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MEDICAL IMAGING

Spiral CT: The Gold Standard for Urinary Tract Stone Detection

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In the past, the standard technique used for detecting urinary tract stones was the Intravenous Urogram (IVU). Limitations of this technique however, including non-radiographically opaque stones (15%), the use of potentially nephrotoxic intravenous contrast material (particularly in diabetics and patients with renal function impairment), and poor visualisation in obese patients and those with abundant intestinal gas, which have resulted in a considerable number of missed urinary tract stones.

Unenhanced spiral computed tomography (CT) has proved to be an accurate, safe and rapid examination used in the diagnosis and treatment of patients presenting with acute flank pain. During the past decade, unenhanced computed tomography has become the standard of reference in the detection of urinary calculi owing to its high sensitivity (>95%) and specificity (>98%) in this setting. Bowel cleansing, which is required prior to standard IVU and is frequently inadequate, is not necessary for unenhanced CT making it more comfortable for the patient and avoiding delays in the diagnostic process.

The spiral CT examination performed for suspected ureterolithiasis is conducted without intravenous or oral administration of contrast material. Because most ureteral stones are small, narrow collimation of 5mm is recommended. Most institutions perform helical CT with a pitch of 1, although there is no documented disadvantage to increasing the table speed. Multiplanar reconstructions are seldom necessary, but they can be used to illustrate stone location or other anatomic relationships.

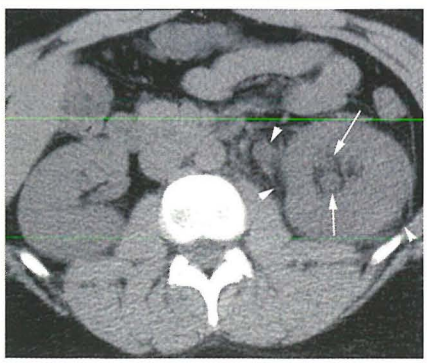

Figure 1. *Axial CT scan shows stranding of the fat surrounding the left kidney and proximal left ureter (arrow heads) In addition, the left kidney is enlarged, with dilatation of the intrarenal collecting system (arrows).*

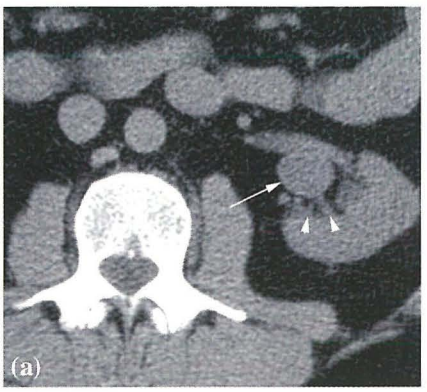

Figure 2(a). *Extrarenal pelvis. Axial CT scan shows apparent dilatation of the left renal pelvis (arrow), however note that the calyces are not dilated (arrow heads).*

Interpretation of the CT scans begins with inspection for secondary signs of urinary tract obstruction. The secondary signs of obstruction described, include asymmetric stranding of the perinephric fat, dilatation of the intrarenal collecting system, hydroureter, and unilateral renal enlargement (Figure 1). An extrarenal pelvis, a normal variant, should not be misinterpreted as a secondary sign of urolithiasis (Figure 2).

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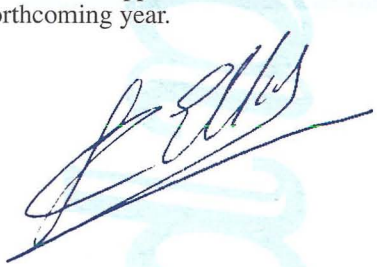
Editor's Word

Locally last year was characterized by a national health reform, spanning from a restructuring within the Ministry of Social Policy to the completion of migration of services to Mater Dei. Internationally we have also seen the onset of the credit crunch and collapsing markets, seriously jeopardizing the introduction of new drugs to our market. The impact on our healthcare system is still to be experienced. Equally 2009 will present its own challenges, possibly presenting more mergers between pharmaceutical giants and further research in personalised medicine and genetic testing with all the ethical implications which these may entail. On our part, the start of the new year has seen a revamped Synapse website, reflecting a considerable investment in IT infrastructure by The Synapse management team. We recognize that obtaining and understanding accurate and complete information is not easy. We also recognize that it is not the unexpected that causes problems. It's what ignored, unavailable or untrue. This is why we pledge our allegiance to all this ... this is why we strive so much to improve our service provision to you.
On a final note, we wish you health and happiness in the forthcoming year.



