..

by **Marika Azzopardi**

"I had always fancied joining the Services, perhaps due to my fascination with the air scouting movement as a youth. There was a certain something that lured me to join and sure enough I was immediately thrown in at the deep end. Between 1962 and 1965, I served as a young battalion medical officer on the border with Northern Yemen in desert and mountain areas. There were no roads and we relied on air supplies brought in by planes that also airlifted emergency cases down to Aden. Aeroplanes had to land on makeshift landing grounds. At night we would light up landing grounds by parking Land Rovers and other vehicles with their headlamps lit up. This guided the pilots to find their way on territory that had to be blacked-out because of enemy fire."

It was an experience that saw him facing all sorts of dangers but also a wealth of new challenges that your average doctor would not have encountered in his ward rounds. The main responsibility was to care for Arab soldiers stationed in this far-flung outpost, and in the simplest scenario this involved long sick parades. These were men who faced ambushes, mortar attacks and road mines on a daily basis. Primary care was extended to the troops' families and also to the local tribes. Franco Grima's responsibility was particularly trying since there were no other



doctors along the border with Northern Yemen. The Imam of Yemen claimed Aden and all of Southern Arabia and he kept inciting tribes and rebels to cause trouble.

"It was not just about injuries, burns and serious trauma but also about treating the locals who presented with a lot of gross pathology. There was an incredible number of tropical diseases, some of which were particularly common, as in the case of helminths, malaria and other fevers. I also encountered several tropical tumours like mycetomas, as well as cases of trachoma. I frequently doubled up as dentist and for the purpose used a discarded airplane seat asa dental chair as it proved to be particularly strong and steady." Tribal women were often taken to him during the last stages of childbirth when both mother and child were at risk. The more extreme cases, like ruptured uteri, complicated births or severe haemorrhages generally had to be air evacuated.

Talking about some of the more traumatic experiences, Franco Grima relates something of the struggle for independence and the military threat which the country found itself in at the time. He mentions the Radfan campaign, north of Aden, when a number of SAS soldiers went to locate rebel strongholds

beyond

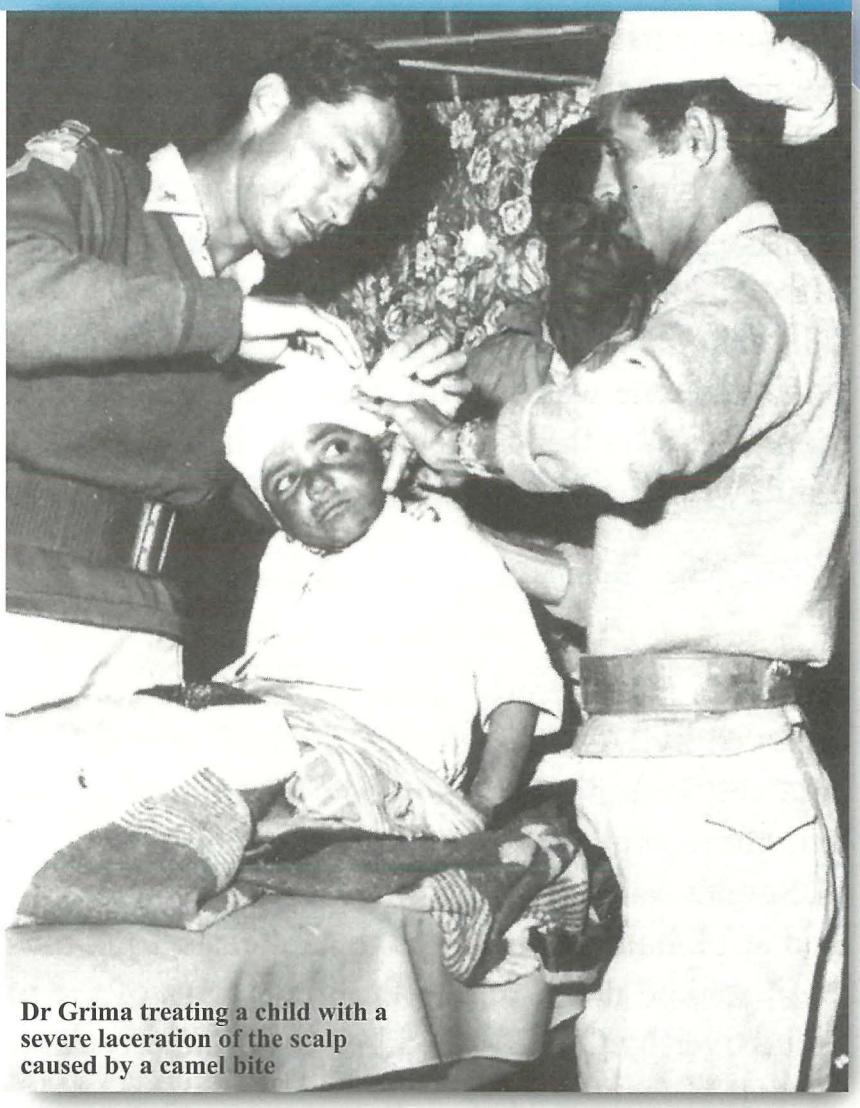
in the Radfan Mountains. "Some of the soldiers were unfortunately caught, killed and decapitated. International media reported they were beheaded but in reality the men had been first killed and then decapitated, the heads being taken as trophies of war. Eventually the heads were recovered for a ransom some months later. But in the meantime, we had to retrieve the bodies of these men. Intelligence reports indicated the whereabouts of the bodies and we went into the mountains to get them. I was the one who picked up those bodies." And he goes on to recount his close shave with death when a landmine blew up a truck behind him just after he passed a stretch of road. "The gravel or sandy roads were peppered with mines. The rebels would cover the plunger with flat bread to protect it from sand and gravel so the mine did not explode immediately but only when enough pressure had been placed on it to trigger it off."

