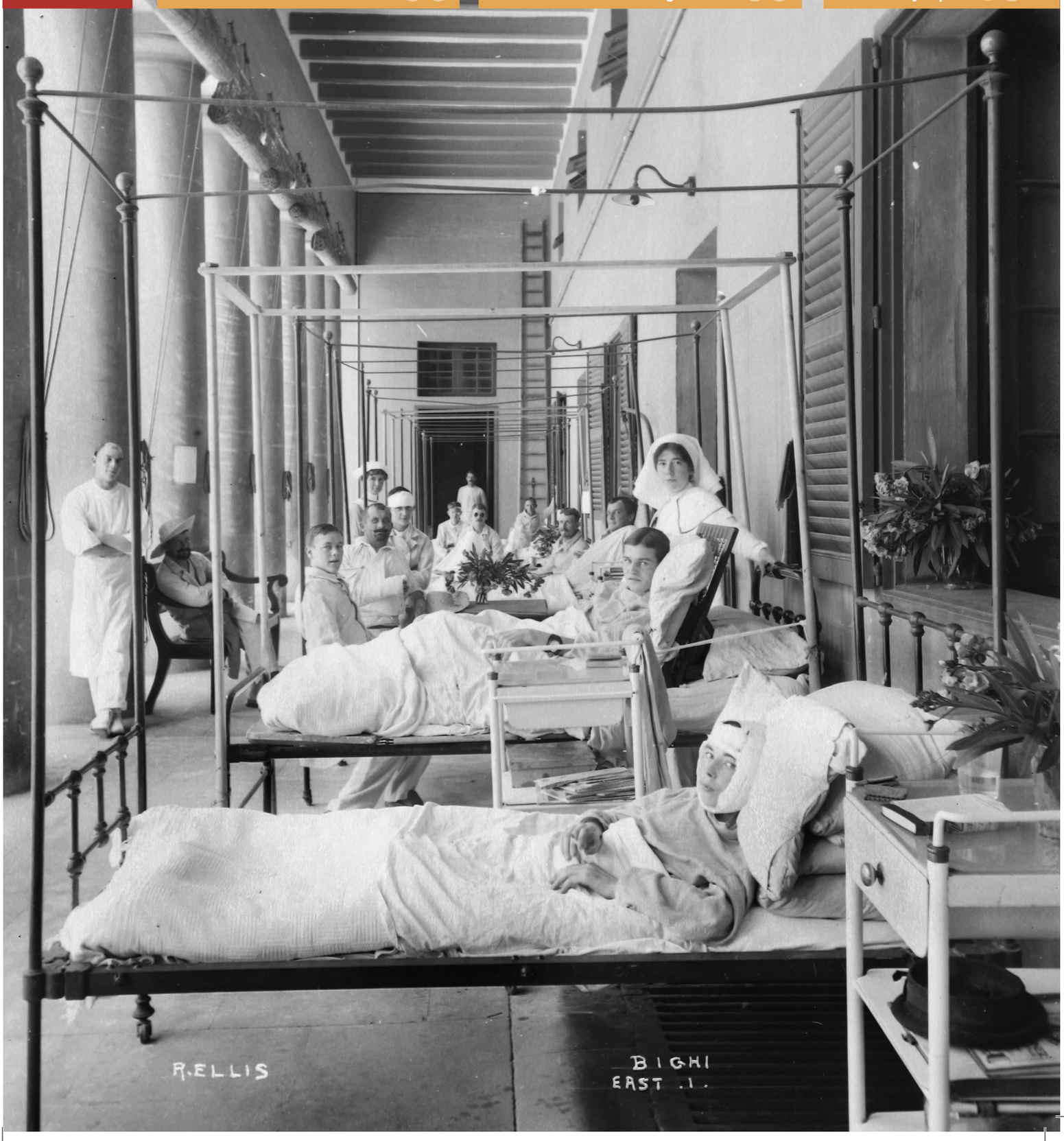
NEWSPAPERPOST

TheSynapse

The Medical Professionals' Network

Issue 02/12



Lipanthyl® 145mg: white, film-coated tablets. **Indication:** in patients who fail to respond to diet and other non-drug therapeutic measures. Secondary hyperproteinaemias (e.g. dyslipidaemia in diabetes mellitus). **Dosage:** The recommended dose is one tablet containing 145mg fenofibrate taken once daily. *Renal-Impairment:* reduce the dose. **Contra-indications:** Hepatic insufficiency, renal insufficiency, hypersensitivity to fenofibrate or any component of this medication, known photoallergy or phototoxic reaction during treatments with fibrates or ketoprofen, gallbladder disease, in children, chronic or acute pancreatitis, (except acute pancreatitis due to severe hypertriglyceridaemia), patients hypersensitive to sucrose, peanut or arachis oil or soya lecithin or related products. **Special warnings and precautions for use:** Secondary cause of hypercholesterolaemia, for hyperlipidaemic patients taking estrogens or contraceptives containing oestrogens it should be ascertained whether the hyperlipidaemia is of primary or secondary nature. *Liver function:* as with other lipid lowering agents, increases have been reported in transaminase levels in some patients; discontinue if ASAT and ALAT levels increase to >3 times the upper limit of normal range or 100 IU. *Pancreatitis:* pancreatitis has been reported in patients taking fenofibrate. *Muscle:* Muscle toxicity, including very rare cases of rhabdomyolysis, has been reported with administration of fibrates and other lipid-lowering agents. The risk of muscle toxicity may be increased if the drug is administered with another fibrate or an HMG-CoA reductase inhibitor (statins), especially in cases of pre-existing muscular disease. *Renal function:* Treatment should be interrupted in case of an increase in creatinine levels > 50% and ULN (upper limit of normal). This medicinal product contains lactose, therefore patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. This medicinal product contains sucrose, therefore patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or Sucrose-isomaltase insufficiency should not take this medicine. Lipanthyl® 145mg should not be taken in patients allergic to soya lecithin or related products due to the risk of hypersensitivity reactions. **Interactions:** Oral anticoagulants: Fenofibrate enhances oral anticoagulant effect and may increase risk of bleeding. Cyclosporin: Some severe cases of reversible renal function impairment have been reported during concomitant administration of fenofibrate and cyclosporin. HMG-CoA reductase inhibitors and other fibrates: The risk of serious muscle toxicity is increased if a fibrate is used concomitantly with statins or other fibrates. Cytochrome p450 enzymes: In vitro studies using human liver microsomes indicate that fenofibrate is not an inhibitor of cytochrome (CYP) P450 isoforms CYP3A4, CYP2D6, CYP2E1, or CYP1A2. They are weak inhibitors of CYP2C19 and CYP24A6, and mild to moderate inhibitors of CYP2C9 at therapeutic concentrations. **Pregnancy and lactation:** There are no adequate data from the use of fenofibrate in pregnant women. Animal studies have not demonstrated any teratogenic effects. Embryotoxic effects have been shown at doses in the range of maternal toxicity. This medicinal product should be used during pregnancy after a careful benefit/risk assessment. This medicinal product should not be used in nursing mother. **Undesirable effects:** Abdominal pain, nausea, vomiting, diarrhoea, flatulence,moderately elevated levels of serum transaminases. Pancreatitis, gallstones, rashes, pruritus, urticarial or photosensitivity reactions, serum creatinine and urea increases. Thromboembolism (pulmonary embolism, DVT). Alopecia, diffuse myalgia, myositis, muscular cramps, weakness, decrease in haemoglobin and leukocytes, sexual asthenia, headache. Episodes of hepatitis, cutaneous photosensitivity (with erythema, vesiculation or nodulation or exposed skin), rhabdomyolysis, interstitial pneumopathies. **Overdose:**No cases of overdoses have been reported. No specific antedote is known. Instruction for use/handling:None. MA Holder:Laboratoires Fournier SA MA Number: AA166/00101

A New Dawn

After months of long hard work and planning we have recently launched a new version of TheSynapse Portal (www.thesynapse.net). Although the changeover happened in just one eventful afternoon, the process is still ongoing and we are still fine tuning the system. Although most comments were highly encouraging, a tiny minority expressed scepticism to the need for such a change, given the already high standard of the service. After all, change is always a challenge, is never smooth and is always expensive...so why bother?

We bother because TheSynapse is deeply committed to provide members of all the medical professions with the news, services and resources they need to provide the best possible service to the most important member of the team ... the patient.

Like the older version, which is still available in its old form for those who wish to see how it looked back then, TheSynapse features news from most authoritative and reliable sources, as soon as they are released.

eLearning is another important facet for TheSynapse and we are indeed very proud to have recently launched another eLearning module in collaboration with the Malta Foundation Programme. This module is entitled 'Informed Consent to Medical Care'. It fills us with further enthusiasm to have another three eLearning modules in progress and awaiting launch this year. We encourage you to participate. You will find it an interesting experience and we promise to provide you with all the support we can offer. We are also open to your ideas in the field of eLearning development.

TheSynapse Events section serves as a list of conferences and other events which have medical professionals as a target audience. For event organisers this section will not only serve as a promotional platform, but from a logistic perspective it will obviously help organisers avoid organising events on the same date. For our members, this should provide a quick reference, one stop area for members. We invite organisers to list their forthcoming events and promote via TheSynapse.

A new addition has been TS ADS which give you the opportunity to basically advertise any product or service to other users. There are many possibilities how one can make use of the service including but not limited to the availability or the need for locum services. The possibilities are, in reality, endless. This service is not necessarily a giant step in terms of innovation as such but it encourages members to interact between themselves on TheSynapse platform. Indeed it has always been the aim of TheSynapse to act as a network for medical professionals and this was way before the advent of social networks.

Writing about user interaction I cannot fail to mention Share IT section. Members can share interesting medical links, videos and images. In the section you can also find a whole archive of articles from TheSynapse magazine and an archive of all articles and news published in TheSynapse website from many years back. This will be useful for those members who regularly use TheSynapse services for their research purposes.

Other services are being introduced which facilitate further interaction and networking - these will be rolled out in the coming months. These will include a forum, and a social networking section.

Love it or hate it, social networking is with us and dominates a substantial part of our lives. Each article of TheSynapse now has a 'share' button which members can use to share interesting articles to their social networking profile.

Undoubtedly, two of the most important services provided by TheSynapse are the eNews which is published every Saturday and painstakingly gives a synopsis of all news published during the week, and the equally informative TheSynapse eInfo which are sent out on a regular basis.

For those who have not visited TheSynapse for some time, I would like to invite you to explore the network. For those who have yet to join, you are most welcome – your free registration is just a couple of clicks away.

For the past fifteen years TheSynapse has been in a process of regular development and several transformations. We are never happy enough with the status quo and will continue to develop services that are useful to our members. This is the beginning of a new dawn.

Ian Ellul

GALVUS and EUCREAS

COMPREHENSIVE POWER TO ADVANCE TYPE 2 DIABETES TREATMENT

GALVUS is a DPP-4 inhibitor that improves glycemic control through powerful islet enhancement[1]

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

Galvus® 50mg (vildagliptin) tablets

PRESENTATION: Each tablet contains 50 mg of vildagliptin **INDICATIONS:** For the treatment of type 2 diabetes mellitus: As monotherapy ♦ in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. 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:** When used as monotherapy or in combination with metformin or thiazolidinedione the recommended daily dose of vildagliptin is 100mg, 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. Galvus is not recommended for use in patients less than 18 years old. The recommended dose for patients with moderate/severe renal impairment is 50mg once daily. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients **WARNINGS / PRECAUTIONS:** ♦ 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. ♦ There is no experience of vildagliptin use in clinical trials in patients with NYHA functional class III-IV and therefore use is not recommended in these patients. 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. Galvus should not be administered during pregnancy or lactation. ♦ Should be used with caution in patients with renal impairment. **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, abnormal liver function tests, hepatic dysfunction (including hepatitis). *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. *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. Frequency not known: urticaria, pancreatitis **LEGAL CATEGORY:** POM PACK SIZES: 7, 28 tablets **MARKETING AUTHORISATION** HOLDER: Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **MARKETING AUTHORISATION NUMBERS:** EU/1/07/414/001, 003. **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. 2012-MT- GAL-03-Feb- 2012

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

PRESENTATION: 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:** 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 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 **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. LFTs 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.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) angiodema,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

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NOVARTIS

Galvus® vildagliptin

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

Eucreas® vildagliptin/metformin

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CLASSIFIED

TheSynapse is now accepting classified adverts from members.
Adverts may for example include locum availabilities, job searches or items for sale. If you are interested please send an email to mpl@thesynapse.net or contact 2145 3973 for more details

ERRATA CORRIGE

• With reference to the article by Dr David Grech published in Issue 1/12 of TheSynapse Magazine, published under the title of 'Hypertonic Saline Irrigation in the management of allergic rhinitis and chronic sinusitis', it was erroneously featured under the heading of Advertorial instead of Review article. We apologise for this genuinely unintentional misprint.
• With reference to the article by Dr Pierre Vassallo published in Issue 5/11 of TheSynapse Magazine, published under the title of ' Imaging Right Iliac Fossa (RIF) Pain', the images erroneously featured wrong legends. A correct version is available on www.thesynapse.net. We apologise for this genuinely unintentional misprint.

contents

COVER:
Patients in an open-air corridor at Bighi Hospital

Patients, some with bandaged heads resulting from wounds received in World War 1, are seen convalescing under one of the colonnades. Hospital staff are also seen posing with them. The sunshades above the collonnades are rolled up. During World War 1, Malta was nicknamed the Nurse of the Mediterranean. Some 2,000 officers and 55,000 men wounded in the Dardanelles and Salonika campaigns on the Gallipoli Front, were treated in the island. Bighi Hospital accommodated a very large number of them but medical centres and camps were set up all over Malta. Ghajn Tuffieha, for instance, had 3,000 beds for ranks while beds for officers were provided at the Dragonara and Verdala Palace.

