NEWSPAPER POST

TheSynapse

The Medical Professionals' Network

MEDICAL IMAGING

Conditions that may mimic Primary Pancreatic Cancer

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A number of anatomic variants and pathologic conditions in and around the pancreas may simulate primary pancreatic cancer on routine abdominal cross-sectional imaging.

An ambiguous lesion whose appearance suggests a pancreatic origin requires a broad differential diagnosis that can subsequently be narrowed on the basis of both clinical history and features at optimal computed tomography (CT) and magnetic resonance (MR) imaging. Recently introduced curved planar reconstruction techniques used with CT and MR studies, may help avoid potential diagnostic pitfalls. These techniques can help identify and characterize a mass in multiple viewing planes, thereby helping distinguish a true pancreatic neoplasm from peripancreatic enlarged lymph nodes or from a tumor of the adjacent small bowel. The correct localisation of a lesion would guide lesion-specific work-up and treatment and may avoid unnecessary tests or procedures, including surgery.

Although there are various modalities for imaging the pancreas, spiral CT is by far the most useful technique use to assess the structure of the pancreas and its anatomical relationship to surrounding structures. MR and Ultrasound (US) are also useful, with the former serving mostly as a secondary investigation when additional information is deemed necessary. US does not usually visualise the whole pancreas, but may be used particularly for lesions of the pancreatic head and when vascular abnormalities are suspected.

Normal anatomic structures and congenital anomalies of the foregut are common entities that may simulate primary pancreatic cancer. The normal fourth portion of the duodenum or proximal jejunum borders the pancreatic tail and unopacified adjacent bowel (figure 1) or

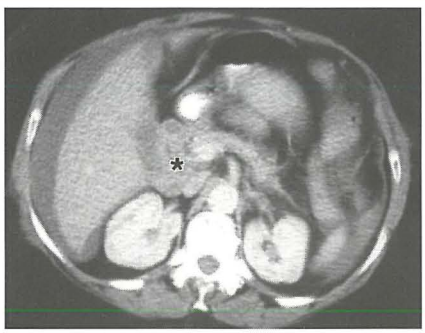

Figure 1a. *CT scan showing a normal unenhanced duodenum mimicking a pancreatic mass (*)*

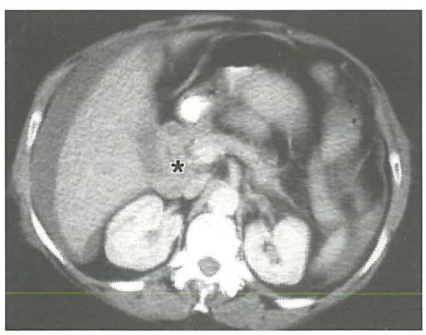

Figure 1b. *CT scan obtained with additional oral contrast material shows a normal pancreatic head, with contrast material in the duodenum (arrow) and gallbladder (*).*

an undistended gastric fundus may simulate a mass. Such cases can be easily clarified with the use of oral contrast material at CT. Variations in the lateral contour of the pancreatic head and neck are common and may also mimic pancreatic masses.

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Editor's Word

Welcome to the 4th issue of TheSynapse magazine for 2008. Besides the regular and, as always, informative radiology contribution we are featuring other very interesting articles in this publication **'The Genetics of the Muscular Dystrophies'** presented by Dr Christian Scerri, **'The New Death Certificate: Your Role as Certifiers'** by Dr Kathleen England, **'Benzodiazepines and older people'** written by Marise Gauci and an informative article by Kirsten Pulis on the **'Modern management approaches for children with Autism'**. We are also publishing the first part of a contribution on **'Philosphy of medicine – is there such a thing?'** besides the usual **'Update on the Avian Influenza'**. In this issue, we also take a closer look on a top health priority in Malta, through an **interview with Dr Charles Scerri**, one of the founding members of The Malta Dementia Society.

Although your profession entails a continual responsibility may the month of August give you the chance to enjoy the relaxing summer bequeathing you with more strength to gear up for the upcoming wintry period.

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Conditions that may mimic

Anatomic distortions from prior surgery, including nephrectomy, Whipple procedure, and Puestow procedure[A] (figure 2), may also appear as pancreatic masses due to unopacified afferent loops or pancreatic displacement.

Pancreas divisum (figure 3) results from aberrant fusion of the embryologic dorsal and ventral pancreatic ducts, and is the most common congenital anatomic variant of the pancreas, with a prevalence approaching 10% in the general population. Its clinical relevance is most often discussed in the context of recurrent pancreatitis; rarely, however, it may cause enlargement of the pancreatic head and be mistaken for a mass.

Annular pancreas is the second most common congenital pancreatic anomaly and results in pancreatic tissue partially or completely encircling the second part of the duodenum (figure 4). A diagnosis of annular pancreas may be suspected if barium studies show narrowing of the duodenum at the level of the major papilla. Endoscopic retrograde cholangiopancreatography (ERCP) or noninvasive MR cholangiopancreatography can be performed to delineate the pancreatic duct encircling the duodenum.

Duodenal duplications (figure 5) and diverticula may also be misinterpreted as pancreatic masses at CT or MR imaging. Duplications are usually noncommunicating and are most often located on the mesenteric side of the second and third portions of the duodenum. Affected patients typically present with symptoms of intestinal obstruction but may also develop biliary obstruction and pancreatitis. At barium examination, the duodenum usually appears compressed by an external mass along its mesenteric

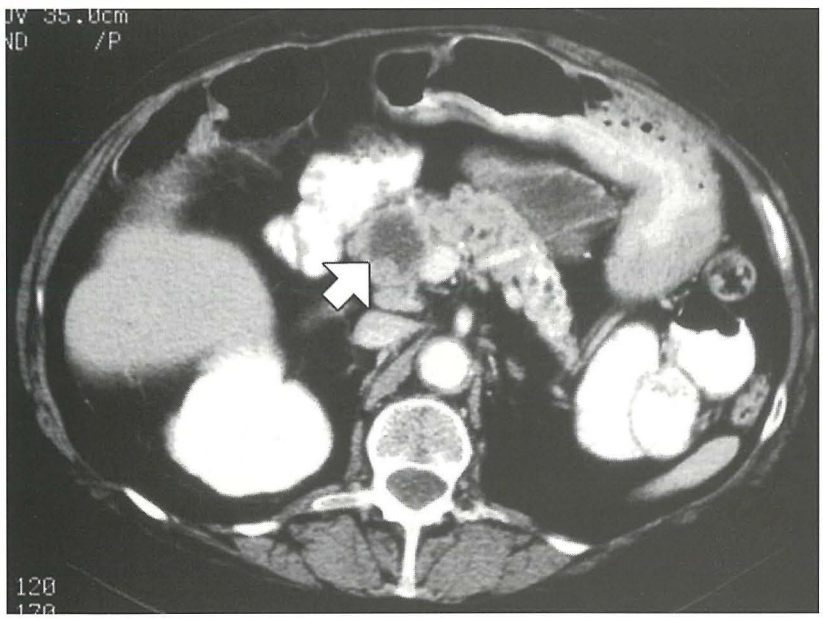

Figure 2. *Chronic pancreatitis treated with a Puestow procedure, CT scan shows anastomosis of a dilated pancreatic duct with a jejunal loop mimicking a cystic pancreatic mass (arrow)*

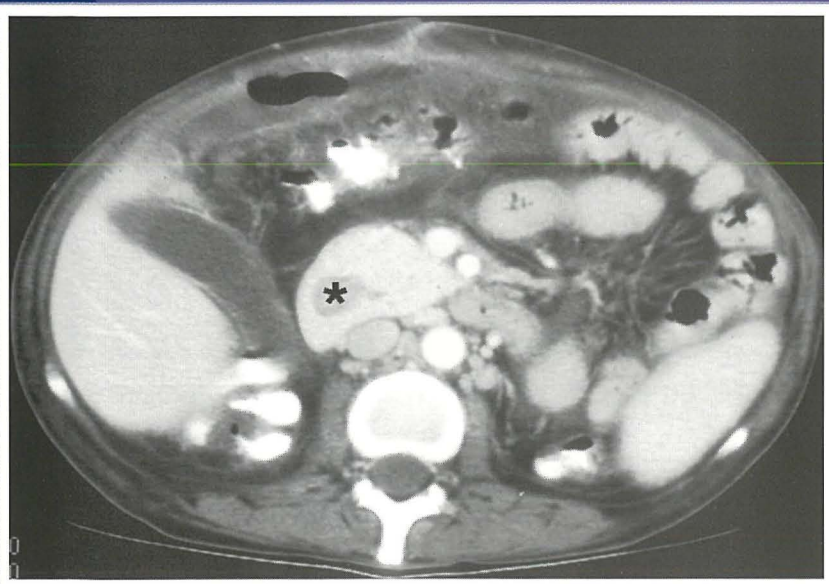

Figure 4. *CT scan showing an annular pancreas encircling the duodenum (*).*

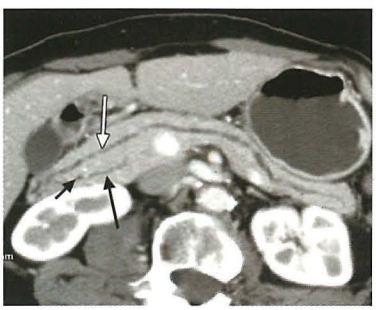

Figure 3a. *Curved-planar CT reconstructions following the course of the ducts through the gland depicts the wider dorsal duct (long white arrow), the narrower ventral duct (long black arrow), and the common bile duct (short black arrow). This is the dominant dorsal duct sign*

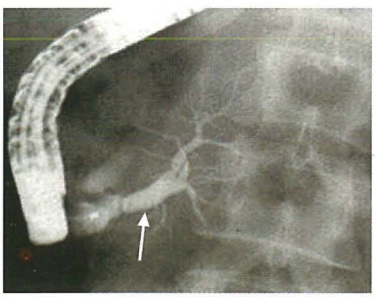

Figure 3b. *ERCP shows contrast material injected through the major papilla filling the dilated ventral duct (arrow), which branches and tapers within the head of the gland and does not communicate with the dorsal duct*

Primary Pancreatic Cancer

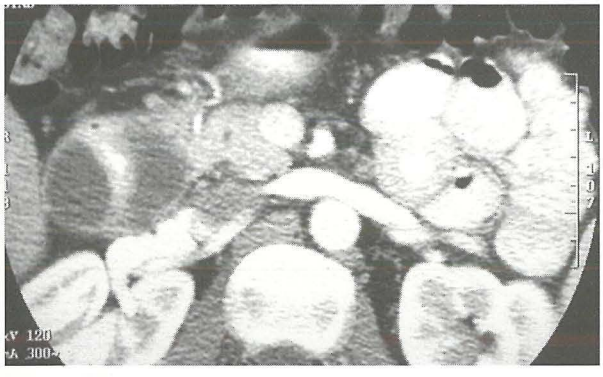

Figure 5. *CT scan shows a fluid-filled structure, the duodenal duplication, encircling the duodenum; the lumen of the duodenum contains oral contrast material*

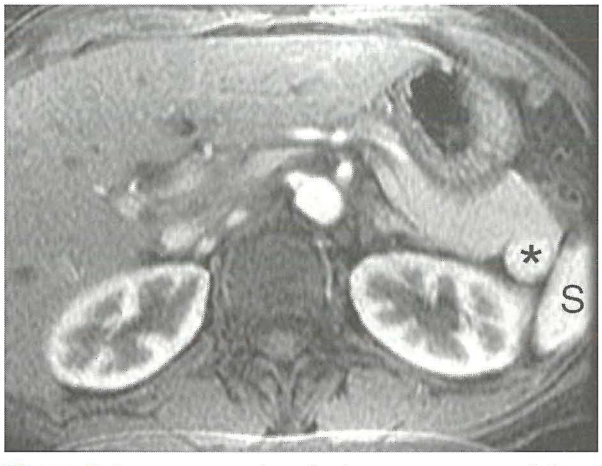

Figure 6. *Intrapancreatic splenic rest seen on axial contrast-enhanced spoiled gradient-echo T1-weighted MR image as a lesion (*) that is isointense relative to the spleen (S)*

border. CT scan the duplication appears as a smoothly rounded, fluid-filled cyst located in or adjacent to the wall. Duodenal diverticula may be of either the congenital intraluminal or, more commonly, the acquired extrinsic pulsion type. Most intraluminal diverticula are found within the second portion of the duodenum appearing as a contrast material–filled pouch projecting into the true lumen.

