

# The Synapse

The Medical Professionals' Network

Issue 01/12

'You are barren and have borne no children...' - Part I **06**

Management of allergic rhinitis & chronic sinusitis **09**

Bilateral Acanthamoeba keratitis **14**



R. ELLIS.  
MALTA





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- No bleaching or staining

The image represents an average patient experience, and does not show an actual patient.

**References:** 1 Terpstra IJ, Acne treatment with 4% erythromycin and 1.2% zinc acetate. Cardiff 1988; 255-259. 2 Stainforth J et al. Dermatol Treat 1993 4: 119-122. 3 Schachner L et al. J Am Acad Dermatol 1990; 22(3): 489-495.

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**Presentation:** After constitution, Zineryt® contains 40 mg/ml erythromycin and 12 mg/ml zinc acetate, as an erythromycin-zinc complex. **Uses:** Topical treatment of acne vulgaris. **Dosage and administration:** For children, adults and the elderly: Apply twice daily over the whole of the affected area for a period of 10 to 12 weeks. **Contra-indications:** Contra-indicated in patients hypersensitive to erythromycin, macrolide antibiotics, zinc, di-isopropyl sebacate or ethanol. **Other warnings and precautions:** Cross-resistance may occur with macrolide antibiotics, with lincomycin, or clindamycin. Contact with the eyes and mucous membranes of the nose and mouth should be avoided. **Use in pregnancy and lactation:** Not-contra-indicated. **Side-effects:** Occasionally a burning sensation or slight redness of the skin due to the alcohol base of Zineryt®; this is transient and of minor clinical significance. **Overdosage:** Not expected in normal use. In idiosyncratic hypersensitivity wash well with soap and water. Zineryt® is a Registered Trademark. Please refer to the full Summary of Product Characteristics before prescribing.

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# The Prince[ess] and the Pea



Everyone heard about the literary fairy tale penned by Hans Christian Andersen, first published in 1835 about a young woman whose future was determined by her awareness of a small pea. Even though she was unaware of the pea, that very same (small) pea caused her (great) discomfort all night long. However it also meant that this very same (temporary) discomfort, in the end, meant that she was to have a better life. Now, everyone also heard about what happened in parliament in January. Now I ask, are there any similarities between the two events, albeit one is fictional and the other is not?

And such similitude also applies to everything else which really matters. Do you recall my last editorial when I quoted what Jobs said about his firing from Apple “[it] ... was awful-tasting medicine, but I guess the patient needed it.” At times such physical or emotional discernment is necessary to have a better tomorrow. Although some may argue that this may be true, the better tomorrow can well indeed be enjoyed by third parties not involved in any of the turmoil caused directly or indirectly by the aforementioned parties! But that is life, after all ...

And incidentally, this year we have already seen a myriad of initiatives from the government. These include the following:

- The launch of *My Health*, whereby patients are now able to access their medical information online and share this with a doctor of their choice. The service will include hospital discharge summary reports, lab results, radiology reports and medicine entitlement information. Another innovative aspect of this service is that patients can tag any registered doctor (like social

networking sites) to view their results and guide them in analysing the information.

- The launch of the e-tender concept which will replace the current tendering procedures used to buy medicine and which is claimed to reduce the shortage problem and reduce cost.
- Malta together with another 21 EU member states has become a signatory to the Anti-Counterfeiting Trade Agreement (ACTA) on the 26<sup>th</sup> January (however, the final vote for the ACTA ratification will be cast in the European Parliament next June). ACTA is a plurilateral agreement for the purpose of establishing international standards for intellectual property rights enforcement, including medicinal products. This has been shrouded in controversy, even locally, since some state that it could have a negative effect on trade in generic medicines. And now even the Commission is having its doubts on this agreement!
- A memorandum of understanding was signed by the health ministers of Libya and Malta in February, outlining open-ended collaborations in the field. Indeed, our Health Minister presented Libyan Health Minister Fatma Hamroush with a box of steroids, tetanus and pain medication as a token.
- The first reading of the in vitro fertilisation law which should take place in the coming days.

And one cannot but remember what Henri Queuille, three times French Prime Minister once said, “Politics is the art of postponing decisions until they are no longer relevant.” But not when we are in election mode, I must add!

Needless to say, the backbone of what great things are to come is IT and social networking. We have already discussed the former. With respect to the latter, we could mention Henry Ford Hospital (Detroit, US) which, a few months ago, became one of the first hospitals to Tweet a live procedure from an operating room. And social sites like Inspire nowadays provide a popular forum for patients to share their health problems and questions about treatments with other patients, as well as qualified medical personnel. Even locally, the Ministry of Health, Primary Health Care Department, Malta Health Promotion and Disease Prevention Directorate, as well as various private entities including The Synapse, use Facebook to reach out to the ever increasing community 196,000 local users (which translate into 81.45% of internet users) (Source: <http://www.socialbakers.com/facebook-statistics/malta>)

It is with this mentality that we at The Synapse are continuing to invest in a new revamped website to further increase networking – this will include the addition of a forum and facilities that promote social networking between members. The new portal will include new sections such as the provision of better facilities for promotion of job vacancies as well as sale / exchange of any items between members. All is aimed to promote a healthy interaction between members of the various medical professions. If you require more information, simply send an email to [editor@thesynapse.net](mailto:editor@thesynapse.net)

*Ian Ellul*

Ian Ellul

## TheSynapse Front Page Pictures

For the past two years, TheSynapse front page pictures featured images of plants which are found in Malta and traditionally had medicinal properties. We thank Mr Guido Bonett for generously contributing these images. This year we decided to change the theme and it was extremely difficult to find material of a comparable quality. We still wanted prestigious high quality images with the broad theme of Malta and Medicine. In December 2011 we came across the 4th volume of ‘Richard Ellis – the Photography Collection’ and thanks to the generous cooperation of Mr Ian Ellis, the editor, we will be featuring some prestigious photographs from the collection. The collection is unique. It not only shows Malta pictorially, as one would expect, but it is also a vast source of information related to Malta’s social, political and industrial history. We strongly recommend that you have a copy of the photography collection by Richard Ellis in your library.



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No data available for use in patients with severe hepatic impairment. No relevant use in the paediatric population. If a dose is missed, the next dose should be taken at the usual time the next day. **CONTRAINDICATIONS:** Hypersensitivity to the active substance, to lactose or to any of the other excipients. **WARNINGS/PRECAUTIONS:** **Asthma:** •ONBREZ BREEZHALER SHOULD NOT BE USED IN ASTHMA. **Paradoxical bronchospasm:** • If paradoxical bronchospasm occurs Onbrez Breezhaler should be discontinued immediately and alternative therapy substituted. **Deterioration of disease:** •Not indicated for treatment of acute episodes of bronchospasm, i.e. as rescue therapy. **Systemic effects:** •Indacaterol should be used with caution in patients with cardiovascular disorders (coronary artery disease, acute myocardial infarction, cardiac arrhythmias, hypertension), in patients with convulsive disorders or thyrotoxicosis, and in patients who are unusually responsive to beta2-adrenergic agonists. **Cardiovascular effects:** •Indacaterol may produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, blood pressure, and/or symptoms, ECG changes. 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Onbrez Breezhaler should only be used during pregnancy if the expected benefits outweigh the potential risks. •Not known whether indacaterol / metabolites are excreted in human milk. A decision must be made whether to discontinue breast-feeding or discontinue Onbrez Breezhaler therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. **INTERACTIONS:** •Concomitant administration of other sympathomimetic agents may potentiate the undesirable effects of Onbrez Breezhaler. 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Onbrez Breezhaler 300mcg - carton containing 30 capsules and one Onbrez Breezhaler inhaler. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **MARKETING AUTHORISATION NUMBERS:** EU/1/09/593/001, 002, 007. Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma Services Inc, Representative Office Malta P.O. Box 124, Valletta, VLT 1000 Malta. Tel: +356 22983217 2011-MT-02-ONB-027-Apr-2011

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**COVER:**  
Victor's Pharmacy on Tower Road Sliema

Victor's Pharmacy on Tower Road Sliema was already serving customers in 1934. It was one of a number of Sliema Pharmacies; the oldest run by Dr Perini having opened in 1872. Victor's pharmacy put on a display of Horlick's Malted milk products for this formal photograph. It is unclear whether this photograph was commissioned by the local Horlick's agents or the owners of Victor's pharmacy. These photographs of shop fronts of which the Ellis collection contains quite a number, are testimony to the early days of product marketing and promotions.