Photography: Richard Ellis

Published by Medical Portals Ltd.
The Professional Services Centre
Guzi Cutajar Street
Dingli, Malta
Email: editor@thesynapse.net
Web: www.thesynapse.net

Editor: Wilfred Galea
Scientific Editor: Ian C Ellul
Administration Manager: Carmen Cachia

Production: Outlook Coop
Printing: Europrint Ltd

'You are barren and have borne no children, but you shall conceive and bear a son' -

VICTOR GRECH
CLARE THAKE-VASSALLO
IVAN CALLUS

Fertility in prehistory, history and contemporary culture - Part II

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

The tendency for cultural scripts to underplay fostering and adoption, thus avoiding any of the above hazards, is also pointed out, along with the legal issues that arise out of infertility treatments, such as the problematisation of what constitutes a natural parent in the setting of egg and sperm donation, surrogate motherhood and same gender families, a notion prefigured in Piercy's famous novel *Woman on the Edge of Time* (1976).[19] The legal controls and punishments inflicted by the state in the setting of mothers who abuse alcohol or recreational drugs that may result in teratogenic effects on the unborn child are also elucidated, along with the impunity which males are afforded despite being partly or totally responsible for the environment that promotes such abuse, and often supplying these substances.[20] Interestingly, little is made of male problems leading to infertility, although this still results in the female bearing the brunt of invasive and potentially hazardous treatments in order to bear her chosen partner's children.

Impotence has also been the target of writers, and for example McLaren's *Impotence: A Cultural History* (2007) guides readers through 2,500 years of impotence and attempted cures in various cultures, cures which are as varied as they are bizarre, including urinating through a church keyhole, whipping, flagellation, electric shocks to the testicles, and countless modern gadgets and drugs that may be bought over the Internet.[21]

Infertility in non-Western cultures has also been extensively addressed by Michie and Cahn, including the more extreme modulations of the impact of infertility in overtly patriarchal cultures on women, who seek help not only from Western medicine, but also from indigenous practitioners of traditional medicine, sometimes simultaneously, to their detriment.[22] More specifically, for example, Bharadwaj argues that the rapid transfer and assimilation of infertility treatments to India is only part of the indigenization of Western technoscience and biomedicine in India, and contends that the success or failure of said techniques, when framed by the Hindu faith, becomes 'a powerful critique of the incompleteness of the "Western" science of conception'.[23]

Conversely, Kahn discusses the ways in which orthodox Jews

Internet has become a key source of all sorts of medical information (including that regarding pregnancy and infertility) but must be viewed with extreme caution

use traditional strategies and new media, such as the Internet, to cope with infertility in the presence of new reproductive technologies by establishing networks that provide support, information and education, along with unique frameworks that permit close collaborations between rabbis, doctors and other clinic personnel. These ensure that fertility treatments are conducted with strict attention to Jewish legal concerns, particularly with regard to incest, adultery, and traditional practices regarding bodily emissions, becoming 'a set of tools and strategies that can be readily appropriated and harnessed to a particular set of individual and collective goals'.[24]

At this juncture, it must be pointed out that the Internet has become a key source of all sorts of medical information (including that regarding pregnancy and infertility) but must be viewed with extreme caution, as shown by Okamura, who reviewed 197 infertility-related websites using the *Journal of the American Medical Association* minimal core standards for responsible print. Only 2% of these websites met all four recommended standards, and the authors naively concluded that women's health clinicians should assume the new responsibility of information monitor, an unlikely prospect when one considers the rate with which new websites mushroom all over the web.[25]

This paper will now briefly review some fictional works that deal with infertility, and it is intriguing to note from the outset that most narratives also deal with the aforementioned middle-class stereotype, implying a normative progression of heterosexual marriage, fertility, pregnancy and childbirth, unlike Science Fiction, which, as we shall see, perhaps due to its multicultural and intertextual nature, deals with infertility in much more diverse scenarios, such as infertility in aliens and in inhuman creations.

It appears that the first fictional narratives to foreground centrally the treatment of infertility are P. D. James's, *An Unsuitable Job for a Woman* (1972)[26] and Barbara Vine's, *A Dark Adapted Eye* (1986),[27] and both deal with an infertile woman and surrogate motherhood.

More specifically, Mary Higgins Clark's, *The Cradle Will Fall* (1980)[28] and *I'll Be Seeing You* (1993),[29] both deal with the idiom of misplacement, the covert and illicit transfer of ova from the body of one woman to another, with resultant confusion in the identity of the offspring. Both narratives involve parents who recognise other parents' children as their own solely by visual resemblance, with the first story also involving a doctor who heads a fertility clinic and kills to keep secret the fact that he transferred aborted but still living embryos whose abortion he coerced, harking back yet again to the mad/criminal fraudster scientist. In more populist vein, Danielle Steel's, *Mixed Blessings* (1992) narrates the events that overcome five infertile characters, one of which undergoes fertility treatment, miscarries, and in an even more normative ending becomes pregnant with twins, without any medical intervention, despite being well past forty years of age.[30]

In conclusion, overall, current Western texts that deal with infertility, both factual and fictional, uphold a rhetoric that promotes the middle-class progression of heterosexual relations, marriage, fertility, pregnancy and childbirth, and fail to account for more liberal attitudes, such as same-sex couples – or even more extraordinary phenomena, since ...

'[n]ew reproductive technologies have split apart categories that were previously coterminous - birth mother, psychological mother, familial father, sperm donor, egg donor, and so forth - transforming the relations of kinship that used to play such a fundamental role in the rhetorics and practices of identity formation.'[31]

Moreover, many medical options, while seemingly science fictional (and several of these advances were actually prefigured by science fiction) are now considered routine in the field of advanced reproductive techniques, which has come a long way from the first test tube baby in 1978,[32] to the extent that Chris Hables Gray opines:

'In the future, many different sexes are likely to be produced, driven by desire (to create and live) and fear (of death and sterility) […]. Cyborgism could well be a bridge to different types of posthumans, some with male bodies, others clearly female, others yet who are hermaphrodites, and still more people who will be quite genderless. And there will be new sexes.'[33]

Conventional stances will undoubtedly stumble when confronted by circumstances that do not conform to formulaic and stereotypical viewpoints. Conversely, it behoves the scientists to exercise extreme caution in this modern age, where ongoing work in genetic engineering, biochemistry, eugenics and advance reproductive techniques have given us the opportunity to manipulate life at a fundamental level, 'something previously exclusively reserved to nature and chance.'[34] S

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ABRIDGED PRESCRIBING INFORMATION: AVAMYS

Please refer to Summary of Product Characteristics before prescribing

PHARMACEUTICAL FORM: Nasal spray suspension; each spray actuation delivers 27.5 micrograms of fluticasone furoate. **INDICATIONS:** Treatment of the symptoms of allergic rhinitis **DOSAGE AND METHOD OF USE:** For administration by the intranasal route only. Duration of treatment should be restricted to the period that corresponds to allergenic exposure. **Adults and adolescents (12 years and over):** two spray actuations in each nostril once daily. **Children (6-11 years of age):** one spray actuation in each nostril once daily; dose may be doubled if no adequate response is achieved. **Maintenance:** Reduce to one spray actuation in each nostril once adequate control of symptoms is achieved. **CONTRAINDICATIONS:** Hypersensitivity to any of the active substance or to any of the exipients. **PRECAUTIONS:** severe liver disease; concomitant administration with ritonavir; higher than recommended doses may result in clinically significant adrenal suppression; use lowest dose possible to achieve effective control of rhinitis. Monitor regularly the height of children receiving prolonged treatment; if impairment of adrenal function is suspected care must be taken when transferring patients from systemic steroids to fluticasone furoate. Close monitoring is warranted in patients with a change in vision or with a history of increased intraocular pressure, glaucoma and/or cataracts. **DRUG INTERACTIONS**: Administration with ritonavir is not recommended as it may increase systemic exposure of fluticasone furoate. **ADVERSE EVENTS**: *Very common:* epistaxis. *Common:* nasal ulceration. *Rare:* Hypersensitivity reactions including anaphylaxis, angioedema, rash and urticaria. Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged perioids. **PREGNANCY AND LACTATION:** consider only if the expected benefits to the mother outweigh the potential risks to foetus or child. **PRESENTATION:** Available in one pack size: 120 sprays. **LEGAL CATEGORY:** POM. **MA HOLDER:** Glaxo Group Ltd., UK. **MA NUMBER:** EU/1/07/434/001-3.

For further information and full prescribing information contact GlaxoSmithKline (Malta) Ltd. Tel: 21 238 131

Date of revision of text: December 2010

MT/11-024/AVA

Pediatric Bipolar disorder, in Malta is it under-diagnosed?

Abigail Cassar Parnis
Nigel Camilleri
Anthony Zahra
Joseph Cassar

Key Words

Pediatric, Bipolar disorder, Under-diagnosed, Malta

Abstract

The objective of this retrospective study was to determine the frequency of Bipolar Disorder in children and adolescents referred to the Child Guidance Clinic (CGC), St. Luke's Hospital, Malta, over a year. Diagnostic criteria were analyzed and compared to current literature.

Of 141 children, none were diagnosed with Bipolar Disorder. Further awareness of clinicians is advised, to identify Bipolar Disorder, thus limiting its long term morbidity and mortality.

Introduction

Pediatric bipolar disorder (BD) is a disorder of affective regulation; it is a serious mental illness with significant morbidity and mortality. BD is a chronic relapsing remitting mental disorder, which has a profound impact on morbidity and mortality.[1] BD is ranked 7th of the world-wide causes of non-fatal disease burden.[2]

Most studies indicate that the onset of BD is frequently between ages 15-30 years. Recently it has been reported that BD starts before the age of 10, though this is rare, it does occur.[3] The prevalence of BD is estimated at 0.1 to 2% among adolescents.[4] The rate of bipolar affective disorder 1 (episodes of mania and depression) and bipolar affective disorder 2 (episodes of hypomania and depression), in adolescents is around 0.99% whereas using the wider BD spectrum classification (and BD NOS), studies report prevalence rates of up to 3%.[5]

Bipolar symptoms in young children mimic those in adulthood but with minor differences.[6] These children most commonly present with symptoms such as irritability, depression, impulsivity, out-of-control behavior, delinquent behavior, inappropriately happy mood, constantly on the move, lack of judgment and inflated self-esteem, delusions of grandeur, rapid and pressured speech, flight of ideas, suicidal ideation and behavior.[7] The symptoms that were more prevalent in preschool children include irritability / dyscontrol, temper tantrums, poor frustration tolerance, impulsivity, increased aggression, decreased attention span, and hyperactivity.[8] Symptoms similar to adult presentations of depression, mania and psychosis were more prevalent in children with a bipolar diagnosis at a later age (7-12 years).[8] Patients with childhood-onset bipolar disorder (before 12 years of age) were more frequently males and had a more frequent co-morbidity with attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD) when compared to adolescent-onset bipolar disorder.[9] Patients with BD-NOS had an earlier age at onset and had frequent co-morbidities such as ADHD and ODD. These follow a chronic rather than an episodic course.[10]

Longitudinal studies suggest that pre-pubertal BD may be more difficult to treat than later onset BD.[11]

Evidence suggests BD is often co-morbid to ADHD, conduct disorder, ODD, anxiety disorders, including obsessive-compulsive disorder and generalized anxiety disorders, substance and alcohol abuse and personality disorders.[11,12]

Effective pharmacotherapy and management are critical in order to minimize relapses and long term disability, morbidity and mortality.[12] Delays in initiation of mood stabilizers, confers an elevated risk for suicidal behavior, poor social adjustment and more hospitalizations. Greater surveillance screening for bipolar illness may help to diminish these adverse outcomes.[4]

The objective of this study was to determine the frequency of BD in children and adolescents referred to the Child Guidance Clinic (CGC) St Luke's Hospital Malta, over a period of a year. The frequency of bipolar affective disorder locally was compared to that reported in the literature. Diagnostic criteria used in Malta, were also compared to those used in other centers abroad.