Splenic variants, such as accessory spleens or splenosis, may also mimic a pancreatic mass (figure 6). Accessory spleens occur in approximately 10% of the population, and intrapancreatic accessory spleens are found in the pancreatic tail in roughly 16% of these patients. Imaging with reticulo-endothelial system targeted contrast agents may be used to differentiate splenic from pancreatic tissue. These include technetium 99m (^{99m}Tc) sulfur colloid scintigraphy or MRI enhanced with iron oxide tagged particles (SPIO – superparamagnetic particulate iron oxide).

Choledochal cysts are rare congenital malformations of the bile duct that usually manifest in infancy and childhood. They appear as cystic or fusiform dilatation of the extrahepatic biliary tree and may simulate a cystic mass in the head of the pancreas (figure 7). MR cholangiopancreatography (MRCP) allows confirmation of the diagnosis and noninvasive delineation of the anatomy. Biliary contrast-enhanced CT or MR imaging may also be used for this purpose.

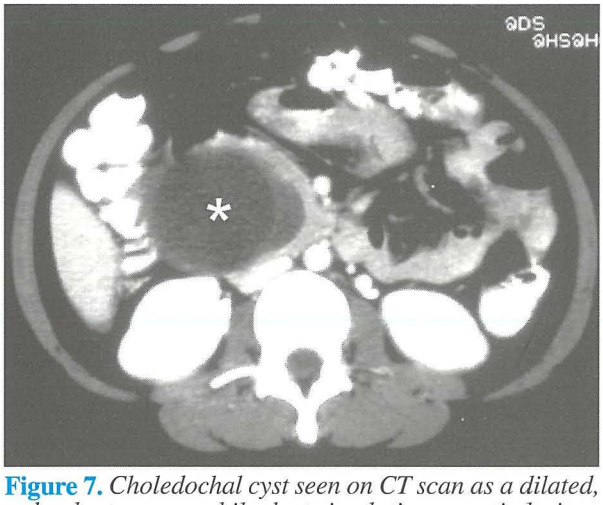

Figure 7. *Choledochal cyst seen on CT scan as a dilated, redundant common bile duct simulating a cystic lesion within the pancreatic head (*)*

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The Genetics of the Muscular Dystrophies

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When one mentions muscular dystrophy, the mental picture that emerges is that of Duchene Muscular Dystrophy (DMD). In reality, the term muscular dystrophy refers to around six, heterogenous groups of inherited disorders characterised by progressive muscle wasting and weakness. The common feature of all the dystrophies is the histological picture of muscle biopsy with the typical signs of muscle fibre variation, muscle necrosis and increased fat and connective tissues.

Attempting to classify muscular dystrophy is not easy and straight forward but Walton and Nattrass in 1954 formulated a classification (further elaborated by Walton in 1964) that is based on two principles – mode of inheritance and the predominant affected muscle group (Figure 1). Though this classification is still in use today, the identification of molecular genetics defects underlying particular dystrophies have distorted this clinical classification, Due to editorial constraints, this article shall attempt to give an overview of the molecular pathologies underlying the major classes of muscular dystrophy.

Clinically, the common feature of these disorders is muscle weakness, but the prognosis of the disorders shows great variability.

Duchene-Type Muscular Dystrophy

The commonest form of Muscular Dystrophy is the Duchenne-type. It is inherited as an X linked recessive trait and therefore predominantly affects boys. It is characterised by progressive muscle wasting and weakness and usually results in inability to walk by age 12 and death in the 20's. Some degree of intellectual impairment might be present in up to a third of cases. A similar but clinically milder condition, Becker-type muscular dystrophy (BMD), has an onset in the teenage years or early 20's, with loss of ability to walk occurring much later and survival is beyond middle age.

The gene was localized in 1982, discovered in 1987 with its protein product identified as dystrophin. The gene is the largest gene associated with a disease (2.4 million base pairs) contains 85 exons with the introns making up 98% of the gene. Being a cytoskeletal protein located beneath the sarcolemma, dystrophin is localised at the periphery of muscle fibres. The discovery of the protein, helped in the definition of the pathophysiological difference between Duchenne-type and Becker-type dystrophies, with the former showing complete absence of the protein and the later showing a reduced presence. Dystrophin forms part of a complex of proteins called the Dystrophin-Glycoprotein Complex (DGC) – a complex of five classes of proteins (dystroglycans, syntrophins, dystrobrevins, sarcoglycans and sarcospan) assembled with either dystrophin or its autosomal homologue utrophin (Figure 2). Utrophin is developmentally controlled i.e. it is highly expressed in muscle tissue during the foetal and neonatal period, but is suppressed and confined ot the sarcolemma after birth. This complex binds the cytoskeleton to the sarcolemma and is thought to help maintain the structure of muscle cells.

The DGC proteins have also been found to be expressed in non-muscle tissues especially in the brain and retina, and might explain the abnormalities present in these tissues in DMD patients.

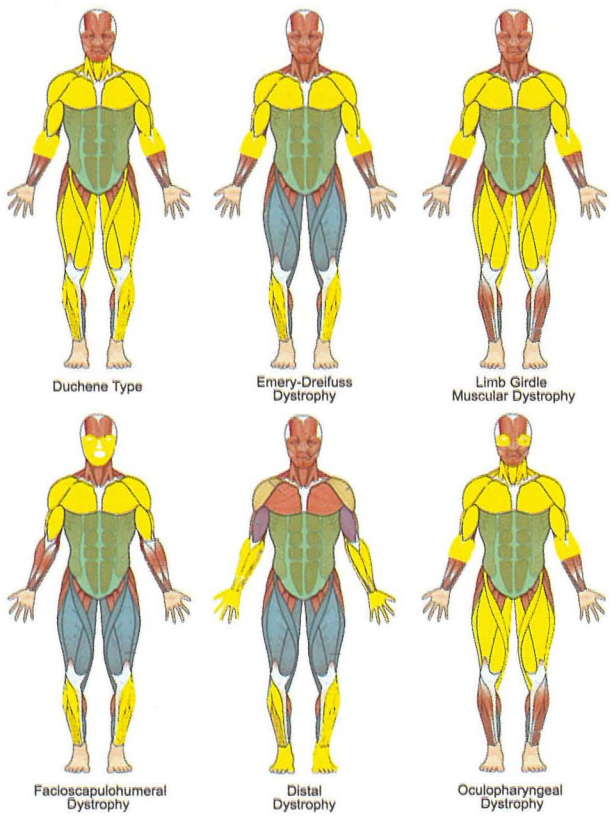

Figure 1: *Distribution of predominant muscle weakness in different types of dystrophy*

Facioscapulohumeral Muscular Dystrophy

Facioscapulohumeral Muscular Dystrophy (FMD) is characterized by weakness of the facial, scapulohumeral, anterior tibial and pelvic girdle muscles with retinal vascular disease, sensory hearing loss and in some cases, abnormalities of the central nervous system. The responsible gene is located on chromosome 4, and the condition is inherited as an autosomal dominant trait. Individuals suffering of the condition are usually mildly affected though some may later become dependent on wheelchairs.

Almost all the patients with FSHD have been found to have a deletion within the D4Z4 repeat region (chromosome 4q35). However, studies have failed to identify a gene within the region of the D4Z4 repeats and the molecular mechanism is still under study.

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Presentation: Tablets containing 50mg vildagliptin and 850mg metformin or 50mg vildagliptin and 1000mg metformin. **Indications:** Type 2 diabetes mellitus in 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:** initiate at 50mg/850mg bd or 50mg/1000mg bd (morning and evening) based on patient's current dose of metformin. Dosing with or just after food may reduce gastrointestinal symptoms associated with metformin. There is no clinical experience of vildagliptin and metformin in triple combination with other antidiabetic agents. Vildagliptin/metformin tablets are not recommended in patients aged >75yrs or in patients <18yrs due to lack of data on safety and efficacy in these groups. **Contra-indications:** Hypersensitivity to the active substance or to any of the excipients; renal failure/dysfunction (CrCl <60 ml/min); acute conditions with potential to alter renal function (e.g. dehydration, severe infection, shock, i.v. administration of iodinated contrast agents); acute or chronic disease which may cause tissue hypoxia (e.g. cardiac or respiratory failure, recent MI, shock); hepatic impairment, including patients with pre-treatment AST or ALT >3xULN; acute alcohol intoxication, alcoholism; lactation. **Precautions:** Vildagliptin/metformin tablets should not be used in patients with type 1 diabetes. Lactic acidosis (characterized by acidotic dyspnoea, abdominal pain, hypothermia, coma, decreased blood pH, plasma lactate levels >5mmol/l, increased anion gap and lactate/pyruvate ratio) can occur due to metformin accumulation (e.g. in significant renal failure, hepatic impairment). Other risk factors for lactic acidosis should be assessed (e.g. poorly controlled diabetes, ketosis, prolonged fasting, excessive alcohol intake, conditions associated with hypoxia). If metabolic acidosis is suspected, treatment should be discontinued and the patient hospitalised immediately. Serum creatinine should be monitored at least once a year in patients with normal renal function and 2-4 times a year in patients with serum creatinine levels at the upper limit of normal and in elderly patients. Special caution should be exercised in elderly patients where renal function may become impaired (e.g. when initiating antihypertensives, diuretics or NSAIDs). It is recommended that LFTs are monitored prior to initiation of Vildagliptin/metformin tablets, at three-monthly intervals in the first year and periodically thereafter. If transaminase levels are increased, patients should be monitored with a second liver function evaluation to confirm the finding and be followed thereafter with frequent liver function tests until the abnormality(ies) return(s) to normal. If AST or ALT persist at 3xULN, vildagliptin/metformin tablets should be stopped. Patients who develop jaundice or other signs of liver dysfunction should discontinue vildagliptin. Following withdrawal of treatment with vildagliptin and LFT normalisation, treatment with vildagliptin should not be reinitiated. In keeping with routine care of the diabetic patient, monitoring for skin disorders, such as blistering or ulceration, is recommended. Vildagliptin/metformin tablets should be discontinued 48 hours before elective surgery with general anaesthesia and should not usually be resumed earlier than 48 hours afterwards. Vildagliptin/metformin should be discontinued prior to, or at the time of, the administration of iodinated contrast agent and not reinstituted until 48 hours afterwards, and only after renal function has been re-evaluated and found to be normal. Patients who experience dizziness as a side effect should avoid driving vehicles or using machines. **Drug interactions:** Vildagliptin has a low potential for interactions with co-administered medicinal products, including drugs that are substrates, inhibitors or inducers of CYP450 enzymes. In pharmacokinetic studies, no interactions were seen with pioglitazone, metformin, glibenclamide, digoxin, warfarin, amlodipine, ramipril, valsartan or simvastatin. As with other oral antidiabetic medicinal products the hypoglycaemic effect of vildagliptin may be reduced by certain active substances, including thiazides, corticosteroids, thyroid products and sympathomimetics. Close monitoring of glycaemic control, dose adjustment within the recommended posology and changes in diabetic treatment should be considered when cationic medicinal products that are eliminated by renal tubular secretion (e.g. cimetidine) are co-administered. Glucocorticoids, beta-2-agonists, diuretics and ACE inhibitors may alter blood glucose. The patient should be informed and more frequent blood glucose monitoring performed, especially at the beginning of treatment. If necessary, the dosage of Vildagliptin/metformin tablets may need to be adjusted during concomitant therapy and on its discontinuation. **Side-effects:** The majority of adverse reactions were mild and transient, not requiring treatment discontinuations. **General** (vildagliptin), rare cases of hepatic dysfunction (including hepatitis). ALT or AST elevations ≥3xULN for vildagliptin 50mg od (0.2%), vildagliptin 50mg bd (0.3%) compared to 0.2% with comparators in clinical trials. Rare cases of angioedema at similar rates to controls. Vildagliptin and metformin in combination **common:** tremor, headache, dizziness, nausea, hypoglycaemia; **uncommon:** fatigue. Vildagliptin monotherapy **common:** dizziness; **uncommon:** headache, constipation, arthralgia, peripheral oedema, hypoglycaemia; **very rare:** upper respiratory tract infection, nasopharyngitis. Metformin **very common:** Nausea, vomiting, diarrhoea, abdominal pain and loss of appetite; **common:** metallic taste; **very rare:** LFT abnormalities or hepatitis, skin reactions such as erythema, pruritis and urticaria. **Legal Category:** POM **Packs:** 60 tablets; Vildagliptin/metformin (Eucreas®) 50mg/850mg tablets, Vildagliptin/metformin (Eucreas®) 50mg/1000mg tablets (EU/1/07/425/001-018). **Marketing Authorisation Holder:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB. Full prescribing information is available on request from Novartis Pharma, P.O. Box 124, Valletta, VLT 1000, Malta. Tel +356 22983217.

