

The Synapse

The Medical Professionals' Network



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Breast Masses in Children - Part II

by **Pierre Vassallo**

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Discovery of breast masses in children and adolescents often causes tremendous parental and physician concern because of the high prevalence of breast cancer in the adult population.

However, the prevalence of breast cancer in this age group is low, and knowledge of the spectrum of pathologic conditions and radiological findings that affect the pediatric breast is important in guiding management...

Benign Breast Tumours

Fibroadenomas are benign fibroepithelial tumors and are the most common breast masses in girls younger than 20 years of age. The mean patient age at diagnosis is 15–17 years. Most patients present with a slowly enlarging, painless mass that may cause breast asymmetry. At physical examination, the mass is well circumscribed, rubbery, and freely movable; it is most often located in the upper outer quadrant. Fibroadenomas are oestrogen-sensitive and may grow faster during pregnancy, although they usually do not vary in size during the menstrual cycle. Fibroadenomas in males have been reported but are rare because males have no terminal duct-lobular units.

The main consideration in the differential diagnosis of fibroadenoma is phyllodes tumor, a fibroepithelial neoplasm that may be malignant. The histopathologic and imaging features of the cellular subtype of fibroadenoma known as juvenile fibroadenoma and phyllodes tumor overlap considerably, such that they are indistinguishable at imaging. The finding of peripheral cysts at ultrasound suggests phyllodes tumor, but definitive diagnosis requires tissue sampling. Rate of growth is also an important distinguishing factor between fibroadenomas and phyllodes tumours. However benign phyllodes tumours grow slowly like fibroadenomas, while juvenile fibroadenomas show rapid growth as do malignant phyllodes tumours.

The term giant fibroadenoma refers to a fibroadenoma 5-10cm in diameter and most of these entities are juvenile fibroadenomas.

Ultrasound is very sensitive in the detection of fibroadenomas. The typical sonographic appearance of a fibroadenoma is a well-circumscribed, round, oval (Figure 1), or macrolobulated mass with fairly uniform

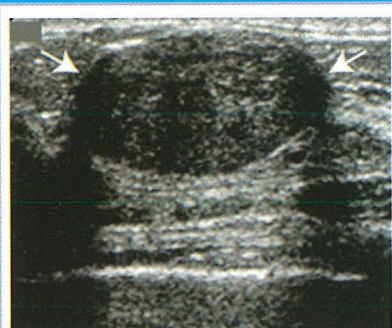


Figure 1. Fibroadenoma seen on ultrasound as a well circumscribed, hypoechoic nodule with dorsal enhancement and a long axis parallel to the chest wall.

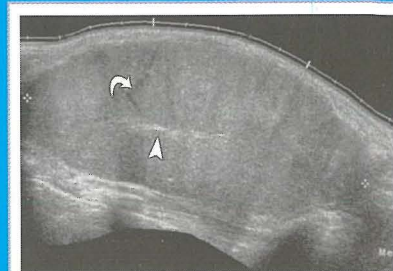


Figure 2. A juvenile fibroadenoma seen on ultrasound as a well circumscribed, homogeneously hypoechoic mass (straight arrow) within the fibroglandular breast tissue (*), with the pectoralis muscle deep to the mass (curved arrow).

hypoechoogenicity. These masses may appear almost anechoic with low-level internal echoes. Slender, fluid-filled clefts may be seen within juvenile fibroadenomas (Figure 2). In ovoid lesions, the growth pattern is horizontal or parallel; that is, the long axis of the mass is parallel to the chest wall. During a colour Doppler evaluation, these lesions may appear avascular or may demonstrate some central vascularity.

Juvenile papillomatosis is a localized, proliferative disorder of young women and older adolescents. Patients present with a firm, well-defined, mobile mass in the periphery of the breast and without nipple discharge. The resected mass appears well circumscribed and contains multiple small cysts (<2 cm) within a dense fibrous stroma, an appearance that has given rise to the term *swiss cheese disease*. This appearance is also evident on ultrasound (Figure 3).

Other causes of masses include infection, trauma, and cyst formation.

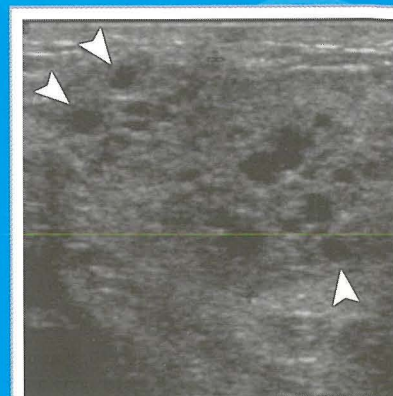


Figure 3. Juvenile papillomatosis appears as a slightly hypoechoic mass that contains multiple, small anechoic cysts (arrowheads) on ultrasound.

Malignant Breast Lesions

Phyllodes tumor, or cystosarcoma phyllodes, is a rare fibroepithelial neoplasm that accounts for only 1% of breast lesions in children and adolescents,

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Bedroom Politics ... Recession, Research & Development

At the beginning of this year, in the annual letter to his shareholders, Warren Buffet, who is currently the world's second richest man, illustrated the financial and economic meltdown with the following words ...

"Participants seeking to dodge troubles face the same problem as someone seeking to avoid venereal disease: It's not just whom you sleep with, but also whom they are sleeping with."

Indeed, exactly one year after Lehman's fall from grace, we are being comforted by the European Commission claiming that the recession in Europe is releasing its grip. Obviously this is good news. However it was only a few months ago that an apocalyptic vision was being projected by all, and in fact over the past year we have seen numerous mergers, take-overs and buy-backs extending horizontally within practically all markets. And obviously the healthcare system was not immune to this. My past editorials have included a plethora of examples. And in case one needs further examples ... just a few days ago we have seen Abbott communicate that it is to buy Visigen for \$400 million in cash to boost its position in intraocular lens technology for cataracts. Besides, it is also to acquire the 90% of outstanding shares of Evalve that it does not already own, for up to \$410 million to strengthen its vascular business. Whilst on the other hand, Boehringer Ingelheim has confirmed that it will cut up to 900 sales representatives, almost 30% of its sales force, in response to market changes affecting the pharmaceutical industry. Thus as one can see the recession has brought green shoots for some companies and dark clouds for others.

Ironically, in August we have also seen the mayor of New York, Michael Bloomberg, defend the very cause

which may have triggered the recession ... Bloomberg has been quoted as claiming that US companies and their CEOs "don't make a lot of money". It is however the opinion of the editor that a fair and just balance has to be sought, respecting the fact that history has the habit of repeating itself. This goes beyond simply trying to prevent a scenario where companies go bust or workers get laid off. Indeed, Research and Development by pharmaceutical companies, including lead finding and clinical trials, can only be sustained through cost-effective management based on corporate social responsibility ...

Amidst all this we are seeing China gearing up to begin the first vaccination programme worldwide against H1N1. The first recipients will be people scheduled to take part in the country's National Day celebrations on 1st October who will receive a domestically manufactured vaccine by Sinovac. On the other hand, the US expects to begin an H1N1 vaccination campaign in mid-October, after approving vaccines made by Sanofi-Aventis, Novartis, CSL Ltd. and AstraZeneca's MedImmune unit in September. Interestingly, MedImmune also manufactures a nasal spray vaccine for the seasonal influenza.

On a final note, a biotechnology company hailing from India, Indus Biotech, is also developing a botanical drug for HIV that is also seen as a potential treatment and prophylaxis for H1N1. The development may be of significance, considering the potentially improved safety/toxicity profile ...

Pan Ellus

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Dental Erosion

by **Dr Audrey Camilleri** BChD MScPaed(Lond) MFDSRCS(Edin)
Paediatric Dentist

It is only relatively recent that tooth erosion has been recognized as presenting a dental health problem in both children and in adults. In the UK 55% of 6 year olds were found to have erosion and in 23% of this population it had progressed into the dentine.



Figure 1. Erosion due to soft drink intake daily with loss of enamel on buccal surface of both upper central incisors



Figure 2. Erosion due to excessive fruit juice intake with loss of enamel on lower incisors and lower canines



Figure 3. Enamel loss on mesial surface of upper central incisors

First and foremost one has to understand what dental erosion means. Erosion is the superficial irreversible loss of tooth structure by a chemical process that does not involve bacteria and is caused by acid attack. Erosion usually shows up as hollows in the teeth and a general wearing away of the tooth surface and biting edges. Enamel is the hard, protective coating of the tooth which protects the sensitive dentine underneath. When the enamel is worn away, the dentine underneath is exposed, which is a darker, yellower colour than the enamel, and this may lead to pain and sensitivity. Because the dentine is sensitive a patient's teeth can also become more sensitive to hot, cold or sweet foods and drinks. The teeth also appear highly polished and the loss of tooth surface is generally disproportionate to the age of the subject (Figure 1).

It is equally important to understand the aetiology of dental erosion. Every time one eats or drinks anything acidic, the enamel on their teeth becomes softer for a short while, and loses some of its mineral content. The saliva will slowly neutralise this acidity in the mouth and restore it to its natural balance. However, if this acid attack happens too often, the mouth does not have enough chance to repair itself and tiny particles of enamel can be irreversibly lost. Over time one would start to lose the surface of their teeth.

Dental erosion is multifactorial and the causative factors may be divided into:

Extrinsic factors

(a) Diet including acidic drinks, energy drinks, flavoured water, sugar-containing sports drinks (Figures 2, 3 and 4).

Acidic foods and drinks such as infant fruit juices, particularly citric ones including lemon and orange, can be particularly harmful to teeth. These generally contain natural acids, which can be harmful to teeth. Fizzy drinks are also a cause of enamel erosion. It is important to remember that even the diet brands are still as harmful. Flavoured sparkling waters should equally be considered as potentially erosive, and preventive advice on their consumption should recognize them as potentially acidic drinks rather than just water with flavouring¹.

Relative titratable acidity is a more accurate indicator than the pH value when it comes to dental erosion:

- Grapefruit, apple and orange → high
- Soft drinks, wine → medium
- Beer, sparkling water → low

Interestingly it was found that the titratable acidity of energy drinks was greater than that of regular and diet sodas which in turn was greater than that of pure (not from concentrate) juices and sports drinks ($P < 0.05$).¹

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The Great Pretender

by **Philip Carabot**
Head, Genito-Urinary Clinic
Boffa Hospital

The Pox is back – but did it ever really go away? After a brief illusory dramatic drop in incidence in the mid-80's and early 90's Syphilis has made a dramatic re-appearance on the STI centre stage like the good old trouserer it is. However we seem to ignore it to our own and our patients' peril. It is nothing more than yesterday's HIV disease. I have to admit I have a soft spot for the Pox, which together with the Clap (gonorrhoea) represents the traditional Venereology I have grown old with.