Franco Grima also served in Bahrain in the Gulf and in the Sultanate of Oman during the Dhofar rebellion in the Qara mountains. Back in the UK he served on a number of stations including V-Bomber and Tornado Stations.

Franco Grima was later posted to the Ministry of Defence in London with varied duties including arranging the transport of serious infectious disease cases from overseas, to overseeing occupational hygiene standards. After a Masters degree in Occupational Medicine at London

A stark warning for Amir Shaafel and all the rulers:
"From today we are going to cut off the ears of all collaborators"

National Liberation Front leaflet threatening to cut off the ears of all collaborating rulers



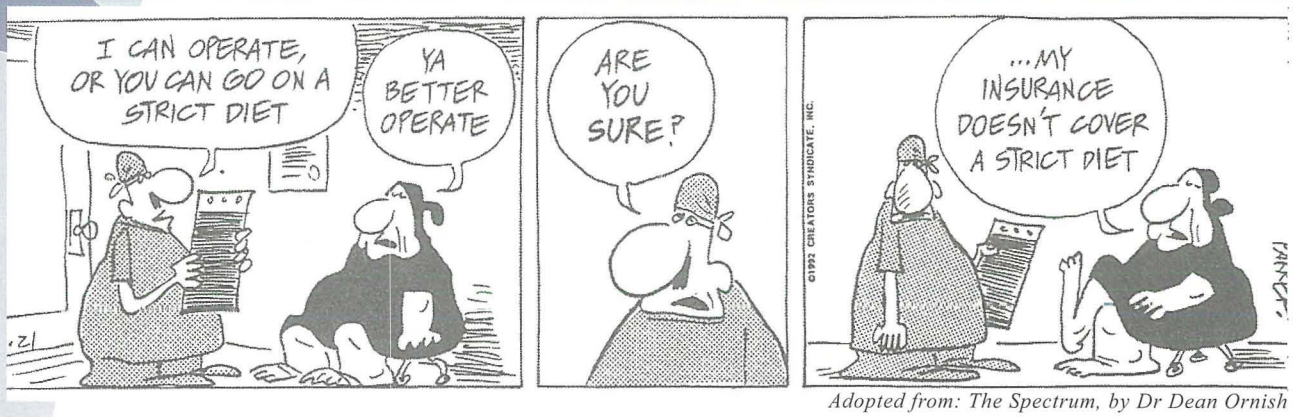
Dr Grima treating a child with a severe laceration of the scalp caused by a camel bite

University, he was posted to the RAF Institute of Community and Occupational Medicine at RAF Halton, Buckinghamshire. He was also subsequently appointed as the first RAF consultant in Occupational Medicine. "One of the projects at hand was measuring noise levels. We had to measure the footprints of RAF aeroplanes as they took off over neighbouring villages. The government provided funding for house owners to fit double glazing if they lived in an area disturbed by high levels of noise pollution caused by military aircraft." Eventually he took over the command of the whole institute which offered training for doctors, nurses and physiotherapists. In the eighties he helped several Maltese medical students whose course was interrupted, to get cadetships to continue their training in London.

Listing all of his varied placements in the RAF is impossible; he did the rounds of many RAF stations around the UK as Senior Medical Officer for a number of years including a two-year post as Hospital Registrar at the RAF Hospital Nocton Hall in Lincolnshire. Franco Grima retired in 1992 with the rank of Group captain. He then worked as an occupational physician at the Atomic Weapons Research Establishment, and in 1995, returned to Malta where he presently offers consultancy services to industry on matters of occupational health.

"Yes, Occupational Medicine is a new area, but one which is becoming increasingly important due to the introduction of stringent EU directives. With the Health and Safety Authority being established in Malta only a few years ago, this is a fledgling field with only 13 specialists to date." Certainly the levels of occupational health he seeks to promote today are a far cry from the conditions he worked in when he was posted in southern Arabia. He concluded that "The RAF has always been professional and disciplined and has proved to be an excellent school for my self-discipline, both on a professional and personal basis."