Of 141 children, none were diagnosed with Bipolar Disorder. Further awareness of clinicians is advised, to identify Bipolar Disorder, thus limiting its long term morbidity and mortality

Method

This retrospective study included all children referred to the Child Guidance Clinic (CGC) at St. Luke's Hospital Malta, over a year from January to December 2007. Inclusion criteria were: first visit to CGC, and patient ages from 8 to16 years (both ages included). Exclusion criteria were a working diagnosis of autism spectrum disorders or mental retardation. Children attending Child Guidance Clinics in Gozo were not included in the study. Children reviewed in the private sector were not included in this study as data was not readily available, although the authors did speak to the relevant consultant psychiatrists and confirmed that no diagnosis of BD was made. The authors are also confident that if a diagnosis of BD 1 was made then admission to hospital for management of the patient would have been required and therefore he would have been referred through the public service route and then picked up as one of the cases at CGC.

Approval to carry out the study was obtained from the head of psychiatry at Mount Carmel Hospital. This study was also registered and approved by the merit award scheme. Data was collected

restrospectively through the case notes and recorded in an anonymous way, the information collected did not influence the management outcome the young person received at CGC.

Data collection was carried out six months after the end of the study period that was, May to June 2008. Case notes were reviewed, and the working diagnosis made by the multidisciplinary team at the CGC, in accordance to the multi-axial system used for children and adolescents, in the International classification of mental and behavioral disorders (WHO 1994), was recorded. This classification is divided in six axes describing: psychiatric disorder, delays in psychological development, intellectual level, medical conditions, psychosocial adversity and adaptive functioning. The most recently allocated working diagnosis was the one we recorded. Special note was taken to pick up any reference or formal diagnosis of BD in the case notes. Also response to treatment was recorded in accordance with the last entry in the file when reviewed by a member of the multidisciplinary team. Treatment resistance by the children and adolescence was recorded.

Data was inputted in Microsoft Excel 2007 and descriptive percentages were tabulated.

Results

Of the 146 case files reviewed, 141 (96.6%) children met the inclusion criteria. The sample consisted of 84 males (60%) and 57 females (40%) with a mean age of 10.9 (±2.2).

The distribution by diagnosis of the 141 children referred to CGC is: 46 (32.6%) were diagnosed with hyperkinetic disorder, 19 cases (13.5%) with adjustment disorder, 18 (12.8%) with conduct disorder, 13 (9.2%) with anxiety disorders and 11 (7.8%) with obsessive-compulsive disorder. Refer to Table 1 for further details on ICD-10 diagnosis of sample. No diagnosis (0%) of BD was made for the 141 children included in the study.

75 (53.2%) of the cohort were reviewed only once by the CGC multidisciplinary team; a working diagnosis and management plan was made but there was no-follow up during the study period and thus outcome could not be clearly established.[12] (8.5%) of all referred patients did not require follow-up and were discharged by the firm consultant due to behavioral presentation being in-keeping with a normal child development and/or the severity of the disorder not meeting criteria for specialist service and/or discharged at requested by the legal guardian.

54 (38.3%) children had attended follow-ups. 36 (66.7%) of these children improved with the management plan given. Best responders were those diagnosed with generalized anxiety disorder, depressive disorder, somatoform disorders, and other behavioral and emotional disorders. 18 (33.3%) children did not respond to the treatment plan, these included youngsters with eating disorders, tic disorders and obsessive-compulsive disorders. From our results, it was noticed that those children diagnosed with ADHD (hyperkinetic disorder)

Table 1: All the children referred to Child Guidance Clinic during 2007. The working diagnosis and their outcome are outlined

Diagnosis	Discharged	Improved	One Review	Not improved	Grand Total
Hyperkinetic disorder	4	10	25	7	46
Adjustment disorder	2	4	10	3	19
Conduct disorder	0	4	13	1	18
Anxiety disorder	0	4	8	1	13
OCD	0	2	7	2	11
Depressive disorder	0	3	2	0	5
Emotional disorders	2	2	0	1	5
Somatoform Disorder	1	2	1	0	4
Eating disorder	0	0	1	2	3
Speech and language disorder	0	0	3	0	3
Tic disorder	1	1	0	1	3
Mixed disorder conduct & emotion	0	0	2	0	2
Other behavioural and emotional disorders	0	2	0	0	2
Phobia	0	0	2	0	2
Drug abuse	1	0	0	0	1
Schizotypal disorder	0	0	1	0	1
Sexual maturation disorder	1	0	0	0	1
Social functioning disorders	0	1	0	0	1
Substance abuse	0	1	0	0	1
Total	**12**	**36**	**75**	**18**	**141**

Reference: 1. Prolia® Summary of Product Characteristics, 2010.

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PRESENTATION: Onbrez Breezhaler 150mcg and 300mcg inhalation powder hard capsules containing indacaterol maleate, and separate Onbrez Breezhaler inhaler. **INDICATIONS:** For maintenance bronchodilator treatment of airflow obstruction in adult patients with chronic obstructive pulmonary disease (COPD). **DOSAGE AND ADMINISTRATION:** Recommended dose is the inhalation of the content of one 150mcg capsule once a day, administered at the same time of the day each day, using the Onbrez Breezhaler inhaler. Capsules must not be swallowed. Dose should only be increased on medical advice. The inhalation of the content of one 300mcg capsule once a day has been shown to provide additional clinical benefit with regard to breathlessness, particularly for patients with severe COPD. Maximum dose is 300mcg once daily. No dose adjustment required in elderly patients, for patients with mild and moderate hepatic impairment or for patients with renal impairment. 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. In case such effects occur, treatment may need to be discontinued. ***Hypokalaemia:*** • Beta2-adrenergic agonists may produce significant hypokalaemia in some patients, which has the potential to produce cardiovascular effects. In patients with severe COPD, hypokalaemia may be potentiated by hypoxia and concomitant treatment which may increase the susceptibility to cardiac arrhythmias. ***Hyperglycaemia:*** •Inhalation of high doses of beta2-adrenergic agonists may produce increases in plasma glucose. Upon initiation of treatment with Onbrez Breezhaler plasma glucose should be monitored more closely in diabetic patients. •During clinical studies, clinically notable changes in blood glucose were generally more frequent by 1.2% on Onbrez Breezhaler at the recommended doses than on placebo. Onbrez Breezhaler has not been investigated in patients with not well controlled diabetes mellitus. Pregnancy and Lactation: •No data available from the use of indacaterol in pregnant women. Onbrez Breezhaler should only be used during pregnancy if the expected benefits outweigh the potential risks. •Not known whether indacaterol / metabolites are excreted in human milk. A decision must be made whether to discontinue breast-feeding or discontinue Onbrez Breezhaler therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. **INTERACTIONS:** •Concomitant administration of other sympathomimetic agents may potentiate the undesirable effects of Onbrez Breezhaler. Onbrez Breezhaler should not be used in conjunction with other long-acting beta2-adrenergic agonists or medicinal products containing long-acting beta2-adrenergic agonists. •Concomitant hypokalaemic treatment with methylxanthine derivatives, steroids, or non-potassium-sparing diuretics may potentiate the possible hypokalaemic effect of beta2-adrenergic agonists, therefore use with caution. •Indacaterol should not be given together with beta-adrenergic blockers (including eye drops) as these may weaken or antagonise the effect of beta2-adrenergic agonists. Where required, cardioselective beta-adrenergic blockers should be preferred, although they should be administered with caution. •Inhibition of the key contributors of indacaterol clearance, CYP3A4 and P-gp, does not raise any safety concerns given the safety experience of treatment with Onbrez Breezhaler. •Indacaterol has not been shown to cause interactions with co-medications. **ADVERSE REACTIONS:** •The most common adverse reactions with Onbrez Breezhaler are: nasopharyngitis, upper respiratory tract infection, sinusitis, diabetes mellitus and hyperglycaemia, headache, ischaemic heart disease, cough, pharyngolaryngeal pain, rhinorrhoea, respiratory tract congestion, muscle spasm, peripheral oedema. •Uncommon: paraesthesia, atrial fibrillation and non-cardiac chest pain. •Please refer to SmPC for a full list of adverse events for Onbrez Breezhaler. **LEGAL CATEGORY: POM PACK SIZES:** Onbrez Breezhaler 150mcg - carton containing 10 or 30 capsules and one Onbrez Breezhaler inhaler. Onbrez Breezhaler 300mcg - carton containing 30 capsules and one Onbrez Breezhaler inhaler. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **MARKETING AUTHORISATION NUMBERS:** EU/1/09/593/001, 002, 007. **Please refer to Summary of Product Characteristics (SmPC) before prescribing.** Full prescribing information is available on request from Novartis Pharma Services Inc. Representative Office Malta P.O Box 124, Valletta, VLT 1000 Malta. Tel. +356 22983217. 2011-MT-02-ONB-027-Apr-2011

References:
1. Gaccola M, Matera MG. Novel long-acting bronchodilators for COPD and asthma. Br J Pharmacol. 2008;155:281-295.
2. Novartis Europharm Ltd. Onbrez® Breezhaler® Summary of Product Characteristics.

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Table 2: Illustration of the distribution of children, their diagnosis, and the percentage improvement over 2007

Diagnosis	Improved		No improvement		
	N=	(%)	N=	(%)	
Hyperkinetic disorder	10	(58.8)	7	(41.2)	100%
Conduct disorder	4	(80.0)	1	(20.0)	100%
Adjustment disorders	4	(57.1)	3	(42.9)	100%
Anxiety disorder	4	(80.0.)	1	(20.0)	100%
OCD	2	(50.0)	2	(50.0)	100%
Other behavioral and emotional disorders	2	(100.0)	0	-	100%
Depressive disorder	3	(100.0)	0	-	100%
Social functioning disorders	1	(100.0)	0	-	100%
Somatoform disorders	2	(100.0)	0	-	100%
Emotional disorder	2	(66.7)	1	(33.3)	100%
Tic disorder	1	(50.0)	1	(50.0)	100%
Substance abuse	1	(100.0)	0	-	100%
Eating disorders	0	-	2	(100.0)	100%
Total	**36**	**(66.7)**	**18**	**(33.3)**	**100%**

did fairly well, as 58.8% responded to the treatment given at CGC. Table 2 illustrates the above.

Limitations

The results may be limited by the following, (a) use of retrospective design; (b) small sample size i.e. over half of the cohort were reviewed only once at CGC, during the study period, thus improvement could not be really assessed; (c) ages of the children considered were 8-16 years; (d) children followed up by psychiatrists in the community could not be included; (e) children followed up at CGC in Gozo were not included. The authors did ask consultant psychiatrists working with children, whether they had reviewed anyone with BD in Gozo over that year, however their reply was negative. The authors are convinced that due to the nature of severity of disorder any child diagnosed with BD 1 would require hospital in-patient treatment and would have come to the attention of the national health service.

Discussion

In comparison, the frequency of children and adolescents diagnosed with BD in Malta is significantly lower than that reported in the literature. Reasons for this could be lack of specific awareness in recognizing and diagnosing pediatric bipolar disorder locally, or due to the diagnostic criteria used. In Child Guidance Clinic, the multi-axial version of ICD-10, is used rather than the DSM IV criteria, which is more quoted in studies. [4,13,14] In the DSM IV diagnosis of BD can be assigned after one manic episode alone, while in ICD-10 the diagnosis is only assigned after the presentation of the second affective episode, one of which is a mixed or manic episode. Thus this could lead to a relative delayed diagnosis of BD.