There have been 90 cases recorded since 2002 (Figure 1). As with all the other STIs notified by the GU Clinic it cannot be assumed that this is all there is. They are simply picked up from those who chose to attend the Clinic. The bulk of the diseases, as well as their contacts are still out there in the community waiting to be diagnosed. For this all practitioners need a high degree of suspicion and a low threshold for testing appropriately.

While 46 cases were latent disease and picked up only on serology (Figure 2), the other 44 cases presented with signs of early disease with primary chancres and rashes or other classical manifestations of secondary syphilis (Figure 3).

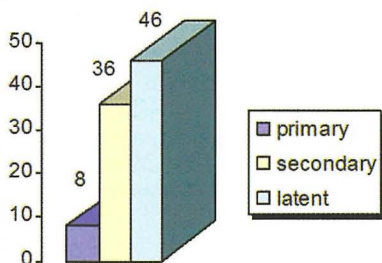


Figure 2. Classification of syphilis cases (2002-2008)

Is that penile/vulval ulcer which should be herpetic but is actually quite painless and not healing as expected still diagnosed as herpetic? Is that funny rash which is hardly noticeable really a 'sun rash'? Are those perianal warts really warts? Could they possibly be *condylomata lata* (Figure 4)? **If in doubt, test.**

For general screening purposes we should specify that we need either a Syphilis EIA IgM/IgG, or a VDRL test (Venereal Disease Research Laboratory) together with a TPHA (Treponema Pallidum Haemagglutination Test). VDRL by itself is NOT a good screening test. The VDRL is often negative in latent

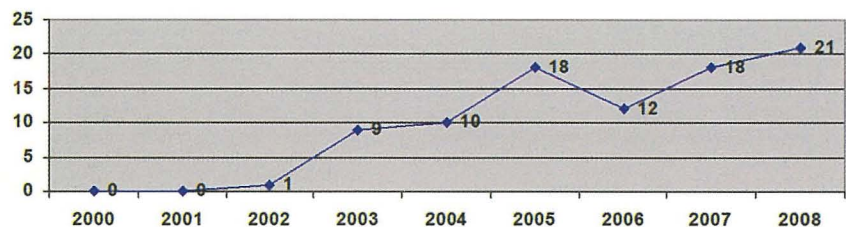


Figure 1. Total Syphilis cases 2000-2008 (GU Clinic)

disease and can also be apparently negative in primary disease (the prozone phenomenon). Therefore cases will be missed if this is all we ask for. While the full battery of tests is available at Mater Dei Hospital, unfortunately there are still laboratories which perform only the VDRL. This practice needs to be challenged.

9 of the patients diagnosed with syphilis were pregnant women. Fortunately, all delivered normal babies free of congenital disease. The recommended practice of screening all pregnant women, irrespective of marital status, for syphilis should be re-introduced.



Figure 3. Rash of secondary syphilis - the great imitator

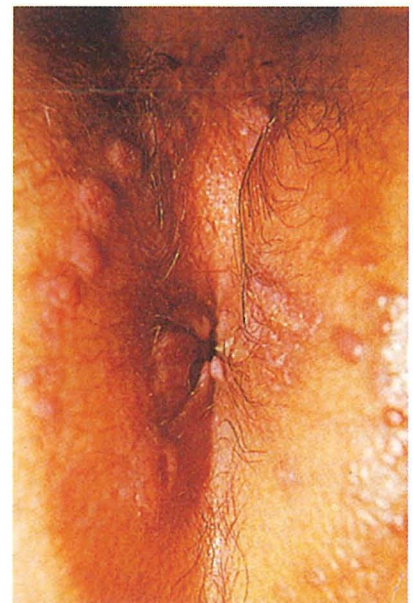


Figure 4: *Condylomata lata* of secondary syphilis

Fortunately *Treponema Pallidum* is still very sensitive to penicillin. We use the long-acting Benzathine Penicillin, not to be confused with Benzylpenicillin which is not an appropriate treatment in adults. Benzathine Penicillin can only be obtained from the Boffa Hospital pharmacy under the GU Clinic's prescription, so all cases of known or suspected syphilis need to be referred there without delay. ☑

For more information please contact the GU Clinic on 229897115/ 21227981 or philip.carabot@gov.mt

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Rare: Angioedema. **Laboratory values:** decrease in haemoglobin and haematocrit, increase in serum potassium. For the hydrochlorothiazide component, other reported adverse reactions include: Aplastic anaemia, bone marrow depression, neutropenia/agranulocytosis, haemolytic anaemia, leucopenia, thrombocytopenia, depression, sleep disturbances, restlessness, light-headedness, vertigo, paraesthesia, dizziness, transient blurred vision, xanthopsia, cardiac arrhythmias, postural hypotension, respiratory distress (including pneumonitis and pulmonary oedema), pancreatitis, anorexia, diarrhoea, constipation, gastric irritation, sialadenitis, loss of appetite, jaundice (intrahepatic cholestatic jaundice), anaphylactic reactions, toxic epidermal necrolysis, necrotising angitis, (vasculitis, cutaneous vasculitis), cutaneous lupus erythematosus-like reactions, reactivation of cutaneous lupus erythematosus, photosensitivity reactions, rash, urticaria, weakness, muscle spasm, interstitial nephritis, renal dysfunction, fever. **Laboratory values:** electrolyte imbalance, including hypokalaemia and hyponatraemia, hyperuricaemia, glycosuria, hyperglycaemia, increases in cholesterol and triglycerides **Legal Category:** POM **Pack sizes:** 7, 28 film-coated tablets **Marketing Authorisation Holder:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **Marketing Authorisation Numbers:** Rasilez HCT 300/12.5 mg - EU/1/08/491/041-060. 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Cervical Cancer Screening and GPs in Italy

by Francesco Carelli & Stefano Alice

Background

All over the world the standard method for cervical cancer screening is Papanicolaou smear (Pap test), introduced more than 50 years ago; routine use of Pap smears, whose false negative rate is 20%, has been associated with a dramatic reduction in the incidence rate of cervical cancer (by 60-90%) and in mortality (by 90%). The test is a simple procedure, which can detect the disease at a pre-cancerous and treatable stage.

Cervical cancer ranks third of the female cancers, after breast and ovarian, that affect women in Italy. The principal risks factors are considered sexual activity at an early age and multiple sex partners for either woman or partner.

According to the Italian Screening Programme, the Pap smear is offered to all women age 25 to 64 years who are sexually active; the screening interval is 3 years.¹ It is estimated that screening efficacy is very high²; it is evaluated that, thanks to the screening programme which started in Italy in 1996, 60% of cervical cancers have been prevented, even if only 66.7% of the target population has been screened, in the period 1999-2005.³

The low rate of eligible women screened is not the only problem in our country; the first smear is done late, on average, at 31 years⁴ and compliance among the unmarried is only 51.8%.^{1,5} In Italy, smear tests are carried out by Gynaecologists and a specific survey shows that GPs involvement in recruiting women in their communities to have Pap smears is very low; only 31% of eligible women are screened on suggestion of their Family doctors^{1,4}.

The role of GPs

We believe that the suggestion of the Pap Test to women eligible for the Screening Programme is a professional task of the GPs, because the characteristics of Family Medicine include the "promotion of health and wellbeing of patients by appropriate and effective interventions"; ultimately Family Medicine "has a specific responsibility for the health of the community".⁶

Furthermore GPs should give information to patients about the test, condition being investigated and possible results of screening and their implications; GPs should be responsible to communicate the results to women and to refer them to specialists when needed. GPs could also take the smears, however this should be done after being appropriately trained example, by attending a specific course.⁶

GPs are normally the first medical contact within the health care system and so they can have a strategic role in a Screening Programme; they have a unique relationship with patients, which is established over time, through effective communication between doctor and patient; thanks to this special, long term relationship of trust, a greater involvement of the GPs in this Public Health programme could be successful in increasing the rate of eligible women screened and in lowering the age of the first smear.

The potential for GPs to promote screening for cervical cancer has been explored by a multi-centre study, published in 1996, by the Centre of Clinical Epidemiology and Biostatistics of the Faculty of Medicine of the University of Newcastle, Australia.

They compared the effectiveness of three different community-based strategies: a television campaign, a television campaign combined with personally addressed letters sent to all women in the community, and a television campaign combined with a GP-based programme. Each intervention was implemented in three different regions in New South Wales, Australia. Three control regions were also included for comparison. Of all three strategies, the combined television campaign and GP-based programme was the most effective tool had the most potential, with an increment of 8% of previously unscreened women being screened; this compares to 2-4% when the television campaign was combined with letters and 1-3% when television was used alone.⁷

Further research is needed to understand which are the barriers for Italian GPs to improve the early detection and management of cervical cancer and the Italian NHS should develop strategies to overcome these. In our opinion the first goal is to improve GPs awareness of the importance of the Pap smear and of the fact that too many women are not adequately screened. This can be done during CME events, by providing GPs Evidence Based information. Financial incentives for computerized recall/reminder systems, could also be useful. Furthermore lately we have also seen the introduction of a new mobile-based technology to assist family doctors and gynaecologists in this respect. ☐