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1. Novartis Europharm Ltd. Galvus® Summary of Product Characteristics 2008.
2. Novartis Europharm Ltd. Eucreas® Summary of Product Characteristics 2008

Eucreas® vildagliptin/metformin

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The Genetics of the Muscular Dystrophies

continued from page 4

Limb Girdle Muscular Dystrophy

Though listed under one title, Limb Girdle Muscular Dystrophy (LGMD) is in fact both clinically and genetically a heterogeneous group of conditions. Seven types (around 10% of all LGMD) are inherited in an autosomal dominant trait (named Type 1A to Type 1G) and are relatively mild, characterised by proximal muscle weakness, beginning in the hip girdle region and later progressing to the shoulder girdle region with distal muscle weakness occurring later (if at all). The autosomal recessive form of LGMD shows an even higher degree of heterogeneity than the autosomal dominant form (11 discrete types named Type 2A to Type 2K). Onset is usually in childhood, but can occur in maturity or middle age. The first evidence of the disease is usually the pelvic or, less frequently, the shoulder girdle, often with asymmetry of wasting when the upper limbs are first involved. Spread from the lower to the upper limbs or vice versa occurs within 20 years. The rate of progression is variable, but usually severe disability with inability to walk sets in within 20 to 30 years of onset. Age at death is variable with the largest number of patients dying in middle age. Though in most cases of LGMD the causative gene has been identified, identifying the underlying genetic defect in particular cases can be a daunting task.

Other Dystrophies

The **Dystal Myopathies** are rare forms of dystrophies associated with wasting and weakness of the distal muscles with minor involvement of other muscle groups. Clinically, the disorder follows a mild course though some individuals do suffer from severe mobility problems. At least four genetically distinct types have been identified so far.

The **Oculopharyngeal Muscular Dystrophy** is an autosomal dominant disorder characterised by late adult onset, progressive ptosis and dysphagia. Other cranial and limb muscles can be involved as well. The gene associated with the disease is located on chromosome 14 and it is postulated that a triplet expansion in the PABPN1 gene might be the causative agent.

As the name implies, the relatively uncommon autosomal recessive **Congenital Muscular Dystrophy**, occurs at birth or early infancy. The child presents with hypotonia and generalised weakness with possible joint contractures. Individuals with the disorder tend to have severe muscle weakness, inability to walk and possible respiratory weakness. In most of the cases the disorder is caused by mutations in the merosin gene (chromosome 6) with some cases due to deficiency of its receptor (integrin α 7).

Pathogenesis and Molecular Management

Though muscle weakness is a ubiquitous feature in all cases of muscle dystrophy and even though most of the pathological molecular defects are known, the actual molecular pathogenesis is still not clear. The basic mechanism seems to indicate that the absence of a protein (or the presence of a mutated protein) in the DGC, and thus within the link between the extracellular matrix and intracellular actin molecules, causes a breakdown in the integrity of the muscle membrane that results in muscle weakness. But the actual mechanism by which this weakness occurs is still obscure.

Apart from the use in counseling, molecular biological techniques are promising to produce important developments in the management of the disease. In addition to supportive measures of a good diet, reduction in weight, physiotherapy, controlled exercise and orthotic and surgical corrections, there

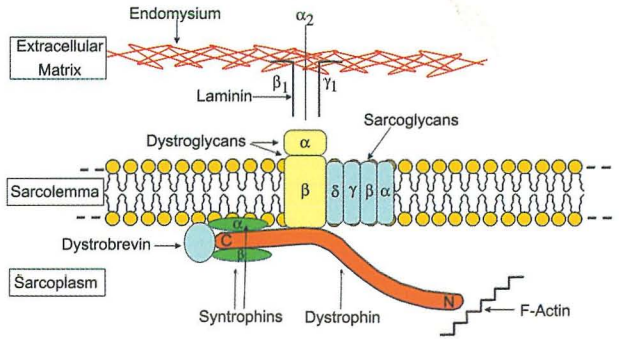

Figure 2: *Dystrophin-Glycoprotein Complex (DGC)*

is the possibility of treating the disease by correcting the underlying defect. It is not surprising to note that as DMD is the most common muscular dystrophy and that the dystrophin gene has been fully characterized and studied, most of the treatment research has been concentrated on this disorder. The observation that the basic molecular pathology difference between DMD and BMD is that the Dystrophin gene is usually either severely truncated or absent in the former, whilst only shortened but partially functioning in the latter, has indicated a possible treatment strategy for DMD cases. There are at present 4 clinical trials (in various phases) that are targeting this approach and are attempting to revert a Duchene-type of mutation into a Becker's type (usually produced by what is known as exon skipping) that should in theory improve the prognosis.

Aminoglycosides have previously been shown to suppress nonsense mutations, allowing translation of full-length proteins in vitro and in animal models. At the moment a number of clinical trials, both in the US as well as in Europe, are underway to determine both the safety and efficacy of Gentamycin IV injections in regenerating dystrophin proteins. Preliminary results have shown that such a treatment can be useful to at least a subset of patients with DMD that can be identified through the type of mutation present. The same approach has been taken through the use of anti-sense oligonucleotides. These are synthetic, short DNA sequences that are complimentary to the area of the DNA that contains the mutation. On binding to this area, the part of DNA is skipped during the translation process. A third clinical trial, that is entering into phase 2, is investigating the use of a small, oral molecule (called PTC124) to induce exon skipping. Preliminary results show that treatment with PTC124 was associated with increases in muscle dystrophin expression.

Other trials include the attempt to introduce the dystrophin gene, initially by direct injection but if successful, by systematic means. Other bio-pharmaceuticals that are at present undergoing clinical trials include the nutritional supplement coenzyme Q10 in conjunction with steroid treatment, creatinine and L-glutamine in steroid naive cases and the 'mast cell stabilizer' oxatomide drug.

Another interesting approach would be to upregulate the dystrophin analogue, utrophin. This approach has been tested in genetically engineered mice with muscular dystrophy with the treated mice showing amelioration. Though this approach offers a novel and relatively safe treatment, the search for a safe compound that upregulates utrophin is still on.

Muscular dystrophy is currently considered to be an incurable disease with an increased degree of morbidity and mortality. Through genetic studies and the use of bio-pharmaceuticals it is hoped that this dim future shall change into one that is brighter and which offers a hope to these patients.

The # 1 Antihypertensive Worldwide[1]

Diovan®/ Co-Diovan®

Powerfully Effective...
Proven Cardioprotective

HIGHER STRENGTHS AVAILABLE NOW

320 mg

1. IMS PADDS Data (53 countries) - MAT Sales April 2008.

Diovan®

Presentation: Valsartan: film-coated tablets of 80 mg, 160 mg and 320mg. **Indication:** Hypertension, post-myocardial infarction, heart failure. **Dosage - Hypertension:** Recommended dose is 80 mg once daily. If the fall in blood pressure is inadequate, dosage may be increased to 160 mg. If additional blood pressure reduction is required, the dose can be increased further to a maximum of 320 mg or another antihypertensive (e.g. diuretic) may be added. **Treatment of post-myocardial infarction:** Starting dose is 20 mg twice daily. Uptitration to a maximum of 160 mg twice daily as tolerated by patient. **Heart failure:** Starting dose is 40mg twice daily. Uptitration to 80 and 160mg twice daily as tolerated by patient. **Contraindication:** Known hypersensitivity to the components of this product, severe renal impairment (creatinine clearance < 10 mL/min), biliary cirrhosis and cholestasis and patients undergoing dialysis, pregnancy. **Precautions/Warnings/Interactions:** Risk of hypotension in sodium- and/or volume-depleted patients. Caution is advised when administering valsartan to patients with renal artery stenosis, hepatic impairment, aortic or mitral stenosis or obstructive hypertrophic cardiomyopathy. Caution should be observed when initiating therapy in patients with heart failure or post myocardial infarction. Caution should be observed with the triple combination of an ACE-inhibitor, beta-blocker and Diovan. In patients with severe heart failure, treatment with Diovan may cause impairment of renal function. Concomitant treatment with potassium-sparing diuretics or potassium supplements may increase serum potassium levels. Caution is advised when driving or operating machines. Avoid use in women planning to become pregnant and whilst breast-feeding. **Adverse reactions:** Generally similar in incidence to patients receiving placebo in placebo-controlled clinical trials, e.g. headache, dizziness, fatigue. The observed incidence of cough with valsartan in controlled clinical trials was significantly less than that observed with ACE inhibitors and similar to that seen with placebo. **The most common adverse reactions are:** viral infections, postural dizziness (reported in heart failure indication), orthostatic hypotension (reported in heart failure indication), neutropenia, upper respiratory tract infection, pharyngitis, sinusitis, hyperkalaemia (reported in post-myocardial infarction and heart failure indications), insomnia, libido decrease, vertigo, hypotension (reported in post-myocardial infarction indication and uncommon in heart failure indication), cough, diarrhoea, abdominal pain, back pain, fatigue, asthenia, oedema, syncope (reported in postmyocardial infarction indication), cardiac failure (reported in post-myocardial infarction indication). **Very rare adverse reactions but potentially serious are:** thrombocytopenia, hypersensitivity including serum sickness, vasculitis, haemorrhage, angioneurotic oedema (uncommon in post-myocardial infarction indication), renal impairment (common in heart failure indication), renal insufficiency, acute renal failure (uncommon in post-myocardial infarction indication). Some patients with heart failure have developed increases in blood urea nitrogen, serum creatinine and potassium, usually minor and transient **Packs and prices:** Country specific. **Marketing Authorisation Holder:** Novartis Pharmaceuticals UK Ltd., Frimley Business Park, Frimley, Camberely, 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, VLT1000, Malta. Tel +356 22983217. 2008-MT-01-Diovan

Co-Diovan®

Presentation: Coated tablets containing 80 mg valsartan (an angiotensin II receptor antagonist) and 12.5 mg hydrochlorothiazide (a thiazide diuretic) or 160 mg valsartan and 12.5mg hydrochlorthiazide or 160mg valsartan and 25mg hydrochlorthiazide or 320 mg valsartan and 12.5mg hydrochlorthiazide or 320mg valsartan and 25mg hydrochlorthiazide. **Indication:** Hypertension. **Dosage:** One tablet of Co-Diovan 80/12.5 mg or 160/12.5 mg or 160/25mg or 320/12.5mg daily or 320/25mg daily. **Contraindication:** Known hypersensitivity to the components of this product or to sulphonamides, pregnancy, severe hepatic impairment, biliary cirrhosis and cholestasis, anuria, severe renal impairment (creatinine clearance < 30 mL/min), refractory hypokalemia, hyponatremia, and hypercalcemia. Symptomatic hyperuricemia. **Precautions/Warnings:** Risk of hypotension in sodium- and/or volume-depleted patients, caution is advised when administering Co-Diovan to patients with renal artery stenosis, renal and liver disease, systemic lupus erythematosus. Disturbance of serum electrolyte balance, glucose tolerance and serum levels of cholesterol, tryglicerides and uric acid. Caution in driving or operating machinery. Avoid use in women planning to become pregnant and while breast-feeding. **Interactions:** Concomitant treatment with potassium-sparing diuretics or potassium supplements may increase potassium levels. Caution if combined with other antihypertensives or lithium (serum lithium monitoring), curare derivatives, NSAIDs, digoxin, antidiabetic agents, allopurinol, amantadine, cytotoxic drugs, anticholergenic agents, cholestyramine, vitamin D, calcium salts and cyclosporine. **Adverse reactions.** headache, dizziness, fatigue. For the hydrochlorothiazide component, other reported adverse reactions include hypokalemia, hyperuricemia and other electrolyte imbalance, postural hypotension and rise in blood lipids. Rare: jaundice, cardiac arrhythmias, blood disorders. Very rare: vasculitis, pancreatitis, pneumonitis, pulmonary edema. Post-marketing experience revealed very rare cases of hypersensitivity (e.g. angioneurotic oedema), and impaired renal function, myalgia and thrombocytopenia. Laboratory findings: Neutropenia, elevations in creatinine and blood urea. **Packs and prices:** Country specific. **Marketing Authorisation Holder:** Novartis Pharmaceuticals UK Ltd., Frimley Business Park, Frimley, Camberely, 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, VLT1000, Malta. Tel +356 22983217. 2008-MT-01-Co-Diovan

NOVARTIS

DIO Ad2 07/08 MT

Benzodiazepines and older people

by **Marise Gauci** *B.Pharm.(Hons.) MSc*
Clinical Pharmacist
Zammit Clapp Hospital

There is a high prevalence of benzodiazepine use among elderly persons despite the fact that this sector of the population is particularly susceptible to the adverse effects of these medicines. Short half-life benzodiazepines are usually preferred for chronic use in older adults because they do not accumulate in the body, although they have a higher potential for dependence and are more strongly associated with withdrawal symptoms. A review of the literature confirms that benzodiazepines should be prescribed with caution, at low doses and for short periods.