Standardized diagnostic assessment tools include: (a) WASH-U-KSADS (semi-structured interview that yields a DSM-IV diagnosis). The WASH-U-KSADS has a provision for documenting the onset and offset of rapid mood swings. Inter rater reliability was 100% reported. (b) Child Mania Rating Scale Parent Version (CMRS-P) completed by parents, and the Young Mania Rating Scale (YMRS) completed by the clinician. The scale measures manic symptoms only[14]. (c) (KSADS-MRS) which is a semi-structured interview, completed by the clinician after interview with the parents and youths sequentially. (d) The Mini International Neuropsychiatry Interview-Kid (MINI-KID) is a structured interview that elicits co-morbid diagnoses in children. This has been used to differentiate BPD from ADHD.[12]

Another finding from this study was that 18 (33.3%) children being treated the at Child Guidance Clinic did not improve on the treatment prescribed. 7 of these youngsters were cases diagnosed with ADHD. The use of a more specific diagnostic tool would help elucidate early clinical diagnosis of BD, thus excluding the possibility of mis-diagnosis. Studies indicate that children with BD alone or with other co-morbid illnesses are amongst the poorest responders to treatment.[15] Research shows that early and the correct psychopharmacology is critical to minimize the risk of morbidity and mortality associated with BD. This mental disorder carries a high risk of substance misuse and risk of suicide hence is a public health concern.[4,16]

The rapid increase in frequency reported for pediatric BD highlights a need for further longitudinal studies following up this cohort of non-responders so as to identify reliable clinical and epidemiological data of BD[17] in clinical practice in Malta.

For the list of abbreviations & references log on www.thesynapse.net

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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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Winners with TheSynapse

During a social event held recently, winners of TheSynapse Photography Competition, TheSynapse eQuiz performance audit as well as the winner of Keral eQuiz were presented with prizes. During the event, Dr Wilfred Galea gave the audience a sneak preview of the new version of TheSynapse and received very positive feedback from members. Dr Galea showed the appreciation to the high level of member participation in the site and explained that members can now benefit from a more interactive site which includes social networking and forum amongst other facilities.

The winners of TheSynapse Photography Competition were Dr Alex Gatt, Mr John Caruana, Mr Dylan Said and Dr Mario Saliba whereas Dr Nadia Cilia was the winner of TheSynapse eQuiz performance audit. Dr John Attard was the winner of the Keral eQuiz and was presented with the prize by Ms Marina Fenech from Menarini.


Dr Alex Gatt


Dr John Attard


Mr John Caruana

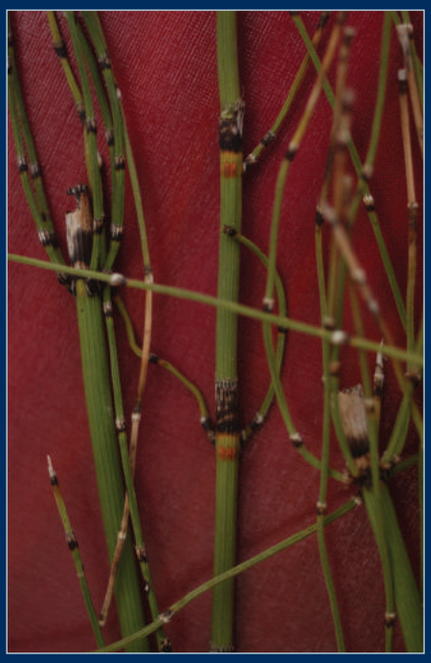

Dr Mario Saliba


Dr Nadia Cilia

These photos are a selection of submissions from members in TheSynapse Members Photo Competition 2011. The Theme of the competition was 'Malta and Medicine'

Kull qaddis jghin by John Caruana. Saints have always had an important role in Maltese culture especially when it comes to health. Many are patron saints of various diseases and when things get serious almost everyone turns to prayers and saints to help get back to normal health.

Enjoying a walk together by Mario Saliba depicts a lovely old couple walking in the Gozo countryside. A happy, healthy relationship is one of the most important factors in life and is known to decrease the effects of stress.



Denb iz-Ziemel by Alexander Gatt Equisetum ramoisissimum (Horsetail; Denb iz-ziemel). The only living fossil of the Equisetaceae which dominated the low growths of the Palaeozoic forests. E ramoisissimum is indigenous to Malta, scarce and found in wet areas. The stem is hollow and its nodal sequence is a logarithmic one. Like other equisetaceae, the plant is remarkable, having no natural predators and is not susceptible to any known disease or virus. In Malta the plant was used as a herbal remedy to treat UTI's and renal stones but has also anti- cancer properties owing to its anti-oxidants. Its striking immunity from diseases may well provide precious clues in our fight against them.

Vintage oven for heat sterilization by Dylan Said. The temperature being raised enough and prolonged adequately to kill all bacteria and spores.

Leitz compound brass and steel microscope that the Maltese bacteriologist Themistocles Zammit used to examine the Brucella species, by Dylan Said. This led to his 1905 discovery of contaminated milk as a vector for transmission of brucella melitensis present in the blood of the goat to humans. This discovery greatly contributed to the elimination of undulant fever from the island and earned Temi Zammit his knighthood.

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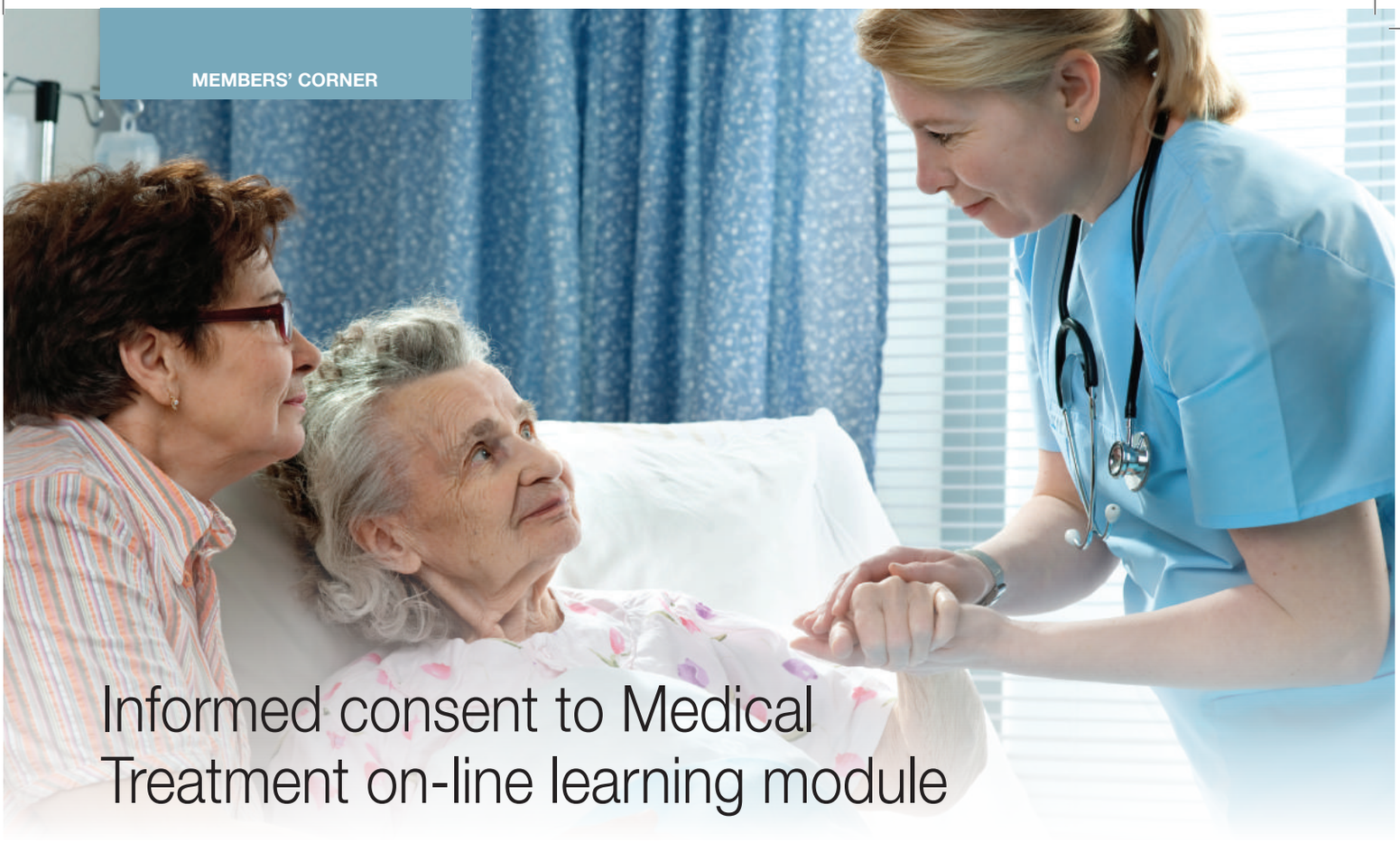

Informed consent to Medical Treatment on-line learning module

The Malta Foundation Programme in collaboration with TheSynapse launched the third online e-learning module - **"Informed Consent to Medical Treatment"**. The e-tutor of this course is Dr Pierre Ellul MD MRCP MSc, Consultant Gastroenterologist, Associate Programme Director, Foundation School, Malta.

The aim of the course is to introduce the important topic of Informed consent for adults with capacity, to Foundation Doctors. Although not fully exhaustive it provides the initial building blocks for a better understanding of this topic.

The eCME (online) modules are the fruit of collaboration between the Foundation Programme (Malta) and TheSynapse. As a result of this collaboration, the modules are available to all Foundation students as well as members of TheSynapse. The content and delivery of each of these modules is guided by experts in eLearning.

We encourage you to participate and wish you success!

How to access this online course

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IDEOS®, chewable tablets. **COMPOSITION*:** Elemental calcium 500 mg (corresponding to 1250 mg of calcium carbonate), cholecalciferol (Vitamin D3) 400 IU (corresponding to 4 mg of cholecalciferol concentrate, powder form). **PHARMACEUTICAL FORM :** Chewable tablets. **THERAPEUTIC INDICATIONS*:** Vitamin D and calcium deficiency correction in the elderly. Vitamin D and calcium supplementation, as an adjunct to specific therapy for osteoporosis, in deficient patients or in patients with a high risk of vitamin D and calcium deficiency. **POSOLOGY AND METHOD OF ADMINISTRATION :** Oral use. For adults only. Suck or chew the tablets. One tablet twice a day. **CONTRAINDICATIONS :** Hypersensitivity to one of the constituents. Hypercalcaemia, hypercalciuria, calcium lithiasis. In patients where prolonged immobilisation is accompanied by hypercalcaemia and/or hypercalciuria, vitamin D and calcium treatment should only be resumed when the patient becomes mobile. **SPECIAL WARNINGS AND PRECAUTIONS FOR USE :** In case of long term treatment, the urinary calcium excretion must be monitored and treatment must be reduced or temporarily suspended if urinary calcium excretion exceeds 7,5 mmol/24 h, i.e. 300 mg/24 h. In case of simultaneous treatment with digitalis glycosides, diphosphonates, sodium fluoride, thiazide diuretics, tetracyclines, see "Interactions". Take into account the dose of vitamin D per tablet (400 IU) in case of simultaneous treatment with another vitamin D preparation. Administration of supplementary vitamin D or calcium should be done under medical surveillance with monitoring of calcaemia and calciuria. The product should be prescribed carefully to patients suffering from sarcoidosis because of the potential increase of vitamin D metabolism into its active form. For these patients calcaemia and calciuria should be monitored. In case of renal insufficiency, adapt the dosage according to creatinine clearance . **INTERACTION WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION*:** Digitalis glycosides, thiazide diuretics, oral tetracyclines, - diphosphonates, sodium fluoride, high doses of vitamin D, phenytoin, barbiturics, glucocorticoids. **PREGNANCY*:** Ideos can be used during pregnancy and lactation. However, the daily dose should not exceed 1500 mg of calcium and 600 IU of vitamin D3. During pregnancy, overdose of cholecalciferol and vitamin D should be avoided. **LACTATION:** Vitamin D and its metabolites enter the breast milk. **UNDESIRABLE EFFECTS :** Hypercalciuria and exceptionally hypercalcaemia, in case of long term treatment in high dosage: constipation, flatulence, epigastric pains, diarrhoea. **OVERDOSE*. PHARMACOLOGICAL PROPERTIES* :** VITAMIN D-CALCIUM SUPPLEMENT (Drug acting on calcium balance - Alimentary tract and metabolism). **PHARMACEUTICAL FORMS AND PRESENTATIONS:** Box of 60 tablets in tube of 15 tablets. MA number: MA093/00201 **MARKETING AUTHORISATION HOLDER:** LABORATOIRE INNOTECH INTERNATIONAL 22 Avenue Aristide Briand 94110 ARCUEIL-FRANCE. **TEXT REVISION DATE:**14 April 2010. ***For complete information, please refer to the therapeutic references.**

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Calcium, Vitamin D and Bone

ANDREW BORG

Abstract

Calcium, protein and vitamin D are the main nutrients relevant to bone health. This short article discusses the importance of vitamin D and its relation to calcium homeostasis. The various causes, clinical manifestations and treatment are outlined.