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Abbreviated Prescribing Information SILGARD[®]
SILGARD, suspension for injection in a pre-filled syringe. Human Papillomavirus Vaccine [Types 6, 11, 16, 18]. PHARMACEUTICAL FORM: Suspension for injection in a pre-filled syringe. Prior to agitation, SILGARD may appear as a clear liquid with a white precipitate. After thorough agitation, it is a white, cloudy liquid. Therapeutic indications: SILGARD is a vaccine for the prevention of premalignant genital lesions (cervical, vulvar and vaginal), cervical cancer and external genital warts (condyloma acuminata) causally related to Human Papillomavirus (HPV) types 6, 11, 16 and 18. The indication is based on the demonstration of efficacy of SILGARD in adult females 16 to 26 years of age and on the demonstration of immunogenicity of SILGARD in 9- to 15-year old children and adolescents. Protective efficacy has not been evaluated in males. Posology and method of administration: The primary vaccination series consists of 3 separate 0.5 ml doses administered according to the following schedule: 0, 2, 6 months. If an alternate vaccination schedule is necessary, the second dose should be administered at least one month after the first dose and the third dose should be administered at least 3 months after the second dose. All three doses should be given within a 1-year period. The need for a booster dose has not been established. Paediatric population: SILGARD is not recommended for use in children below 9 years of age due to insufficient data on immunogenicity, safety and efficacy. The vaccine should be administered by intramuscular injection. The preferred site is the deltoid area of the upper arm or in the higher anterolateral area of the thigh. Contraindications: Hypersensitivity to the active substances or to any of the excipients. Special warnings and precautions for use: As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine. Syncope (fainting) may follow any vaccination, especially in adolescents and young adults. Syncope, sometimes associated with falling, has occurred after vaccination with SILGARD. As with any vaccine, vaccination with SILGARD may not result in protection in all vaccine recipients. SILGARD will only protect against diseases that are caused by HPV types 6, 11, 16 and 18 and to a limited extent against diseases caused by certain related HPV types. SILGARD has not been shown to have a therapeutic effect. The vaccine is therefore not indicated for treatment of cervical cancer, high-grade cervical, vulvar and vaginal dysplastic lesions or genital warts. It is also not intended to prevent progression of other established HPV-related lesions. Vaccination is not a substitute for routine cervical screening. There are no data

on the use of SILGARD in subjects with impaired immune responsiveness. Individuals with impaired immune responsiveness, whether due to the use of potent immunosuppressive therapy, a genetic defect, Human Immunodeficiency Virus (HIV) infection, or other causes, may not respond to the vaccine. This vaccine should be given with caution to individuals with thrombocytopenia or any coagulation disorder because bleeding may occur following an intramuscular administration in these individuals. The duration of protection is currently unknown. Sustained protective efficacy has been observed for 4.5 years after completion of the 3-dose series. There are no safety, immunogenicity or efficacy data to support interchangeability of SILGARD with other HPV vaccines. Interaction with other medicinal products and other forms of interaction: Use with other vaccines: Administration of SILGARD at the same time (but, for injected vaccines, at a different injection site) as hepatitis B (recombinant) vaccine did not interfere with the immune response to the HPV types. The concomitant administration of SILGARD with vaccines other than hepatitis B (recombinant) vaccine has not been studied. Use with hormonal contraceptives: Use of hormonal contraceptives did not appear to affect the immune response to SILGARD. Pregnancy and lactation: Vaccination should, therefore, be postponed until completion of pregnancy. SILGARD can be given to breastfeeding women. Undesirable effects: The following vaccine-related adverse reactions were observed among recipients of SILGARD at a frequency of at least 1.0% and also at a greater frequency than observed among placebo recipients. They are ranked under headings of frequency using the following convention: Very common: pyrexia, erythema, pain, and swelling. Common at the injection site: bruising and pruritus. Post Marketing Experience: lymphadenopathy, arthralgia, myalgia, asthenia, fatigue and malaise. MARKETING AUTHORISATION HOLDER: Merck Sharp & Dohme Ltd, Hertford Road, Hoddesdon, Hertfordshire EN11 9BU, United Kingdom. MARKETING AUTHORISATION NUMBER(S): EU/1/06/358/007, EU/1/06/358/015. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION: 20th September 2006. DATE OF REVISION OF THE TEXT: 02 February 2009. The drug is provided by medical prescription only. This is an abridged Prescribing Information. Before prescribing, please consult the full prescribing information. SILGARD is a registered trademark of Merck & Co., Inc, Whitehouse Station, NJ, USA. For more information please contact MSD Cyprus.

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SILGARD[™]
[Quadrivalent Human Papillomavirus
(Types 6, 11, 16, 18) Recombinant Vaccine]

11-09 GRD-2008-MVD-1273400-J
12-09-GRD-2009-ME-(CY-MA)-1351-J

Update on H1N1 Virus

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

Local situation

Up till 14 September, we had 296 confirmed cases of H1N1 (162 males and 134 females) and 109 confirmed cases of Influenza A (probable cases). 36% of those confirmed cases were found in patients suffering from chronic disease, 12% were health care workers, 4% were pregnant women, 16% were children < 5 years, 14% were hospitalized cases, 8% were cases with severe symptoms, and sentinel cases made up the remaining 10%.

International situation

As of 1 September 3,402 deaths related to the pandemic A/H1N1/2009 were reported worldwide. Epidemics of influenza-like syndromes are evolving differently across the world but A/H1N1 remains the predominant virus circulating in both the northern and southern hemispheres. In southern hemisphere countries (represented by Chile, Argentina, Australia, New Zealand and South Africa), influenza activity continues to decrease. Active transmission persists in tropical regions of America and Asia. Many countries in Central America and the Caribbean continue to report declining activity however, countries in the tropical region of South America (represented by Bolivia, Ecuador and Venezuela) and Asia (like India, Bangladesh and Cambodia) are reporting increasing levels of respiratory disease.

In the Northern Hemisphere influenza activity is variable. In the US, regional increases in influenza activity are being reported. Most of Europe is reporting low or moderate respiratory diseases activity, but parts of Eastern Europe are beginning to report increases in activity.

H1N1 Vaccine

Media is focusing presently on the pandemic vaccines. Most countries have decided to offer the vaccine to those persons at high risk of developing complications to influenza and these include pregnant women, children < 5 years, those suffering from chronic conditions and health care workers.

Preliminary data from clinical trials done by Greenberg et al. in Australia show that a single dose of nonadjuvated vaccine containing the usual 15µg of hemagglutinin (HA) antigen is immunogenic in a high proportion of healthy young and middle-aged adults (75% - 96%). US studies indicate that protection occurs within 8 to 10 days. The study found the same side effects that many people usual experience with influenza vaccines. Approximately 45% of vaccines had moderate reactions like headaches, pains in the arm and redness at the injection site.

In another study by Clark et al. at the University of Leicester, 175 British volunteers aged 18 to 50 who received either 7.5 or 15µg of an adjuvated vaccine, made by Novartis Corp were found to elicit antibody titres. The study found that either dose produced adequate immune response within 14 days.

The obvious advantage of a one-dose schedule is that, in the current time of vaccine scarcity, it doubles the number of people who may be vaccinated with a fixed amount of vaccine. Another advantage is that antibody responses develop sooner. In the present situation of widespread circulation of H1N1 virus occurring in many areas of the world, achieving protection 3 to 4 weeks earlier with one dose, rather than later on a two-dose

schedule, is advantageous. Furthermore, from a logistic standpoint, administering one dose will greatly simplify vaccination programs and should reduce costs.

Data on immunogenicity is difficult to extrapolate to children or to adults who have underlying immune suppression or high-risk conditions. Experience with traditional seasonal vaccines has shown that the immune responses in older children, pregnant women, and immuno-competent adults with chronic conditions are roughly similar to those of healthy non-pregnant adults. So on this basis, the new data suggest that the standard 15µg HA dose of H1N1 vaccine should be immunogenic for these groups. The immune responses in children are unknown. Younger children tend to have inferior responses to inactivated vaccines, as compared with healthy adults so it is likely that in children less than 9 years of age, two doses will be recommended as is done the first year they receive seasonal influenza vaccines.

The EMEA's expert committee on new medicines have started to consider the first three H1N1 swine flu vaccines from GlaxoSmithKline, Novartis and Baxter in September. If all goes as planned, the first swine flu vaccines could be licensed by the European Commission early in October.

Antivirals

CDC has last week issued revised guidance advising against giving influenza drugs as prophylaxis in healthy people, even if they may have been exposed to infected persons.

The CDC recommends treatment with Tamiflu® or Relenza® for anyone hospitalized with a flu-like illness. They also advise prompt treatment at the first sign of symptoms for those at high risk for serious complications, including pregnant women, children < 5 years and people with certain chronic conditions like asthma and heart disease.

As of the 2nd week of September Roche have confirmed that they are aware of 13 cases of Tamiflu®-resistant H1N1 cases around the world; CDC alone has counted 9 in the US. All were single cases. But there has been the first reporting by Health officials in North Carolina of what seems to be the first Tamiflu®-resistant H1N1 virus spreading from one person to another.

Latest recommendations from the WHO on school closures as of 11 September

From data already collected it has been demonstrated that schools amplify the transmission of pandemic viruses both within schools and in the wider community. However the timing of school closures is critically important to be effective in reducing transmission, and also other measures have to be included to ensure that contact between students is limited if the school is closed. One has to ensure that the students are not congregating in another setting like the cinema, shopping mall and other venues, as they will continue to spread the virus and the benefits of closing the school will diminish greatly.

While it is known that school closures can reduce the peak demand on health care systems, one also has to weigh the disruption it may cause to health care services if a number of health care workers would need to stay at home to look after their school-aged children. ☐