Benzodiazepines are often prescribed for elderly patients as hypnotics and anxiolytics. Several problems associated with benzodiazepine use in this patient population are well documented and therefore the topic merits particular attention.

Key concerns

With advancing age, elderly persons are more sensitive to the potential side effects of benzodiazepines because of altered pharmacokinetics and pharmacodynamics. Numerous studies of benzodiazepine kinetics have been conducted and have shown that alterations in the distribution and elimination of these agents occur among older patients. Benzodiazepines with longer half-lives, such as chlordiazepoxide, diazepam, and flurazepam, are more likely to accumulate in the body and cause prolonged sedation.[1] Furthermore, alterations in pharmacodynamics among elderly patients can be more important in explaining the altered response to benzodiazepines. The increased sensitivity of older people to benzodiazepines is due to age-related alterations in the central nervous system receptors.[2]

The use of benzodiazepines among elderly patients has been associated with intellectual and cognitive impairment. Cognitive impairment is characterized by anterograde amnesia, diminished short-term recall and increased forgetfulness. These symptoms are consistent with the early stages of dementia and can lead to a false diagnosis. Cognitive impairment seems to develop insidiously as a late complication of benzodiazepine use and is most commonly associated with long-acting benzodiazepines. Elderly patients with cognitive impairment show improved functioning once the drug has been discontinued.[3]

Benzodiazepines may contribute to psychomotor impairment and increase the risk of falls and automobile accidents. Psychomotor impairment is characterized by slowed reaction time and diminished speed and accuracy of motor tasks. Several studies show evidence of an increased risk of hip fracture and recurrent falls among elderly patients taking benzodiazepines. The risk of falls has been associated with sudden increases in dosage and with continuous use of benzodiazepines.[4]

Benzodiazepine dependence is a serious problem among elderly persons. Factors potentially associated with an increased risk of developing dependency include long-term use, short duration of action, high dose, high potency, alcohol or other drug dependency and personality disorders.[5]

Appropriate prescribing

It is generally advised that, if benzodiazepines are used in the elderly, they should be prescribed half the recommended dose of adults. Benzodiazepines used as hypnotics include nitrazepam which has a prolonged action and may give rise to residual effects the following day, with repeated doses tending to be cumulative. More appropriate options are lormetazepam and temazepam which act for a shorter time and have little or no hangover effect. Alternative hypnotics are the Z drugs e.g. zolpidem which are non-benzodiazepine hypnotics, but act on the benzodiazepine receptors. The Z drugs were developed with the aim of overcoming some of the disadvantages of benzodiazepines but available evidence has not clearly shown these benefits. In fact NICE guidance on the use of Z drugs recommends that because of the lack of evidence to distinguish between these agents and the short-acting benzodiazepine hypnotics, the drug with the lower purchase cost for the patient should be prescribed.[6]

Benzodiazepines can be effective in alleviating anxiety states. Although these drugs are often prescribed to patients with stress-related symptoms, unhappiness or physical disease, their use in many situations is unjustified. In particular, they are not appropriate for treating depression or chronic psychosis.[7] All benzodiazepines work well in anxiety, however, elderly people respond better and experience fewer adverse effects with short or intermediate-acting agents such as lorazepam than with longer acting ones such as diazepam. Occasionally, short-acting agents produce a rebound anxiety effect before the next dose is given. In such cases, a longer acting drug may be preferred.[8]

Reducing use

Benzodiazepine treatment should be limited to the lowest possible dose for the shortest possible time. Stopping the drug is easier if clinicians and pharmacists clarify from the outset that treatment is only for a brief definite period. After continuous use for an extended time, benzodiazepines may be difficult to stop because of psychological and physical reasons. Nevertheless, periodic efforts should be made to stop the drug or at least reduce the dose. Withdrawal should be gradual because abrupt withdrawal may produce confusion, toxic psychosis, convulsions or a condition resembling delirium tremens. Abrupt discontinuation of short-acting benzodiazepines may produce a more severe withdrawal than long-acting agents.[9]

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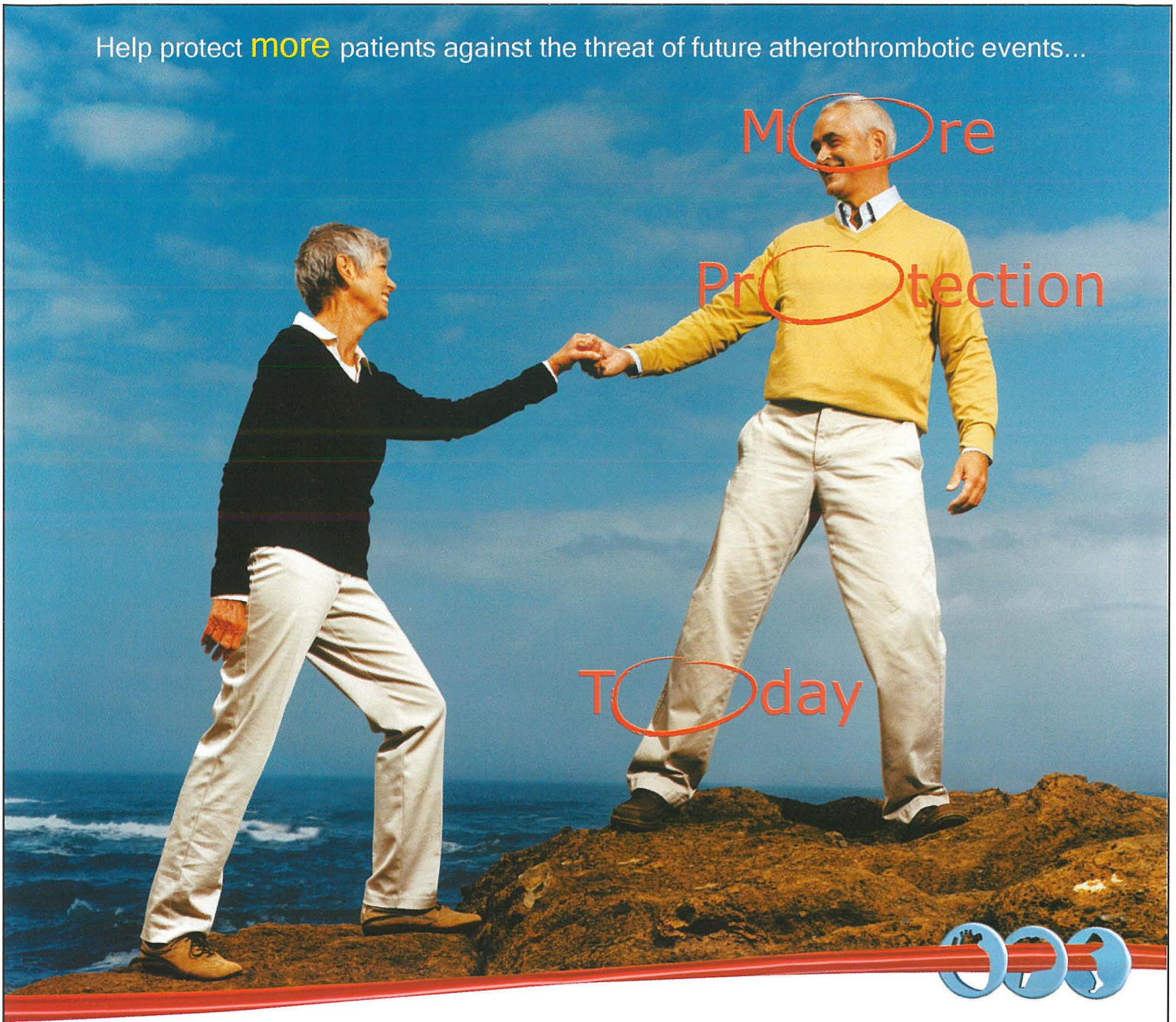

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Clopidogrel 75mg

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NAME OF MEDICINAL PRODUCT: Plavix 75 mg film-coated tablets. COMPOSITION: Clopidogrel hydrogen sulphate 97.875mg. PHARMACEUTICAL FORM Film-coated tablet. THERAPEUTIC INDICATIONS Clopidogrel is indicated for the prevention of atherothrombotic events in: Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease. Patients suffering from non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction) in combination with acetylsalicylic acid (ASA). POSOLOGY AND METHOD OF ADMINISTRATION Adults and elderly: single daily dose of 75 mg with or without food. In patients with non-ST segment elevation acute coronary syndrome (unstable angina or non-Q wave myocardial infarction): single 300 mg loading dose and then continued at 75 mg once a day (with ASA 75 mg-325 mg daily). Since higher doses of ASA were associated with higher bleeding risk it is recommended that the dose of ASA should not be higher than 100 mg. The optimal duration of treatment has not been formally established. Clinical trial data support use up to 12 months, and the maximum benefit was seen at 3 months. Children and adolescents: There is no experience in children. CONTRAINDICATIONS Hypersensitivity to the active substance or to any of the excipients of the medicinal product; Severe liver impairment; Active pathological bleeding such as peptic ulcer or intracranial haemorrhage; Breast-feeding. SPECIAL WARNINGS AND PRECAUTIONS FOR USE Due to the risk of bleeding and haematological undesirable effects, blood cell count determination and/or other appropriate testing should be promptly considered whenever clinical symptoms suggestive of bleeding arise during the course of treatment. As with other antiplatelet agents, clopidogrel should be used with caution in patients who may be at risk of increased bleeding from trauma, surgery or other pathological conditions and in patients receiving treatment with ASA, nonsteroidal anti-inflammatory drugs, heparin, glycoprotein IIb/IIIa inhibitors or thrombolytics. Patients should be followed carefully for any signs of bleeding including occult bleeding, especially during the first weeks of treatment and/or after invasive cardiac procedures or surgery. The concomitant administration of clopidogrel with warfarin is not recommended since it may increase the intensity of bleedings. If a patient is to undergo elective surgery and antiplatelet effect is not necessary, clopidogrel should be discontinued 7 days prior to surgery. Clopidogrel prolongs bleeding time and should be used with caution in patients who have lesions with a propensity to bleed (particularly gastrointestinal and intraocular). Patients should be told that it might take longer than usual to stop bleeding when they take clopidogrel (alone or in combination with ASA), and that they should report any unusual bleeding (site or duration) to their physician. Patients should inform physicians and dentists that they are taking clopidogrel before any surgery is scheduled and before any new drug is taken. Thrombotic Thrombocytopenic Purpura (TTP) has been reported very rarely following the use of clopidogrel, sometimes after a short exposure. It is characterised by thrombocytopenia and microangiopathic hemolytic anemia associated with either neurological findings, renal dysfunction or fever. TTP is a potentially fatal condition requiring prompt treatment including plasmapheresis. In view of the lack of data, in patients with acute myocardial infarction with ST-segment elevation, clopidogrel therapy should not be initiated within the first few days following myocardial infarction. In view of the lack of data, clopidogrel cannot be recommended in acute ischaemic stroke (less than 7 days). Therapeutic experience with clopidogrel is limited in patients with renal impairment. Therefore, clopidogrel should be used with caution in these patients. Experience is limited in patients with moderate hepatic disease who may have bleeding diatheses. Clopidogrel should therefore be used with caution in this population. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucosegalactose malabsorption should not take this medicine. INTERACTION WITH OTHER MEDICINAL PRODUCTS: Warfarin; glycoprotein IIb/IIIa inhibitors; Acetylsalicylic acid (ASA); Heparin; Thrombolytics; Non-Steroidal Anti-Inflammatory Drugs (NSAIDs); Other concomitant therapy: No clinically significant pharmacodynamic interactions were observed when clopidogrel was co-administered with atenolol, nifedipine, or both atenolol and nifedipine. PREGNANCY AND LACTATION Pregnancy: As no clinical data on exposed pregnancies are available, it is preferable not to use clopidogrel during pregnancy as a precautionary measure. Lactation: It is not known whether this medicinal product is excreted in human milk. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: Clopidogrel has no or negligible influence on the ability to drive and use machines. UNDESIRABLE EFFECTS: Haemorrhagic disorders; Haematological disorders; Central and peripheral nervous system disorders: Headache, Dizziness, Paraesthesia and Vertigo; Gastrointestinal system disorders: Diarrhoea, Abdominal pain, Dyspepsia, Gastric ulcer and Duodenal ulcer, Gastritis, Vomiting, Nausea, Constipation, Flatulence. Platelet, bleeding and clotting disorders; Bleeding time increased and Platelets decreased. Skin and appendages disorder: Rash and Pruritus. White cell and RES disorders: Leucopenia, Neutrophils decreased and Eosinophilia. Bleeding: some cases were reported with fatal outcome (especially intracranial, gastrointestinal and retroperitoneal haemorrhage); skin bleeding (purpura), musculo-skeletal bleeding (haemarthrosis, haematoma), eye bleeding (conjunctival, ocular, retinal), epistaxis, respiratory tract bleeding (haemoptysis, pulmonary haemorrhage), haematuria and haemorrhage of operative wound have been reported. Blood and lymphatic system disorders: Thrombotic Thrombocytopenic Purpura (TTP), severe Thrombocytopenia (platelet count ≤30 x109/l), Agranulocytosis, Granulocytopenia, Aplastic anaemia/Pancytopenia, Anaemia. Immune system disorders: Anaphylactoid reactions, Serum sickness. Psychiatric disorders: Confusion, Hallucinations. Nervous system disorders: Taste disturbances. Vascular disorders: Vasculitis, Hypotension. Respiratory, thoracic and mediastinal disorders: Bronchospasm, Interstitial pneumonitis. Gastrointestinal disorders: Pancreatitis, Colitis (including ulcerative or lymphocytic colitis), Stomatitis. Hepatobiliary disorders: Acute liver failure, Hepatitis. Skin and subcutaneous tissue disorders: Angioedema, Bullous dermatitis (erythema multiforme, Stevens Johnson Syndrome, toxic epidermal necrolysis), Rash erythematous, Urticaria, Eczema and Lichen planus. Musculoskeletal, connective tissue and bone disorders: Arthralgia, Arthritis, Myalgia. Renal and urinary disorders: Glomerulonephritis. General disorders and administration site conditions: Fever. Investigations: Abnormal liver function test, Blood creatinine increase. OVERDOSE: No antidote to the pharmacological activity of clopidogrel has been found. If prompt correction of prolonged bleeding time is required, platelet transfusion may reverse the effects of clopidogrel. MARKETING AUTHORISATION HOLDER: Sanofi Pharma Bristol-Myers Squibb SNC, 174 Avenue de France, F-75013 Paris – France. MARKETING AUTHORISATION NUMBER: EU/1/98/069/001a. FURTHER INFORMATION IS AVAILABLE FROM: sanofi-aventis Malta Ltd. Tel: 2149 3022