Vitamin D deficiency and effects on bone

The main nutrients relevant for bone health are calcium, protein and vitamin D. Calcium intake has been shown to be weakly related to bone mineral density and in two recent meta-analysis[1] was found to be associated with a modest reduction of fracture risk. The ideal calcium allowance is unclear. It is reasonable to intervene with calcium supplementation when dietary calcium intake cannot be increased above 800mg/day. The problem is complicated by the observation that

Vitamin D is important in calcium homeostasis and may also need supplementation.

Vitamin D deficiency which occurs with serum 25-hydroxyvitamin D levels below <25nmol/l results in osteomalacia in adults and rickets in children. Commonly patients are asymptomatic or may present with non-specific bone pain, fractures, hypocalcaemia and myopathy.

Vitamin D insufficiency is defined by consensus as a serum 25-hydroxyvitamin D level of <75nmol/l. When vitamin D levels fall below 75nmol/l, parathormone (PTH) secreted by the parathyroid glands starts to rise. The clinical consequences are debatable but it may be associated with osteomalacia, bone aches and poor bone mineralisation.

Pathophysiology

Vitamin D is formed from the effect of UVB-sunlight on 7-dehydrocholesterol in the skin[2,3]. There are 2 forms of vitamin D: vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). Both forms are hydroxylated to the 25-OH form in the liver. Further hydroxylation of the 25-OH vitamin D in the kidney results in production of the active form 1,25-dihydroxyvitamin D. Vitamin D production in the skin declines with advancing age, such that elderly people rely more on vitamin D dietary intake. Some studies[1] have suggested that vitamin D3 may be more active than vitamin D2 but more recently it was demonstrated that they are equally effective.

Vitamin D functions

- Enhances calcium and phosphate absorption from the gut;
- Stimulates osteoblast production;
- Decreases PTH synthesis.

Causes of osteomalacia and rickets

- Dietary deficiency;
- Reduced sun exposure;
- Pseudovitamin D deficiency rickets (autosomal recessive, presents in 1st year of life);
- Hereditary vitamin D resistance rickets (autosomal recessive, presents in infancy);
- Hypophosphataemic vitamin D resistant rickets (X linked, presents in childhood);
- Autosomal dominant hypophosphatemic rickets (autosomal dominant, presents in infancy).

People at risk of vitamin D deficiency

- Elderly particularly those in institutions;
- Excessive use of sunscreen;
- Dark skinned people living at high altitudes;
- Ethnic/religious reasons which may demand coverage of all the skin;
- Malabsorption conditions eg: coeliac disease, short bowel syndrome, cystic fibrosis;
- Chronic liver disease;
- Drugs eg: prolonged anticonvulsant use, cholestyramine, aluminum containing antacids.

Vitamin D insufficiency is not exclusive to the elderly. Studies have shown that up to two thirds of healthy adults have vitamin D insufficiency and this tends to be worse after winter and improves after summer[4,5].

Treatment of vitamin D insufficiency may decrease the risk of hip and nonvertebral fractures. In the elderly vitamin D supplementation has been associated with a reduction in falls and enhanced muscle strength[6]. A meta-analysis[1] demonstrated that vitamin D supplementation resulted in a reduction in falls of about 22% in ambulatory institutionalized elderly subjects, compared with controls. A Cochrane Review[1] including 50 randomized, controlled trials involving close to 100,000 individuals, has found vitamin D3 supplementation to be associated with significant reduction in mortality while other forms of vitamin D (vitamin D2, calcitriol, and alpha-calcidiol) did not.

Lab investigation

- Serum calcium is usually normal, serum phosphate maybe normal or low, serum Alkaline Phosphatase may be normal or raised.
- The level of 25-OH vitamin D is usually < 25nmol/l.
- PTH is usually > 5pmol/l although this does not need to be measured in all patients.
- Other tests such as liver and renal function, anti-TTG, folate and thyroid function may be needed to rule out other associated conditions or conditions which may mimic symptomatology.

Imaging

Pseudofractures (small radiolucent lines through bone cortices) may be seen characteristically in the femoral neck, pelvis and ribs.

In children growth plate abnormalities such as blurring of the growth plate, widening of the epiphyses and splaying of the long bone metaphyses can be observed.

Treatment

Maintenance

The recommended daily intake of vitamin D is controversial. The daily maintenance dose of vitamin D varies by age, but most children and adults generally require 400-2000 IU of vitamin D daily (1 mcg = 40 International Units (IU)). Caution is needed when recommending vitamin D supplements as some brands which are not classified and registered as medicines (and hence do not have to comply with the stringent regulations and quality, medicines have to comply with) may not contain the amount of vitamin D stated on the packaging.

Prevention and treatment of osteoporosis

- 800-1,000 IU orally daily with calcium.

Treatment of Vitamin D deficiency

Cholecalciferol orally

- 50,000 units weekly for 6 weeks
- 20,000 units weekly for 12 weeks

Ergocalciferol im

- 300,000 units stat repeat after 6 weeks if still low.

For the references log on www.thesynapse.net

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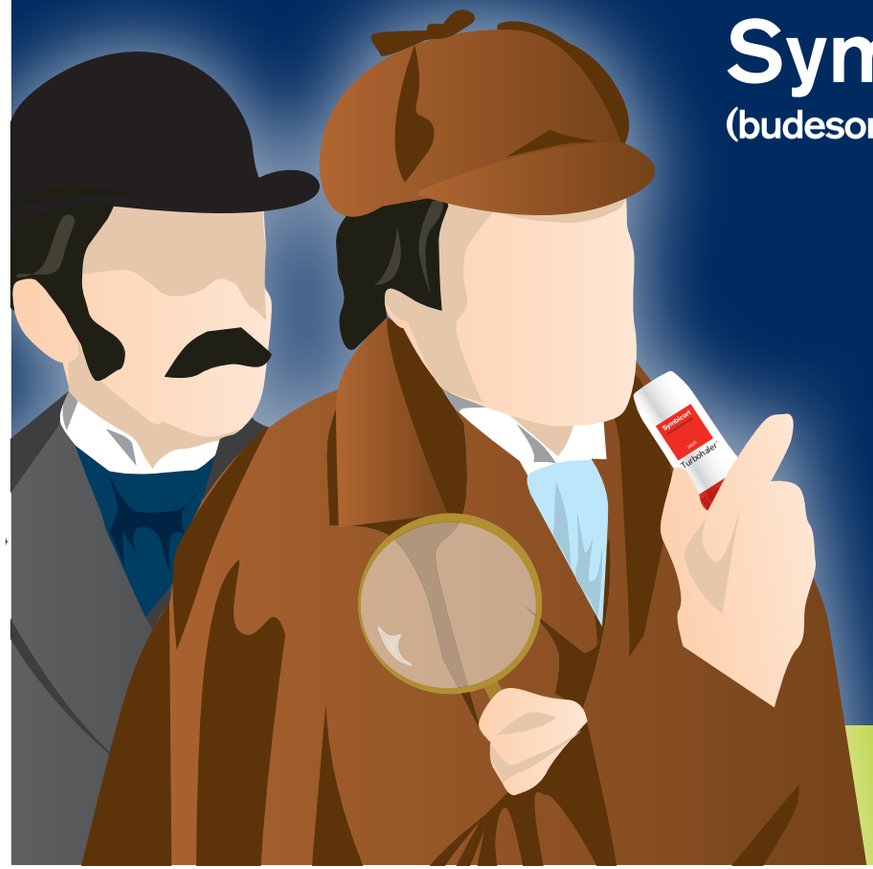

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Symbicort Turbohaler 100/6 is not appropriate for patients with severe asthma. **COPD *(Symbicort 200/6 only):*** Symptomatic treatment of patients with severe COPD (FEV1 <50% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators. **Dosage and Administration: Asthma (Symbicort maintenance therapy – regular maintenance treatment with a separate rescue medication): *Adults (including elderly)*:** 1-2 inhalations twice daily. Some patients may require up to a maximum of 4 inhalations twice daily. ***Adolescents (12-17 years)*:** 1-2 inhalations twice daily. ***Children 6 years and older (Symbicort 100/6 only)*:** 2 inhalations twice daily. Not intended for the initial management of asthma. Dose should be individualised. If an individual patient requires dosages outside recommended regimen, appropriate doses of β_2 adrenoceptor agonist and/or corticosteroid should be prescribed. When long-term symptoms are controlled, titrate to the lowest effective dose, which could include a once daily dosage. ***Children under 6 years:*** Not recommended. **Asthma (Symbicort maintenance and reliever therapy – regular maintenance treatment and as needed in response to symptoms):** especially consider for (i) patients with inadequate asthma control and in frequent need of reliever medication (ii) patients with asthma exacerbations in the past requiring medical intervention. ***Adults (including elderly)*:** 1 inhalation twice daily or as 2 inhalations once daily. For some patients a dose of 2 inhalations twice daily may be appropriate (200/6 strength only). Patients should take 1 additional inhalation as needed in response to symptoms. If symptoms persist after a few minutes, an additional inhalation should be taken. Not more than 6 inhalations should be taken on any single occasion. A total daily dose of more than 8 inhalations is not normally needed; however, up to 12 inhalations a day could be used for a limited period. Patients using more than 8 inhalations daily should be strongly recommended to seek medical advice and should be reassessed; their maintenance therapy should be reconsidered. Patients should be advised to always have Symbicort for reliever use. ***Children and adolescents under 18 years of age*:** not recommended. **COPD *(Symbicort 200/6 only): Adults*:** 2 inhalations twice daily. **Contraindications, Warnings and Precautions etc.:** ***Contraindications*:** Hypersensitivity (allergy) to budesonide, formoterol or lactose (which contains small amounts of milk proteins). ***Warnings and Precautions*:** If treatment is ineffective, or there is a worsening of the underlying condition, therapy should be reassessed. Sudden and progressive deterioration in control requires urgent medical assessment. Patients should have their appropriate rescue medication available at all times, i.e. either Symbicort or a separate reliever. If needed for prophylactic use (e.g. before exercise) a separate reliever should be used. Therapy should not be initiated during an exacerbation. Serious asthma-related adverse events and exacerbations may occur and patients should continue treatment but seek medical advice if asthma symptoms remain uncontrolled or worsen after initiation of Symbicort. Paradoxical bronchospasm may occur, with an immediate increase in wheezing and shortness of breath after dosing. This responds to a rapid-acting inhaled bronchodilator and should be treated straightaway. As with any inhaled corticosteroid, systemic effects may occur, particularly at high doses prescribed for long periods. These may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract and glaucoma. Potential effects on bone should be considered especially in patients on high doses for prolonged periods that have co-existing risk factors for osteoporosis. Prolonged treatment with high doses of inhaled corticosteroids, particularly higher than recommended doses, may also result in clinically significant adrenal suppression. Therefore additional systemic corticosteroid cover should be considered during periods of stress such as severe infections or elective surgery. Treatment with supplementary systemic steroids or inhaled budesonide should not be stopped abruptly. During transfer from oral steroid therapy to Symbicort, a generally lower systemic steroid action will be experienced which may result in the appearance of allergic or arthritic symptoms which will need treatment. In rare cases, symptoms such as tiredness, headache, nausea and vomiting can occur due to insufficient glucocorticosteroid effect and temporary increase in the dose of oral glucocorticosteroids is sometimes necessary. Observe caution in patients with thyrotoxicosis, phaeochromocytoma, diabetes mellitus, untreated hypokalaemia, or severe cardiovascular disorders. As with other β_2 adrenoceptor agonists, hypokalaemia may occur at high doses. Particular caution recommended in unstable or acute severe asthma as this effect may be potentiated by xanthine-derivatives, steroids, diuretics and hypoxia. Monitor serum potassium levels. Hypokalaemia may increase the disposition towards arrhythmias in patients taking digitalis glycosides. In diabetic patients, consider additional blood glucose monitoring. Symbicort contains lactose monohydrate, as with other lactose containing products the small amounts of milk proteins present may cause allergic reactions. ***Interactions*:** Concomitant treatment with itraconazole, ritonavir or other CYP3A4 inhibitors should be avoided unless the benefits outweigh the systemic side effect risks. Symbicort maintenance and reliever therapy is not recommended in patients using potent CYP3A4 inhibitors. Not to be given with beta adrenergic blockers (including eye drops) unless there are compelling reasons. Concomitant administration with quinidine, disopyramide, procainamide, phenothiazines, antihistamines (terfenadine), MAOIs and TCAs can prolong the QTc-interval and increase the risk of ventricular arrhythmias. L-Dopa, L-thyroxine, oxytocin and alcohol can impair cardiac tolerance. Concomitant administration with MAOIs, including agents with similar properties such as furazolidone and procarbazine, may precipitate hypertension. Risk of arrhythmias in patients receiving anaesthesia with halogenated hydrocarbons. **Pregnancy and Lactation:** Should only be used when the benefits outweigh the potential risks. Budesonide is excreted in breast milk, however at therapeutic doses no effects on the child are anticipated. **Undesirable effects:** Undesirable effects include headache, palpitations, tremor, candida infections in the oropharynx, coughing, mild irritation in the throat, hoarseness, tachycardia, muscle cramps, agitation, restlessness, nervousness, nausea, dizziness, sleep disturbances and bruises. Rarely, hypokalemia, cardiac disorders including atrial fibrillation, supraventricular tachycardia and extrasystoles, bronchospasm and immediate and delayed hypersensitivity reactions including exanthema, urticaria, pruritus, dermatitis, angioedema and anaphylactic reaction. Very rarely, psychiatric disorders including depression and behavioural disturbances (mainly in children), angina pectoris, prolongation of QTc-interval, hyperglycaemia, taste disturbance, signs or symptoms of systemic glucocorticosteroid effects (including Cushing's syndrome, adrenal suppression, growth retardation, decrease in bone mineral density, cataract and glaucoma) and variations in blood pressure. As with other inhalation therapy, paradoxical bronchospasm may occur in very rare cases. **Package Quantities:** Each Symbicort Turbohaler contains 120 inhalations. **Legal Status:** POM. **Marketing Authorisation Numbers:** PA 970/28/1-2. **Marketing Authorisation Holder:** AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, UK. **Further information available on request from:** AstraZeneca Pharmaceuticals (Ireland) Ltd., College House, 20 Nassau Street, Dublin 2. Telephone: (01) 6097100, Fax: (01) 6796650. **Abridged Prescribing Information prepared:** 06/11. Symbicort and Turbohaler are trade marks of the AstraZeneca group of companies. **References: 1.** Symbicort SmPC. **2.** Seberova Andersson. Respir Med 2000: 94: 607-611. URN: 11/0286 **Date of Preparation:** September 2011.