Photography: Richard Ellis

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but you shall conceive and bear a son' -

VICTOR GRECH  
CLARE THAKE-VASSALLO  
IVAN CALLUS

# Fertility in prehistory, history and contemporary culture - Part I

Work should be attributed to the Pediatrics Department, Mater Dei Hospital, Tal-Qroqq, Malta and the Faculty of Arts, University of Malta

Fertility has always been a vital and fundamental matter for the human race as evinced by the multitudes of fertility totems and rites that have been created by ancient cultures. Locally, for example, the Maltese Neolithic 'fat lady' statuettes are believed to be representations of Mother Earth, a symbol of fertility.<sup>1</sup> Ancient biblical texts also testify to the importance that fertility has always had for humanity. Genesis recounts that God created male and female, blessed them and enjoined them to be fruitful and multiply. Further examples as to the importance of fertility in the Bible abound. For instance, after the destruction of Sodom and Gomorrah, Lot took up habitation in a cave with his two daughters, who were concerned by the lack of men other than their father. They therefore deliberately drugged Lot with wine and had sex with him, producing two sons in order to propagate the race. The Bible also recounts several scenarios wherein infertile women arranged for their husbands to have children by other women such as in the case of three of the four biblical matriarchs (Sarah, Abraham's wife; Rebecca, Isaac's wife; and Jacob's wives, Leah and Rachel) who were infertile. The Old Testament is amply clear on this subject in that an infertile wife encouraged her husband to have sex and beget children from slaves and servants, and the children would legally belong to husband and infertile wife.<sup>2</sup>

Closer to present day, the infamous papal bull *Malleus Maleficarum* (1446) was used as an excuse to prosecute and generally hunt down and kill an

estimated 50,000 'witches', who were considered as vile as prostitutes, and this is germane to this dissertation as both were considered symbols of sterility.<sup>3</sup>

Interestingly, the first known documented recognition of the principle of physical insemination was documented in the Talmud (central text of mainstream Judaism), with the first successful artificial insemination occurring in 1742 using fish gametes. In 1780, the first canine and human inseminations occurred,<sup>4</sup> with elaboration by the famous obstetrician Sims in 1866, who, 'by a classification of all diseases of the uterus, [...] found sterility to be incident to many of them',<sup>5</sup> and strove to create cures and treatments. However, opposition to these new techniques by Sims' contemporaries was rife including 'as a valid objection to gynecological examinations [was] the likelihood of inducing a lax moral sense in the patient'!<sup>6</sup> And even more drastically, a review of Sims's book concluded the utilisation of procedures such as vaginal examination and other techniques that might elucidate causes of infertility would be detrimental to the medical profession and

'[a]t any rate, if such practices were to be considered the "business of the

Physician", there are a good many of us who would quit Physic for some other calling that would let us keep our sense of decency and self-respect. Better let ancient families become extinct than keep up the succession by such means.'<sup>7</sup>

This paper will now briefly inspect the intersection between infertility and popular culture with particular reference to Helena Michie and Naomi Cahn's *Confinements: Fertility and Infertility in Contemporary Culture* (1997). This book was written by two female authors with personal experience in the fields of both infertility and pregnancy.<sup>8</sup> *Confinements* attempts to provide an analytic framework for the understanding of the metanarrative of infertility, and its bias toward the more affluent Western middle-class couple, principally by analyzing Arlene Eisenberg et al *What to Expect When You're Expecting* (1991) and other works which consist predominantly of self-help and self-empowerment narratives.<sup>9</sup>

Feminist attitudes to pregnancy and infertility are also discussed along with a very brief history of attitudes toward infertility, which until the 19th century was always thought to be the fault of the woman. To some extent this is still portrayed as a female choice

Interestingly, the first known documented recognition of the principle of physical insemination was documented in the Talmud (central text of mainstream Judaism)





for the following reasons: waiting too long to attempt to become pregnant, too stressed, too fat or too thin, using inappropriate contraception (e.g. the pill), sleeping around with too many different partners and developing a sexually transmitted disease or having an abortion. Thus, infertility risks being portrayed dually as a female choice or a cultural responsibility, and as a female disease, while, on the other hand, such empowerment and availability of options may lead to guilt if matters do not take their hoped-for course. It is also ironic that 'pro-choice' invokes the view that a woman should have the choice of whether or not to terminate her pregnancy. This pro-abortion stance implies not only the guarantee of reproductive rights, but also access to sex education, to contraception and fertility treatments and to safe and legal abortion.<sup>10</sup>

Michie and Cahn contend that the idioms of popular pregnancy and infertility manuals romanticise the dream or illusion that expresses the middle-class evolution of heterosexuality, marriage, fertility, pregnancy and childbirth. These progressions are considered normative and create the context from which the rhetoric of infertility arises, along with the disparate circumstances and emotional crises that together constitute infertility treatment. The authors correctly state that 'the rhetoric of choice diverts attention from the constraints within which an individual choice occurs onto the act of choice itself',<sup>8</sup> but the claim that the current infertility epidemic is caused by media attention to middle-class couples who find themselves in this quandary by waiting until both partners have established careers is rather dated, with clear evidence of falling fertility in all classes and races,<sup>11</sup> not to mention the current possibilities of gamete banking whereby couples may bank ova and spermatozoa for later use.<sup>12</sup>

Undeniably, the intertwined and certainly incorrect conflation of the rhetoric of choice in treatment is evident even in the titles of these narratives, such as Kitzinger's *Your Baby, Your Way* (1987).<sup>13</sup> These manuals encourage women to learn

about new reproductive technologies as fast as or even faster than doctors, a common enough situation to doctors in all specialities in these postmodern days of ubiquitous access to the Internet and to freely accessible medical servers, most notably the United States' National Library of Medicine's PubMed server archive.<sup>14</sup>

In turn, women with fertility problems may find themselves coerced, consciously or unconsciously, to opt for fertility treatments in a patriarchal society that values women mostly for their reproductive capacities.<sup>15</sup> Michie and Cahn outline the invasive progression of reproductive therapies and of pregnancy itself, from basic ultrasounds through to laparoscopies and hysterosalpingograms that look inside the female body, and in doing so, render the intimate public, a performatory aspect, exposing the body's working to the healing medical gaze. Indeed, a very recent review of the long-term effect on fourteen Swedish women twenty years after their infertility treatment found that childlessness had a profound and lasting impact on their lives, resulting in high rates of marital breakdown and sexual dysfunction.<sup>16</sup>

The negative medical aspects are also debated, including the lack of complete candour by doctors who do not always give honest estimates of likely outcomes of treatments, and who do not counsel adequately with regard to possible deleterious side-effects. Regrettable medical tendencies to seek fame and profit in this form of treatment are underscored, along with exhortations to select doctors and facilities after careful deliberation.

Michie and Cahn also argue that women are policed through a series of interventions in both infertility treatment and possible subsequent pregnancy in the name of domesticity, supporting Paul Morrison's notion of the 'domestic carceral',<sup>17</sup> foreshadowed by Michel Foucault,<sup>18</sup> almost a form of punishment for infertility, where we must almost 'analyse rather the 'concrete systems of punishment', study them as social

phenomena'.<sup>18</sup> This aspect is even more relevant when infertility treatments are imbricated in explicit or implicit male dominance games, particularly when framed in feminist discourses and idioms, leading to unwitting antifeminist tropes. *S (to be continued in 02/12)*

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# Hypertonic saline nasal irrigation in the management of allergic rhinitis and chronic sinusitis

Allergic rhinitis is a disease characterized by the classic symptoms of rhinorrhea, obstruction of the nasal passage, sneezing and itching, all occurring in a temporal relationship to allergen exposure.<sup>1</sup> Conventional treatment options include antihistamines, decongestants, anticholinergics and corticosteroids.<sup>1,2</sup>

If untreated or in the long term, chronic inflammation of the maxillary sinuses may result in increased secretions from the sinuses and postnasal drip caused by the allergic response. The mucosa becomes swollen and hypertrophic. The impaired drainage of the secretion from the sinuses (especially from the maxillary sinuses) increases the likelihood of recurrent infections. The conventional medical approach to chronic sinusitis includes treatment with local and systemic anti-inflammatory drugs with or without antibiotics.<sup>3</sup>

Many patients with sinusitis also experience chronic cough, fatigue and lassitude characteristic of the disease. The prevalence of chronic sinusitis among patients with respiratory complaints is estimated to be as high as 38% in children older than 10 years of age.<sup>3</sup>

Recent studies have documented interesting results using nasal irrigation as an adjunctive treatment modality in many sinonasal diseases. In this regard, it has also been reported that an increased efficacy could be effected using hypertonic (2 – 3.5% w/v) saline instead of normal saline.<sup>4</sup>

Significant clinical benefits were observed in children with seasonal allergic rhinitis who received a regimen of three-times daily nasal irrigation with hypertonic saline during the pollen season (Figure 1). Indeed, the mean daily rhinitis score was reduced during the study treatment period (6 weeks). Reduced need for oral antihistamines was also observed.<sup>1</sup>

Tamooka et al. have also reported that nasal wash is efficient in the treatment of seasonal allergic rhinitis in adults.<sup>5</sup> These authors documented a significant improvement in the symptoms score after nasal irrigation with hypertonic saline.