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Spiral CT: The Gold Standard fo

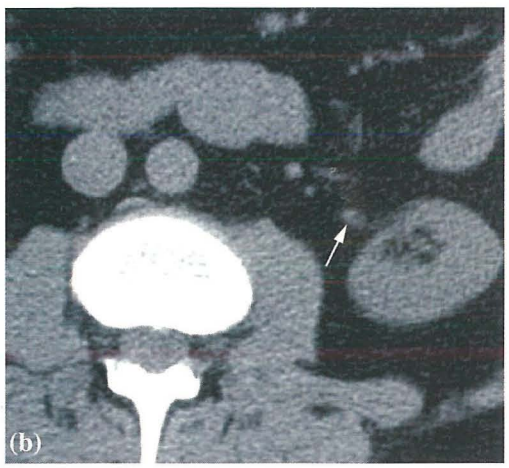

Figure 2(b). *Extrarenal pelvis. Axial CT scan obtained at a slightly lower level shows that the extrarenal pelvis tapers rapidly to a normal proximal ureter that is not dilated (arrow).*

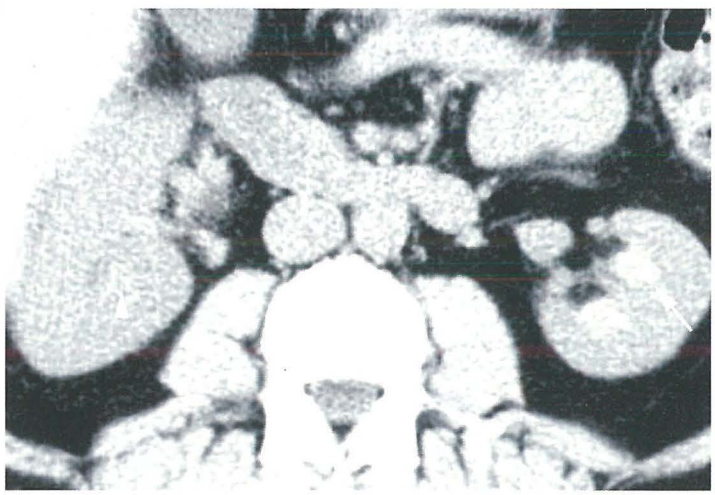

Figure 3. *CT image reveals normal hyperdense pyramids in the left kidney (arrow) and isodense pyramids in the obstructed right kidney (arrow head).*

The extrarenal pelvis is naturally wide and should not be mistaken for secondary widening due to obstruction and increased intrapelvic pressure; important distinguishing CT features include non-dilated calyces and a rapid tapering of the pelvis to a ureter of normal diameter. Unilateral absence of the white pyramid has been described as an additional secondary sign of an obstructing stone (Figure 3).

Further interpretation of CT scans involves following the ureters down to their insertion into the bladder. A thrombosed gonadal vein may occasionally be misinterpreted as an obstructed ureter, however meticulous inspection of each axial image in cine mode will allow the ureter to be followed throughout its course in most cases. Difficulty may be encountered in some cases due to paucity of retroperitoneal fat particularly in the pelvis where the ureter lies between bowel loops and the iliac vessels.

Phleboliths may also cause confusion, however they can generally be clarified by tracing the course of the ureter. The ureterovesical junction is often identified as a high-attenuation, thickened region in the midline of the posterior bladder wall (Figure 4).