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

Lescol[®]/Lescol[®] XL

Presentation: Fluvastatin sodium. Lescol capsules containing the equivalent of 20 mg or 40 mg fluvastatin free acid. Lescol XL prolonged release tablets containing the equivalent of 80 mg fluvastatin free acid. **Indications:** For the reduction of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (apoB), and triglycerides (TG), and the increase in high-density lipoprotein cholesterol (HDL-C) as an adjunct to diet in adults with primary hypercholesterolaemia and mixed dyslipidaemia (Fredrickson Types IIa/IIb) and in heterozygous familial hypercholesterolaemia ♦Slowing of the progression of coronary atherosclerosis in adults with primary hypercholesterolaemia, including mild forms, and coronary heart disease ♦Secondary prevention of major adverse cardiac events in adults with CHD after coronary transcatheter therapy. **Dosage:** Dyslipidaemia and slowing of the progression of coronary atherosclerosis: Prior to initiating Lescol, the patient should be placed on a standard cholesterol-lowering diet; dietary therapy should be continued during treatment. The recommended starting dose is 40 mg (1 capsule Lescol 40 mg once daily) or 80 mg (1 capsule Lescol 40 mg twice daily). 1 tablet Lescol XL 80 mg at any time of the day is recommended for use in adults only. 20 mg (1 capsule Lescol 20 mg) may be adequate in mild cases. Secondary prevention of major adverse cardiac events in adults with CHD after coronary transcatheter therapy: the recommended daily dose is 80 mg. **Contraindications:** Hypersensitivity to the drug or excipients. Active liver disease or unexplained, persistent elevations in serum transaminases. Pregnancy and lactation. **Precautions/Warnings:** Liver function should be monitored ♦Caution is required in patients with a history of liver disease or heavy alcohol consumption, with unexplained diffuse myalgias, muscle pain/tenderness/weakness, and marked elevation of creatine kinase (CK) values. In patients with pre-disposing factors for rhabdomyolysis, the CK-level should be measured prior to treatment initiation. If muscular symptoms like pain, weakness or cramps occur in patients receiving fluvastatin, their CK-levels should be measured. Treatment should be stopped, if these levels are found to be significantly elevated (>5xULN). ♦Caution with co-administration of fibrates, nicotinic acid and ciclosporin ♦Experience in paediatric population is limited to children of 9 years and older and to specific hypercholesterolaemia conditions. **Interactions:** Fibrates; nicotinic acid; fluconazole; ciclosporin; bile acid-sequestrants; rifampicin; phenytoin; oral anticoagulants; glibenclamide; colchicines. **Adverse reactions: Common:** dyspepsia, abdominal pain, nausea, headache, insomnia ♦**Rare cases of hypersensitivity reactions** (mainly rash and urticaria), myalgia, muscle tenderness/weakness, myopathy ♦**Very rare cases of thrombocytopenia, anaphylactic reaction, paraesthesia, dysaesthesia, hypo-aesthesia, vasculitis, hepatitis, other skin reactions** (e.g. eczema, dermatitis, bullous exanthema), face oedema, angioedema, rhabdomyolysis, myositis, lupus erythematosus-like reactions, pancreatitis ♦Elevation of transaminase and CK levels. Marketing Authorisation Number: Lescol 20mg – 088/01601, Lescol 40mg – 088/01602, Lescol XL - 088/01603 **Marketing Authorisation Holder:** Novartis Pharmaceuticals UK Ltd., Frimley Business Park, Frimley, Camberley, Surrey GU16 7 SR, UK. Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma, P.O. Box 124, Valletta, VLT 1000, Malta. Tel +356 22983217. 2009-MT-01-Lescol

E-Learning modules: A healthy collaboration between the Malta Foundation School and TheSynapse

by **Mr Kevin Cassar, Dr Tonio Piscopo**
Malta Foundation Programme Directors

The Malta Foundation School enrolled its first group of doctors into its newly established foundation programme last July. This programme covers the first two years of clinical practice for newly graduated doctors and is the equivalent of the 'housemanship' period. The big difference is that doctors entering this programme will be provided with one-to-one educational supervision throughout the two years, a structured training programme, regular assessment using different tools and various assessors as well as a certificate of successful completion at the end of the programme. This certificate will enable these doctors to apply for basic specialist training programmes both in Malta and in the UK. The completion certificate is recognized in the UK as the same as a certificate awarded by UK foundation schools, since the Malta Foundation school has been accorded affiliate status by the UK foundation programme office.

One important aspect of the foundation programme is that doctors need to achieve and demonstrate achievement of core competences which are laid down in the foundation programme curriculum, a document produced by the Academy of Royal Colleges and the various departments of Health of England, Scotland, Wales and Northern Ireland. This curriculum is revised every 3 years and sets down not only the areas of knowledge that the trainees need to cover but also the skills and attitudes that they need to develop. In an effort to help our doctors cover these areas we have



teamed up with TheSynapse to develop e-learning modules. The aim is to deliver learning solutions to the next generation of healthcare professionals using innovative learning technologies. These online modules will cover key areas of the curriculum and give the trainees the opportunity of learning anytime and anywhere but also to perform self-assessment. The first module being launched and which is written by Principal Pharmacist Mark Zammit covers the area of safe prescribing. Needless to say this is an essential skill that any doctor needs to master and it is also clear that although this module covers an important part of the foundation programme curriculum, this is of interest to doctors in any practice.

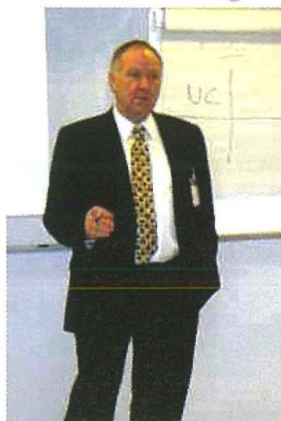
The e-modules that are planned and which will be rolled out gradually will deal with areas that are of interest to the majority of medical practitioners across all specialties. While these modules will provide foundation doctors with an important educational resource to help them cover the curriculum, there is little doubt that these will be of benefit to all practitioners. We are grateful to the TheSynapse team for their support in developing these modules and augur that these modules will serve to improve the standards of medical care in Malta. ☑

Further information may be found on www.fpdoctors.info.

The E-Learning modules are found on <http://cme.thesynapse.net>

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By Mr Rodney J Peyton OBE



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Mr. Peyton was the Principal Tutor in Faculty Development at the Royal College of Surgeons of England and Educational Advisor to the Intercollegiate Examinations Board in Surgery.

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In order to advertise any locum availabilities / opportunities in The Synapse Magazine and/or The Synapse Website, kindly contact us on mpl@thesynapse.net. This is a service offered FREE OF CHARGE to all doctors, pharmacists and dentists.

‘Grape Expectations’

Continuing our Introduction to Wine Enjoyment

by *Albert Cilia-Vincenti*

*“One barrel of wine can work more miracles than a church full of saints”
(Italian proverb)*

Wine storage

This is a major problem because wine hasn't got such a high content of alcohol, and has a far more complex organic chemical composition than spirits, and so is easily damaged and its chemical constituents altered by **high temperatures**. It is of concern, particularly with our hot summers.

Obsessional wine aficionados will insist you need a subterranean wine cellar which is dark, vibration-free, damp and kept at a constant 13°C. Few of us have such ideal conditions. Wine can in fact thrive quite happily, and develop well, in basements that reach 18°C in summer. If your storage place reaches up to 20°C, or just over, you must keep in mind that your wines will mature a bit faster than what you read in wine publications, and you should therefore drink them earlier than the recommended ageing time spans.

Instead of being a drawback, these less than ideal storage conditions are actually better for average mortals like most of us, because they will offer you the opportunity

of enjoying your quality wines earlier. Wines stored at a constant 13°C will evolve so slowly that your grandchildren are the ones more likely to enjoy them at their peak. This point should be kept in mind also by those who own professional wine storage cabinets – keeping wines at a temperature of 17/18°C, rather than at 13°C, will mature them faster, and also safely.

As long as a **constant temperature** is maintained, and any temperature change up to 18-20°C and back down to winter temperature is very gradual, wines will not be damaged. It is important to keep in mind that white wines are more fragile than reds, and if storage conditions are not ideal, ageing times for whites must be more drastically reduced. These simple guidelines should therefore alert you to the fact that wine storage within kitchens or living rooms, where temperature fluctuates rapidly, is not suitable for wine storage.

The level of **humidity** in one's wine storage arrangement is as important as the temperature. A 70-75% level is ideal. Higher humidity levels than 75% will damage the

bottle labels with mould, although this high humidity is perfectly safe for the wine itself. A level of below 40% will dry the corks and potentially shorten the life of the wine. Therefore, one needs to be careful not to use a drying type of air-conditioning in a wine storage compartment – it would need to be a low temperature/high humidity type air-conditioning specifically made for wine storage areas.

Perhaps one of the most common misconceptions with wine storage is that most wines will not improve with storing and ageing. One may go to the trouble and expense of storing wines in the expectation that they are going to improve and offer higher levels of olfactory and gustatory pleasure, but only a minority can actually satisfy this expectation. More on this interesting and controversial wine subject next time. ☐

Albert Cilia-Vincenti is a long-standing member of The Wine Society (1874) of UK and founding committee member of “Il-Qatra” – a 60-member blind-tasting wine club of 10 years standing.

Of Thi Thoug

Today Edward de Bono is known the world over. There is no university that has not considered his methods which are promulgated by a network of some 1200 trainees worldwide. Meeting him in Malta during one of his pauses in between delivering speeches and holding international seminars, provides insight into the personality and the man.

“My methods of thinking can be adopted in any field and certainly they have been adopted by diverse people, multinational companies and artists of world fame. For instance in art and music, they have been taken up by great artists such as Peter Gabriel, the Pet Shop Boys and Eurythmics. Then there are the schools. Research carried out in the UK has shown that there is a tangible increase in the improved performance of students who are taught my thinking methods.”

Certainly de Bono’s thinking skills can be adopted by the very young, even as young as four years of age. This age group can kick off with the Six Hats parallel thinking methods, yet they would only be learning a simplified version of what is taught to top economists around the globe. Lateral thinking has also been found to be extremely useful to the very old, since it empowers the aged to find methods of reducing confusion. Even the parents of schizophrenic children have found the methods helpful in this regard. “I must say that this method has been taken as far afield as Papua New Guinea. There the method has been taught to the populations living in the remote highlands and after they learnt the method, they admitted that it had changed their lives.”

But why do de Bono’s methods clinch such popularity? Why would China set up five pilot projects in five different provinces to teach his methods to thousands of school children? And why would big names, the likes of IBM, Du Pont, British



by **Marika Azzopardi**

He originally qualified in medicine and proceeded to work clinically as well as follow up on research about the interaction of different systems, applying the principles of medicine to those of neurology. His findings ultimately gave rise to the rules of lateral thinking. As early as 1969 just a few years after becoming a doctor, his book ‘Mechanism of Mind’ caught the attention of the American Nobel prize winner Professor Murray Gell-Mann, a physicist who worked on a theory of elementary particles, and whose name became synonymous with the quark.

Thinking Hats and Thought Revolutions

Airways, and Siemens take up his thinking methods? The latter corporation decided to teach his methods to all of its estimated 370,000 employees in a bid to help improve their performance and efficiency. And it is not just about education and big business. In the US the de Bono methods are taught to jurors and in at least three states, this is done under the direct recommendation of the presiding judge. This has been a major change in the US's jurist system.

It all seems simple enough. De Bono speaks about changing thinking patterns. He highlights the inadequacy of our way of thinking and the problems that it tends to lead us into. As he speaks, Dr de Bono discusses various practical methods which people should know of, if they only think the right way, yet still ignore because they believe they have other, simpler solutions to their problems. "Take the classic migraine. Somebody would dash out to buy aspirin to get rid of the pain. But all it takes is one simple paper bag. Breathe in and out of the bag. This will raise CO₂ levels in the blood and stop blood vessels from going into spasm... this will stop you getting the migraine."