It has been shown that the hyperosmolar airway fluids resulting from hypertonic saline nasal irrigation (HSNI) increase ciliary beat frequency, possibly by regulating the use or availability of adenosine triphosphate by the ciliary axoneme. This enhances mucociliary clearance, facilitating the evacuation of potentially allergen- and irritant-containing mucus. The topical antibacterial effect of hypertonic saline solution is also well established in wound dressing and washing of open wounds.<sup>4</sup>

In summary, daily HSNI is a safe, effective and tolerable therapy associated with high patient satisfaction, improved quality of life, decreased antibiotic use, and improved sinus symptoms in both paediatric and adult patients with a history of frequent rhinosinusitis and chronic sinus complaints. Study participants also expressed satisfaction in their perception that at-home use of HSNI reduced the number of trips to their physician and the number of antibiotic prescriptions.<sup>3</sup> S

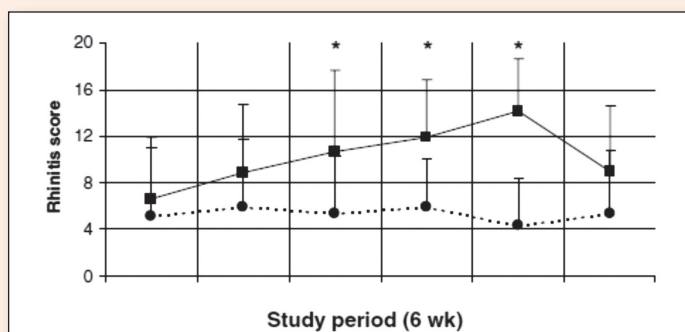


Fig. 1. Mean  $\pm$  SD of the rhinitis score during the 6-week period of the pollen season for both patients treated with nasal irrigation (dotted line) and controls (solid line). Scores represent the sum of scores of four different symptoms: nasal itching, rhinorrhea, nasal obstruction and sneezing. Intensity of these four symptoms was rated according to a 5-grade scale: 0 = no symptom, 1 = slight, 2 = mild, 3 = moderate, 4 = severe and a mean daily rhinitis score for each week of the pollen season was calculated. The mean daily rhinitis score for each week of the pollen season was reduced during 5 weeks of the study treatment period in patients who were prescribed nasal irrigation. This difference resulted in statistical significance (\*) in the 3th, 4th and 5th week of therapy.

**Source:**  
Garavello W et al. Hypersaline nasal irrigation in children with symptomatic seasonal allergic rhinitis: A randomized study. *Pediatr Allergy Immunol* 2003; 14: 140-143

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Administration of the amoxicillin/clavulanate combination to patients with a disturbed liver function should be approached with caution. Liver function should be monitored on a regular basis. Forcid Solutab 875/125 is not recommended for patients with a glomerular filtration rate  $\leq$  30 ml/min. In case of long-term treatment regular checks of renal and hepatic function and haematological studies are indicated. Amoxicillin/clavulanate should be used with care in patients on anti-coagulation therapy, since prolongation of the prothrombin time has been observed rarely. The presence of high urinary concentrations of amoxicillin can cause precipitation of amoxicillin in urinary catheters. Therefore, the catheter should be checked at regular intervals in such cases. Forcid Solutab contains the following quantities of potassium per tablet: Forcid Solutab 500/125: 24.53 mg, Forcid Solutab 875/125: 25 mg. **Pregnancy and lactation:** Following administration of amoxicillin/clavulanic acid to pregnant women, no detrimental effects in the fetus or neonate could be observed. However, a single study in women with premature rupture of the amnion reported that prophylactic treatment with amoxicillin/clavulanic acid can be associated with an increased risk of necrotising enterocolitis in neonates. As a precautionary measure, Forcid Solutab should only be used during pregnancy after benefit/risk assessment by the physician in charge. Forcid Solutab should be avoided during the first trimester of pregnancy. Both substances reach the embryo/fetus via the placenta and are excreted in maternal milk. (Nothing is known about the effects of clavulanic acid on the breast-fed infant). Therefore, diarrhoea and fungus infections of the mucous membranes could occur in the breast-fed infant, so that nursing might have to be discontinued. The possibility of sensitising should be born in mind. **Marketing authorization holder:** Astellas Pharma International BV, Elisabethhof 19, 2353 EW Leiderdorp, The Netherlands.

12-FOR-004



# Mental and Emotional Health

BRIGITTE OHK

Nowadays probably every person came across the term *Psychotherapy*. It seems, however, not to be so clear what psychotherapy actually means. Besides that, it seems to be not so clear, what a Psychotherapist does and how s/he can assist someone, who finds himself temporarily in distress. When we speak about psychotherapy, we refer to a form of therapeutic interaction or intervention which usually addresses emotional issues.

Accredited psychotherapists are highly trained people, who have undergone strictly regulated schooling in one or more of the officially recognized forms of psychotherapy. This training takes up to four years and even more. During their training course psychotherapists have to undergo their own personal therapeutic journey. Following accreditation, a psychotherapist is asked to take part in supervision groups, personal development groups and to attend seminars and workshops to further his knowledge and education. The therapist's on-going personal and professional journey will equip him for his métier with the right amount of empathy and experience to choose from the best instruments available the most appropriate one to work with the individual patient's issues.

Persons can avail themselves of the support of a psychotherapist as individual patients, groups, couples, or families. The session's focus will address the person's or the group's environment, since human beings do not live isolated from one another. Fundamentally we all are historically - somewhat coarsely expressed - gregarious animals.

The journey of discovering the roots of the difficulties experienced throughout a momentary phase of life might bring into awareness issues with every day contacts like the partner, members of the patient's close family, work, school, or any other social group.

Confidentiality in psychotherapeutic sessions is of critical importance and stipulated in the regulatory statutes of the psychotherapeutic organization's code of ethics. A psychotherapist who does not respect those statutes is in danger of losing his credibility, and also his right to practice in his profession. A trained professional would unlikely want to risk that.

When it comes to the topics that can be dealt with in psychotherapy there is hardly anything that cannot be addressed. Psychotherapists however, might have specialized themselves in a particular field. In such a case, a patient can be referred to a colleague with the respective specialized background.

Psychotherapy can improve the response to prescribed medication and help the patient to recover quicker. Vice-versa the psychotherapist might decide that it would be of advantage for the patient to see a medical practitioner to evaluate the possibility of introducing medication. The psychotherapist and the medical practitioner can thus decide together on the management of the patient by monitoring the improvement of the patient's emotional rebalancing.

Psychotherapy aims to help patients to cope better with their lives and the challenges, learn about conflict management and self-growth, and to reach their full potential. Within the therapeutic setting, the psychotherapist creates an environment that is

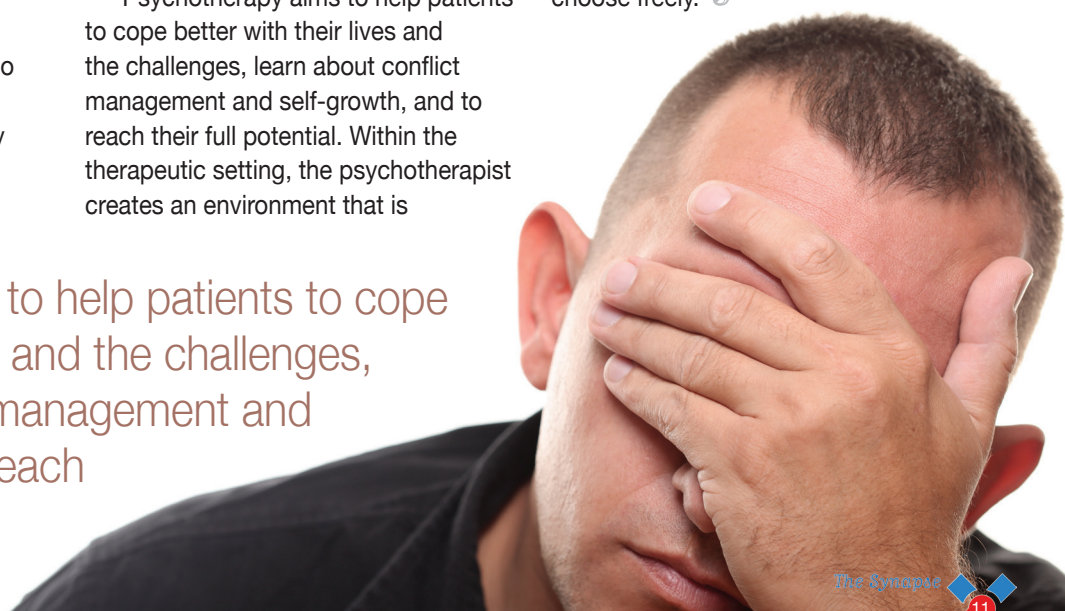
potentially healing for the patient. Mental and emotional health and fitness are efficient allies when it comes to seriously tackling all sorts of crisis. Therefore, the psychotherapist's aspiration will be that of strengthening both, be it as prevention for future hardships, or as cure for a momentary deadlock in a difficult life-situation.