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ALBERT CILIA-VINCENTI

THE SERIES

Healing & Disease Reversal

This series reviews Dean Ornish's evidence-based claims of healing & disease reversal by dietary and lifestyle changes. He is a California University Professor of Medicine in San Francisco. This instalment discusses health benefits of spices and probiotics in foods.

The foods we have been discussing in this series may also prevent various cancers because they may contain anti-angiogenic factors. Primary tumour growth (or growth of metastatic deposits, causing cancer recurrence) depends on chemical signals the tumour cells send out to stimulate new blood vessel formation (angiogenesis) which feeds it. Many fruits, vegetables and whole-grains have anti-angiogenic factors, and this is one mechanism by which these foods may help prevent cancer development or its progression or recurrence. The British Health Service recently claimed that accumulated scientific evidence points that increased consumption of fruits, vegetables and whole-grains, less consumption of red meats and alcohol, less smoking, and more regular exercise, could decrease cancer incidence by almost 50 percent.

Spices not only enhance the taste of foods, but can also help you feel better. They contain many protective phytonutrients, which may inhibit tumour formation and progression. One of the most exciting is turmeric, an Indian spice providing the yellow colour in curries. It is said to have anti-inflammatory and anti-oxidant properties, and may help prevent or even treat Alzheimer's disease. The prevalence of Alzheimer's disease is much lower in India than in the West, affecting only 1 percent of over-65-year-olds in some Indian villages. There have been claims that curcumin (one of the most active substances in turmeric) may reduce Alzheimer's type plaques by 50 percent, and that rats given turmeric also perform better in maze-based memory tests. Turmeric also enhances immune function, improves digestion and its anti-inflammatory properties have been claimed to be comparable to corticosteroids.

Ginger is another spice whose health benefits, particularly its gastrointestinal distress-reducing properties, have been recognised for centuries. Besides claimed anti-oxidant and anti-inflammatory effects, ginger is very effective in preventing the symptoms of motion sickness, especially seasickness, and is very useful in reducing the nausea and vomiting of pregnancy. Its potent anti-inflammatory substances (gingerols) help reduce pain and improve function in osteoarthritis and rheumatoid arthritis.

Sage, oregano, thyme, rosemary, fennel, turmeric, caraway, anise, coriander, cumin and tarragon are claimed to have some cancer-preventing activity. Some of them contain terpenoids that may prevent or slow tumour progression. Cinnamon, garlic, sage, nutmeg and clove may inhibit bacterial growth and help prevent cooked food from spoiling. Paprika and saffron may boost immunity. Chili peppers may help block tumour formation. Rosemary contains substances claimed to stimulate immunity, increasing brain blood flow and mental concentration, improving digestion, and contains anti-inflammatory compounds claimed to reducing the severity of asthma attacks.

Probiotics are health-enhancing bacteria found mainly in the mouth, bowels and vagina. They live in a complex ecological equilibrium with other bacteria, helping keeping the harmful ones in check, and some produce vitamin K and B vitamins. They may aid digestion, improve nutrient absorption, help reduce carcinogen formation, and enhance immune function.

Many forces can throw off this delicate balance, such as ageing, alcohol, poor diet, stress, chronic illness and, especially so, antibiotics. When the gut flora balance is disrupted, some harmful bacteria grow too numerous causing diarrhoea or worse. Probiotics such as Lactobacillus reduce the risk of diarrhoea during antibiotic use as well as shorten the course of infectious diarrhoea after such antibiotic use. .

The vagina, like the gut, contains bacteria in a dynamic equilibrium, and antibiotics, spermicides, contraceptive hormones and the menopause may disrupt this internal ecology resulting in bacterial vaginosis. Since dairy products are a common source of probiotics, regular consumption of yogurt (with or without live Lactobacillus) is said to significantly reduce the risk of bacterial vaginosis.

Probiotics may be helpful in irritable bowel syndrome, Crohn's disease and ulcerative colitis, lessening recurrences. They also help prevent allergic reactions, such as reducing the risk of eczema in children. Neonates' digestive tracts contain only small populations of Bifidobacterium, but breast milk contains these bacteria and breast-feeding raises newborns' good bacterial gut flora within a few days. This is one reason why breast-feeding reduces risk of infectious diarrhoea.

The easiest way to incorporate probiotic bacteria into one's life is to eat a few servings of live-culture yogurt a week. Probiotic supplements are another option, but they vary in quality and potency, are largely unregulated, and there is likely more variability in numbers and type of probiotic bacteria in them than in foods. S

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Dean Ornish, The Spectrum: a scientifically proven program to feel better, live longer, lose weight, and gain health, 2007, 57-61, Ballantine Books, US.

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Therapy over at least 10 days is indicated in the treatment of infections with beta-haemolytic streptococci in order to prevent late complications (e.g. rheumatic fever, glomerulonephritis). However, Forcid Solutab should not be used for more than 14 days without assessing the liver function of the patient. **Adults and children over 40 kg body weight:** The usual posology of 500/125 mg is 3 times a day (every 8 hours). For severe, chronical and relapsing infections, this dosage may be doubled. The usual posology of 875/125 mg is 2 times a day. The single dose should be taken at regular intervals throughout the day; ideally at 12 hours interval. **Elderly patients:** Posology as for adults. **Patients with impaired renal function:** In patients with renal insufficiency the excretion of clavulanate and amoxicillin through the kidneys is delayed. Forcid Solutab 875/125 tablets may only be given to patients with a glomerular filtration rate > 30 ml/min. No dose adjustment is required then. **Patients with impaired liver function:** The combination amoxicillin/clavulanate should be administered cautiously to patients with liver impairment. The liver function should be monitored at regular intervals. There are, as yet, insufficient data on which to base a dosage recommendation. **Method of administration:** To prevent possible gastro-intestinal undesirable effects, Forcid Solutab should be taken at the start of the meal. Forcid Solutab tablets can be swallowed whole with a glass of water, or first dissolved in a 1/2 cup of water (at least 30 ml) and stirred thoroughly before swallowing. **Contraindications:** Hypersensitivity to amoxicillin, clavulanic acid or to any of the excipients. Hypersensitivity to any other ß-lactam antibiotic like penicillins and cephalosporins. A previous history of amoxicillin/clavulanate associated jaundice or hepatic dysfunction. Patients with infectious mononucleosis (glandular fever) and patients with lymphatic leukaemia have a higher risk of exanthema and consequently amoxicillin/clavulanate must not be administered in these diseases for concomitantly occurring bacterial infections. **Special warnings and precautions for use:** Serious and occasionally fatal cases of hypersensitivity (anaphylactic reactions) have been reported for patients on penicillin treatment. These reactions are more common for patients with a history of hypersensitivity. Treatment with Forcid Solutab must be stopped immediately and replaced by another suitable therapy. Suitable therapy to treat symptoms of an anaphylactic reaction may be necessary, such as immediate administration of epinephrine, intravenous steroids and the treatment of respiratory insufficiency. Forcid Solutab should be used with caution in patients with known severe allergies or asthma since such patients are more likely to respond with allergic reactions. Cross-hypersensitivity and cross-resistance between the penicillins and cephalosporins can exist. As is the case for other broad spectrum antibiotics, superinfections may occur, particularly in patients with chronic diseases and/or dysfunctioning immune responses. Mucocutane candida infections have been observed. If superinfections occur, the medicinal product should be discontinued and/or an appropriate therapy should be initiated. Patients with severe gastrointestinal disturbances with vomiting and/or diarrhoea should not be treated with Forcid Solutab since adequate absorption can not be guaranteed. In case of severe and persistent diarrhoea, the possibility of pseudomembraneous colitis must be considered and if not refuted, therapy should be discontinued and appropriate measures should be taken. The necessary measures should also be taken if haemorrhagic colitis occurs. The use of antiperistaltics is contraindicated in such cases. 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 ≤ 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 interval 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 foetus or neonate could be observed. However, a single study in women with premature rupture of the amnion reported that prophylactic treatment with amoxicillin/clavlanic 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/foetus 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

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CHARMAINE GAUCI

Update from the Health Promotion and Disease prevention Directorate

With 40 to 44% of children and 58% of adults being overweight or obese, excess weight in both children and adults in Malta has become a major concern. Obesity has considerable effects on mortality and morbidity. It reduces life expectancy, significantly reduces health-related quality of life and increases the risk of onset of several chronic diseases. Obesity is responsible for a significant proportion of cases of diabetes, heart disease and high blood pressure. The health consequences of being overweight and obesity are also important in children, who are more commonly exhibiting health conditions related to obesity, including low self-esteem and mental health symptoms.

The Healthy Weight for Life Strategy launched in February 2012, identifies multi-sectoral areas for action which are effective and designed to lead to containment and reversal of the epidemic. One of the areas for action is to re-orient public health services to increase the importance of health promotion and disease prevention

Research conducted at Harvard University by David Cutler and colleagues found that the rising obesity is primarily the result of consuming more calories which is associated with technological innovations such as reduced food prices as well as the changing sociodemographic factors such as increased urbanization and increased female labour force participation. This research also looked at cooking patterns across several cultures and found that obesity rates are inversely correlated with the amount of time spent on food preparation. **The more time a nation devotes to food preparation at home, the lower its rate of obesity.** In fact, the amount of time spent cooking predicts obesity rates more readily than female participation in the labor force or income.

We are seeing a majority of our population in Malta consuming ready prepared food which is usually high in salt, fat and sugar content. The Malta Standards Authority Food consumption survey published in 2010 showed that a high proportion of our adult population eat sweets, biscuits and chocolate for breakfast, mid morning snack and afternoon snack. A study on university students showed that half of the students had only between 1 and 2 servings of fruit and vegetables daily, more than half chose the less healthy food, less than half had a regular healthy breakfast, while one third consumed daily soft drinks.

Preparing meals at home is an essential way to exert control over the nutritional quality of the whole family's diet. Cooking whole, fresh foods at home usually means less saturated fat and salt, and more whole grains, fruits, and vegetables. As a health care professional you have an important role to encourage people to limit food high in sugar, fat and salt content and opt more for home prepared meals.

However evidence shows that telling people to eat healthier is one thing but teaching them how to do it, is a completely different matter. Hence the Health Promotion and Disease Prevention Directorate will be focusing this year's obesity campaign on enhancing healthy cooking skills in the public.

For more information and material on this campaign contact the directorate on health.pro@gov.mt or 2326 6000.