MT CLO 08 03 01

The new Death Certificate: Your role as Certifiers

by **Kathleen England** *MD MSc (Public Health Medicine)*
Medical Officer, Department of Health Information and Research

Information recorded on death certificates is used to produce population-based mortality statistics. Mortality data is used both in health monitoring and resource allocation as well as epidemiological research.

Inaccuracies of death certificate information can occur as a result of errors at a number of the steps in the certification process. Resulting inaccuracies in information undermine the quality of the data derived from death certificates.[1] These steps include:

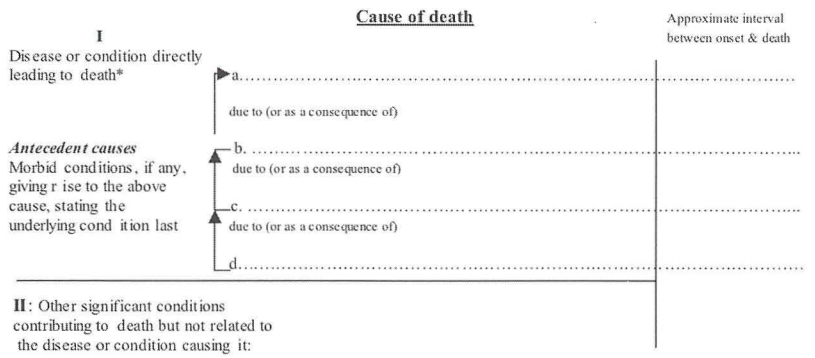
- Inadequate or misinterpreted clinical information can lead to erroneous ante mortem diagnosis, which are then recorded by the physician on the death certificate.
- Information can also be recorded wrongly on the death certificate due to lack of training in how to fill in death certificates.
- Modification of cause of death statement to avoid autopsy and distress to relatives.
- The final step in the process is coding of causes of death by a person who is usually trained. Studies have shown that this is relatively accurate and measures to improve coding and comparability between countries are being implemented.

During 2006-2007 the Department of Health Information and Research participated in an EU Project aimed at improving the quality of mortality statistics through improvements at certification and codification process depending on the individual needs of participating countries. This project led to the updating of the death certificate according to WHO and EU recommendations as well as the creation of training material aimed to assist certifiers in completing correctly the 'cause of death' section of the death certificate.

International form of the medical certificate for cause of death

Part I of the certificate provides 4 lines, on which the sequences of events leading to death are recorded. The condition thought to be the **underlying cause of death** (UCD) should appear on the last (lowest) completed line of part I and is usually the cause used in mortality statistics.

International form of the medical certificate for cause of death



* This does not mean mode of dying e.g. respiratory failure. It means the disease, injury or complication that caused death.

WHO defines the underlying cause of death as: the disease or injury that initiated the train of morbid events leading directly to death, or the circumstances of the accident or violence that produced the fatal injury.[2]

An example with 4 steps in the chain of events leading directly to death is:

a) line I a: Pulmonary embolism
b) line I b: Pathological fracture
c) line I c: Secondary carcinoma of femur
d) line I d: **Carcinoma of breast ← (UCD)**

There must always be an entry on line I a. This condition may be the only condition reported in part I of the certificate only if it was not due to, or did not arise as a consequence of any disease or injury that occurred before the immediate cause of death (E.g. 'Viral Myocarditis' was present at death).

Part II is for any other significant conditions that contributed to the fatal outcome, but were not related to the disease or condition directly causing death.

In a questionnaire sent to a number of doctors who are commonly involved in death certification they were asked to complete examples of medical parts of death certificates. A number of frequent errors emerged:

- **Major errors:**
  - Mechanism of death or non-specific condition listed without an underlying cause e.g. cardiac arrest, respiratory failure. Because there could be hundreds of different causes leading to the same mechanism of death, this kind of description provides no useful information for cause of death statistics[3] and therefore should not be used. The cause of non specific conditions such as heart failure should always be specified e.g. due to ischaemic heart disease.
  - Improper sequencing e.g. underlying cause of death written on first line (line a) followed by other causes on subsequent lines.
  - Competing causes: two or more causally unrelated, etiologically specific diseases listed in part I e.g. breast cancer, diabetes listed in part I.
  - Not writing down the method of injury e.g. not writing the fall as cause of a fractured femur.
  - Limiting underlying cause of death to recent past e.g. not taking account of the effects of a cerebrovascular accident which occurred two years before.
- **Minor errors:**
  - Absent time intervals
  - Use of abbreviations.

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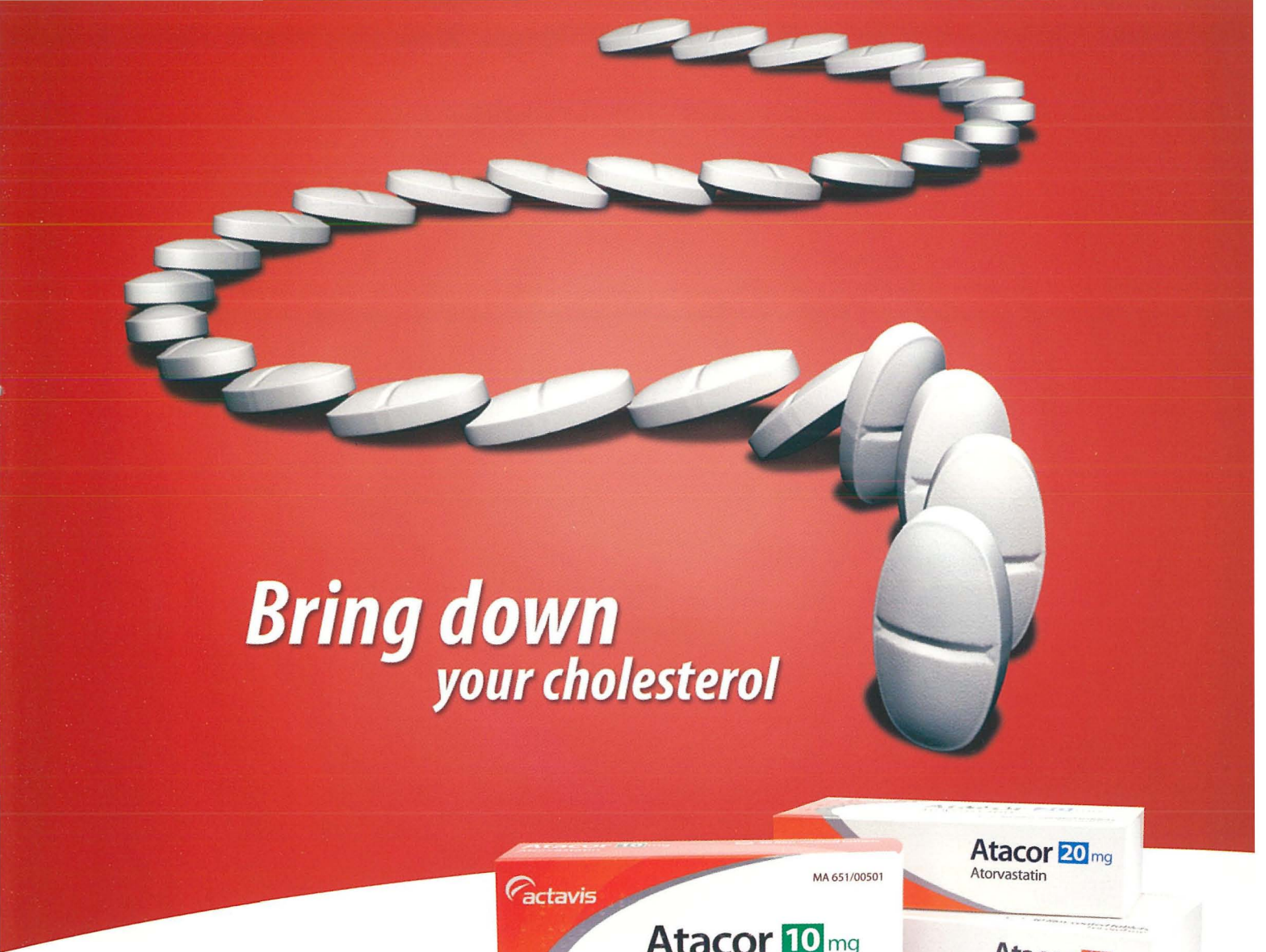

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Atorvastatin

10mg, 20mg, 40mg tablets

Lipid Reducing Agent

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

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SMS4Health . . . health promotion and disease prevention – a novel use of the mobile phone

Thinking Prevention – a Symposium organized by SMS4health and Bupa

Prof. Albert Fenech's quote of an old Chinese proverb: "The superior doctor prevents sickness; The mediocre doctor attends to impending sickness; The inferior doctor treats actual sickness"

A symposium on "Thinking Prevention", which was chaired by Dr Mario Grixti – President, Malta College of Family Doctors, was held for medical professionals at all levels of health care highlighting the importance of Preventive Healthcare and the benefits that may be reaped especially for the patient but also for the doctor. Another important role of the doctors is to use their trusted influence for the patients to lead a healthier way of life so as minimize the main critical ailments in the Maltese Society and compliment the national promotion strategies. This was precisely stressed by Dr Charmaine Gauci, Director for Health Promotion and Disease Prevention.