During each session the psychotherapist strives to increase awareness, insight and understanding. To reach this goal the therapist will use different techniques. Amongst others the therapist will aim to support the patient to recognize his behaviour or thinking patterns that once might have been useful but now sabotages the patient's well-being. Through broader awareness the patient can ultimately expand his capacity for self-observation, become more aware to undesired behaviour, develop insight and empathy.

Be it with medication or without, through the interventions given by the psychotherapist, the patient will with time be able to change his thoughts and feelings and as a result change his patterns and his behaviour. Through this changed behaviour the patient will increase his sense of well-being.

Coming to the end of this therapeutic journey, the patient will be able to cope better with discomfort and distress, and his perception of reality will be balanced, so that he can clearly see the variety of his choices - and choose freely. §

Psychotherapy aims to help patients to cope better with their lives and the challenges, learn about conflict management and self-growth, and to reach their full potential





# Herbal medicine - Drug Interactions

In today's Western world, herbal medicine is used alongside conventional medicine. Herbal medicines may interfere with conventional medicines by several mechanisms, the most typical being via cytochrome P450 and/or P-glycoprotein systems. The cytochrome P450 family (officially abbreviated as CYP) is a large and diverse group of enzymes (Table 1). P glycoproteins (P-gp) are part of a larger superfamily of efflux transporters found in several organs, with the role of protecting the body from harmful substances. These mechanisms alter the plasma concentrations and/or alter the clearance of drugs, hence leading to a potentiated or diminished therapeutic effect. Most of the over-the-counter herbal medicines are relatively safe. However, the patients should be advised on the concurrent use of conventional and herbal medicines. Patients suffering from chronic

conditions, such as hypertension and diabetes, are usually stabilised on a number of medications. The introduction of a herbal medicine unfortunately may destabilise the patient leading to episodes of hypo or hyperglycaemia in diabetic patients, and hypo- or hypertension in hypertensive patients, for instance.

The most utilised herbal medicines, with potential herb-drug interactions, include St. John's wort, echinacea, garlic, ginkgo, ginseng, black pepper, kava, and goldenseal. In the context of this article, the herbs mentioned above will be discussed one by one on their potential interactive effects (Table 1).

St. John's wort (*Hypericum perforatum*), also known as nature's Prozac, is a broad spectrum P450 inducer and a p-glycoprotein inducer.<sup>1</sup> St. John's wort contains several phytochemicals, particularly flavonoids (such as quercetin, rutin and

hyperoside), other phenylpropanoids, naphthodianthrones (hypericin), and acylphloroglucinols (hyperforin). Hyperforin is the most active constituent, increasing the gene expression of CYP3A4 isoenzyme through the pregnane X receptor activation, is also a potent competitive inhibitor of CYP3A4 and induces P-glycoprotein transport (cyclosporine and digoxin).

*Echinacea purpurea* L. preparations have been used in tradition as an antimicrobial and an immune-booster. It contains phenylpropanoids (cichoric acid, chlorogenic acid, echinacoside), flavonoids, unsaturated alkamides, polysaccharides and a trace amount of non-hepatotoxic pyrrolizidine alkaloids. Cichoric acid and the alkamides are primarily involved in the cytochrome P450 isoenzyme inhibition.

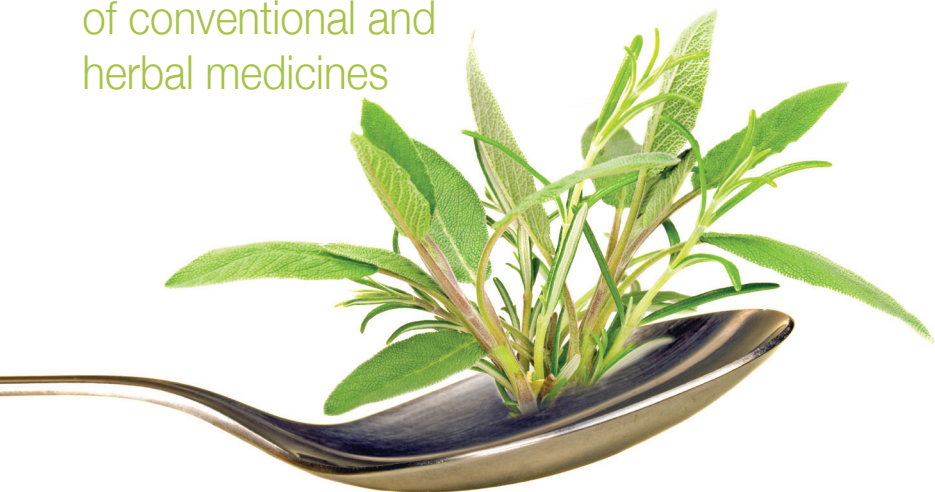
Garlic (*Allium sativum* L.) may be regarded both as food and medicine. However, it is medicinally used for the

**Table 1:** Interactions of some frequently used herbal medicines in Malta

CYP or P-gp	St. John's wort	Echinacea	Garlic	Ginkgo	Panax spp.	E. senticosus	Black pepper	Kava	Goldenseal	Substrate/s for CYP isoenzymes or glycoprotein	Activity
CYP1A2		-				-				theophylline, caffeine	Metabolism
CYP2C9				+		-			-	warfarin	Metabolism
CYP2C19	+			+						antiepileptics, TCAs, NSAIDs, warfarin, omeprazole	Metabolism
CYP2D6					-				-	warfarin	Metabolism
CYP2E1	+		-					-		Chlorzoxazone, acetaminophen, theophylline, ethanol	Metabolism
CYP3A4	+	-	+	-	-		-		-	benzodiazepines, antivirals, oestrogens, anticonvulsants, imatinib	Bioavailability and Metabolism
P-gp	+				-		-			Tricyclic antidepressants, Cyclosporin, digoxin antiretrovirals, phenytoin, rifampin	Transport




Most of the over-the-counter herbal medicines are relatively safe. However, the patients should be advised on the concurrent use of conventional and herbal medicines



The two most significant *Piper* species are kava (*Piper methysticum*) and black pepper (*Piper nigrum*).<sup>4</sup> Kava is a popular medicine for the treatment of anxiety. It contains kava lactones (kawain, methysticin, yangonin and their derivatives). Kava interferes with GABA receptors, hence benzodiazepines, and inhibits CYP2E1. Black pepper contains piperidine amides (mainly piperine, chavicine and piperetine). It inhibits CYP3A4 isoenzyme and the P-glycoprotein transporter.

Goldenseal (*Hydrastis canadensis*) is used as an antimicrobial and an immune-booster, as for Echinacea. The main active constituents are alkaloids (hydrastine and berberine). Goldenseal rhizome extract is one of the strongest CYP3A4 iso-enzyme inhibitor. However it also inhibits CYP2C9 and CYP2D6 iso-enzymes.<sup>4</sup>

As demonstrated in this article, herbal medicines may increase or decrease drug bioavailability through the P-glycoprotein or via the Cytochrome P450 iso-enzyme systems. In some instances, contradictory activities have been established. This is because the quality of constituents and their quantity, affect which mechanism predominates in a particular situation. Therefore, herbal medicines should be evaluated on a case by case basis. 

prevention of atherosclerosis and the control of hypercholesterolaemia. The main active constituents are the organosulphur compounds allicin, alliin, S-allyl cysteine and their derivatives. It has been reported that garlic interferes with anticoagulant activity leading to a risk of bleeding in patients on warfarin. These sulphur compounds are also responsible for the inhibition of the CYP2E1 and the induction of the CYP3A4 isoenzyme.<sup>2</sup>

*Ginkgo biloba* leaf extracts are mainly used for the enhancement of memory and control of Alzheimer's disease, peripheral vascular disease and tinnitus. The main active constituents in these extracts are the ginkgolides and bilobalides (diterpenic and sesquiterpenic lactones, respectively), flavonoids and ginkgolic acids (6-alkylsalicylic acids). The P-glycoprotein is inhibited by flavonoids but induced by terpenoids, pregnane X receptor is induced by terpenoid, while

CYP3A4 is inhibited by flavonoids but induced by organic acids. The most significant activity is the induction of the CYP2C19 isoenzyme that affects the metabolism of several drugs.<sup>3</sup> The terpenic lactones exhibit antiplatelet activity and are claimed to block the platelet-activating factor receptor.