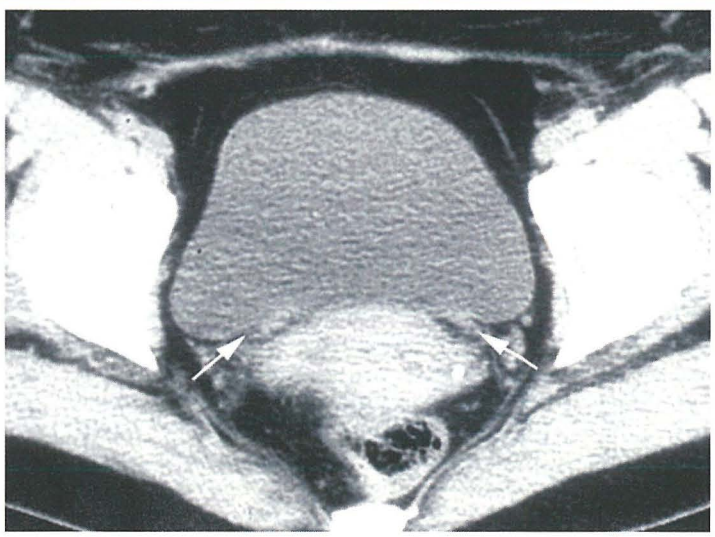

Figure 4. *Normal ureterovesical junctions. Axial CT scan shows bilateral hyperattenuating areas of focal thickening of the posterior bladder wall (arrows), an appearance that represents normal ureterovesical junctions.*

r Urinary Tract Stone Detection

From this region, the distal ureter can be traced back, so that continuity of the calcification with the ureter can be either verified or excluded.

The soft-tissue rim sign can be used when the ureter cannot be confidently identified by any of the above methods (Figure 5); the ureteral wall around a passing stone is inflamed and appears as a thick rim around the stone. Although not all ureteral stones have this sign, approximately 77% of them are surrounded by a rim of soft tissue. Less than 10% of phleboliths have a soft-tissue rim.

Another pitfall may be encountered if a stone lies at the ureterovesical junction, as the tissue surrounding the stone may be so thin as to be imperceptible (Figure 6). This misleading appearance may lead to the conclusion that the stone has passed into the bladder. In such cases, rescanning the patient in the prone position helps one differentiate between passed stones that fall anteriorly and stones within the ureterovesical junction that do not.

Although virtually all stones previously considered radiolucent on plain radiographs, such as uric acid stones, are readily identified on CT scans, the recent use of protease inhibitors to treat HIV has led to an increasing prevalence of urinary tract obstruction caused by deposition of crystals that are nonopaque on CT scans. The presence of secondary signs of obstruction on the symptomatic side in the absence of an identifiable calculus typically prompts a differential diagnosis of a passed stone, pyelonephritis, or obstruction unrelated to stone disease. However, in a patient undergoing therapy with the protease inhibitor indinavir, the same constellation of findings should suggest the diagnosis of indinavir crystal deposition (Figure 7). Because demonstration of indinavir crystals requires gas chromatography, which is not available in most hospital laboratories, intravenous CT urography or retrograde urography should be used as they provide a rapid way to confirm the diagnosis of crystal deposition disease suspected on the basis of CT findings and clinical history.