Profs. Albert Fenech, Chairman, Cardiology Department, Mater Dei Hospital, in his much awaited habitually ingenious talk strongly supported these initiatives to encourage the general Maltese public change their present lifestyle and customs so as to lower the potential development of cardiovascular related diseases and their life damaging results. Profs. Fenech also stressed on the importance of preventive healthcare quoting the Chinese proverb : "The superior doctor prevents sickness; The mediocre doctor attends to impending sickness; The inferior doctor treats actual sickness"

Dr Wilfred Galea, Managing Director of SMS4Health, explained how, with SMS4Health, both preventive healthcare and promoting a better lifestyle for the patients can be practiced so simply and consistently. The system which has been successfully tested in his practice is now being rolled out in other practices thus bridging the gap of both the patients' and doctors' expectations. SMS4Health is a subscription based service. On enrollment, the doctor prescribes an individual health programme according to the age, gender and medical history. The patient will then receive an sms message on the given mobile number as a reminder of each next due medical check up. Besides, the service offers regular health promotion tips and medical alerts always sent via sms messages.

Bupa Malta manager Adriana Zarb Adami also delivered a presentation on Bupa's commitment in support of health. *"In line with its primary objective to provide the very best in health care in a professional, caring and understanding manner, Bupa has recently extended its support for this newly launched platform that facilitates health promotion – **SMS4Health**."*

For further information on SMS4Health, visit the website www.sms4health.com, contact Medical Portals Ltd on 21453973 and 79453972 or send an email at sales@sms4health.com

Claims that a Fish Oil Extract is a Breakthrough Treatment for Depression, Myalgic Encephalomyelitis and other Brain Function Disorders

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

Scientific evidence indicates that diet and lifestyle influence gene expression, and that the old notion that you "cannot change what's in your genes" is exactly that – old hat. Natural medicine is emerging as an important adjunct to conventional medicine, and it therefore behoves physicians to be receptive to its claims that it may provide safer remedies than pharmaceutical drugs and surgeons' implements.

Professor Basant Puri, a distinguished London medical scientist, expert in psychiatry, neuroscience and MRI brain scanning, claims that depression can be beaten with a purified fish oil extract. Marine oil contains two essential fatty acids, Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA) – important components of all our cell membranes, including those of neurons and their synapses. Puri not only believes that a deficiency of these fatty acids in neuronal membranes is linked to mood disorders, chronic fatigue syndrome / Myalgic Encephalomyelitis and to attention deficit and hyperactivity, but that EPA is the beneficial fatty acid involved in these conditions. He claims DHA hinders EPA, and that the best results are achieved with a pure EPA preparation specially developed for his research. He claims pure EPA is a therapeutic breakthrough and, unlike anti-depressive drugs, has no unpleasant side-effects and prevents recurrence.

Puri claims his MRI scans show shrunken grey cortex in mood disorders and ME, and that the grey cortex returns to normal thickness after successful treatment with pure EPA. He also claims it is beneficial in schizophrenia and Huntington's disease, and that it is better than pharmaceutical drugs for attention deficit and hyperactivity states. Further information on EPA, as well as Puri's books on these subjects are available from www.igennus.com. References to Puri's scientific publications are on *Google*.

Professor Cilia-Vincenti is a former teacher of disease mechanisms at London and Malta medical schools, and has a longstanding interest in natural medicine.

Reminder

All medical doctors who have not yet paid their registration fee to the Medical Council are kindly requested to do so immediately. Queries may be addressed to the Medical Council on 21255540 or medicalcouncil.mhec@gov.mt

Philosophy of medicine – is there such a thing? – Part I

by **Pierre Mallia** *MD MPhil PhD MRCP FRCGP*
Associate Professor of Family Medicine and Patients' Rights
Department of Family Medicine, Medical School
University of Malta

The first thing we need to ask is whether philosophy of science matters at all for medicine; and indeed what do we mean by philosophy of science anyway? Perhaps the best way is to answer the question whether medicine, as a science, depends on tradition, and secondly, if there is a tradition, what are the goals of this tradition. Prima facie most doctors would agree that there is a tradition of medicine, which is to heal patients and to do good. Yet this tradition is being challenged when some doctors feel it their duty of assist in ending the life of a suffering individual. When one asks whether this is or should be the goal of medicine, one is making an inquiry about the philosophy of one's practice. Even if it is not the aim, the *ethos*, of medicine, it may still be within the grasp of the general aim of scientific method. To illustrate this better, we can use reproductive technology or stem cell research as an example. Scientific advances in these areas by no means hold back the medical profession from using them; at least the former. Yet some may still challenge them on moral grounds outside medicine and then ask whether it should be within the scope of medical practice to host these technologies which some (or many) may question on moral grounds.

There are two principal movements in the philosophy of science, which can be applied to medicine, which have made their voice heard even in circles not inherent to the field. These are those of Karl Popper and Thomas Kuhn. Both did not concern themselves with medicine, but with philosophy of science per se. Popper is portrayed as the more objectivist and traditional, putting science on a level of challenges.[1] We uphold a theory until it is challenged by a better one. The good scientist thus allows his theory as a working tool but is open to challenges and indeed may challenge it himself. Kuhn, on the other hand can be thought of more as coming from the American Pragmatic school and is considered more liberal and indeed relativist, saying that science moves forward by the practice or thought of the day, which he called *paradigms*.[1] These paradigms create small revolutions in themselves and scientists work around them. It is therefore more authoritarian and based on historical research as well. This historicism is a learning experience, if you may, on which one builds. Yet when a paradigm changes, all the material of the previous thoughts are put aside. Kuhn was a physicist and limited his discussion to this field. A clear example was theoretical physics which at the time was passing through a revolution of thought because of general relativity and quantum physics. Cosmology, with the 'Big Bang', created this new paradigm of thought and cosmologists work around this theory even though some still challenge the Big Bang concept.

We uphold a theory until it is challanged by a better one

Do we do the same in medicine? In many ways, we do. We speak of current thoughts in medical practice and historical development do take their toll. If one asks whether medicine is liberal or indeed relativist, there are indeed those who would go to all means in order to cure patients, or indeed to gain external advantages, given the necessity of industry to push forward medical research and development. Thus some would little question the embryo once this is for the gain of benefits obtained by stem cell research. Yet medicine has its long tradition and we take joy in speaking about the Hippocratic Oath and such. When it comes therefore to the teaching of bio- and medical ethics, one often appeals to tradition; but this tradition does change with the times. The principle of respecting autonomy has, for example, challenged paternalism – the notion that the doctor knows all and the patient must obey.

Does this matter at all? Indeed if medicine is to maintain its repute as doing good, it does. Doctors who are paternalistic are not only challenged but may face trouble. Whereas in the past it was relatively fine to take organs from dead bodies for research and study purposes; today medicine has fallen in line with obtaining consent and indeed has pioneered the concept of 'informed' consent – something which the business world, for example, including those giving out medical insurance, must still master. Moreover medicine has become *socialized*. Example, today people are more and more aware of their cholesterol and weight, and exercise. Far from what certain authors say, that medicine has manipulated the world, this is the result of society. The very fact that many other social factors come into play in medicine – politics, insurances, pharmaceutical industry etc, implies that there are more than doctors and paramedics involved in health care. This breeds the question – should these not all have the same ethics? Should they be obliged to follow the rules of medicine?

If we can speak of a philosophy of medicine, then we can answer in the affirmative. This would oblige insurances, politicians, and even brands promoting a certain product to follow the same rules – that of respecting the principles which we as doctors uphold – respecting autonomy, beneficence, nonmaleficence and justice. Whilst the latter would apply mostly to politicians, we would not tolerate advertising which works upon scare-mongering techniques – if you do not choose this product you may be at a disadvantage; or manipulation – such as facial creams 'approved' by dermatological foundations sponsored by the same company producing the cream. As conflicts of interest apply to doctors, they should apply to anyone who is in any way making a profit on patients.

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Benzodiazepines and older people

continued from page 8

Symptoms may develop at any time up to 3 weeks after stopping a long-acting benzodiazepine, but may occur within a few hours in the case of a short-acting one. The British National Formulary includes a suggested withdrawal protocol involving transfer to an equivalent dose of diazepam and slowly reducing the dose. This may help those patients who experience symptoms when reducing their intake of original benzodiazepine.[7] Gradual tapering of benzodiazepines has been shown to be at least as effective among elderly patients as among younger patients. Schweizer and colleagues[10] compared the severity of withdrawal symptoms and clinical outcomes in a matched sample of elderly and young patients. The elderly patients showed significantly less severe withdrawal symptoms during a gradual taper and did equally well in terms of outcomes as their younger counterparts. The authors speculated that a slower clearance of the medication may attenuate withdrawal symptoms and that diminished neuronal capacity among elderly persons causes less rebound overactivity.

Conclusion

When prescribing benzodiazepines for older people, careful consideration should be given to minimizing doses and duration of treatment. Medication reviews are particularly important in this sector of the population when decreasing doses or discontinuing drugs which are no longer appropriate for the patient. Moreover, effective communication with the patient and carers is imperative since resistance to withdrawing these agents is often encountered.

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Update on Avian Influenza

by **Tanya Melillo Fenech** *MD MSc*
Principle Medical Officer at Infectious Disease Prevention and Control Unit
Department of Health Promotion and Disease Prevention

The cumulative number of confirmed cases of human avian influenza since the beginning of the year is 34 cases with 26 deaths. The HPAI subtype H5N1 is unprecedented since there are no records of an epizootic having lasted so long a time and having covered such a wide geographical area in such a short period of time. Up till the end of May this year, 12 countries/territories have notified the reoccurrence of HPAI H5N1 following its previous eradication, thus indicating that the virus is continuing to circulate. These are the Republic of Korea, Hong Kong (SARPRC), India, Iran, Israel, Japan, Laos, Switzerland, Thailand, Turkey, Ukraine and the United Kingdom (wild birds).

First EU prepandemic vaccine

Last May, GSK's new vaccine Prepandrix was the first prepandemic vaccine to obtain a centralised marketing authorisation. It is formulated with a novel adjuvant system designed to achieve high immune response to a low dose of antigen which is long lasting and active against a broad range of H5N1 strains. The current age indication is 18-60 years. During clinical trials it was found to be well tolerated and showed cross protection.

Scientists publishing in *Nature* call for diversification of antiviral stockpiles

The potential impact of pandemic influenza makes effective measures to limit the spread and morbidity of virus infection a public health priority. Antiviral drugs are seen as essential requirements for control of initial influenza outbreaks caused by a new virus, and in prepandemic plans there is a heavy reliance on drug stockpiles.

The principal target for these drugs is a virus surface glycoprotein, neuraminidase N1, which facilitates the release of the virus and thus the spread of infection. The presence of N1 neuraminidase on both avian H5N1 and human seasonal influenza A subtype H1N1, shows that both virus sub-types have the same mechanism of resistance to oseltamivir. This data adds weight to the hypothesis that because the molecular structure of zanamivir is a minimal modification of the natural sialic acid substrate, use of zanamivir should minimize the viability of any drug resistant mutations at the enzyme active site, and thus reduce the chances for development of resistance. Due to these findings, scientists recommend the diversification of pandemic stockpile with both types of neuraminidases.

Modern Management Approa

by **Kirsten M. Pulis** *BSc(Hons) Communication Therapy MA (Autism)*

Autism is a developmental disorder characterised by a triad of impairments, namely communication, social interaction and imagination. It was first described by Leo Kanner and Hans Asperger almost simultaneously in the 1940s, and since then has continued to gain momentum in the clinical, educational and lay world. In fact, prevalence estimates have escalated in recent years, going from 0.4% in 1978 to 1% in 2006, making autism the third most common childhood disorder after intellectual disability and language impairment.[1]

Just as autism may be described as a spectrum of disorders, ranging from severe to high-functioning, so its treatments may also be seen as falling along a 'rainbow' of management options. This variety results, in part, from the fact that no single causation has as yet been attributed to autism.[2] Yet, it may be said that all interventions have the same goal i.e. "to promote normal development and acquisition of skills, and to reduce or eliminate maladaptive behaviours"[3], enabling children to function in their everyday lives and be included in all aspects of their community.