There are several species classified as Ginseng. These include Korean/Asian ginseng (*Panax ginseng*), American ginseng (*Panax quinquefolius*) and Siberian ginseng (*Eleutherococcus senticosus*) amongst others.<sup>2</sup> *Panax ginseng*, which contains mainly ginsenosides, interacts with phenelzine. It has been shown that it inhibits the CYP2D6 isoenzyme. However, *Panax ginseng* and *Panax quinquefolius* (polysaccharides, mainly) inhibit CYP3A4 and P-glycoprotein. *Eleutherococcus senticosus*, containing eleutherosides, inhibits CYP1A2 and CYP2C9 iso-enzymes with minimal effects on CYP2D6 and CYP3A4.

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# Bilateral Acanthamoeba keratitis

MARK CACHIA MARKHAM  
FRANCO MERCIECA

## Abstract

Acanthamoeba keratitis is a rare eye infection commonly misdiagnosed as herpes simplex or fungal keratitis. Failure to include it in the differential diagnosis in any contact lens wearer with the typical features of an eye infection, results in a delay in the appropriate treatment with eventual complications and even blindness. This report describes the first case of bilateral Acanthamoeba keratitis ever reported in Malta, which occurred in a young female contact lens wearer.

## Introduction

Acanthamoeba keratitis (AK) is a rare, acute sight-threatening infection of the cornea, caused by the Acanthamoeba species – an organism ubiquitously found in the environment.<sup>1,2</sup>

Approximately 85% of cases are associated with the use of contact lenses.<sup>3</sup> The initial symptoms are often nonspecific, with redness, tearing, disproportional excruciating pain, and photophobia being the most common

complaints.<sup>4,5</sup> Corneal nerve infiltration and an immune ring are the typical signs of this infection.

## Case Report

A 17-year old female (MB) presented at Mater Dei Hospital with redness in both eyes, photophobia, severely impaired vision and excruciatingly painful eyes. The patient denied any previous ocular trauma and was not on any steroid treatment before. MB also stated that she swam with the contact lenses three days prior presentation.

On examination, both eyes were watery but there was no discharge. A slit-lamp examination of the left eye revealed multiple abscesses while that of the right showed multiple abscesses with corneal oedema. Corneal scrapings which were carried out were negative for Gram stain and culture. MB was admitted, prescribed topical moxifloxacin 0.5% three times daily, topical dexamethasone 0.1% three times daily, ciprofloxacin 750mg twice

daily and timolol maleate 0.5% twice daily, for both eyes, together with oral fluconazole 200mg daily.

The following day both eyes showed corneal oedema with prominent corneal infiltration, multiple stromal infiltrates and abscesses, with minimal fluorescein uptake. A working diagnosis of bilateral fungal keratitis was made, and topical amphotericin B 0.1% was added on an hourly regime in addition to the previous medication. The patient was referred to a corneal specialist for an opinion who in addition, also noted bilateral corneal nerve infiltrates and an immune ring in the right eye. These findings changed the working diagnosis to bilateral acanthamoeba keratitis.

At this point, the topical dexamethasone was stopped and atropine 1% twice daily together with dibromopropamide 0.15% twice daily were added. In the meantime, propamide isethionate, 0.02% chlorhexidine and 0.02% polyhexamethylene biguanide were ordered from abroad as they are



unavailable locally. Corneal scrapings were repeated the next morning with the following being sent for investigation: one scalpel blade plus two fluid samples from the right eye, and two scalpel blades plus one fluid sample from the left (enough material was collected from one fluid sample). The results were positive for *Acanthamoeba polyphaga* in the right eye. No bacteria/fungi were grown.

After waiting for the medication to arrive from abroad (16 days following admission), MB was started on the standard treatment for bilateral acanthamoeba keratitis, i.e. topical 0.02% chlorhexidine and topical 0.02% polyhexamethylene biguanide every two hours and topical 0.1% propamidine isethionate every hour. Atropine and dibromopropamide were still being administered to the patient. An improvement was noted within four days, at which point atropine and dibromopropamide were stopped while topical fluorometholone acetate 0.1%, acyclovir 3% ointment and ciprofloxacin 750mg were prescribed twice daily for both eyes. 21 days after admission, the patient was discharged, with further follow-ups both locally and abroad at the Moorfields Eye Hospital in London.

## Discussion

*Acanthamoeba* species are extremely resistant protozoa<sup>6</sup>, and exist in two forms – the active trophozoite form, and the inactive cystic form. The latter is reported to be resistant even to contact lens solutions, antimicrobials and the majority of anti-amoebals.<sup>7,8</sup>

A breach in the corneal epithelium is not a prerequisite for *Acanthamoeba* infection, however, contact lens-induced changes in the cornea may partly explain how the organism invades the eye.<sup>8,9</sup>

Contamination with *Acanthamoeba* in itself does not cause any discomfort to the contact lens wearer<sup>2,4</sup> however, proteins building up from tear secretions on the surface of the lens act as a culture medium for bacteria<sup>10</sup> and other microorganisms. These microorganisms are then utilized by *Acanthamoeba* for growth. The trophozoites, in favourable conditions,

are liberated from the cysts, and adhere to the contact lens surface.<sup>2,3,11</sup> When wearing the contact lenses, numerous trophozoites and cysts are apposed to the corneal surface, and in the presence of a minor epithelial defect, the amoebae make their way into the anterior stroma of the corneal epithelium.<sup>2,3,11</sup> The parasites then phagocytose and deplete the keratocytes, starting anteriorly then proceeding deeper into the cornea. The devitalized stroma is quickly infiltrated by inflammatory cells followed by stromal necrosis from leukocytic and parasitic collagenolysis.<sup>3,5</sup>


The fact that the patient swam with the contact lenses, only three days before symptoms started, strongly suggests that this might be the main causative factor. MB also claimed that the disinfecting procedure she used with the lenses and cases was not in accordance with the manufacturer's guidelines. In fact MB sometimes missed disinfecting the lenses after use, and instead placed the lenses in their cases after use. Moreover, it cannot be excluded that the patient made use of an expired contact lens solution. These three factors probably made the invasion by *Acanthamoeba* an easier task. The solution used by our patient contained neither isopropyl alcohol nor 3% hydrogen peroxide – two ingredients proved to be very effective disinfectants for soft lenses.<sup>10-13</sup> It is of concern that companies producing contact lens solutions are not required to demonstrate activity against *Acanthamoeba*.

Treatment of bilateral AK is often difficult because of the possibility of long term therapy and toxicity of anti-amoebic medication.<sup>12,13</sup> The time which elapsed from onset of symptoms till starting treatment against AK probably allowed deeper stromal invasion by the organism, making medical therapy more difficult. The fact that specific anti-AK drugs are not readily available in Malta could have played a role in allowing the infection to invade deeper into the cornea.

## Conclusion

It is imperative that any contact lens wearer presenting with the features of

an eye infection should be screened for *Acanthamoeba* keratitis in order to avoid serious complications. Awareness of such a condition must therefore increase among general practitioners, optometrists and ophthalmologists.

Following a strict disinfecting procedure on a regular basis (ideally instructed by an eye specialist), avoiding any water contact with the contact lenses/cases and ensuring the use of proper disinfecting solutions, should allow adequate protection against this sight-threatening condition. Other recommendations of note include the frequent changing of the lens storage cases, avoiding overnight contact lens wear and maintaining strict personal hygiene especially when handling the lenses and cases. 