He speaks of the way people become entrenched in what seems to be the most secure way of thinking – a pattern that is hard to break. Motivation to explore diverse potentials can only be gained by means of certain tools which you can learn, no matter what your age is.

"The Greek gang of three – Socrates, Plato and Aristotle, utilised truth, logic and argument to prove their points. Since then, 2,400 years hence, universities have followed on their teachings and as in their great part, universities eventually belonged to the church,

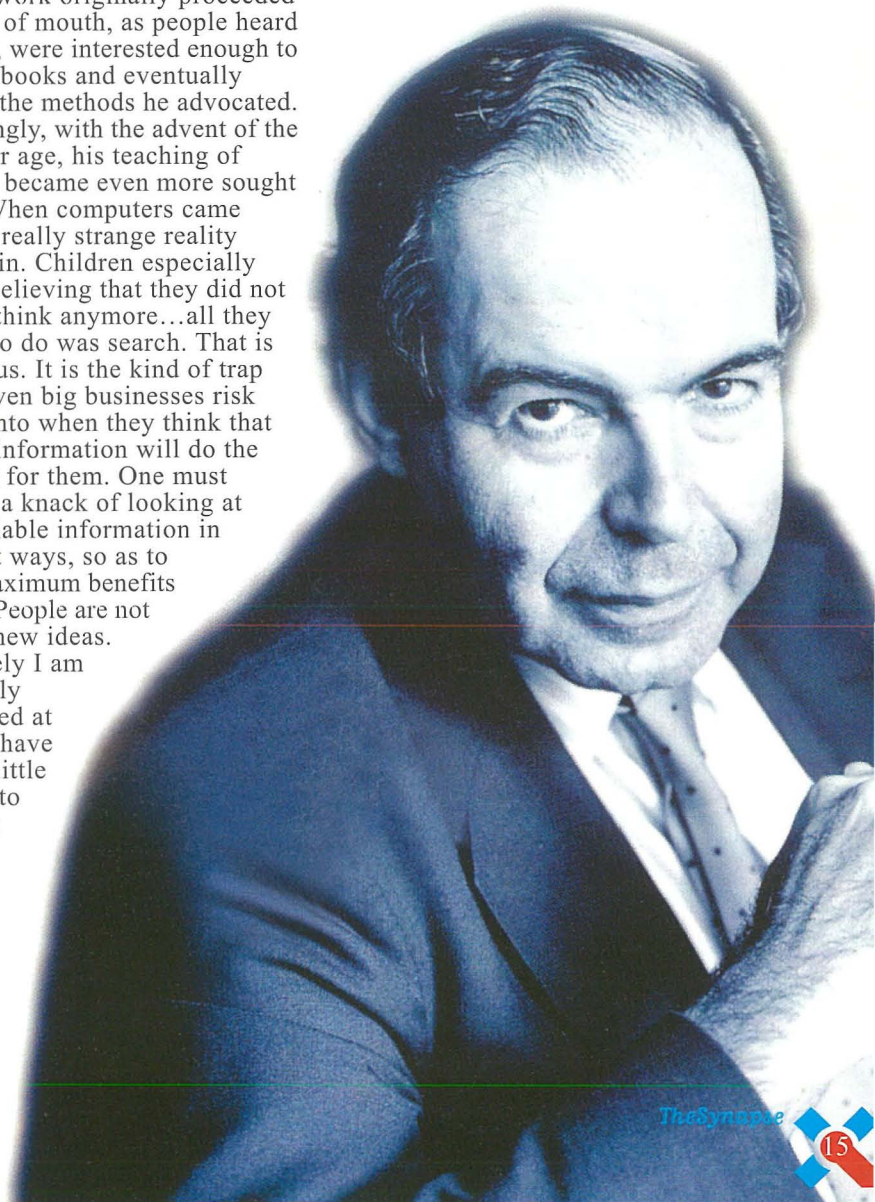
they didn't encourage creative or designer thinking, and this has come down to us today. Our existing thinking is about judgement not about designing a way forward. We are still depending on methods which were adopted when creativity was crushed, and yet our world is craving for creativity and innovation."

With some 72 books to his credit, and translations of same to 41 languages to date, de Bono admits that his work originally proceeded by word of mouth, as people heard him talk, were interested enough to read his books and eventually adopted the methods he advocated. Surprisingly, with the advent of the computer age, his teaching of thinking became even more sought after. "When computers came along, a really strange reality stepped in. Children especially started believing that they did not have to think anymore...all they needed to do was search. That is dangerous. It is the kind of trap which even big businesses risk falling into when they think that enough information will do the thinking for them. One must develop a knack of looking at the available information in different ways, so as to glean maximum benefits from it. People are not against new ideas. Ultimately I am constantly astonished at how we have paid so little thought to thinking itself."

As we
end off
the

interview, Dr de Bono admits he travels a great deal, working with corporations, in the field of education, and writing. He utilises his self-same credo to produce his several books, each and every time. "I only need one week to write a book. I can be very focused in my thinking and have specific techniques that allow me to produce better and faster."

It is what most people hanker for isn't it? [☞](#)



Healing & Disease Reversal

by **Albert Cilia-Vincenti MD FRCPATH**

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

Professor Dean Ornish's clinical research over more than 30 years shows that the progression of even severe coronary heart disease can often be reversed by making comprehensive lifestyle changes. These include a very-low-fat diet containing mainly fruits, vegetables, whole grains, legumes and unrefined soy products; moderate exercise such as walking; various stress management techniques; and enhanced family and social support.

His research has also documented that other chronic diseases may be reversible simply by making comprehensive lifestyle changes. The results of a randomised controlled trial he conducted with Drs Peter Carroll (Chair, Urology Department, University of California) and the late William Fair (Chief of urologic surgery and Chair of urologic oncology, Memorial Sloan-Kettering Cancer Center, New York) showed that the progression of early-stage prostate cancer may be slowed, stopped, or perhaps even reversed by making similar changes in diet and lifestyle. This may be the first randomised controlled trial showing that the progression of *any* cancer may be modified just by changing what we eat and how we live. As we'll see later in this series of features, what's true for prostate cancer may also be true for breast cancer.

However it's important to substantiate and validate whatever health promises are made. In 2000, Dean Ornish was appointed to the White House Commission on Complementary and Alternative Medicine Policy. In the US, more money is spent out-of-pocket for alternative medicine than for traditional medicine, because many people have become disenchanted with conventional medicine. However, Ornish believes that many of these alternative medicines do not have robust scientific evidence to support their claims. Seen from this perspective, **his programme is one of the most scientifically documented alternative medicine approaches to health and healing.**

Beginning in 1977, Ornish's cardiac studies found that with diet and lifestyle modifications, patients experienced a 91% angina frequency reduction after only a few weeks, and most of them became pain-free. These were patients with very severe coronary heart disease, many of whom could not walk across the street without getting severe chest pain and shortness of breath, when they were enrolled. After one year, there was a 40% average reduction in LDL cholesterol levels, comparable to what is achievable with statin drugs like atorvastatin, without the costs or side-effects (both known and unknown).

In the Lifestyle Heart Trial, after only one year, there was significant reversal in coronary artery blockages in the group that went through Ornish's programme, whereas those in the randomised control group showed a worsening of their coronary artery blockages. Most patients continued to follow the programme for 5 years

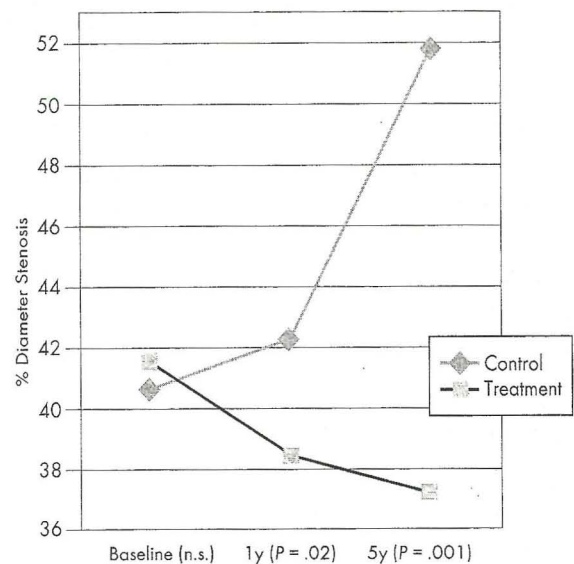


Figure 1. Changes in Quantitative Coronary Arteriography

even though they had initially volunteered only for a one year study. It was found out that there was even more reversal in coronary artery blockages after five years than after one year, whereas randomised control patients showed even more worsening. These differences were highly statistically significant (Figure 1).

Figure 2 depicts what reversing heart disease looks like in a typical patient. This subject entered Ornish's study in

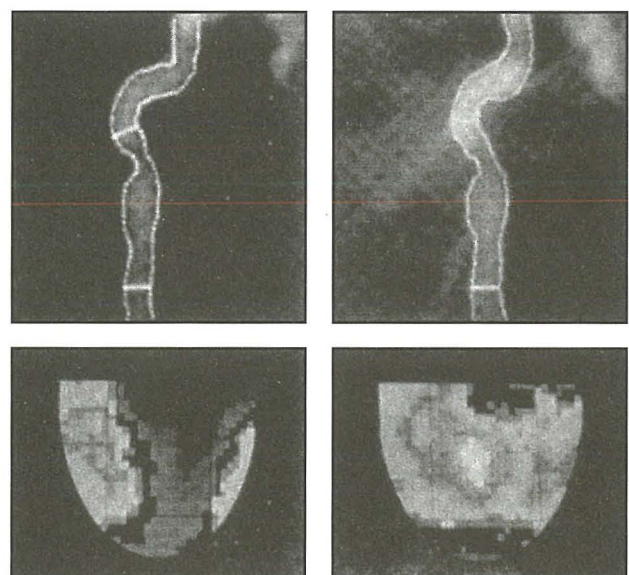


Figure 2. Top section represents comparative angiograms whilst lower section shows cardiac PET scans

continues on page 23

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References:

1. Philipp T. et al. Clin Therapeutics 2007; 29 (4) 563-580
2. Poldermans D. et al. Clin Therapeutics 2007; 29(2); 279-289

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Presentation: Amlodipine and valsartan 5 mg/160 mg, 10 mg/160 mg film-coated tablets. **Indications/Posology:** Treatment of essential hypertension in patients whose blood pressure is not adequately controlled on amlodipine or valsartan monotherapy. Recommended dose is one film-coated tablet per day (5 mg amlodipine and 160 mg valsartan, or 10 mg amlodipine and 160 mg valsartan).