However, treatment may have a different focus depending on whether individuals fall at the severe or high-functioning ends of the autistic continuum, and this focus may change again across an individual's lifespan as behavioural symptoms change.[4] Apart from that, programmes may be founded on different schools of thought, namely the traditional behaviourist school (e.g. the Lovaas method[5]), the more recently advocated semantic-pragmatic model (e.g. Developmental, individual-difference, relationship based [DIR][6]), or a school of thought that falls somewhere in between, into what are known as contemporary behavioural models (e.g. Pivotal Response Therapy[7]). They may target autism as a whole i.e. comprehensive approaches such as the Treatment and Education of Autistic and Related Communication Handicapped Children [TEACCH][8]; or be more specific, such as speech therapy or play therapy[9], and may be based in the home, centre or school environments. Some approaches are more physical, such as Daily Life Therapy[10], which emphasises physical exercise, whereas others could be described as more psychological (e.g. EarlyBird counselling[11]).

Treatment options may also be classified as educational versus medical. The former includes schooling and any program where the child is taught skills that will enable him/her to function in everyday life. The recent trend towards inclusion has resulted in a shift in the type of schooling methods advocated for children with autism, from segregation in special schools to integration into mainstream ones[12]. Full inclusion in school, however may not be the best solution for all children with autism, or, indeed, for one individual at different points in time, and thus, alternative educational opportunities must be made available[13].

Medical management involves the use of medication, special diets or vitamin supplements to reduce behavioural symptoms such as obsessions, hyperactivity and aggressiveness. In this way, individuals with autism are more able to engage in study, play and social interactions; although medications should never be used as a substitute for psychological, social and educational interventions[14]. Rather, they should serve to increase the individual's ability to benefit from them. It should be noted, however, that most medication available to children with autism has not been tested on children, or specifically on children with autism, and must thus be used with caution[13,15].

Lastly, it is important to distinguish between therapies which are substantiated by research from those where the evidence is at best anecdotal (e.g. Options/Son-Rise[16], aromatherapy)[17]. This is crucial because subjecting a child to a treatment program which is unlikely to work will be detrimental in that it might diminish the exposure of that child to a more beneficial therapy option, as well as taxing the parents financial reserves unnecessarily.

Of course, just as the colours of a rainbow merge together at their borders, it must be noted that there is also a lot of overlap between types of management strategies for autism, and it is often the case that a variety of treatment approaches are used in tandem[9].

Two of the most widely researched and substantiated programmes for autism are Early Intensive Behavioural Intervention (EIBI) and TEACCH. EIBI is based on the behaviourist school of thought, and on applied behavioural analysis (ABA) specifically. Behavioural approaches have followed the principles of learning to teach appropriate behaviours and eliminate inappropriate ones in people with autism[18]. An ABA program works on the premise that when reinforcing consequences follow a child's response, the child is likely to give that response again, so learning can be shaped by reinforcement[9]. Eventually, the aim is that the child will give the response even without the reward. Each skill is practised repeatedly in a series of drills, starting from the smallest learnable part, and building up to the whole skill until it is mastered[13]. These methods have been criticised as being unnaturally "stiff" and artificial, but their proponents hold that for autistic children, who find it hard to learn in 'normal' environments due to their specific learning and attentional deficits, these very repetitive, predictable interactions with the therapist are *reassuring*[19], as well as compatible with their unique way of processing information[2].

These concerns fuelled the development of more functional approaches, such as the contemporary behavioural techniques and semantic pragmatic–developmental (SP-D) approaches, which emphasise the importance of learning functional skills in natural environments and in natural ways[19]. Perhaps one of the best known and most widely used SP-D approaches is TEACCH[20]. This is a highly structured teaching approach, focusing on the visual, rather than auditory/verbal, pathway to the presentation of information, thus playing on the strengths of individuals with autism[21]. The learning environment is structured in such a way as to make clear demarcations of different areas by using screens or differently coloured carpets so that individuals are clear about what activity occurs there. TEACCH can be used by individuals of all ages and degrees of severity of autism[14]; and its principles can, and should, be applied to different settings. TEACCH strategies give predictability to the individual, thus reducing anxiety

ches for Children with Autism

and resulting challenging behaviour. By helping the individual understand the environment, TEACCH fosters independence by decreasing dependence on other people, which is one of the problems encountered in many behaviourist approaches.

TEACCH is not without its criticisms, however. Unlike most behavioural approaches, which try to help people with autism adapt to their environment, TEACCH's philosophy is one of acceptance of the condition, and therefore, instead of putting strategies in place to eliminate or cope with problem behaviours, TEACCH aims to prevent them from happening. This philosophy has been criticised as being too accommodating, since it may not always be possible to modify each and every environment or situation an individual may encounter.

Although autism is a developmental disorder for which there is as yet no known cure, this does not mean that improvements cannot be made. Problems with sleeping, eating and temper tantrums can diminish over time[22], and many management approaches are available to ameliorate the symptoms of the condition. What is clear, though, is that there is no one treatment option for autism, as evidenced from the great variability in intervention outcomes[23]. Thus, an individualised approach should be encouraged, because different therapies work for different people[22]. In fact, recent research is beginning to focus on trying to match individuals with autism with efficacious treatments[23]. It is important that 'individualised' is not only taken to mean how one person's plan differs from another's, but how that plan will be revised and updated according to how that person responds to intervention and to how his/her developmental profile changes with age.

Another point to remember is that such children benefit from a multidisciplinary approach, since they typically require services from a number of different professionals. These include neurologists, general practitioners, speech -language pathologists, occupational therapists and psychologists, to name but a few. Parents must also be considered as members of these teams, because it is they who spend most time with the child, and will thus be more aware of his/her specific needs. An important role of every professional in contact with individuals with autism is to keep up to date with recent literature about possible treatment approaches in order to be able to guide parents with their choice of management strategies.

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Remembering not to Forget

by **Marika Azzopardi**

It has been voiced time and again over recent years – Dementia should be a top health priority in Europe. As much has been stressed by a number of MEPs at the European Parliament, a substantial 70 so far, endorsing the recommendations of Alzheimer Europe following the launch of the Paris Declaration way back in 2006 in a bid to raise awareness about this disease. Dementia should also be placed at the top of the health agenda in Malta. The Malta Dementia Society strongly backs this whilst lobbying with local policy makers, and making valid suggestions on what it entails and what needs to be done. To find out more about the reasons behind this urgency around the issue of dementia, I meet up with Dr Charles Scerri who is the Secretary of the Malta Dementia Society and a newly elected board member of Alzheimer Europe.

Dr Scerri's name has been constantly linked with the study of dementia over the past years. Although he began his medical career as a pharmacist, he soon honed in on increasing his understanding of what happens within the brain in this particular disorder and what chemical agents could be valuable in slowing down the significant brain cell loss observed. This led him to read for an MPhil in Behavioural Pharmacology followed by a Doctorate studying the various biochemical, pathological and pharmacological aspects of Alzheimer's Disease at the University of Dundee in Scotland in 2004. That same year saw the official launch of the Malta Dementia Society of which he is a founding member and a vociferous one at that.

"Dementia is not something new although it is being recognised as the epidemic of our times. We live in a modern world having better sanitary and medical care which is enabling us to live longer. It is a side-effect of longevity if you want, and with an increasingly ageing population, things can only get worse. So much so that in Alzheimer's disease (which accounts for 60% of all dementia cases) the worst struck are women as these tend to live longer than their male counterparts."

Attending an international conference on dementia

With this predicament for a backdrop, Dr Scerri provides deeper insight into this neurological disease which is a very subjective illness. "Each person who develops dementia develops it in his or her own manner and very often it is the relatives who recognise the subtle abnormalities which can sound the first alarm bells. True, memory loss could be precipitated by other factors such as malnutrition, certain drug therapies or brain tumours, but more often than not, when people reach a certain age, unusual and recurrent forgetfulness can very possibly be due to some form of dementia."

The crux of the matter seems to be early diagnosis. Dr Scerri bemoans the fact that, together with other health care professionals, the current armies of doctors trained in Malta don't have enough knowledge on dementia with respect to diagnosis, pharmacological management and long-term care. This is obviously not aided by the fact that academic preparation in this specific area at tertiary level is currently very limited. This results in very slow diagnosis, and my interviewee stresses insistently that the biggest problem is that 'we don't reach them early enough!'

With a possible 4,500 people in Malta being diagnosed with dementia, numbers peaking sharply in the octogenarian age group, the Maltese population must wake up to the fact that in the here and now, 1% of the general population is forgetting fast. By 2035, this percentage will have almost doubled. Who will care for these people?

"That is just one of my fears. With a serious lack of long-term planning plaguing our health care facilities which are already seriously handicapped financially, the government will find itself facing a scenario wherein family carers are less and less, and itself being called upon to offer services. Care for people with dementia is a 24/7 affair. The government authorities had better wake up to some mind-boggling facts: individuals with dementia live long lives and the average time-span from diagnosis to decease is approximately 11 years. This long co-habitation with dementia has harsh effects on the immediate family structure. Most often, family members have to stop working to care for their relative

Members of the Alzheimer European Board

and this leads to further social, psychological and financial problems. Epidemiological studies suggest that 60% of the relatives who act as carers resort to psychiatric assistance at some point or other due to extreme stress levels. When institutionalisation of the individual with dementia occurs, the strain on the public structures becomes enormous." Then again, Dr Scerri pinpoints a huge financial crevice around dementia as, according to the WHO, the disease is costing the national health services of developed countries way beyond cancer and cardio vascular disease put together. With the current costs of medication reaching close to some Euro 150 per month locally, no part of which expense is subsidised by government, the individual families of dementia sufferers are having an even harder time. But giving the medication for free, although helpful, is not the only answer.

Apart from the evident lack of training to support healthcare professionals and the lack of awareness of policy makers, individuals with dementia must also face the lack of awareness of the man in the street who pooh-poohs the problem away, or even worse, stamps it with a derogative stigma that can only make matters worse. It leads to the sufferer being emarginated and negatively affects the dignity of the individual.

"We need to educate, educate, educate at all levels. I have visited several countries in my quest to learn more about dementia and so far I can see we lack far behind in terms of adopting a patient-centred care strategy placing training as the essential link in the chain." Being a lecturer in Neuropathology and Neuropharmacology at the University of Malta certainly helps Dr Scerri push the message home. He can speak to his students of current and future research strategies aimed at investigating factors that play an important role in brain cell loss in dementia and other neurological disorders. He strongly believes that keeping away from stress, adopting a healthy lifestyle coupled with plenty of exercise and keeping one's mind active can help in keeping dementia at bay. With a love for drama, theatre and writing, he keeps his mind active by resorting to script-writing, having been awarded the 2001 Broadcasting Authority Award for Best Radio Drama with 'Zaren'. But even as he speaks of this love for writing and poetry, Dr Scerri's words revert back to the topic in question and his constant urge to get things moving in the right direction. "We are all potential dementia sufferers.... we'd better stand up and take note."

Doing to and being with

MALTA DEMENTIA SOCIETY

Further information on dementia and the Malta Dementia Society may be obtained from www.maltadementiasociety.org.mt or email info@maltadementiasociety.org.mt

On stage

Conditions that may mimic

continued from page 3

Chronic pancreatitis can be associated with a range of anatomic abnormalities of the pancreas, including pancreatic atrophy or enlargement and ductal dilatation.

When enlargement is focal with parenchymal changes due to chronic inflammation, it may be virtually indistinguishable from adenocarcinoma on the basis of morphologic features or enhancement pattern at MR imaging and CT (figure 8). Clinical and imaging follow-up findings usually confirm this diagnosis.