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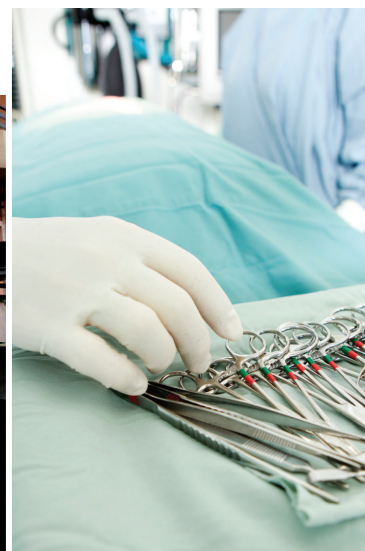
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## Update from the Health Promotion and Disease prevention Directorate

2012 is the European Year of Active Ageing and Solidarity between Generations (EY2012). Active ageing is the process of optimizing opportunities for health, participation and security in order to enhance quality of life as people age. Of all Member States, Malta has the second highest share (21.5%) of persons aged 50 to 64 years as per total population. Moreover Malta has a fertility rate (1.4 per woman) below EU average whilst life expectancy is one of the highest (78 to 80 years). These demographic changes will increase the proportion of elderly persons in our population and hence the need to put active ageing high on the agenda as a sustainable model.

A National Committee was set up within the Ministry for Health, the Elderly and Community Care with the aim of translating the EY2012 aims and objectives in Malta. Keeping in mind the broad scope of the EY2012, the inter-ministerial and multi-stakeholder Committee streamlined the objectives of the year in four main areas:

- Older persons' participation in formal employment;

- Active ageing by means of health (biopsychosocial) literacy and healthy ageing initiatives;
- Older persons' participating in volunteering; and
- Solidarity between generations.

As we get older we have a tendency to slow down. That does not have to mean daytime television and comfort eating. Elderly people can be as fit and healthy as younger people. In order to reach these objectives the elderly have to be motivated to eat healthy, work and exercise. Obviously the latter two objectives have to be carried out in a feasible manner

Exercise is the primary driver for reversing age-related functional decline. There are various types of exercise one can do, including aerobics, which are helpful to maintain and recover the heart/lung/vascular fitness. Weight training is important to start the muscle-building process and hence remain strong. Elderly often suffer from lack of flexibility, bad posture and endurance. Various forms of exercise can help including Yoga, Pilates, and stretching and balance exercises. However, physical activity doesn't necessarily mean joining an exercise class. Gardening, walking to the shops and housework can all count as types of

activity too. Apart from exercise, good nutrition is essential to remain fit and healthy. It is very important that food choices are nutritionally dense, which means one still need to eat a variety of foods to get all the necessary vitamins and minerals, but with fewer calories.

If a person is overweight or obese, it's even more important to be calorie conscious. Advice to restrict fat intake, particularly cutting saturated fat to improve heart health, remains equally true for older people who want to be fit and well. High-fibre cereal foods, fruit and vegetables are important for the prevention of chronic diseases and prevention of constipation which is common in the elderly. Older people should limit foods and drinks that are rich in sugar, as it can impair dental health and contribute to weight gain.

The Health Promotion and Disease Prevention Directorate offers advice to all groups of people including the elderly on healthy food options and physical activity. Apart from the advice, this directorate is also working hard to reverse the obesity epidemic which is also affecting the elderly. As a health care provider you too have a role to play in achieving the aims of the EY2012. §



Walk into a pharmacy and meet the pharmacist, get your pills and walk back out. What about the pharmacist? The one I get to meet for this interview is 29-year-old Gabriel Micallef. I meet him in between his locum hours, curious to find out what his brush with film-making is all about.

# FROM PHARMACY TO FILM

I graduated in 2005 from the University of Malta after the usual studies in pharmacy which included a stint in London as an Erasmus student. After graduating I spent five years working with the Medicines Authority at the Regulatory Affairs Department. However at a certain point in time I moved on to become a community pharmacist doing locum placements and part-time jobs. I am quite enjoying the experience...”

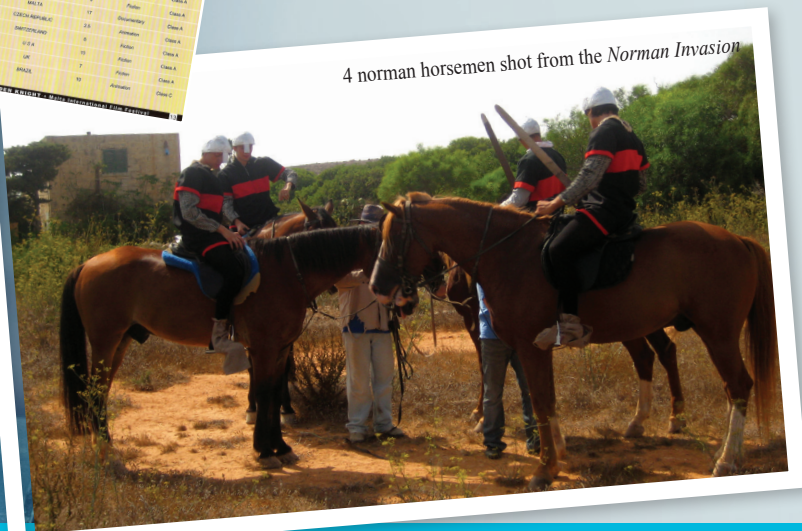
So where does film come in? It actually comes in pretty early on. At age 11 Gabriel had already filmed his first movie. “I ‘borrowed’ my dad’s camera, kidnapped my friends and proceeded to make a movie. It was my first brush with the experience of holding a camera and making things happen from behind the lens. In those days, the camera was pretty rudimentary of course – I could only use the VHS play/record system and my only editing tools were the record/pause buttons on the machine.”

Entry in the Golden Knight Malta International Film Festival of 2009



Golden Knight Malta International Film Festival		DAY 3	
Friday 20th November 2009 - 7:30 pm		09	
CHUCK DAVIS	USA	1	10:00
SPIDER	USA	2	10:30
THE FIGHTER	USA	3	11:00
THE FIGHTER	USA	4	11:30
THE FIGHTER	USA	5	12:00
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THE FIGHTER	USA	10	2:30
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THE FIGHTER	USA	99	11:00
THE FIGHTER	USA	100	11:30

4 norman horsemen shot from the *Norman Invasion*





Ready for action, me and my camera



clips – part one and part two, with each part not being longer than 17 minutes. I figured out that as a viable production, I could always invest in presenting the work as a TV documentary, one out of a series tackling varied epic moments in Maltese history.”

The movie participated in the festival and was subsequently uploaded on YouTube from where it registered 1000+ hits over a relatively short period of time. In the meantime Gabriel had been keeping busy promoting it. “I had shown it to most of the local TV stations and whilst the production was appreciated, I found that there is really very little financial back-up to support young people like myself.”

“The fact that a short film is a low budget film makes it possible for me to produce it with minimal expense knowing that I cannot dream of paying actors, have to use all my own equipment and consume up all of my spare time. At the end, if all extra work is done by myself, by searching for sponsors I can only hope to recuperate costs or at least break-even.”

So why do it? “For the passion of it all. I am inspired by a number of big producers who started out as short film producers and have made it big..... Take Robert Rodriguez whose first film was ‘El Mariachi’. Then there is the great Quentin Tarantino of course. Short films are usually low-budget movies, anyone can make them and will have no famous actors. Producers have to make do with very little, and then of course there are different grades of low-budget movies as well. I like to listen to the directors’ remarks on their films as such comments are always greatly inspiring and provide a window onto all the background work that went into each production.”

As his portfolio grows, Gabriel has taken on a number of short films for local youth communities and the like. In the meantime, he is studying for an MBA, working hard in varied pharmacies and keeping his Iphone handy – “I use it to make a note of every idea that crops up during my day – and working in a pharmacy is a great opportunity to learn more about human nature and human realities. Who knows what my next film will be about ?” Maybe a series about a Pharmacist! S

Still, it worked out well and his friends and himself were pretty satisfied with the outcome. They became overnight stars, at least within their personal circle of family and friends. The young film-maker was soon in business... “I started creating innovative school projects. Film-taking came in pretty handy for this purpose and every time I was assigned a school project, I filmed it all. It certainly attracted attention from the teachers who were used to the normal stuff – scrap books, papers, paintings ... certainly not sit-down movies in class.”

Over the years, as he grew up, Gabriel started refining and honing his skills as well as increasing his equipment according to his budget and savings. “Today I have my own lights, my own equipment. Certainly I don’t have everything, but I have the essential basics which I purchased slowly, carefully and with my humble budget. I have to pay a loan on a house as most people do, so the pay packet can only stretch so far. But I work with what I have and so far have reached milestones which have reaped results.”