Contraindications: Hypersensitivity to any component of Exforge or to dihydropyridine derivatives. 2nd and 3rd trimesters of pregnancy. Severe hepatic impairment, biliary cirrhosis or cholestasis. Severe renal impairment (GFR <30ml/min/1.73 m²) and patients undergoing dialysis. **Precautions/Warnings:** Risk of hypotension in sodium- and/or volume-depleted patients. Beta-blocker withdrawal should be gradual.

No data available in patients with unilateral or bilateral renal artery stenosis, stenosis to a solitary kidney or after recent kidney transplantation. Monitoring of potassium levels and creatinine in moderate renal impairment. In patients with mild to moderate hepatic impairment without cholestasis, the maximum recommended dose is 80mg valsartan. As with all other vasodilators, special caution in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy. Exforge has not been studied in any patient population other than hypertension. When driving vehicles or operating machines it should be taken into account that occasionally dizziness or weariness may occur. Avoid use in women planning to become pregnant and while breast-feeding. Not recommended during the first trimester of pregnancy. Not recommended in patients below 18 years of age. Caution when using potassium supplements, potassium-sparing diuretics, salt substitutes containing potassium or any other medicinal product that may increase potassium levels. Primary hyperaldosteronism. In a long-term, placebo controlled study (PRAISE-2) of amlodipine in patients with NYHA III and IV heart failure of nonischaemic aetiology, amlodipine was associated with increased reports of pulmonary oedema despite no significant difference in the incidence of worsening heart failure as compared to placebo. **Interactions:** Caution is required with concomitant use of CYP 3A4 inhibitors (eg. ketoconazole, itraconazole, ritonavir), CYP 3A4 inducers (eg. carbamazepine, phenobarbital, phenytoin, fosphenytoin, primidone, rifampicin, Hypericum perforatum). Caution is required when used together with NSAIDs, COX-2 inhibitors, acetylsalicylic acid and non-selective NSAIDs. Concomitant use is not recommended however if the combination proves necessary, caution and monitoring of serum potassium levels is required when used concomitantly with potassium supplements, potassium sparing diuretics, salt substitutes containing potassium, or other drugs that may increase potassium level and serum lithium levels when used with lithium. **Adverse reactions: The most common adverse reactions are:** Nasopharyngitis, influenza, headache, oedema peripheral, pitting oedema, facial oedema, fatigue, flushing, asthenia, vertigo, tachycardia, palpitations, orthostatic hypotension, cough, pharyngolaryngeal pain, diarrhoea, nausea, abdominal pain, constipation, rash, erythema, joint swelling, back pain, arthralgia, dizziness, somnolence, dizziness postural, paraesthesia. Peripheral oedema, a recognised side-effect of amlodipine, was generally observed at a lower incidence in patients who received the amlodipine/valsartan combination than in those who received amlodipine alone. **Rare adverse reactions but potentially serious are:** Hypersensitivity. **Additional potentially serious adverse experiences reported in clinical trials with amlodipine monotherapy are:** Gastritis, gingival hyperplasia, gynaecomastia, leucopenia, myalgia, pancreatitis, hepatitis, thrombocytopenia, vasculitis. **Additional potentially serious adverse experiences reported in clinical trials with valsartan monotherapy are:** Viral infections, upper respiratory infections, sinusitis, rhinitis, neutropenia, insomnia. Altered renal function, especially in patients treated with diuretics or in patients with renal impairment, angioedema and hypersensitivity (vasculitis, serum sickness) can occur. Please refer to SmPC for a full list of adverse events. **PACK SIZE:** 14, 28 film-coated tablets. **LEGAL CATEGORY:** POM. **MARKETING AUTHORISATION NUMBER:** EU/1/06/370/002 - 3/ EU/1/06/370/10-11. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblesbury Road, Horsham, West Sussex, RH12 5AB, United Kingdom. Consult full Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available upon request from: Novartis Pharma, P.O. Box 124, Valletta VLT 1000, Malta. Tel +356 22983217 (2009-MT-01 EXF Mar-2009).

 **NOVARTIS**

Problems facing biobanks

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

Biobanks – collection of samples for genetic research – are the future of research into linking genetic-related diseases, especially those of a non-Darwinian mode of inheritance, to their epigenetic environment.

Pharmacogenetics is also the ‘Newfoundland’ where information will considerably help with the choice of pharmaceuticals individualized for patients. For this kind of research large quantities of samples from populations are needed together with a detailed amount of data from the person. The data is kept by a controller who will then give the samples (anonymised) to those carrying out research. Since this is a relatively new mode of research and the person making the donation of the sample, or acknowledging that a sample may be used for scientific research, does not know for what kind of research the sample is to be used, this has made this area problematic.

Many documents however have considered this problem and there are ongoing projects, even at EU level, to make further recommendations. Mainly the areas of concern are how one should obtain consent to use such samples, and secondly how one can use such samples in the best interests of patients and indeed give something back to the donor if it is found relevant to his or her health. The problem lies within the fact that many biobanks accept donations only from patients who would agree that they are not given any information derived from their sample. The reason is indeed to protect the patient from any abuse from insurances or employers, who may make use of genetic information. Whilst insurances do want to assess risk, it would be unfair to use genetic information of subjects if such subjects have altruistically consented to a sample to be used for research purposes, whilst the rest of the population does not reveal (because it does not know) this information.

Laws which protect patients from insurances, such as in the United States, have largely failed because the latter are allowed to ask patients to waive this protection right. Conversely countries like Canada, where insurance provision is on a national level, genetic tests do not matter because insurances do not analyse risk on an individual level but make a national risk assessment.

When it comes to obtaining consent, a broad consent is necessary. This still involves the usual provisions for obtaining informed consent: information, understanding why the sample is being taken, a voluntary choice, competence, and of course a consent process. Indeed however a more detailed process carried out by a competent individual is necessary to explain what genetic testing does; it has been shown that people do have a general idea of what genetics is, but when it comes to research they will usually wish to know that their sample will be used for legitimate purposes and that it would not be used to label any particular group or for purposes to which they may have a moral objection – such as pharmacogenetics on contraception, to mention but an example.


... many biobanks accept donations only from patients who would agree that they are not given any information derived from their sample

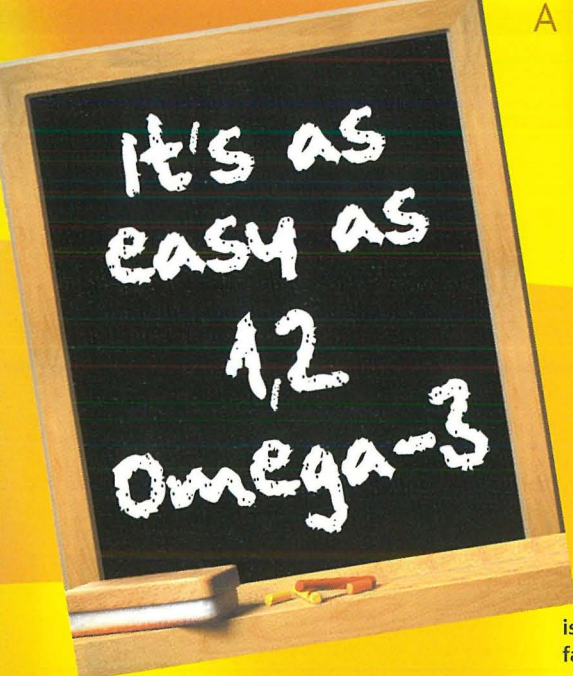
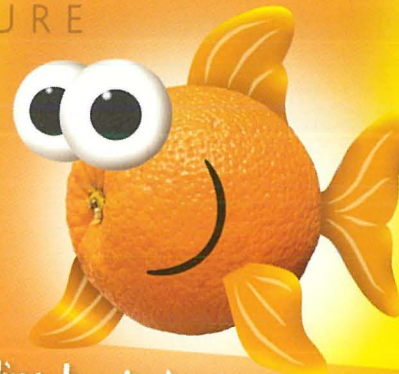
The Biobanks Ethics and Guidance Council is an ‘oversight body’ in the UK which sees that biobanks use their samples and data appropriately and that researchers are transparent, accountable and consistent in their practices. However one major area of concern, which varies from legislation to legislation, and which therefore should be explained to patients before obtaining the sample, is the definition of what constitutes *data*. Some would say that *data* is simply obtained from the sample, but is not the sample itself. What if the patient requests that his or her *data* be destroyed, thus opting out of the biobank system? – a right which is always given. Clearly we have to explain to patients their rights and

inform them correctly that if they want to opt out they may also have to request that the sample be destroyed. Furthermore it does not resolve the question of destruction of *information*. Legislations so far have not seen this coming, unfortunately.

There have been instances where data controllers have handed samples to research companies, who have then used them for further tests, either not going to patients for consent, or requesting consent themselves. This leaves the data controllers out of control and usually they do not have the money or the time to pursue such issues legally. Certainly such occurrences can harm science in the long run by losing public trust.

Finally one has to consider how information can be given back to people without putting them in danger of discrimination. It has been argued that much of the research is still at a stage where it is really not relevant to individual health. Conversely, when information does become relevant, even if someone has signed a consent form, protecting him from information, he should be given enough guidance on how to seek information if he wants to. Publishing an article in a peer reviewed journal is not convenient and certainly does not make information accessible ‘publicly’. The answer lies in explaining to people which sites and public media to search.

On the other hand, some people will only donate samples if they are given the right to know about anything which is relevant to their health. We are still in the early stages of biobanking and in the UK a biobank would simply not take the sample unless the person consents to the limits discussed. What may be necessary is for people to be allowed *not* to give genetic information to potential employers and insurances, and not be guilty of fraudulent behaviour in the process. These legal implications are being studied in the EU FP6 PRIVILEGED project, which is an extended project on the EU directive on data protection with particular relevance to genetic information. At the end of the day we want to protect the trust that people have in science! 



Thousands of children will be heading back to the classroom this September for another gruelling year of exams and homework. And after the long summer holiday, boosting their concentration levels will be essential for the new term ahead.