'Warriors of Arabia – Memoirs of a Medical Officer in Aden and Beyond' by Franco Grima, published last June. The book is available at Agenda outlets and all leading bookshops. For enquiries contact the author on francogrima@onvol.net



Adopted from: The Spectrum, by Dr Dean Ornish

Healing & Disease Reversal - II

by **Albert Cilia-Vincenti** *MD FRCPath*

This article is the second part of a series looking into Dean Ornish's work, emphasising that there is more to medicine than pharmaceutical drugs and surgery. His clinical research findings on disease reversal, in particular, may not be exactly what you learnt at medical school. He is Clinical Professor of Medicine and Founder President of the non-profit Preventive Medicine Research Institute, California University, San Francisco.

Until recently most doctors considered it impossible to reverse the progression of heart disease. They thought that, at best, diet and lifestyle changes might slow down disease progression but, in the end, it could only get worse. Now that professor Ornish's clinical trials have proven that coronary heart disease, and other chronic diseases, can often be reversed by making comprehensive lifestyle changes, these misconceptions have slowly began to change. *However, although many American physicians believe that Ornish's diet and lifestyle programme works, they tend to think that the majority of people can't follow it because it's too strict, too hard, and too boring – so why bother?*

Ornish admits that when he published his research findings, he thought these would significantly change medical practice, but later realised he was a little naive. *The stark reality was that with all the talk of evidence-based medicine, we were actually in an era of "funding-based medicine".* It wasn't enough to have good science; one needed to change the way medicine was funded. *Doctors do what they are paid to do, and are trained to do what they are paid to do.* If one could change funding, both medical practice and medical education would be improved.

Beginning in 1993, Ornish's team began training personnel, in more than 50 hospitals and clinics around America, on their diet and lifestyle programme, via their non-profit research institute, and they conducted three demonstration projects with three prominent medical insurers. Alexander Leaf, professor of medicine at Harvard Medical School, co-ordinated the data centre for the demonstration projects. They found that 80% of patients eligible for coronary bypass heart surgery or angioplasty were able to safely avoid it for at least 3 years. In the first year it saved medical insurers $30,000 per patient. By then, more than 40 insurance companies were covering Ornish's programme. One insurer, Highland Blue Cross Blue Shield, found that the programme reduced its overall health costs by 50% in the first year and by an additional 20 to 30% in subsequent years.

Medicare, the biggest American medical insurer, was then approached to see if it would provide coverage for the Ornish programme, but initially said no. Its Director later told Dean Ornish that *before they could consider his programme, they needed a letter from the National Heart, Lung and Blood Institute, stating that his programme was safe.* Ornish could not believe it. *He was being asked to get a letter saying that it was safe for older Americans to walk, meditate, quit smoking, and eat fruits and vegetables!* He met the Director of the National Heart, Lung and Blood Institute to review the medical literature evidence. Not surprisingly, they found that Ornish's programme was not high-risk, especially when compared with having your chest sawed open for a bypass operation. His earlier research had shown that with his programme older patients improved as much as young ones. Considering that the risks of bypass surgery and angioplasty increased with age, these lifestyle changes were especially beneficial for older patients in the Medicare population. Four years later, in 1999, with strong bipartisan political support from President Clinton and the Republicans, Medicare agreed to conduct a demonstration project.

At that stage professor Ornish remarked that we had gotten to a point in medicine, where it's considered "conservative medicine" to cut open someone's chest, or to inflate balloons and put stents inside his/her coronary arteries, even when there is inconclusive data supporting these approaches in the prevention of heart attacks or in the life-extention of stable patients with heart disease, yet it's considered high risk or even radical to ask people to walk, meditate, stop smoking, and eat fruits and vegetables.

In 2005, his team completed the Medicare demonstration project, and after its results were reviewed, Medicare agreed to provide coverage for their programme for reversing heart disease, and other similar programmes. This was a major breakthrough – *it was the first time that Medicare covered an integrative-medicine programme of comprehensive lifestyle changes.* Because funding/reimbursement is a major determinant of medical practice and medical education in America, Medicare coverage may help make comprehensive lifestyle change programmes more sustainable and widely available to those who need them most.

Medicare coverage in America is, for practical purposes, analogous to coverage by Malta's NHS and by our private medical insurers. In Malta we are still at the stage where Dean Ornish was 15 years ago, that is, Maltese health providers will cover pharmaceutical drugs and

continues on page 24

new

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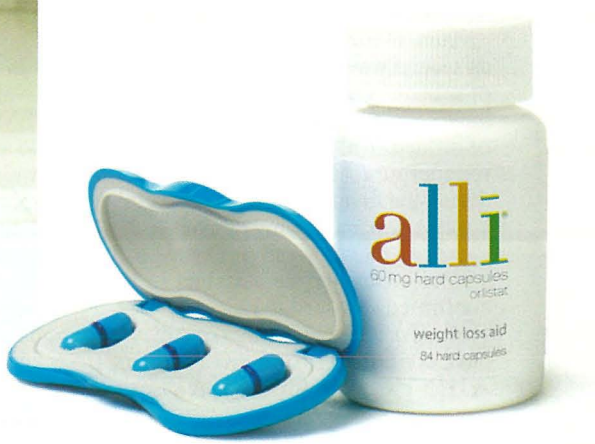