In fact, Gabriel Micallef has already participated in a number of short film festivals over the years. The first short film which he submitted was for a local film festival held in 2004. The film was called, ‘You can’t always get what you want.’ Second movie – second film festival – ‘How to change your life in a minute’ and that was in 2005.

His third and latest complete short movie was for the Golden Knight Malta International Film Festival held in 2009. “This time, things were different. By then I had more equipment, such as a semi-professional camera plus increased knowledge of what I wanted to do. So I decided I’d go to a documentary styled film. I am very much into history and decided to tackle one period in time – the Norman invasion of Malta.”

The film was a mega job compared to his previous experiences. With some 16 actors on board, he wrote, filmed, produced and edited the movie himself. “As a docu-drama film it was only hampered by one regulation – its duration. To make it worth its while, I decided to divide it into two short



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# Imaging Groin Hernias

Clinical differentiation of direct inguinal hernias, indirect inguinal hernias, femoral and Spigelian hernias can be difficult particularly with small hernias and in obese patients. Diagnostic imaging can detect and characterize hernias more reliably, allow better surgical planning and possibly even prevent unnecessary surgery. Detection of complications occurring in groin hernias is also of importance. Hernial incarceration is particularly evident on ultrasound (US) performed during rest and abdominal straining (Valsalva maneuver) in both the supine and erect postures. Hernial strangulation is visible both with US and with computed tomography (CT) with fluid appearing around the hernial sac contents.

Detecting and characterizing groin hernias with cross sectional imaging techniques requires an accurate knowledge of regional anatomy and

particularly of the landmarks that can help identify the type of hernia.

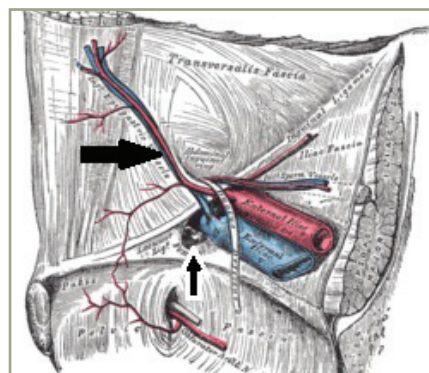
Figure 1 shows a schematic image of the anterior abdominal wall with the locations of four types of groin hernias that are commonly encountered in clinical practice: direct and indirect inguinal hernias, femoral hernias and spigelian hernias. The two important landmarks indicated here are the inferior epigastric artery and the inguinal ligament.

The inferior epigastric artery originates from the external iliac artery within the pelvis and extends superiorly and medially towards the umbilicus coursing deep to the peritoneum that lines the internal aspect of the lower abdominal wall (Figure 2). The second important landmark is the inguinal ligament. The groin can thus be divided into the supra and infra-inguinal compartments and the supra-inguinal compartment is further divided into medial and lateral compartments.

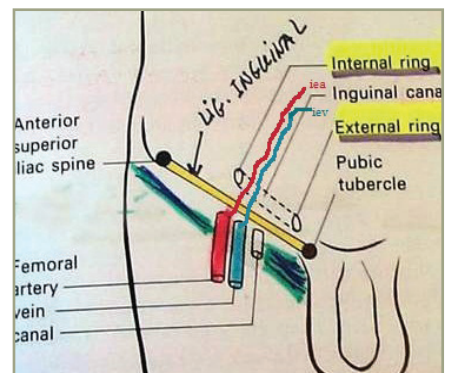
Indirect inguinal hernias pass through the inguinal canal along with the spermatic cord in males or the round ligament in females. They enter through the internal inguinal ring into the inguinal canal and exit through the external inguinal ring (Figure 3). The internal inguinal ring lies lateral to the inferior epigastric artery, so an indirect inguinal hernia enters the abdominal wall lateral to the said artery and courses medially anterior to it. US and CT can visualize the inferior epigastric artery and also the neck of the hernial sac (Figures 4 & 5) lying lateral and then anterior to the said artery. Indirect inguinal hernias are five times more common than direct hernias. In boys, indirect inguinal hernias are the result of a congenital defect of a patent processus vaginalis. In adults, they are acquired due to weakness and dilatation of the internal inguinal ring.



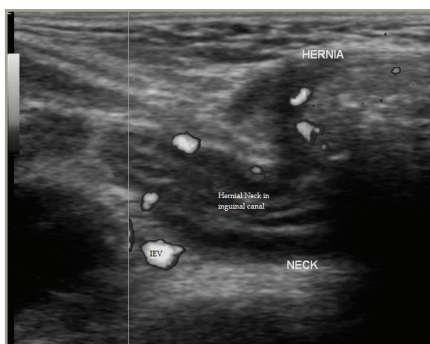
**Figure 1.** Anatomic location of various groin / lower anterior abdominal wall hernias. Red line in right lower quadrant indicates inferior epigastric artery. S = spigelian hernia; I = indirect inguinal hernia; D = direct inguinal hernia; F = femoral hernia.



**Figure 2.** Gray's diagram showing internal view of lower abdominal wall with inferior epigastric artery (large arrow) and femoral canal (small arrow).



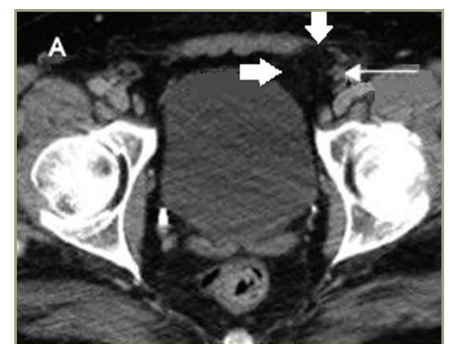
**Figure 3.** Drawing showing locations of the inguinal rings, the inguinal canal (passing in front of the inferior epigastric vessels) and the femoral canal.



**Figure 4.** US of indirect inguinal hernia with the neck of the hernia in the inguinal canal passing anterior to the inferior epigastric vein (iev) from lateral to medial.



**Figure 5.** CT of indirect inguinal hernia (white arrows) located lateral to the inferior epigastric vessels (black arrows).



**Figure 6.** CT of direct inguinal hernia (larger arrows) located medial to the inferior epigastric vessels (smaller arrow).



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#### Eucreas® (vildagliptin/metformin hydrochloride) film-coated tablets

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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 < 30 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. **WARNINGS / PRECAUTIONS:** 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 reinstated until 48 hours afterwards and only after renal function has been re-evaluated and found to be normal. 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), amiodipine, 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, abnormal liver function tests, hepatic dysfunction (including hepatitis) have been reported with vildagliptin. **Vildagliptin Monotherapy:** Common (>1/100 to <1/10): dizziness, Uncommon (>1/1,000 to <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. Frequency not known: urticaria, pancreatitis. For a full list of Adverse reactions, please refer to the SmPC. **LEGAL CATEGORY:** POM. **PACK SIZES:** 30, 60 film-coated tablets. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **MARKETING AUTHORISATION NUMBER:** EU/1/07/425/002-003, EU/1/07/425/008-009. Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available upon request from: Novartis Pharma Services Inc, Representative Office Malta, P.O. Box 124, Valletta VLT 1000, Malta. Tel +356 22983217 - 2011-MT- EUC-07 Dec-2011



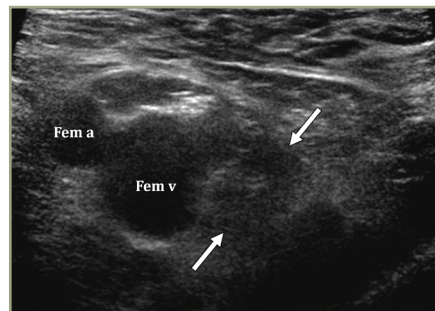
A direct inguinal hernia emerges medial to the inferior epigastric artery passing directly through the posterior wall of the inguinal canal into the external inguinal ring. Weakness of the posterior wall in the inguinal canal may be congenital or acquired, in the latter case due to excessive abdominal wall strain. Both US and CT can identify the inferior epigastric artery (Figure 6) as well as the orientation of the neck of the hernia sac relative to the inguinal ligament. Valsalva maneuver performed during US or CT will help identify spontaneously reducing inguinal hernias that are commonly bilateral (Figure 7).



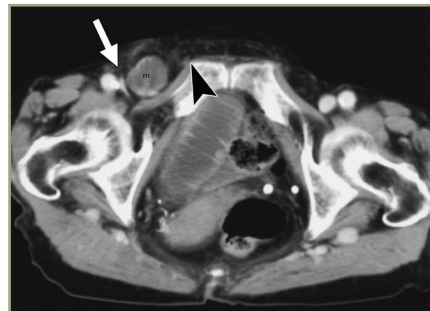
**Figure 7.** CT with Valsalva (abdominal straining) better shows bilateral direct inguinal hernias (arrows).