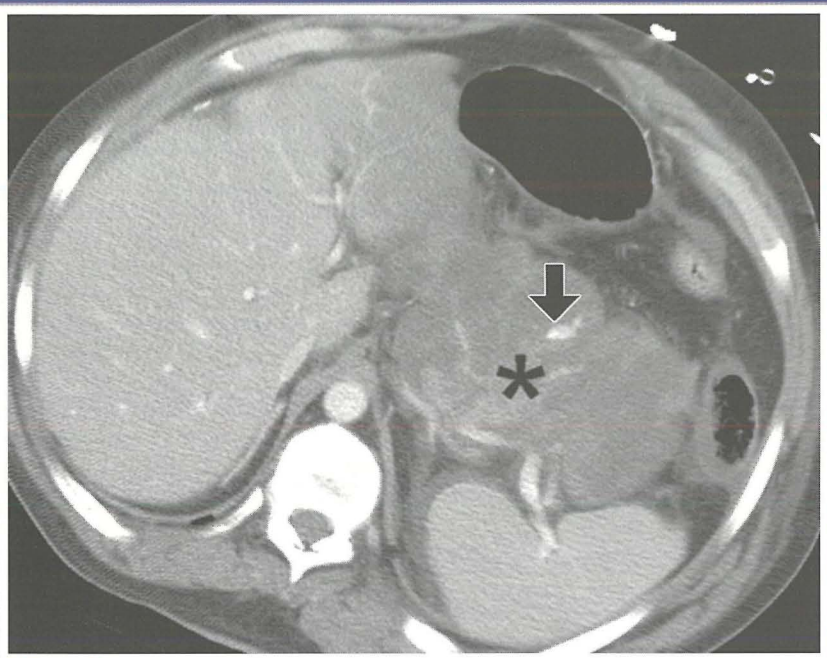

Figure 8. *CT scan demonstrates hemorrhagic pancreatitis as a heterogeneous mass in the area of the pancreatic bed (*) that mimics a pancreatic tumor. Arrow indicates active haemorrhage*

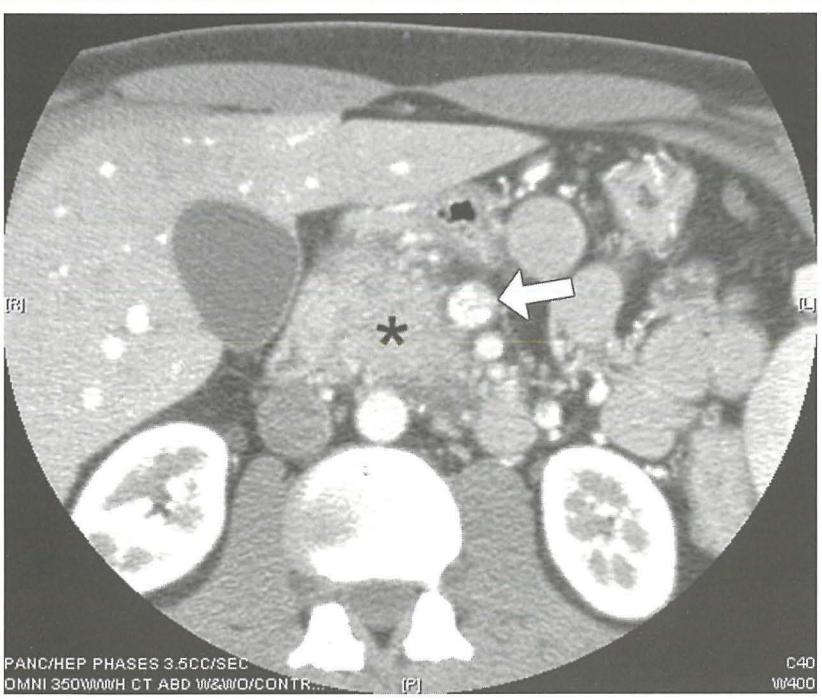

Figure 9. *CT scan demonstrates an enlarged, heterogeneous pancreatic head (*) due to autoimmune pancreatitis (associated with ulcerative colitis) with perivascular inflammation simulating neoplastic vascular involvement (arrow)*

Although autoimmune pancreatitis typically manifests with diffuse pancreatic enlargement, the focal type may manifest as a distinct mass in the pancreatic head (figure 9). In the context of a coexisting autoimmune disease such as primary sclerosing cholangitis or ulcerative colitis, suspecting this diagnosis will help avoid unnecessary surgical intervention.

Certain nodal chains, when involved in neoplastic, inflammatory, or infectious disorders resulting in lymphadenopathy, may mimic lesions of the pancreas. Bulky lymphadenopathy due to lymphoma, usually non-Hodgkin B-cell type (figure 10) or metastatic disease from a variety of primary malignancies such as those occurring the esophagus, stomach, colon, breast, adrenal gland, and kidney may manifest with lymph node involvement, that can mimic a pancreatic carcinoma. Inflammatory disorders associated with lymphadenopathy include granulomatous disorders such as sarcoidosis and angioproliferative disorders such as Castleman disease. Although nonspecific, sarcoidosis may be diagnosed if concomitant lesions are present in the liver or spleen and the typical perihilar and paratracheal adenopathy or parenchymal lung changes are present. Castleman disease may sometimes manifest with variably but intensely enhancing adenopathy. Tuberculosis of the pancreas and peripancreatic lymph nodes, although rare, may also mimic a tumor of the pancreatic head.

Abnormalities such as aberrant vessels or pseudoaneurysms (figure 11) secondary to complicated pancreatitis or vascular surgical anastomoses may mimic a pancreatic mass. Pseudoaneurysms complicate 10% of cases of acute pancreatitis, most commonly affecting the splenic artery. Colour Doppler US will clear demonstrate the extent of such an aneurysm and the presence of thrombus within it. A thrombosed distended portal vein may also mimic a pancreatic neoplasm and is well characterised by Colour Doppler US.

Primary Pancreatic Cancer

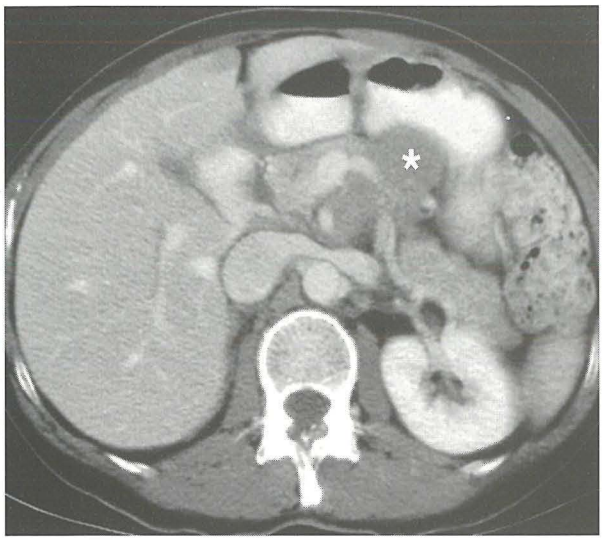

Figure 10. *Intraabdominal lymphoma (*) noted on CT scan simulating a primary pancreatic mass*

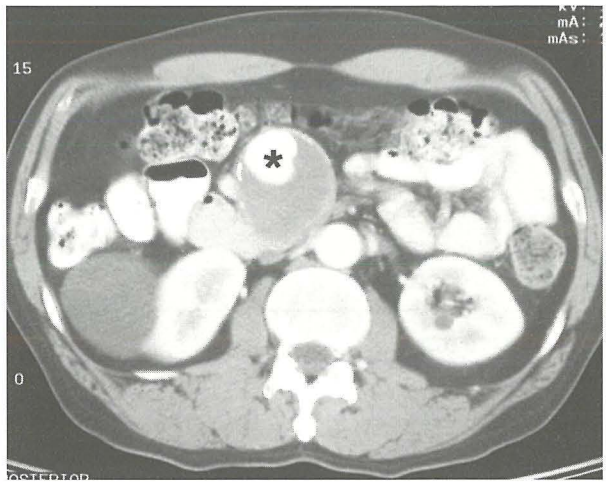

Figure 11. *Contrast-enhanced CT scan shows a superior mesenteric artery aneurysm with an enhancing lumen (*) surrounded by mural thrombus mimicking a primary pancreatic lesion*

Primary retroperitoneal processes such as a hematoma, fibrosis, or neoplasms may mimic a pancreatic mass (figure 12). Some mesenteric processes (eg, retractile mesenteritis) or masses (eg, carcinoid tumors, desmoid tumors, sclerosing mesenteritis) may pose diagnostic difficulty unless a clear plane of separation is identified.

Metastatic lesions to the pancreas are found at 3%–12% of autopsies performed in patients who died of advanced malignancies, and most patients with metastatic pancreatic lesions also had extrapancreatic metastatic disease. Primary tumors that commonly metastasize to the pancreas include those involving the lung, gastrointestinal tract, breast, and kidney, melanoma, lymphoma, and (osteo)sarcoma. The use of US- or CT-guided fine-needle biopsy for the diagnosis of lesions prompts appropriate clinical studies and treatment whilst avoiding open pancreatic biopsy.

Focal pancreatitis may be the result of abnormal sensitivity to certain pharmaceuticals (eg Protease Inhibitors).

We have discussed a variety of anatomic variants and diseases in and around the pancreas that simulate primary pancreatic tumours. Knowledge of these variants and disease entities is important for initiating the appropriate work-up while avoiding unnecessary tests or procedures. Advanced CT and MR imaging techniques and in selected cases US can greatly improve the ability to identify pancreatic malignancies.

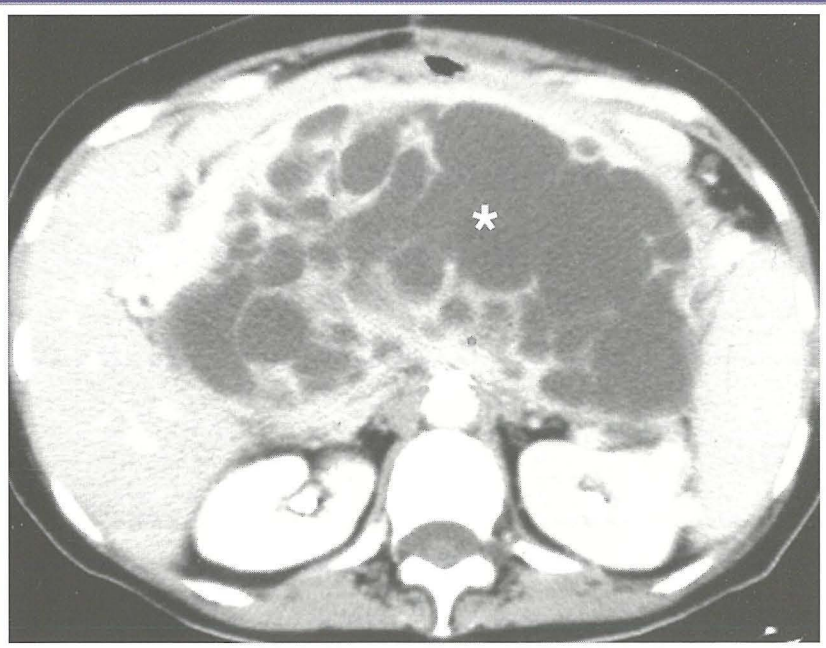

Figure 12. *A retroperitoneal fibrohistiocytoma (*) mimicking a pancreatic mass on CT scan; this was initially diagnosed as a mucinous adenocarcinoma of the pancreas*

[A] The Puestow procedure involves creating a longitudinal incision along the pancreas which opens the main pancreatic duct longitudinally from the head of the organ to its tail followed by anastomosis with a loop of the small intestine (pancreatico-jejunostomy) oversewn to the exposed pancreatic duct to allow drainage.

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The new Death Certificate: Your role as Certifiers

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Improving the quality of death certification

Selection of a single underlying cause of death becomes more difficult in those who are older and have more morbid conditions. Diabetes mellitus presents a particular problem as this can be regarded as both an underlying cause of death giving rise to ischaemic heart disease and other complications, or it can be regarded as a contributing risk factor.

Training remains an important tool in improving the standard of the information written on death certificates.

Training tools available include:
- **Training leaflet**
- **Training manual**
- **Web-based training tool**

These can be accessed from the Department of Health Information and Research website on: http://www.sahha.gov.mt/pages.aspx?page=41

The intended use of this package is to assist certifiers in providing quality information in areas where common mistakes occur, by giving instructions and practical examples on the correct completion of the medical part of death certificates.

Medicine is becoming more and more evidence based. This increases the value of the information being collected, however it also emphasizes the need of more reliable data on which policy makers can base their decisions.

The attending physician is the individual best able to prioritize the medical history to determine, in his or her best judgement, what disease process initiated the sequence of events leading to death.[3]

All information requested on the death certificate form should be written in a clear and legible manner. Abbreviations should not be used. All information regarding the deceased as requested on the death certificate should be completed.

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3. Kircher T, Anderson RE. Proper completion of the death certificate. *Journal of the American Medical Association* 1987; 258:349-52.