MARIKA AZZOPARDI

WITH SPORTS IN

Some people are born to be something others will never be. That much is true of Dr Danica Bonello Spiteri. Sports being imprinted in her genes, she is perhaps more widely known for her sporting proficiency, rather than for her actual profession which is medicine, with the latter, being also sport-related.

Her father, like herself a past President's Award sports person, has been her constant inspiration. "As a young girl, I vividly recall browsing through his logbook, all carefully handwritten with black and white photos and knew I wanted to achieve a Gold Award too. I remember 'playing' with my dad's trophies and once I told him I wanted to win bigger trophies than his when I grew up! He was the school record holder for certain race distances and 'Sportsman of the Year Award' in 1964 for the Sliema district. As I grew up, I managed to beat some of his timings!"

Although sports did not always feature in her early family life, she was encouraged to try different sports so that she eventually discovered triathlon as the sports most suited to her abilities and tastes. She has persisted in triathlon since she was 14.

"My father has been a source of support and encouragement in my sports career from my first races (where he always came to watch me and have a bar of chocolate ready and waiting for my post-race recovery!) Up till today, he is also involved in the Malta Triathlon Association and keeps tabs of my progress. I was offered the opportunity to achieve the President's Award when I was studying at St. Aloysius College, and I worked hard in order to cover all four aspects of the Award – Sports, Skill, Community work and Expeditions. This led me to being presented the President's Gold Award aged 18." Eventually she was awarded the Sportswoman of the Year 2010, as well as the SportMalta Award for 2011, which are the two most prestigious sports awards in Malta.

Receiving SportMalta Award 2011, Malta's most prestigious sport award, by Hon. Clyde Puli

With sports being a lifelong feature, she has nonetheless shouldered new challenges in life, including a career in medicine. How does she juggle this, including family life? Danica explains her way of life, "I have been involved in a number of sports, since I was two, so sports has 'grown' on me. It's not easy, but I'm very self-disciplined, hard-working and try not to waste time – it's all about time management and multi-tasking. The main problem is that any free time on my hands is used to 'get things done in advance!' My husband - Malta's top cyclist Etienne Bonello- sometimes has to actually tell me to stop and have a break in the evenings! I still try to keep up with my social network of friends, meeting them for a swim, bike -ride or run, rather than a coffee!"

The interview touches upon Danica's studies. Why medicine? "Sciences were always a favourite at school and this led me to medical school. I graduated in 2004. It seemed a natural progression, perhaps because I enjoy being of help to other people. My other option had I not become a doctor, would have been to become a Biology or Physical Education teacher."

Initially studying internal medicine, she veered off towards something more to her liking. "I seriously wanted to combine my sports interest with my career, so sports and exercise medicine seemed a viable option. This specialization helps me on a personal sporting level. I have lectured at UOM's Institute of Physical Education and Sports for three years, something which allows me to progressively develop my teaching skills."

Sports and Exercise Medicine as a specialization is actually quite vast and not just about athletes. "*Sports Medicine* involves Musculoskeletal Medicine - joints, muscles, tendons, ligamentous and soft tissue injuries. The commonest cause of musculoskeletal disorders is inactivity and sedentary office-based jobs! We deal with active people doing all forms of exercise - DIY jobs actually keep us quite busy! People typically visit

Run in Wetherby Triathlon, 2012

HER BLOOD

GPs with shoulder, elbow, hip, back or knee problems. Following repeated consultations they tend to end up in front of an orthopaedic surgeon, yet surgery is not a feasible option. Here is where musculoskeletal medicine helps link the bridge." *Exercise Medicine* is about getting chronically ill people to increase activity to improve health and well-being. Danica is particularly interested in cardiac and pulmonary rehabilitation through exercise, as well as the provision of tailor-made exercise for diabetics.

Having an 'athlete's way of thinking' is essential in this specialization. With musculoskeletal problems, dealing with active/athletic people and their expectations and demands, is different from dealing with inactive people. Being able to understand specific sport demands and being familiar with the body's response to exercise, how exercise is measured, how personalised exercise prescriptions and rehabilitation programmes are prepared, allows her a holistic approach with patients.

"I am in a training post at ST4 level, based in Leeds, undergoing specialist training for the next three years to complete my competency requirements. At 31years of age sports keeps me very fit and young. My daily life is quite full and I make the most of it. I believe opportunities come along only once, and it is up to us to grasp them, rather than let them go by, as we have no guarantee of our tomorrows. As doctors, we face death on a daily basis and this has re-enforced such belief. I totally believe life is not made up by the number of breaths we take, but by the number of moments that take our breath away. I am lucky to state that I have had innumerable such moments!"

All African Triathlon Championship - bike segment (2nd overall, 1st in Age group), 2008

Presently Danica is taken up with preparations for her involvement in the London Summer Olympics 2012 – not as an athlete, but rather as a medical professional. She was selected to form part of the sports medicine team, working alongside Olympians - a once-in-a-lifetime opportunity. Plans for the future are varied but as she admits, "In the long term, I am working hard towards finishing my specialization and hope to bring this to Malta, but I leave my options totally open, depending on what life throws at me. I am also focusing on upgrading my triathlon career, and my decision to move to the UK has greatly helped in this aspect, as I have higher standard triathlon competitions and training opportunities. We'll wait and see what the future brings forth…" S

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Breast MR Imaging in Mammographically Benign-Appearing Breast Lesions

PIERRE VASSALLO

Breast cancer is the most common malignancy in women. The most common pathologic subtypes of breast cancer originate in the terminal duct lobular unit in either the ducts (ductal carcinoma) or lobules (lobular carcinoma). These subtypes account for 80%–85% of primary breast cancers. The origin of the breast cancer can only be determined by the microscopic appearance of the cancer cells obtained at biopsy.

Usually, breast cancers manifest as irregularly shaped masses, with or without microcalcifications. Therefore, many breast cancers are diagnosed on the basis of these findings at mammography or ultrasonography (US).

Although most well-circumscribed breast lesions are benign, 10%–20% of breast malignancies are also well-circumscribed; these malignant masses include papillary, mucinous, medullary, and metaplastic carcinomas, as well as malignant phyllodes tumors. Such lesions may be difficult to recognize as malignant using conventional imaging modalities such as mammography and US.

MR imaging has been widely used for detecting and assessing breast lesions. MR imaging is sensitive for detecting breast cancers, with a sensitivity as high as 100% for invasive breast cancers, and therefore has emerged as an adjunctive breast imaging modality to mammography and US. MR imaging has limitations in lesion characterization, but it is still useful as an adjunct for differentiating between benign breast lesions and benign-looking breast cancers. It is also useful for evaluating dense breasts.

Papillary Carinomas may be located in a duct or within a cyst and are therefore mostly located in the retroareolar region. The lesions may be in-situ or invasive. On mammography, papillary carcinomas appear as well-defined dense lesions (Fig 1a). On US, intracystic lesions tend to show internal haemorrhage and also contain solid components within the cyst (Fig 1b). The solid component may show hypervascularity on Doppler US. MR imaging will show smooth lesion margins, areas of haemorrhage (fig 1c), cystic fluid (fig 1d), strong contrast enhancement of the rim and solid polypoid components (fig 1e) and a temporal contrast enhancement pattern indicative of malignant disease (fig 1f). Invasive and non-invasive papillary cancers have similar appearances on US, mammography and MR imaging.

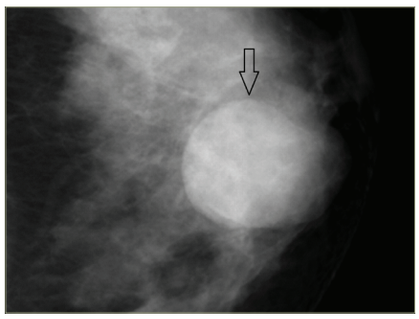

Figure 1a. Mammogram showing an intracystic papillary carcinoma as an oval well-circumscribed high-density mass (arrow).

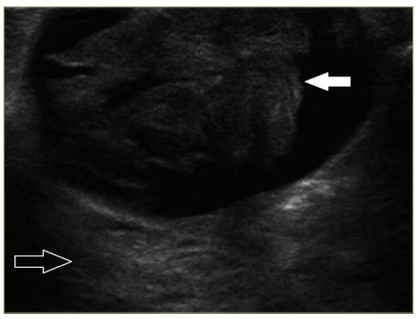

Figure 1b. US demonstrates a solid mass (solid arrow) within a cystic lesion with mild posterior acoustic enhancement (open arrow).

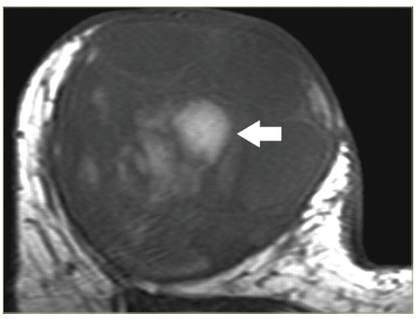

Figure 1c. T1-weighted MR scan of an intracystic papillary carcinoma showing central high T1 signal (bright area) (arrow) within the lesion that is compatible with haemorrhage.

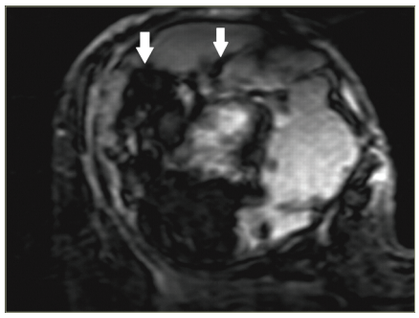

Figure 1d. T2-weighted MR scan of an intracystic papillary carcinoma showing areas of high T1 signal (bright areas) within the lesion compatible with cyst fluid. Black areas (arrows) within the lesion are due to deposits of haemosiderin resulting from older haemorrhage.

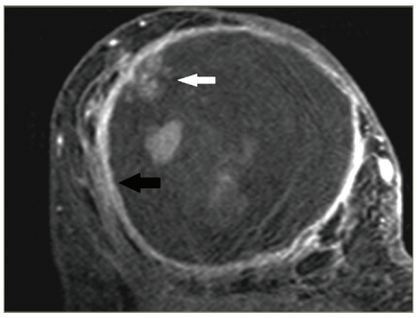

Figure 1e. Axial contrast material–enhanced T1-weighted MR image demonstrates marked enhancement of the cystic wall (black arrow) and mural nodules (white arrow).

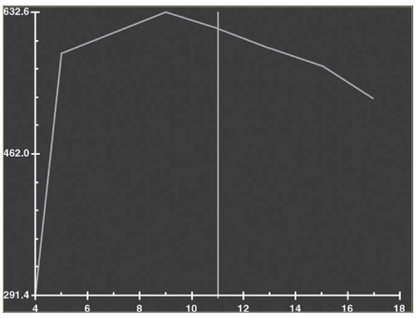

Figure 1f. The dynamic enhancement pattern (signal intensity y axis against time x axis) following (Gadolinium-based) contrast agent injection shows marked early enhancement and also an early washout pattern in the solid portion of the lesion that are features of malignancy (Type III pattern).

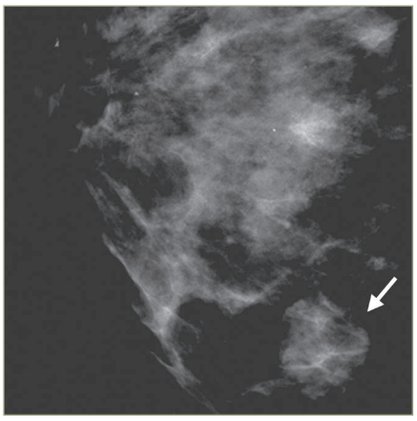

Figure 2a. Mucinous carcinoma on a mammogram shows a lobular well-circumscribed mass lesion (arrow).

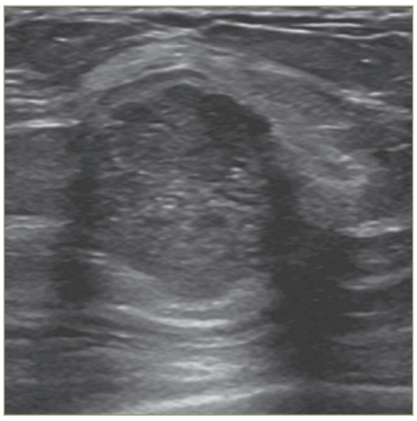

Figure 2b. Mucinous carcinoma on US seen as a round microlobulated mass with posterior acoustic enhancement.