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Product Information **alli** 60 mg hard capsules (orlistat) **Indication** Weight loss in adults BMI ≥ 28. **Dosage** *Adults (18 or over)* One capsule within an hour of each of three main meals. Max 3 caps/day for up to 6 months. Use with lower fat mildly hypocaloric diet. If no weight loss within 12 weeks refer to HCP. Diet and exercise should start prior to treatment. **Contraindications** Hypersensitivity to ingredients, concurrent treatment with oral anticoagulants or ciclosporin, chronic malabsorption syndrome, cholestasis, pregnancy, breast-feeding. **Special warnings and precautions** See HCP if on amiodarone or medication for hypertension, hypercholesterolemia or diabetes as control of these conditions may improve necessitating alteration of therapy. Risk of GI symptoms increases with fat consumption. Take multivitamin at bedtime. See GP if rectal bleeding. Oral contraceptive efficacy may be reduced if severe diarrhoea, use additional contraception. **Drug interactions** Ciclosporin, oral anticoagulants, fat soluble vitamins, acarbose, amiodarone. **Pregnancy and lactation** Do not use during pregnancy or lactation. **Side effects** See SPC for full details. Predominantly gastrointestinal eg oily stools, urgency, usually mild and transient, risk reduced by low fat consumption. Hepatitis, cholelithiasis, abnormal liver enzymes, anxiety, hypersensitivity reactions including anaphylaxis, bronchospasm, angioedema, pruritus, rash, and urticaria, bullous eruption. **Legal category** P. **Marketing Authorisation Holder** Glaxo Group Limited, Greenford, Middlesex, UB6 0NN. **MA Number** EU/1/07/401/007 & 009. **Last revised** November 2008. **References** 1. **alli** Summary of Product Characteristics. GlaxoSmithKline Consumer Healthcare.

Update on H1N1 Virus

by **Tanya Melillo Fenech** *MD MSc*
Resident Specialist
Head, Infectious Disease Prevention and Control Unit
Department of Health Promotion and Disease Prevention

Epidemiological update worldwide

The total number of deaths up to 7 November in the 27 EU and 4 EFTA countries is 1079 and in the rest of the world it is 9971.

In Europe, 17 EU countries reported widespread activity in the past week, most experiencing medium to very high influenza intensity. Increasing activity is still being reported in Eastern and Southern European countries while a decline in activity is starting to be seen in Northern, Western and Central European Countries (Belgium, Bulgaria, Belarus, Ireland, Luxemburg, Norway, Serbia, Ukraine and Iceland).

Over 99% of subtyped influenza A viruses in Europe were pandemic H1N1 (2009).

In the United States and Canada, influenza transmission is still present but there are signs that influenza activity has peaked. In East Asia, influenza transmission remains active while most countries in Central and South America are reporting declining influenza activity. In the southern hemisphere, little pandemic influenza activity has been reported.

Epidemiological update – The Local Scenario

Malta, like the rest of the world started its second wave in October with the start of schools. Over the past 10 weeks we have seen a steady increase in the rate of influenza-like illness through our sentinel surveillance with a slight drop during the first two weeks in November but it is now increasing again.

Since 4 October we have had 162 confirmed cases (high risk cases and sentinel cases). Since the 1of July we have confirmed 615 cases of Influenza A H1N1 and 146 Influenza A cases.

Over the past two weeks we have seen a number of increased absenteeism in particular classes in different schools all over the country. Risk assessments done by the Infectious Disease Prevention and Control Unit on particular schools confirmed that the majority of children away from school were suffering from influenza-like illness. Primary school children have been mostly affected.

We expect to continue seeing a rise in school absenteeism until school closure for the Christmas recess.

For the last 10 weeks since we started our second wave we have not had any deaths and have had 27 hospitalizations of confirmed cases.

The Pandemic Vaccine for Malta

The pandemic vaccine that will be shortly available in Malta is Pandemrix™, manufactured by GlaxoSmithKline. It will be provided to all those who are at high risk of developing complications from influenza.

It is a split virion, inactivated, adjuvanted vaccine. It is a monovalent vaccine containing 3.75 micrograms of antigen. The antigen used is A/California/07/2009 (H1N1)v-like strain (X-179A), propagated in fertilised hens' eggs. The vaccine contains an adjuvant (AS03) to help boost the immune response. AS03 adjuvant is composed of squalene, DL-α-tocopherol and polysorbate 80.

Pandemrix™ contains five micrograms of thiomersal as a preservative. This is added to prevent bacterial contamination occurring during the preparation and subsequent storage and use of the vaccine. There is no evidence of risk from thiomersal-containing vaccines, including for children, pregnant women and their offspring.

In 2004, the European Agency for the Evaluation of Medicinal Products (EMEA) concluded that studies show no association between vaccination with thiomersal-containing vaccines and specific neurodevelopmental disorders. A more recent study has also shown no association between neuropsychological functioning at the age of seven to ten years and exposure to mercury during the prenatal period, the neonatal period and the first seven months of life[1]

Doses for Pandemrix™

Children aged 6 months to under 10 years - Two doses of 0.25ml (i.e. half the normal dose) given at least three weeks apart.
Adults and children aged 10 years and above - A single injection of 0.5ml
Immunocompromised individuals aged 10 years and above -Two doses of 0.5ml given at least three weeks apart.
Pregnant Women A single injection of 0.5ml

The influenza A(H1N1) vaccine can be given at the same time as other vaccines including seasonal influenza vaccine and other childhood vaccines. Vaccines should be given at separate sites, preferably in different limbs.