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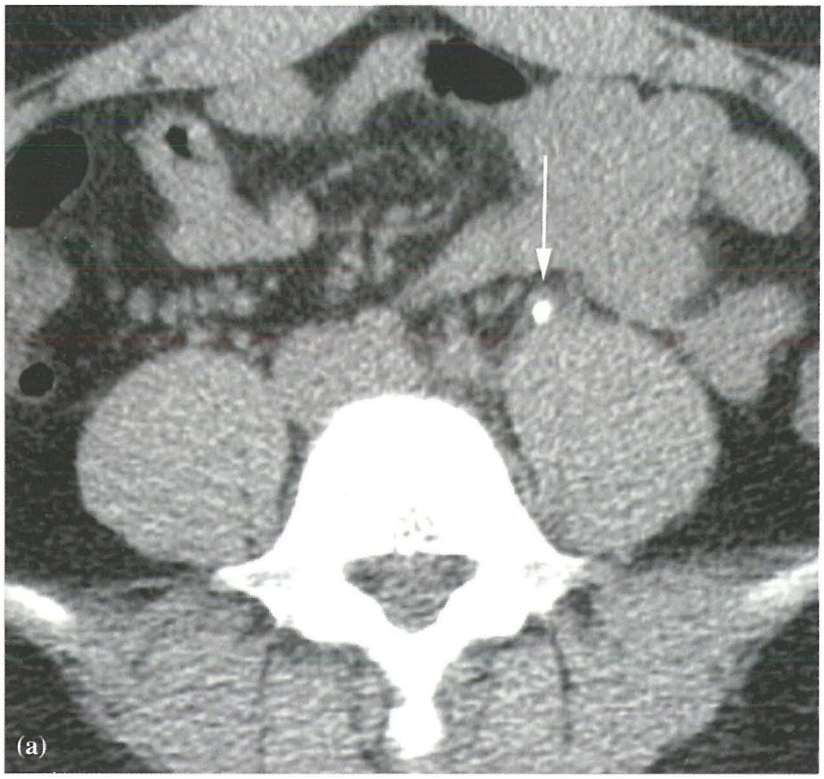
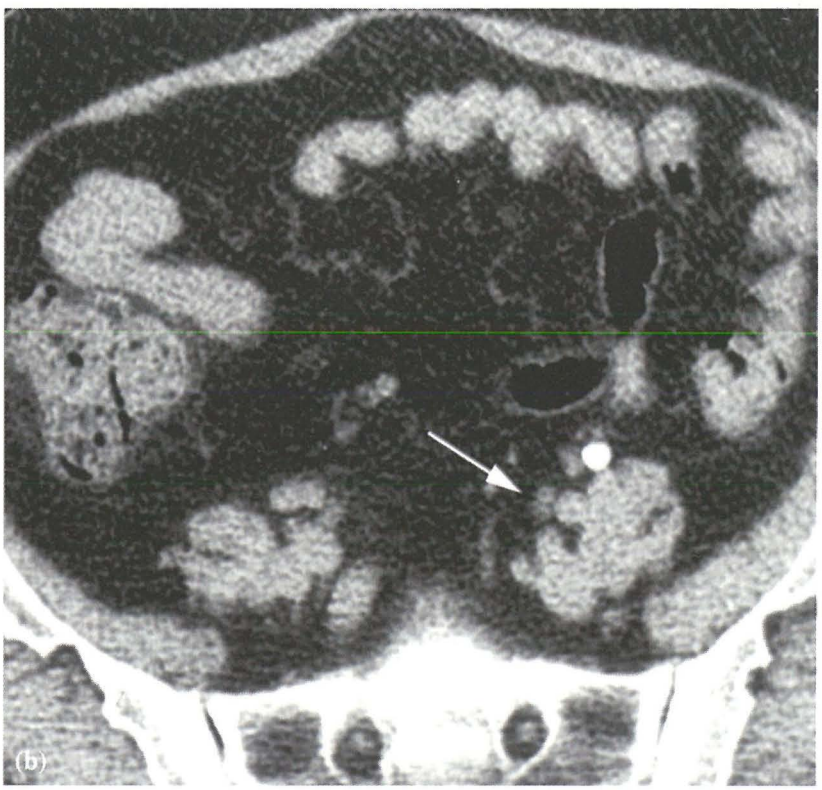


Figure 5. *(a) Axial CT scan shows a rim of soft tissue surrounding a stone in the midportion of the left ureter (arrow). (b) On an axial CT scan of a different patient, no soft tissue is present around a gonadal vein phlebolith. The normal left ureter was followed from above and identified as separate from the calcification (arrow).*



A practical and comprehensive overview of PET/CT – Part III

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Presently, the list of advantages of oncology PET/CT is growing longer as more studies are being published. Although PET/CT seems relatively expensive, it should now be considered a first choice investigation for staging and re-staging of most cancer pathologies, together with complementary imaging and laboratory investigations. The advantages outweigh the apparent 'expense drawback' since the increased sensibility, specificity and accuracy of this methodology over stand-alone CT allows better therapeutic planning and follow-up, and this could substantially reduce overall costs, where and when available[1,2].