60% of the brain structure is fat and is vitally important to brain function. The fat required by the brain is the long-chain polyunsaturated fatty acid Omega-3, and it is this that contains

the rich nutrients DHA (docosahexaenoic acid) and EPA (eicosapentaenoic acid), which are naturally found in oily fish. Increasing evidence suggests that children's dietary intake of Omega-3 is related to mental performance and concentration levels.

The Secret of Omega-3

Both EPA and DHA are beneficial for good health, however DHA can offer the greatest benefit for the brain, as EPA does not occur to any great extent in brain tissue. DHA is in fact the most important nutrient in the brain after water making up 25% of fat material. Intake during pregnancy is key as DHA forms a significant part of key tissue structure such as brain, grey matter, the retina and the nerves. Its structural significance is additionally supported by its presence in human breast milk¹. Furthermore, during childhood DHA plays a key role in maintaining healthy brain function and concentration levels.

Omega-3 and Concentration

Over 23 schools and 120 children, aged between 6 and 11, took part in one of the largest multicentre studies across the UK to find out whether a daily dose of Omega-3 with vitamins would help their concentration and behaviour in school and at home². The results showed that supplementing with Omega-3 with vitamins substantially improved the children's behaviour and concentration levels by 35%, with teachers and parents noticing improvements in attention and conscientious levels and that the children were generally more alert and focused.

Omega-3 and Intelligence

When something new is learnt the brain cells send messages to one another. High levels of Omega-3 increase the fluidity of cell membranes and speeds the transfer of electrical signals between brain cells. Effectively, DHA fills the gap around the brain cells allowing communication to be passed quickly. Omega-3 also assists the development of new connections.

The formation of brain cells are largely completed during the last trimester and first year of life - therefore Omega-3 intake during this period is vital in the development of IQ potential.

There's evidence that a lack of Omega-3 inhibits development of intelligence. A recent UK study looked at the intake of Omega-3 by 7,000 pregnant women. The study found that those women who did not consume much Omega-3 during pregnancy gave birth to offspring, which when tested for IQ showed a 6 point deficit compared to children born to mothers with a good level of Omega-3 intake³.

Omega-3 and Behaviour

Studies show that children born to mothers who ate fish during pregnancy have better behaviour, better cognitive development, better eyesight and better communication skills. One UK study in particular followed a group of young offenders. Results showed that when they were given an Omega-3 and vitamins supplement, their anti-social behaviour was markedly reduced in comparison to that of the placebo group⁴.

Summary

Many studies have revealed overwhelming evidence to support the benefits of Omega-3 supplementation for children's healthy brain development and function.

Haliborange Omega-3 for Children

Haliborange offers the best tasting range of health supplements for growing children, with the widest choice of vitamin and Omega-3 protection for general health and well-being, healthy growth and development, and brain development and function.

Haliborange Omega-3 has been specially formulated with children in mind, and is a delicious range that combines Omega-3 with the important A, C, D and E vitamins. There are a variety of products within the range to suit children of all ages and preference in supplementation format. Each Haliborange Omega-3 product offers a controlled delivery of Omega-3 in a pleasant tasting, convenient presentation.



Haliborange Omega-3 Product	Format	Flavour	Omega-3 content per dose	of which DHA per dose	of which EPA per dose	Daily Dosage	Age Range
Haliborange Omega-3 Orange Syrup	Syrup	Orange	600mg	300mg	150mg	10ml	3-12 years
Haliborange Omega-3 Orange Chewable	Chewable capsule	Orange	260mg	200mg	28mg	2 capsules	3-12 years
Haliborange Omega-3 Blackcurrant Chewable	Chewable capsule	Blackcurrant	260mg	200mg	28mg	2 capsules	3-12 years
Haliborange TeenSense	Chewable capsule	Orange	520mg	400mg	56mg	Up to 2 capsules	Teenagers

Giving them Haliborange Omega-3 every day as part of a healthy diet could be helping them physically, mentally, and at school.

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For further information or for your copy of the Clinical Guide to Omega-3 for Children's Brain Development, please contact Associated Drug Company Ltd. Tel no. 22 77 8000.

Dental Erosion

continued from page 4

(b) Habits including occupational exposure to acids.

Erosion has also been reported in swimmers who are in contact with pool water for several hours a week when the acidity of the pool water is below a pH value of 5.² Frequent exposure of the teeth to wine, as occurs among professional wine tasters, is deleterious to enamel, and constitutes an occupational hazard.³

Intrinsic factors

- (a) Buffering capacity of saliva;
- (b) Solubility of tooth structure in acid;
- (c) Relationship between hard and soft dental tissues;
- (d) Presence of gastro-oesophageal reflux (Figure 5);
- (e) Bulimia (acid in gastric regurgitation);
- (f) Gastric regurgitation and Cerebral Palsy (patients with cerebral palsy are known to have a high incidence of feeding difficulties, including problems with swallowing and vomiting);⁴
- (g) Gastric irritation due to asthma medication.⁵

Preventing erosion entails the following measures:

- Limit acidic products and fizzy drinks to mealtimes to reduce the number of acid attacks on teeth;
- Drinks should be drunk quickly without holding in or 'swishing' around the mouth. Ideally one should use a straw to help drinks go to the back of your mouth and avoid lengthy contact with teeth. Chilled drinks have a lower erosive potential than drinks at room temperature;
- A meal should preferably finish with cheese or milk as this will help neutralise the acidity content of meals;
- Sugar-free chewing gum should be used after eating to help produce more saliva to help cancel out acids which form in the mouth after eating;

Frequent exposure of the teeth to wine, as occurs among professional wine tasters ... constitutes an occupational hazard

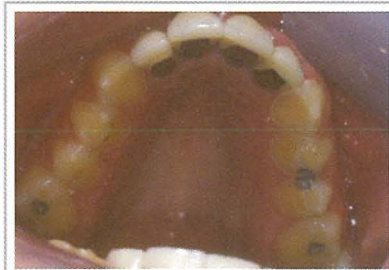


Figure 4. Enamel loss on mesial surface of upper central incisors



Figure 5. Loss of enamel on occlusal surface of posterior molars and premolars due to acid regurgitation

- One should wait for at least one hour after eating or drinking anything acidic before brushing the teeth. This gives teeth time to build up their mineral content again;
- One should brush teeth twice a day with a small-headed brush with medium to soft bristles together with a good fluoride toothpaste;
- Healthy foods such as fruit and fruit juices are not always the best options for teeth if patients have too much of them;

- If antacids are being prescribed the liquid form should be sugar-free so as to avoid dental decay.

Dental erosion does not always need to be treated. With regular check-ups one can prevent the problem getting any worse and the erosion going any further. Study casts of the patient's teeth are prepared to monitor tooth tissue loss and compared at subsequent visits. However in some cases, it is important to protect the tooth and the dentine underneath to prevent tooth decay and sensitivity. In these cases, simply bonding a filling onto the tooth will be enough to repair it. Nevertheless in more severe cases one may need to fit a dental veneer (Figure 5).

In those cases where a medical condition is causing the erosion it is important that the patient's family doctor liaises with the dentist and ensures that the patient is attending for regular dental check-ups. In view of its increasing prevalence we need to be more aware of the diagnostic features, recognise any predisposing factors and diagnose the symptoms at an early stage in order to prevent further tooth loss. [□](#)

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Breast Masses in Children - Part II

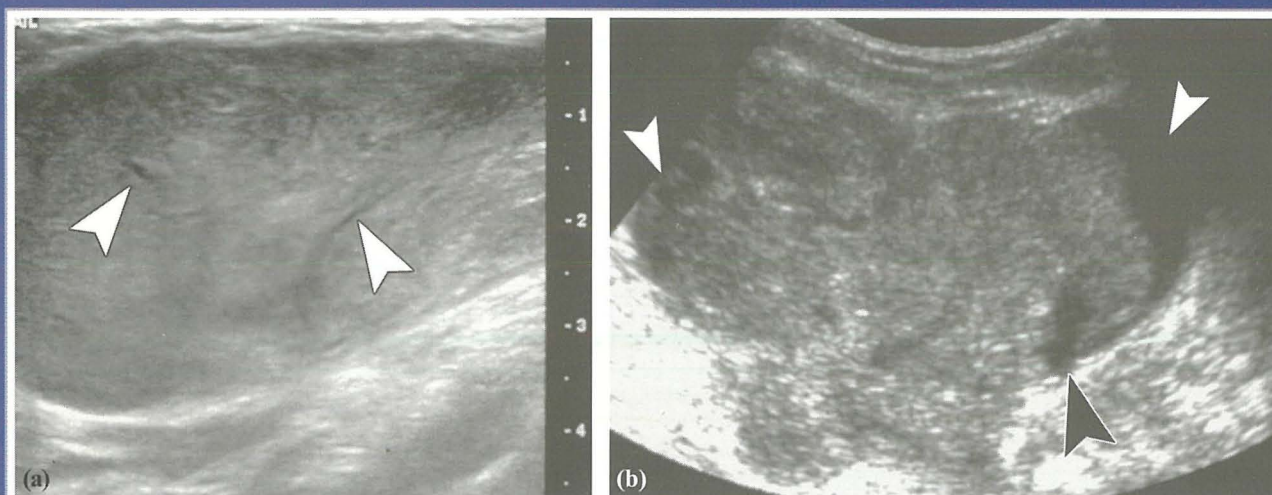


Figure 4. (a) Ultrasound scan of a benign phyllodes tumour reveals a fairly homogeneously hypoechoic, sharply circumscribed mass with dorsal enhancement and anechoic linear clefts (arrowheads). These findings are similar to the appearance of a juvenile fibroadenoma. (b) Ultrasound scan of a malignant phyllodes tumor reveals a partially circumscribed hypoechoic mass with posterior sound enhancement and anechoic foci (arrowheads), some of which are round and others are curvilinear.

but it is the most common primary mammary malignancy in this age group. Its peak age of prevalence is in the 4th decade of life, but about 5% of phyllodes tumors occur in girls younger than 20 years of age. Phyllodes tumor shares many clinical, pathologic, and imaging features with juvenile fibroadenoma. Phyllodes tumors demonstrate a wide spectrum of biologic behavior, and some have the potential for invasive growth, recurrence, or metastasis in rare cases. Most phyllodes tumors in adolescents are histologically benign; on ultrasound these show smooth margins, have a moderately hypoechoic texture and contain linear clefts (Figure 4a) as do fibroadenomas. The findings of foci of hemorrhage or necrosis suggest malignancy (Figure 4b).