Adverse Reactions

The main adverse reactions include headache, fever, fatigue, arthralgia, myalgia, induration, swelling, pain and redness at injection site. Other common reactions include lymphadenopathy, increased sweating, shivering, influenza-like illness, and injection-site reactions such as ecchymosis, warmth and pruritus.

Association with Guillain-Barre Syndrome

A recent study in the UK found that there is no association between Guillain-Barré syndrome (GBS) and seasonal flu vaccines although there is a strong association between GBS and influenza-like illness. GBS has been reported very rarely after immunisation with influenza vaccine (one case per million people vaccinated in one US study.[2] Information regarding the association of GB with the pandemic vaccine is presently underway since no official data has been released so far. So we can only compare the association with the seasonal influenza.

Fever in children after second dose

The European Medicines Agency is warning that young children (below 6 years of age) may experience fever (above 38°C) after their second dose of the pandemic influenza vaccine Pandemrix™. It is important to tell parents to monitor the temperature of the vaccinated child and, if necessary, take measures to lower the fever. Ongoing clinical trials have shown that there was more soreness at the site of injection and more general symptoms such as drowsiness, irritability and loss of appetite after the second dose.

The study also showed that a single dose of vaccine triggered a good immune response in young children, but that the second dose further increased the immune response.

Report received on 8.12.09.

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Qlaira® is not only the first oral contraceptive to provide natural estradiol, it is also the first pill to have been extensively studied in women up to the age of 50[1-5]. After all, when it comes to reliable contraception that is in harmony with a woman's body, what matters is the revolutionary formula that reflects nature – not women's age.

In harmony with a woman's body.

Indication: oral contraception. Composition: Active ingredients: Each wallet (28 film-coated tablets) contains in the following order: 2 dark yellow tablets each containing 3 mg estradiol valerate (EV), 5 medium red tablets each containing 2 mg EV and 2 mg dienogest (DNG), 17 light yellow tablets each containing 2 mg EV and 3 mgDNG, 2 dark red tablets each containing 1 mg EV, 2 white tablets do not contain active substancesContraindications: Qlaira® is contraindicated, if one of the following conditions is present. Should any of the conditions appear for the first time during COC use, the product should be stopped immediately: Deep venous thrombosis or pulmonary embolism present or in history; arterial thrombosis present or in history (e.g. myocardial infarction) or prodromal conditions (e.g. angina pectoris and transient ischemic attack); cerebrovascular accident present or in history; presence of a severe or multiple risk factor(s) 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 or 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, amenorrhea, dysmenorrhea, 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 wallet. Interactions with other medicinal products: contraceptive failure and breakthrough bleeding have been described for the concomitant use of hydantoins, barbiturates, primidone, carbamazepine and rifampicin. Such interactions are also suspected for oxcarbacepin, 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. Warnings: If any of the conditions/risk factors mentioned below is present, the benefits of combined oral contraceptive use should be weighed against the possible risk for each individual women. In the event of aggravation, exacerbation or first appearance of any of these conditions or risk factors, the woman should contact her physician. The physician should then decide on whether COC use should be discontinued. All the following warnings and precautions are derived from clinical and epidemiological data of ethinyl estradiol containing COCs. Whether these warning and precautions apply to Qlaira® is unknown.: Vascular disorders with or without indication of arterial or venous thrombosis. The risk is increased for individuals with a respective family history, increasing age, smoking, obesity, dyslipoproteinemia, hypertension, diabetes, immobilization, valvular heart disease, atrial fibrillation, systemic lupus erythematosus, hemolytic-uremic syndrome, chronic inflammatory bowel disease, migraine, sickle cell disease. Tumors: breast cancer risk is slightly elevated for women taking combined oral contraceptives. Breast cancer is rare in women under 40 years of age, and the excess risk potentially caused by hormone intake gradually disappears during the course of the 10 years after cessation of combined oral contraceptive use. Experiences from clinical studies do not provide evidence of a causal relation between the use of combined oral contraceptives and an increased incidence of breast cancer. An increased risk of cervical cancer in long-term users of COCs has been reported in some epidemiological studies. Annual routine checks by a physician are recommended. Special precautions: Contraceptive safety is impaired if one or more tablets have been missed. Qlaira® is not indicated during pregnancy. Further details see package insert leaflet, valid 16-October 2008. Bayer Schering Pharma AG, European Business Unit Women's Healthcare, 13342 Berlin, Germany, www.bayerscheringpharma.de

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EU.WH.12.2008.0046

'Grape Expectations'

Continuing our Introduction to Wine Enjoyment

by *Albert Cilia-Vincenti*

"Wine awakens and refreshes the lurking passions of the mind, as varnish does to the colours which are sunk in a picture, and brings them out in all their natural glowings"

(Alexander Pope)

A grape is juice, flesh, skin and pips – and that is the 'embryo' of wine. The wine's flavours depend on the grape variety. How it matures and changes with ageing depends on the potential of the particular grape. The wine style, whether sweet or dry, fizzy or fortified or still, depends on the different grape variety's peculiar characteristics. Some grapes love the kiss of oak, others loathe its warm embrace. Wines from different wine regions taste differently, but without the consistent character of each different grape variety, mere comparison of place would be meaningless. However much we delve into all the things that influence wine flavours, it all comes back to the grape.