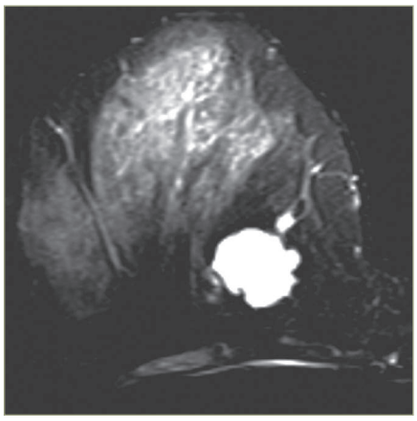

Figure 2c. T2-weighted MR image shows a homogeneously hyperintense lobular mass with a smooth margin.

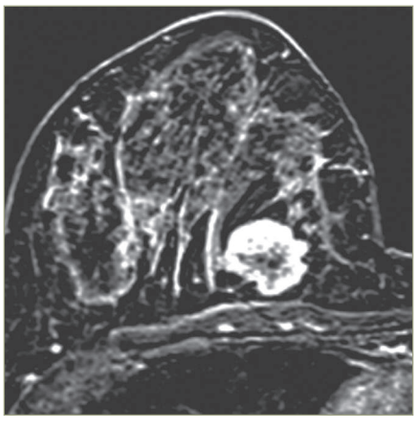

Figure 2d. Contrast-enhanced MR image shows peripheral rim enhancement and an internal nonenhancing portion.

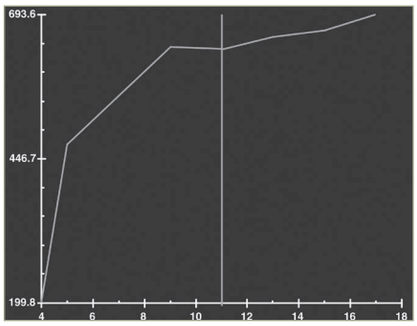

Figure 2e. The dynamic enhancement pattern is the type I persistent pattern phyllodes tumor (arrows).

Mucinous (or colloid) carcinoma contains large amounts of extracellular extraluminal mucus in direct contact with the stroma. It is more common in elderly women and usually has a good prognosis. Areas of invasive ductal cancer are however often intermixed within these lesions, which makes the prognosis less favorable. Mucinous carcinoma commonly presents as a well-circumscribed round, oval, or lobular mass on mammography (Fig 2a) and US. Mixed cystic and solid components and the presence of posterior acoustic enhancement may be seen at US (Fig 2b). Mucinous carcinoma shows variable signal intensity on T1-weighted MR images, depending on protein concentration within the tumor (Fig 2c), and is homogeneously or heterogeneously hyperintense on T2-weighted images (Fig 2d), which correlates with the large mucinous component at histologic examination. Dynamic contrast enhanced T1 weighted scans show marked early enhancement with washout (as in Fig 1f) or persistent enhancement (as in Fig 2e).

Medullary carcinoma is an uncommon tumor that accounts for less than 5% of all breast cancers. It has been reported to account for 11% of all breast carcinomas diagnosed in women 35 years and younger and has a relatively favorable prognosis. Medullary carcinoma manifests as a round, oval, noncalcified mass with a well-circumscribed margin at mammography (Fig 3a) and as a well-circumscribed hypoechoic lesion with no dorsal enhancement at US (Fig 3b). Medullary carcinomas show marked homogeneous enhancement on MRI (Fig 3c) with a plateau phase (ie no washout) (Fig 3d).

Metaplastic breast carcinoma is regarded as a ductal carcinoma that has undergone metaplasia into a nonglandular growth pattern, including squamous cell, spindle cell, and heterogeneous mesenchymal growth patterns. It is a rare type of cancer accounting for only 1% of cases and presents more commonly after the age of 50 years. Metaplastic carcinoma usually presents as a rapidly growing mass with no axillary lymphadenopathy. It appears as a well circumscribed lesion on mammography (Fig 4a) and US, being hypoechoic or heterogeneous with mixed solid and cystic components on US (Fig 4b). T2-weighted MRI scans demonstrate the lesion as bright due to the cystic components (Fig 4c). On the other hand contrast-enhanced T1-weighted scans show rim enhancement (as cystic components do not enhance) (Fig 4d). A type III enhancement pattern is seen on dynamic MR study (Fig 4e).

Phyllodes tumors are composed of a mixture of epithelial elements and a connective tissue stroma. Most are benign but intermediate and malignant forms also occur. All three forms of phyllodes tumors have a high recurrence rate. On mammography, a phyllodes tumor appears as a large relatively well-circumscribed soft-tissue mass, showing an appearance similar to a fibroadenoma. US shows a solid hypoechoic mass often with cystic areas, the latter being more common in malignant lesions. T2-weighted MRI scans demonstrate the cystic components, while contrast enhanced T1-weighted MRI shows heterogeneous enhancement (Fig 5a). Dynamic MR studies show a Type III contrast enhancement pattern (Fig 5b).

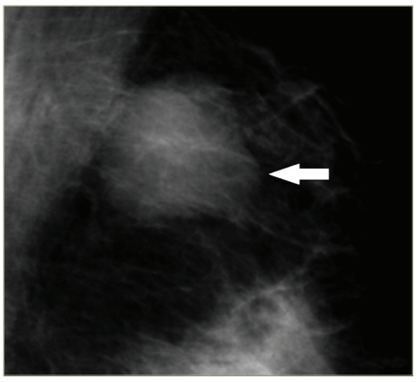

Figure 3a. Medullary carcinoma in a 28-year-old woman presents as a lobular mass (arrow) on mammography.

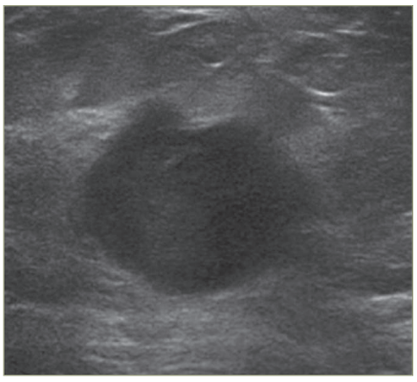

Figure 3b. US of the same lesion shows a lobular hypoechoic mass with a well-defined margins and no dorsal enhancement.

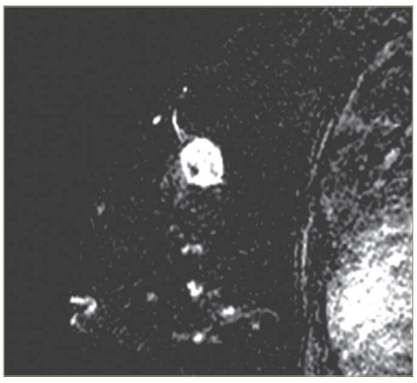

Figure 3c. Medullary carcinoma appears as a rounded well-defined lesion homogeneous contrast enhancement on MRI.

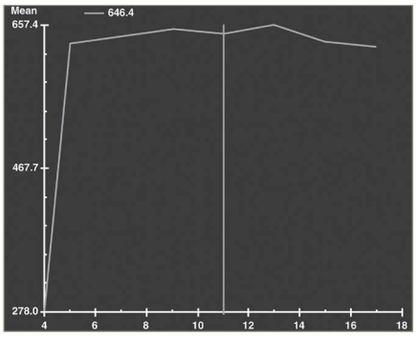

Figure 3d. Dynamic contrast examination shows a type II pattern with rapid and sustained enhancment.

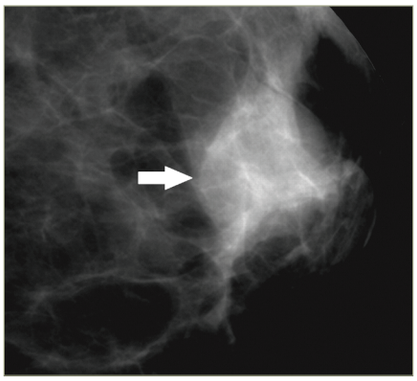

Figure 4a. Focal compression mammography shows a metaplastic carcinoma with mostly well-defined margins (arrow).

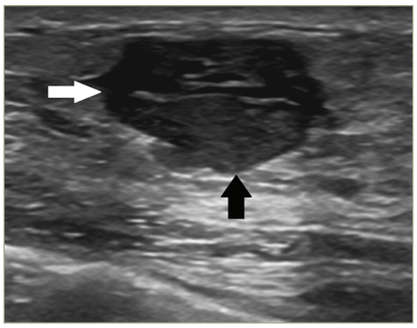

Figure 4b. US shows the same lesion with well-defined margins and heterogeneous internal texture with solid (black arrow) and cystic (white arrow) componements.

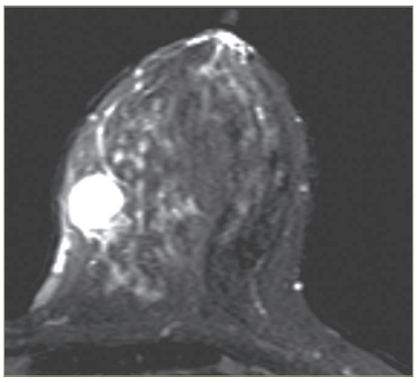

Figure 4c. T2-weighted MRI scan of the same lesion shows high signal due to cystic components.

In summary, a number of malignant lesions have a benign appearance on mammography and US. MR morphology, contrast uptake and dynamic enhancement pattern analysis serve as a valuable adjunct for correct diagnosis in these cases. High T2 signal, strong and rapid contrast uptake with sustained enhancement or early washout are features of malignant disease. S

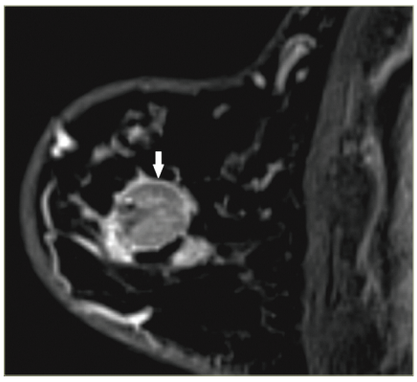

Figure 4d. Contrast enhanced T1-weighted MRI scan shows ring enhancement (arrow) of the lesion.

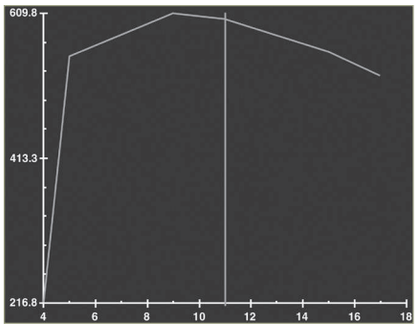

Figure 4e. Dynamic contrast MR study shows a Type III enhancement pattern.

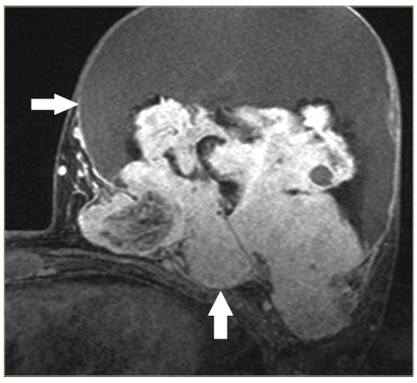

Figure 5a. Contrast-enhanced T1-weighted MRI scan showing heterogeneous enhancement in a

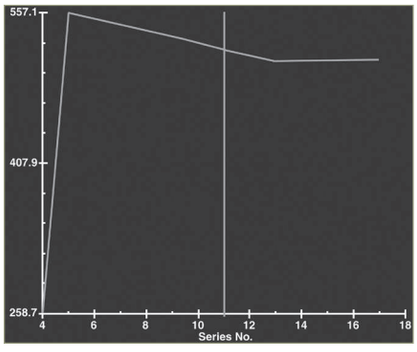

Figure 5b. A type III contrast enhancement pattern is seen in a phyllodes tumor.

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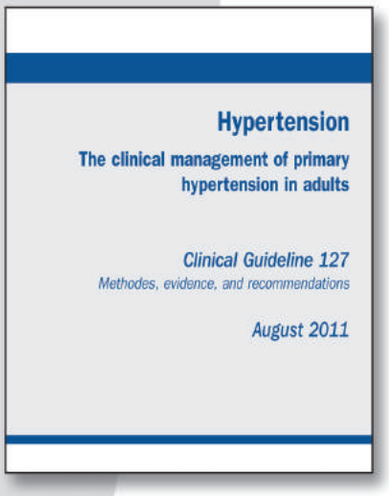
NEW British Hypertension Guidelines[1]



New 2011 Guidelines

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1. National Clinical Guideline Centre UK. Hypertension – the clinical management of primary hypertension in adults. August 2011. http://guidance.nice.org.uk/CG127

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