Breast cancer is exceedingly rare in children. The age-adjusted incidence of carcinoma in 2004 was 0.03 cases per 100,000 in patients younger than 20 years of age. On ultrasound, carcinoma typically appears as a hypoechoic mass with irregular margins, inhomogeneous internal echoes, a long axis perpendicular to the chest wall, and variable posterior acoustic shadowing; these features are similar to those seen in an adult (Figure 5).

Metastatic disease and haematologic malignancy are the most prevalent malignant tumors of the breast in children and adolescents, most commonly rhabdomyosarcoma, neuroblastoma, and haematolymphoid malignancies. The sonographic appearances of breast metastases are variable, but most demonstrate lobulated or irregular margins and heterogeneous, hypoechoic internal echotexture with hyperechoic foci. Posterior acoustic shadowing or lack of dorsal enhancement is typically seen. Metastatic disease to the breast is frequently multifocal.

Summary

The vast majority of conditions that cause breast masses or breast enlargement in children and adolescents are benign. Bilateral enlargement most commonly occurs because of

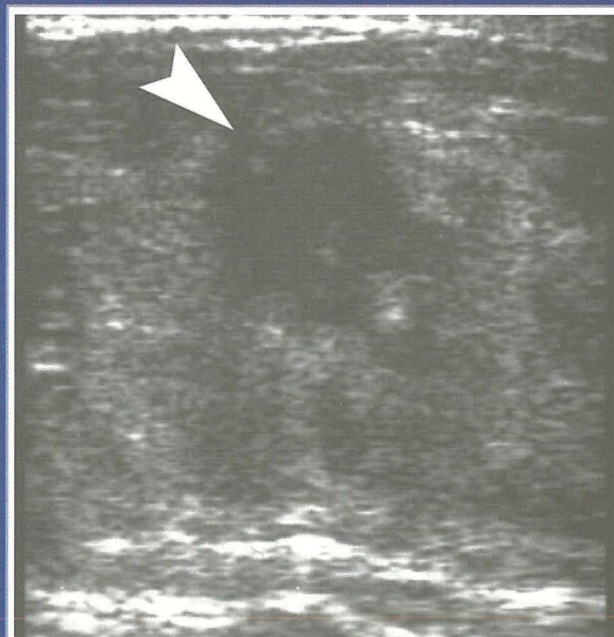


Figure 5. Secretory breast cancer: Ultrasound scan reveals a hypoechoic mass (arrowhead) with irregular borders and an anti-parallel growth pattern.

normal or abnormal development. These conditions are usually self-limited and do not require therapy, but, occasionally, inappropriate breast development may be a sign of a more serious condition, such as a hormonally active gonadal or adrenal tumor that causes feminisation. After onset of puberty, most cases of breast enlargement arise from benign fibroadenoma in girls and gynecomastia in boys. □

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

Healing & Disease Reversal

1986 at age 64 with severe atherosclerosis involving all his major coronary arteries and had been advised to undergo coronary bypass surgery due to severe angina. When he entered the study, he was unable to walk more than a few steps without severe chest pain. After 6 weeks, he was pain-free and was no longer advised to undergo bypass surgery. By the end of the first year, during which he lost 30 pounds due to diet and lifestyle changes, he was able to climb 130 floors per day on a StairMaster® with no angina. His cardiac PET scan revealed a 300% improvement in myocardial blood flow, and his angiogram showed reversal of coronary atherosclerosis. The angiogram illustrated in the upper left hand corner of figure 2 showing significant artery narrowing is significantly wider (upper right hand corner) after one year. The patient's cardiac PET scans at the bottom also show substantially improved myocardial blood flow, represented by brighter areas in the lower right hand picture.

Ornish's programme stopped or reversed heart disease progression in 99% of patients, besides 2½ times fewer cardiac events (heart attacks, bypass surgery, angioplasties and hospital admissions). He found a direct correlation between the amount of dietary and lifestyle changes and the amount of changes in coronary artery disease after both one and after five years (Figure 3). In other words, **the more people changed, the better they got.** ☐

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

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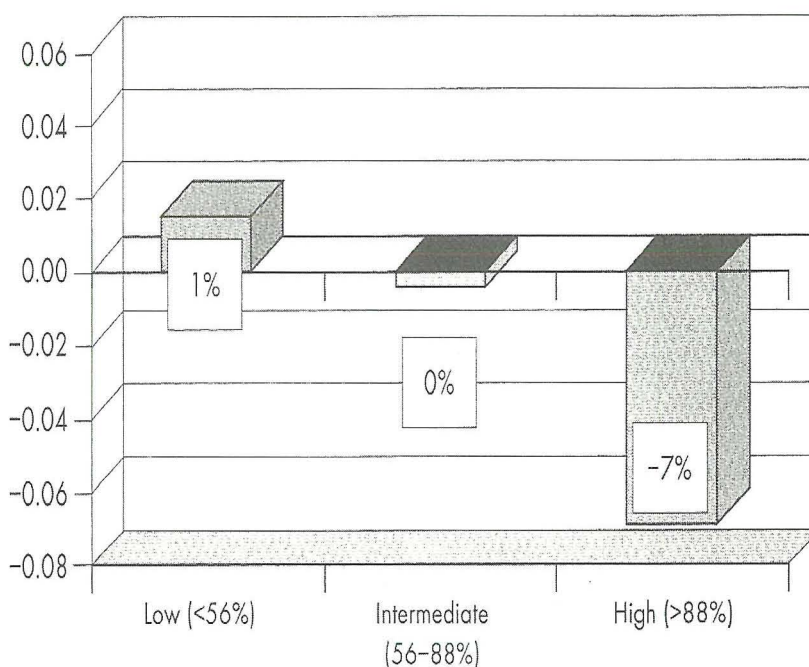


Figure 3. Adherence and change in Coronary Atherosclerosis after five years

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Composition: COVERAM Each tablet contains perindopril arginine, a long-acting ACE inhibitor, and amlodipine besylate, a calcium channel blocker. Coveram 5 mg/5 mg: one tablet contains 3.395 mg perindopril equivalent to 5 mg perindopril arginine and 6.935 mg of amlodipine besylate equivalent to 5 mg of amlodipine. Coveram 10 mg/5 mg: one tablet contains 6.790 mg of perindopril equivalent to 10 mg of perindopril arginine and 6.935 mg of amlodipine besylate equivalent to 5 mg of amlodipine. Coveram 5 mg/10 mg: one tablet contains 3.395 mg of perindopril equivalent to 5 mg of perindopril arginine and 13.870 mg of amlodipine besylate equivalent to 10 mg of amlodipine. Coveram 10 mg/10 mg: one tablet contains 6.790 mg of perindopril equivalent to 10 mg of perindopril arginine and 13.870 mg of amlodipine besylate equivalent to 10 mg of amlodipine. **Excipient:** contains lactose monohydrate. **Indication:** Perindopril arginine/amlodipine is indicated as substitution therapy for treatment of essential hypertension and/or stable coronary artery disease, in patients already controlled with perindopril and amlodipine given currently at the same dose level. **Dosage and administration:** Oral route. One tablet daily, preferably taken in the morning and before a meal. The fixed-dose combination is not suitable for initial therapy. If a change of dosage is required, the dose of perindopril arginine/amlodipine can be modified or individual titration with free combination may be considered. **Contraindications:** Absolute: Known allergy to perindopril or to any other ACE inhibitor, history of angioedema associated with previous ACE inhibitor therapy, hereditary or idiopathic angioedema, pregnancy, lactation, severe hypotension, hypersensitivity to amlodipine or to any other dihydropyridines, shock including cardiogenic shock, obstruction of the outflow tract of the left ventricle (high-grade aortic stenosis), unstable angina pectoris, heart failure after acute myocardial infarction during the first 28 days. Relative: combination therapy with lithium, potassium salts, potassium-sparing diuretics and certain medicines that cause heart rhythm disorders, estramustine. **Concomitant use to be taken into consideration. Drug interactions:** Diuretics, sympathomimetics, gold, nonsteroidal anti-inflammatory drugs, antidiabetic agents, dantrolene, CYP3A4 inducers (rifampicin, hypericum perforatum, carbamazepine, phenobarbital, phenytoin, fosphenytoin, primidone), CYP3A4 inhibitors (itraconazole, ketoconazole), beta-blockers in heart failure, baclofen, corticosteroid, tetracosactide, alpha-blockers, amifostine, tricyclic antidepressants, antipsychotics, anesthetics, immunosuppressive agents. **Side effects:** Asthenia, dizziness, headache, mood swings and/or sleep disturbance, cramps, hypotension, allergic reaction, skin rashes, gastrointestinal disorders, dry cough, dry mouth, risk of dehydration in the elderly and in patients suffering from heart failure, blood test abnormalities. **Precautions:** Assess renal function before and during treatment. Renovascular hypertension. Surgery/anesthesia. Renal failure: the dose should be cautiously adjusted in accordance with the creatinine clearance (refer to complete data sheet). Symptomatic hypotension is rarely seen, but is more likely to happen in volume depleted patients, those receiving diuretics, or with the first two doses. In patients taking diuretics, stop the diuretic 3 days before starting perindopril arginine/amlodipine. A diuretic may be given later in combination if necessary. Potassium-sparing diuretics are not recommended. Patients with impaired hepatic function: amlodipine's half-life is prolonged. Drug should be administered with caution and with close monitoring of liver enzymes. In one third of patients with heart failure, amlodipine was associated with increased reports of pulmonary edema, although there was no significant difference versus placebo. Patients should be treated with caution. Precautions should be taken according to concomitant therapy (ie, drug interactions). KEEP OUT OF THE REACH AND SIGHT OF CHILDREN. **Presentations:** Canister of 30 tablets. Keep the container tightly closed to protect against moisture. Prescribing information may change from country to country. Please refer to the complete data sheet supplied in your country. www.coveram.com

References: 1 - Bahl UK. Fixed dose perindopril and amlodipine in moderate to severe hypertension. 14th World Congress of heart disease 2008. Toronto, Canada. 2 - Dahlöf B. et al. for the ASCOT Investigators. The Lancet 2005; 366:895-906. 3 - Coversyl Arginine 5mg and 10mg Summary of Product Characteristics. 4 - Acercyl Summary of Product Characteristics. 5 - EUROPA Investigators. The Lancet 2003; 362:782-788. 6 - Bangalore S. et al. Fixed dose combinations improve compliance: a meta analysis. Am. J. Med. 2007 Aug; 120(8):713-9.

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