If you are given a glass of pale golden green wine, with a wonderful scent of gooseberry, passionflower and lime, and you taste it and the acidity freshens your mouth, with the exhilarating attack of citrus fruit scouring your palate clean and making your mouth drool for food, but if you're asked who made the wine? No idea. If you're asked where it comes from? It could be the French Loire Valley, South Africa, Chile, Spain, Northern Italy or New Zealand – the four corners of the world, really. But the grape variety? When it smells and tastes like that, you *know* it is Sauvignon Blanc. The wine's uniquely recognizable character is traced to the grape variety – Sauvignon Blanc – above all else. It is *refined* by the talents of those who grow the grape and vinify the wine. It is *modified or intensified* by the local conditions under which it grows, but the *flavour's core* comes from the grape.

Sauvignon Blanc is a dramatic grape, but so is Viognier with its apricot and mayblossom scent. So is Gewürztraminer with its explosion of musky rose petals, and so is Muscat with its overpowering aroma of hothouse grapes. Riesling is more subtle, but the balance of high acidity with floral notes and citrus fruit is unique to the grape. Chardonnay's nutty, oatmealy, buttery ripeness is created with oak barrel ageing, but no other grape achieves quite that taste, however similarly you treat it, wherever it is grown.

Red wine grapes are frequently less outspoken, and presently the obsession with over-doing new oak ageing is spoiling the thrilling individuality of many grapes' flavours – although good varieties still shine through. Tannic sturdiness and blackcurrant fruit mark out Cabernet Sauvignon in a way no other grape can replicate. The ethereal scent and wild strawberry/cherry fruit of Pinot Noir, the damson fruit and violet perfume of Malbec, the sour cherry and herbal rasp of Sangiovese, the brilliant chocolate and smoky black plum blast of Shiraz – all of these experiences are above all else due to the particular characteristics of the grape variety.

So it is remarkable how, for so long, grapes seemed to have been relegated to a subordinate role when they are so evidently of such massive importance. Until the advent of 'New World' winemaking techniques that allow the winemaker to pinpoint the flavour of the grape and maximise it, few people – winemakers, wine writers and wine drinkers – actually had much idea of what grape variety was supposed to taste like. It was easier to say that a wine's particular taste derived from where it was grown, and that it tasted of '*terroir*'. Indeed, the wines often did have a minerally or earthy flavour, which probably emanated from the vineyard and from old-fashioned winemaking, rather than from the grape itself. That's why, until recently, many experts and critics were obsessed with the minutiae of a wine's birthplace rather than its chief component – the grape juice itself.

Everything changed when the 'New World' producers brashly barged their way through into our wine consciousness. The Australians, Californians, New Zealanders, South Africans and Chileans didn't have much of a story to tell about traditions and historical importance of their young vineyards. *The one story they could tell, and the one their ultra-modern winemaking allowed them to tell, was that of the grape itself and the flavour it imparted to the wine.*

Albert Cilia-Vincenti is a long-standing member of The Wine Society (1874) of UK and founding committee member of "Il-Qatra" – a 60-member blind-tasting wine club of 10 years standing. He can be contacted on acvincenti@onvol.net

continued from page 10 MEDICAL ETHICS

Ethical issues in Vocational Training and quality with Patient Registration

Certainly conditions must be satisfied for GPs to have patients registered with them. The first is a minimum number of hours in their practice – usually 20 hours have been suggested. Secondly they should be networked to cover for out-of-hours and emergency calls and when one is on leave. Networking works just as good in other countries as group practices, which have not proved popular yet. This has been the case in Italy from where colleagues have explained their system. It will also prevent business-like services, bringing in doctors from other countries who are not on the specialist register of their own country or have not done vocational training to practice here at the expense of quality and due care.

But the fact we are seeing a silver lining is indeed a step forward for patients and doctors alike. The effort invested by many over the years and especially in recent months is paying off.

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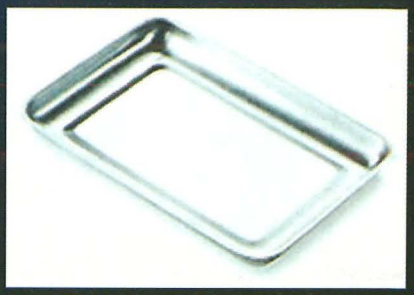

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MEDICAL IMAGING

Imaging Diffuse Liver Disease – Part I

Visualization of the distribution pattern of Lipiodol, an iodised oil used for intraarterial embolization of liver tumors is another indication for nonenhanced hepatic CT.