Femoral hernias exit below the inguinal ligament and protrude through the femoral ring medial to the femoral vein and artery in the femoral canal; they lie medial to the common femoral vein which they often compress (Figures 8 & 9). Femoral hernias are relatively uncommon, with a prevalence less than one-tenth that of inguinal hernias. They have a female predominance of 4:1, which is thought to be secondary to dilatation of the femoral ring connective tissues due to the hormonal and physical changes of pregnancy. For unclear reasons, femoral hernias are twice more common on the right than on the left.

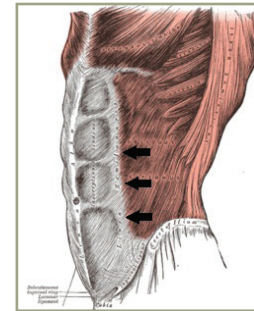
Spigelian hernias are distinct from inguinal and femoral hernias in that they are not related to the inguinal canal or the inguinal ligament. However their relative proximity to the aforementioned hernias and their relative frequency particularly in the young sportive population makes them worth mentioning here. Spigelian hernias occur through a slit-like defect in the anterior abdominal wall adjacent to the semilunar line (Figure 10) that runs along the lateral margin of the rectus



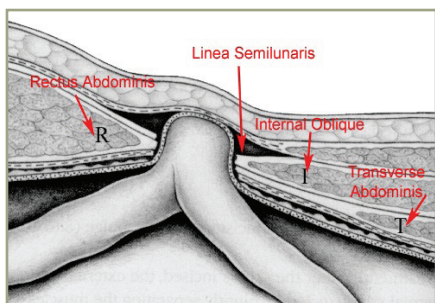
**Figure 8.** US of a femoral hernia (arrows) located medial to the femoral vein.



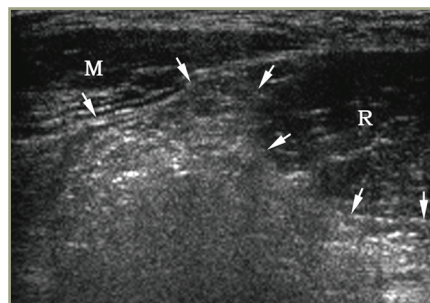
**Figure 9.** CT shows a femoral hernia located medial to the compressed femoral vein (white arrow) and lateral to pubic tubercle (arrowhead).



**Figure 10.** Gray's diagram showing the semilunar line (arrows).



**Figure 11.** Defect in the transversus aponeurosis that connects the rectus muscle sheath medially with the three-layered lateral abdominal wall muscles (internal and external oblique and transversus abdominis muscles).



**Figure 12.** US of Spigelian hernia (arrows) seen in relation to the rectus muscle (R) and the lateral abdominal wall muscles (M).



**Figure 13.** CT of right Spigelian hernia containing bowel (arrow) lateral to the semilunar line (arrowhead).

abdominis muscle. Most spigelian hernias occur in the lower abdomen where the posterior sheath of the rectus abdominis is deficient. The hernia ring is a well-defined defect in the transversus aponeurosis (Figure 11). Both US (Figure 12) and CT (Figure 13) are capable of visualizing spigelian hernias, establishing their contents and detecting complications.

Hernias could contain virtually any organ or tissue found in the lower abdomen. These may include but are not limited to fat, small or large bowel, a portion of the bowel wall (Richter hernia), omentum, incarcerated appendix (Amyand hernia), bladder, Meckel diverticulum (Littre hernia), and gonads. Femoral hernias are the most likely to strangulate, whereas direct inguinal hernias are the least likely to complicate. Other complications include intestinal obstruction, incarceration, volvulus, perforation, appendicitis or diverticulitis, and tumors that may be found incidentally in the hernia.

CT and US are useful for detecting all the above hernias and their complications to allow timely surgical planning. S

# Procoralan<sup>®</sup>

1 Tablet in the morning + 1 Tablet in the evening



Approved by the  
European Medicines  
Agency for use in  
heart failure



European Medicines Agency Press release EMA/CHMP/196375/2011 - [http://www.ema.europa.eu/ema/index.jsp?curl=pages/home/Home\\_Page.jsp&mid](http://www.ema.europa.eu/ema/index.jsp?curl=pages/home/Home_Page.jsp&mid)

**Presentation and composition:** Procoralan 5 mg: film-coated, scored tablet containing 5 mg ivabradine; Procoralan 7.5 mg film-coated tablet containing 7.5 mg ivabradine. **Therapeutic indication: Treatment of coronary artery disease:** Symptomatic treatment of chronic stable angina pectoris in coronary artery disease adults with normal sinus rhythm. Ivabradine is indicated : in adults unable to tolerate or with a contra-indication to the use of beta-blockers or in combination with beta-blockers in patients inadequately controlled with an optimal beta-blocker dose and whose heart rate is > 60 bpm. **Treatment of chronic heart failure:** Ivabradine is indicated in chronic heart failure NYHA II to IV class with systolic dysfunction, in patients in sinus rhythm and whose heart rate is  $\geq$  75 bpm, in combination with standard therapy including beta-blocker therapy or when beta-blocker therapy is contraindicated or not tolerated. **Dosage and administration: Treatment of coronary artery disease:** The usual recommended starting dose of ivabradine is 5 mg twice daily. After three to four weeks of treatment, the dose may be increased to 7.5 mg twice daily depending on the therapeutic response. If, during treatment, heart rate decreases persistently below 50 beats per minute (bpm) at rest or the patient experiences symptoms related to bradycardia such as dizziness, fatigue or hypotension, the dose must be titrated downward including the possible dose of 2.5 mg twice daily (one half 5 mg tablet twice daily). Treatment must be discontinued if heart rate below 50 bpm or symptoms of bradycardia persist. **Treatment of chronic heart failure:** The treatment has to be initiated only in patient with stable heart failure. It is recommended that the treating physician should be experienced in the management of chronic heart failure. The usual recommended starting dose of ivabradine is 5 mg twice daily. After two weeks of treatment, the dose can be increased to 7.5 mg twice daily if resting heart rate is persistently above 60 bpm or decreased to 2.5 mg twice daily (one half 5 mg tablet twice daily) if resting heart rate is persistently below 50 bpm or in case of symptoms related to bradycardia such as dizziness, fatigue or hypotension. If heart rate is between 50 and 60 bpm, the dose of 5 mg twice daily should be maintained. If during treatment, heart rate decreases persistently below 50 beats per minute (bpm) at rest or the patient experiences symptoms related to bradycardia, the dose must be titrated downward to the next lower dose in patients receiving 7.5 mg twice daily or 5 mg twice daily. If heart rate increases persistently above 60 beats per minute at rest, the dose can be up titrated to the next upper dose in patients receiving 2.5 mg twice daily or 5 mg twice daily. **Properties:** Procoralan is a pure heart rate-lowering agent, acting by selective inhibition of the cardiac pacemaker if current that controls spontaneous depolarization in the sinus node and regulates heart rate. Procoralan dose-dependently reduces heart rate, and provides a significant anti-ischemic and antianginal efficacy. Procoralan on top of optimal background therapy (including Beta-Blockers) provides additional efficacy on all exercise tolerance test (ETT) parameters at the trough of drug activity. And in patients with limiting angina, Procoralan reduces the risk of having heart attack and getting hospitalized for acute MI or heart failure. **Contraindications:** Hypersensitivity to Procoralan, resting heart rate below 60 bpm prior to treatment, cardiogenic shock, acute myocardial infarction, severe hypotension, sinoatrial block, third-degree AV block, severe heart failure (NYHA class III-IV), severe hepatic insufficiency, pregnancy and lactation, coadministration with strong CYP 3A4 inhibitor. **Interactions:** Combination with heart rate-reducing agents, combination with QT-prolonging medicinal products, CYP 3A4 inhibitors. **Precautions:** Use with caution in patients with severe renal insufficiency (Creatinine clearance  $<$ 15 mL/min), use with caution in patients with second-degree AV-block, with cardiac arrhythmias, or stroke. **Side effects:** Phosphenes, bradycardia, ventricular extrasystoles, headache. **Presentation:** Pack of 56 tablets of Procoralan 5 mg, Pack of 56 tablets of Procoralan 7.5 mg. Please refer to the complete summary of product characteristics. **LES LABORATOIRES SERVIER France. MAH: SERVIER INTERNATIONAL: 50, rue Carnot – 92284 Suresnes Cedex – France.**