Further advantages of current PET/CT Technology

1. Economical aspects: For example Zubeldia *et al*[1] (University at Buffalo, New York) analysed in detail the costs of adding ^{18}FDG-PET to CT preoperatively in colorectal cancer patients with resectable hepatic metastases[1]. CT with and without ^{18}FDG-PET was compared among patients with colorectal cancer in staging for surgical resection of hepatic metastases. Complication rates and costs for CT, ^{18}FDG PET/CT, and surgical procedures were also obtained. The average expected surgical cost per patient when ^{18}FDG-PET was used to determine the presence of extrahepatic disease was US$16,278 compared to $21,547 for conventional management: a net savings of $5,269 which results from the unique ability of ^{18}FDG-PET in excluding patients with extrahepatic disease, and avoiding unnecessary surgical expenses. Another group of researchers supported by the Ontario Ministry of Health and Long Term Care have recently published a similar study for non-small cell lung carcinoma (NSCLC)[2]. In NSCLC, staging with PET/CT better identifies those patients with mediastinal and extrathoracic disease, sparing some from stage-inappropriate surgery. Once again, this strategy has an economic impact by avoiding costs related to unnecessary surgery, besides the costs related to staging abdominal CT and bone scan (an average total of $900 per patient for the latter two investigations), and also impacts on patient safety by avoiding CT-associated radiation exposure and risk of nephrotoxicity (due to contrast medium). PET/CT imaging for the preoperative assessment of potentially resectable NSCLC is now being used widely in Ontario. One must also keep in mind that with one dose and one examination a whole-body scan is acquired, therefore all organs are examined for metastases.

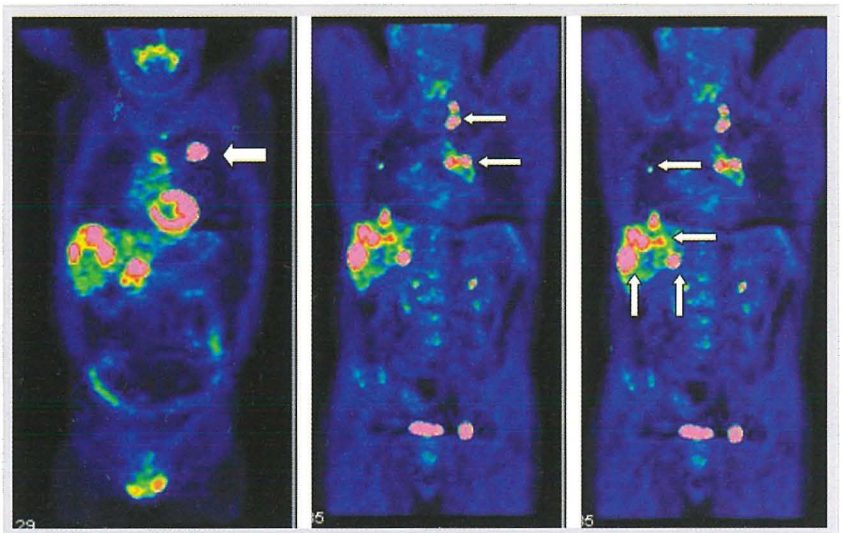

Figure 1. *A single whole-body scan allows comprehensive TNM staging of disease both at diagnosis and during follow-up. In the first image on the left, the primary T is marked by the arrow. Mediastinal Lymph Nodes are marked in the middle image. Liver and lung metastases are shown in the third image on the right. Images courtesy of San Raffaele Hospital, Milan.*

2. Earlier diagnosis and assessment of response to treatment: Another practical example is the early diagnosis of peritoneal carcinomatosis with ^{18}FDG PET/CT which shows superior sensitivities and positive predictive values over stand-alone CT.[3] Already discussed in the previous article is the usefulness of PET/CT in the earlier identification of the cause of rising tumour markers. Assessment of response to therapy has also been extensively discussed previously. Of particular interest is the essential role of PET/CT in lymphomas.