Blood circulation in the liver is based on two major components: the hepatic artery and portal vein. Because of this dual-source hepatic blood supply, the patterns of extracellular parenchymal contrast material uptake and the associated changes in tissue attenuation over time follow a complex multicompartmental model. The overall hepatic perfusion cycle can be separated into three idealized perfusion phases: (a) arterial phase, (b) redistribution or portal venous phase, and (c) equilibrium or hepatic venous phase.

Timing of injection of contrast material in CT can be performed in two ways, either arbitrarily assuming normal cardiac output or through aortic bolus tracking. The latter technique uses serial CT scans performed during contrast injection from which serial density measurements are taken in the abdominal aorta to detect peak contrast concentration. Peak aortic enhancement is achieved approximately 10sec following initiation of contrast injection with normal cardiac output.

The early arterial phase of liver enhancement occurs approximately 10 seconds after peak aortic enhancement. In this phase, enhancement of the hepatic artery is observed; usually, no enhanced portal venous blood is evident. In the late arterial phase, at approximately 20 seconds after peak aortic enhancement, the hepatic artery and its branches are best demonstrated; however, a minimal admixture of enhanced portal venous blood may already have occurred. The redistribution or portal venous inflow phase, imaged about 30 seconds after scan initiation, allows visualization of the intrahepatic and extrahepatic portal veins sharply contrasted against still unenhanced hepatic veins. Maximum enhancement of the portal venous vasculature is reached after approximately 40 seconds. The hepatic venous phase can be reached at 60 seconds after peak aortic enhancement, during which simultaneous enhancement of hepatic and portal veins occurs. Because of retained contrast agent, hepatic pathologic conditions such as confluent hepatic fibrosis or cholangiocarcinoma benefit from further delayed hepatic imaging, after the parenchymal contrast agent has mostly been eliminated from physiologic liver parenchyma (Figure 3).

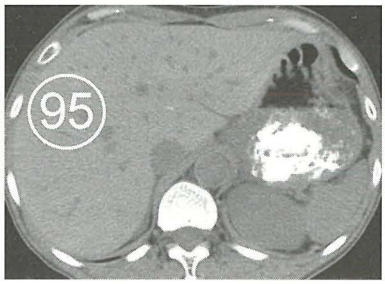

Figure 2. *Histologically proved Wilson disease in a 41-year-old man. Nonenhanced CT scan shows increased attenuation of the hepatic parenchyma.*

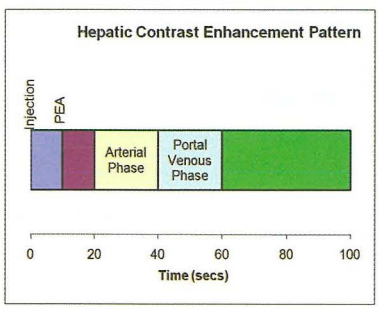

Figure 3. *Timing of hepatic enhancement following IV injection of contrast material. PEA - Peak Aortic Enhancement.*

Dr Pierre Vassallo can be reached at the DaVinci Hospital on 21 491 200 or by email on pvassallo@davincihospital.com.mt

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REGULATORY AFFAIRS

Counterfeit Medicines

The commitment to continuously improve the availability and affordability of medicines on a national and European level should be recognized as a cornerstone of healthcare in Europe if the problem is to be adequately addressed. It is essential that medicines legislation is strictly enforced and that Court cases involving counterfeit medicines are adjudicated without undue delay. Counterfeit medicines do not only affect 'the weak consumer' but impact the health and well-being of the public as a whole. Medicines legislation must therefore reflect the seriousness of public health violations as a matter of public policy.

The author is currently reading for a Doctor of Laws degree at the University of Malta, with a special interest in Medical and Pharmaceutical Law. She is currently researching the EU and US legal frameworks for medicines and their impact on the pharmaceutical industry and public health.

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New Gastrointestinal Diagnostic Modalities: Capsule Endoscopy

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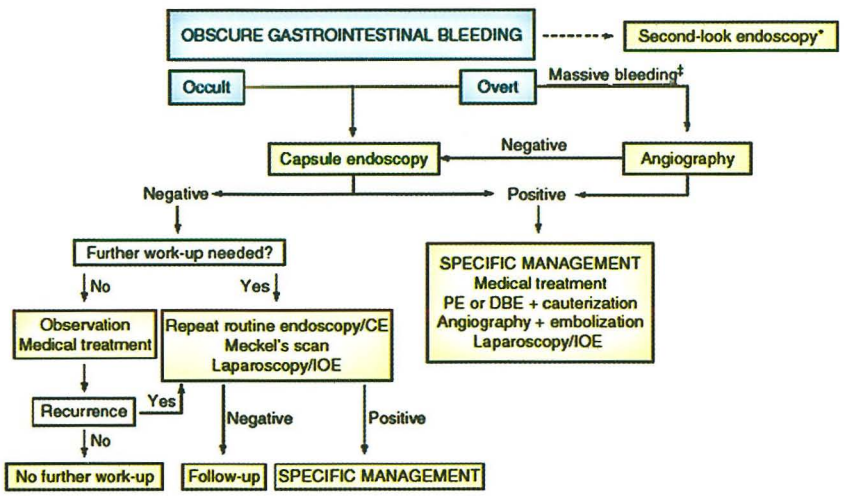