3. Clear characterisation of findings: Other studies demonstrate how high resolution conventional radiological techniques manage to identify unsuspected, clinically silent adrenal lesions (incidentalomas) morphologically, but fail to distinguish benign from malignant. A distinguishing methodology is essential in such cases considering that most incidentalomas are benign adenomas (70-94%) and that adenomas are common in the general population (2-9%). ^{18}FDG PET/CT reaches a specificity and sensitivity close to 100%.[4,5] As already explained in the previous article, PET/CT is very useful in the characterisation of most pulmonary nodules, especially those which are difficult to reach with a biopsy needle. The same concept applies for indeterminate pancreatic, liver or spleen lesions, and residual masses after therapy.

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References:
1. Philipp T. et al. Clin Therapeutics 2007; 29 (4): 563-80
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Psoriasis – New Insights into an Old Disease

by **Christian A Scerri** *MD PhD(Molecular Genetics)*
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With an estimated worldwide incidence of about 2%[1], psoriasis is the most common autoimmune disease in the world with about 80 million affected persons, 20 million of whom being affected in a moderate to severe way. Though psoriasis is common in people of all ages, it appears more frequently in early adulthood.

Environmental factors, immunology and genetics all play an important role in the onset of the disease[2,3]. Due to its chronic nature, physical appearance and high degree of morbidity, the disease can have significant effects on a person's physical and mental health as well as social life. Typically the condition is characterized by the presence of red scaly skin plaques[4]. The histopathological features of psoriasis include growth and dilation of the superficial blood vessels (redness) and hyperplasia of the epidermis (plaques and scales). The epidermic hyperplasia is the result of a rapid proliferation and maturation of keratinocytes resulting in incomplete granular keratinocytes and squamous corneocytes terminal differentiation. Thus, the squamous keratinocytes retain intact nuclei (parakeratosis) and reduce their release of extracellular lipids that normally are responsible for the adherence of the corneocytes. This lack of adherence results in the characteristic scale or flakes of the psoriatic lesions.

An understanding of the pathogenesis of psoriasis requires knowledge of the immunologic processes occurring in the skin. Together with the peripheral lymph nodes and circulating immunocompetent T lymphocytes, a number of immunological actions within the skin layers, effectively render the skin an important lymphoid organ. This collection of antigen-presenting cells (APCs), the epidermotropic T cells, the dermal capillary endothelial cells, cytokine-synthesizing keratinocytes, and the draining lymph nodes form what has become known as skin-associated lymphoid tissue (SALT). In addition, through the effect of different cytokines and chemical mediators, other cells such as mast cells, tissue macrophages, granulocytes, fibroblasts, and dendritic cells, interact with one another.

The cellular physiological picture of psoriasis can be split into the induction phase and the elicitation phase. During the induction phase, APCs in the epidermis process antigens (autoantigens or bacterial antigens) and once in the lymph nodes, present this information to the CD4 helper and CD8 T-cells. An immune reaction occurs with the proliferation and release of both effector and memory T cells (elicitation phase). Through the release of neutrophil, monocyte and keratinocytes chemotactic and activating cytokines, these cells increase the inflammatory reaction in the epidermis.