Figure 3: *Proposed Management of Obscure GI Hemorrhage (ICCE 2005). Abbreviations: PE - push enteroscopy; DBE - double balloon enteroscopy; IOE - intra-operative enteroscopy*

Inflammatory Bowel Disease

Small intestinal involvement is the often elusive, defining pattern in Crohn's Disease. Given that there is no 'gold standard' in diagnosing small intestinal Crohn's Disease, CE appears to be more sensitive, especially for early and more proximal small intestinal mucosal lesions, than all other imaging modalities. This includes small bowel series, CT enterography and Magnetic Resonance Imaging.[7] CE has consequently been shown to be useful in the investigation of indeterminate colitis with 29 – 40% of studied populations diagnosed with small intestinal lesions, therefore Crohn's, with important management sequelae.[7, 8, 9, 10]

Small Bowel Tumors

CE has also rendered the diagnosis of small bowel tumors earlier with a corresponding better prognosis, still however critically dependent on the histologic subtype. Small Bowel tumors are diagnosed in 2.5 – 12% of investigations performed in adult patients. The most common indication in patients subsequently diagnosed with tumors is anemia or obscure gastrointestinal hemorrhage. Most tumors (60%) are malignant, including adenocarcinoma, carcinoid, melanoma and lymphoma. Benign lesions include gastrointestinal stromal tumors (GIST), hemangiomas and hamartomas.[11]

Coeliac Disease

The diagnosis of Coeliac disease requires a combination of characteristic histologic abnormalities, and response to a gluten free diet. Capsule endoscopic abnormalities include duodeno-jejunal areas of fissuring, loss of villi and a scalloping mucosal pattern. CE is as accurate as histology in identifying severe spue,[12, 13] and is useful in determining the extent of involvement[14] and detection of associated small intestinal malignancy – notably T-cell lymphoma and adenocarcinoma.

Complications and Limitations of Capsule Endoscopy

Problems with CE are rare, the commonest being inability to ingest the capsule. Capsule retention or failure of complete passage through the intestine is exceedingly rare but cannot be predicted by prior normal small bowel series. The passage of a sham dissolvable capsule obviates both the patient's ability to swallow the capsule and the potential for retention of the same-sized device capsule. More commonly (15 – 20% of cases in some series), slow gastric emptying or delayed small intestinal transit time may lead to incomplete small intestinal visualization. Measures including prokinetics and positioning appear to improve the diagnostic yield from CE.

The limitations of CE include the inability to biopsy abnormal areas and the potentially limited number of images of areas of interest which can be taken. Although a steerable device is being studied, the ability to direct biopsies appears distant. Centers of excellence have evolved programs including push- or double balloon enteroscopy to allow controlled visualization and biopsy of CE detected abnormalities.

In summary, CE appears to be a safe diagnostic modality that has an established niche in the investigation of diverse gastrointestinal disorders in children and adults; most notably obscure gastrointestinal bleeding, including unexplained anemia, suspected inflammatory bowel disease or indeterminate colitis. It is promising in the detection of small bowel tumors, polyps and coeliac disease.

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Healing & Disease Reversal - II

surgery but not comprehensive dietary and lifestyle change programmes, nor do they cover food supplements such as purified fish oil extracts (as the Japanese health ministry does). Teaching of healing methods in our Medical School covers little more than information about pharmaceutical drugs and surgery. In the meantime, Dean Ornish's team are training health professionals worldwide and offering them free licences in an open-source model. These include physicians, nurses, dieticians, clinical psychologists and exercise physiologists.

Ornish's research has shown that our body has remarkable capacities to heal itself (and much more quickly than people once realised) when the underlying causes of illness are addressed. The choices we make every day as to what we eat and how we live are among the most important underlying causes.

When prescribed medications for hypertension, hyperlipidaemia or diabetes, patients are usually told that they would have to take them for the rest of their lives. Why? *Because the underlying causes are not being addressed.* It's important to treat not only the problem but also its underlying causes, otherwise the same problem often recurs, a new set of problems may emerge (such as drug adverse effects), or even worse, there may have to be rationing of medical services (such as keeping 47 million Americans from having health insurance because it's too expensive to treat everyone with the drugs and surgery that they may need).

Ornish's team found that many people with coronary artery disease, diabetes, hypertension, hypercholesterolaemia, and other chronic conditions, are able to reduce or even discontinue these medications (under doctor's supervision) when they make the diet and lifestyle changes that will be outlined in future articles.

Professor Cilia-Vincenti is a former London University Teacher of disease mechanisms at Charing Cross and The Middlesex Hospital medical schools, and at the Malta Medical School. He is currently steering group chairman of the Academy of Nutritional Medicine of Cambridge, UK, a charity sponsoring teaching and research. He may be contacted on *acvincenti@onvol.net*.

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