Drug	Molecular Action	Physiological Action
Methotrexate (most widely used systemic drug)	• competitive inhibitor of the enzyme dihydrofolate reductase - inhibits thymidylate synthesis	• inhibits the replication and function of T and B cells • suppresses the secretion of cytokines • suppresses epidermal cell
Cyclosporin	• binds cyclophilin, (immunosuppressant-binding protein). The complex binds to and inhibits the enzyme, calcineurin, resulting in blockage of signal transduction pathways that are dependent on the transcription factor, NF-AT (nuclear factor of activated T cells)	• inhibition of the cytokines IL-2 and IFN-γ (inhibits T-helper cell activation and proliferation)
Phototherapy (widely used treatment in moderate to severe psoriasis)	• formation of photoadducts with DNA	• direct effect on the proliferation of epidermal keratinocytes • reduces the dendritic (Langerhans) and cytotoxic T cells • reduces cytokine secretion
Mycophenolate mofetil (also used in prevention of organ transplant rejection and in the treatment of rheumatoid arthritis)	• inhibits the enzyme,inosine monophosphate dehyrogenase	• inhibits purine synthesis in lymphocytes and thus reduces lymphocyte proliferation, antibody production, and the formation of adhesion molecules in response to antigenic or mitogenic stimulation
Hydroxyurea (mainly used in haematological malignancies and in sickle cell disease)	• inhibits ribonucleotide diphosphate reductase, the enzyme that converts ribonucleotides to de oxyribonucleotide triphosphates	• depresses basal cell replication in the epidermis • reverses the abnormal keratin proliferation in psoriatic plaques • inhibits vascular proliferation in the dermis • lowers the neutrophil count in the skin with decreased formation of pustules and microabscesses in psoriatic plaques
Thioguanine	• chemical analogue of guanine and adenosine - incorporated into DNA in place of guanine, leading to DNA derangement	• suppresses lymphocyte and keratinocyte proliferation
Liarozole	• inhibitor of the cytochrome P450 pathway	• decreases the number of CD11+ cells • decreases ICAM-1 expression • decreases keratinocyte proliferation
Fumaric acid esters	• induction of preferential apoptosis in activated T cells through NF- B pathway	• inhibits T-cell activity and causes a shift from a Type 1 helper T cell response to a Type 2 helper T cell response
Pimecrolimus	• binds to FKBP-12 protein – inhibits the enzyme, calcineurin resulting in blockage of signal transduction pathways that are dependent on the transcription factor, NF-AT (nuclear factor of activated T cells)	• specific inhibitor of the production of proinflammatory cytokines from T cells and mast cells • reduces proliferation of T cells after antigen-specific or nonspecific stimulation

Figure 1: *Pharmacological action of drugs used in psoriasis*

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Psoriasis – New Insights into an Old Disease

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The trigger for the abnormally increased T-cell infiltration is thought to be either due to a dysregulatory response or due to the continuous activation of the APCs. Bacterial, viral (retrovirus) and keratinocyte proteins (autoreactivity) have been implicated as the causative antigens.

From the genetic point of view, psoriasis is a genetically heterogenous disorder with multiple genes involved as well as complex environmental interactions that can explain the heterogeneity of both the severity and location of the disease manifestation.

Two main genetic loci on chromosomes 6p and 17q have been reported in genome scans. The HLA-Cw6 phenotype has been found to increase the risk of psoriasis by about 10 fold. Similarly to other HLA-linked conditions (eg. Coeliac Disease), though the HLA locus is an important risk factor, the fact that around 10% of the population carry the phenotype and only 2% have the condition, indicates that other genetic/environmental factors are at play. In fact, the PSORS1 locus near the HLA-C has been estimated to account for 30% to 50% of the genetics contribution to psoriasis.

Two regions within chromosome 17q have been associated with psoriasis and being relatively distant from each other, seems to indicate that they have an independent effect on the disorder. The two genes within the first peak are SLC9A3R1 and NAT9 whilst RAPTOR has been identified within the second peak.

SLC9A3R1 is a scaffold protein, linking plasma membrane proteins to the actin cytoskeleton in epithelial cells. External signals can lead to changes in signal transduction and cell growth via this protein. Thus disruption of this scaffold, could prolong the time that the antigen is presented to the T cell receptor, leading to prolonged inflammation. The actual DNA change, seems to be the loss of a RUNX1 site lying between the two genes. This variant is quite common in the population, so the actual associated susceptibility risk is low (this is a running theme with other variants predisposing to complex disease, that is, they are common in the general population and thus require additional susceptibility factors). RUNX1 is a major transcription factor in the development of haematopoietic cells. Though the actual consequence of loss of this particular RUNX1 site is unknown, alterations in RUNX1 sites in other genes predispose to other autoimmune diseases (systemic lupus erythematosus and rheumatoid arthritis).

RAPTOR is a binding and regulatory factor of mTOR, a major regulator of T cell function and growth, through the cytokine-triggered protein kinase cascade that leads to the phosphorylation of the eukaryotic initiation factor, PHAS-1, in activated T lymphocytes. Rapamycin binds to and blocks the function of mTOR, leading to immunosuppression.

Other susceptibility loci for psoriasis reside on chromosomes 1q21, 3q21, 4q, 7p, 8, 11, 16q and 20p. A recent study has identified over 1300 altered gene expression within lesional skin when compared to uninvolved skin.[5]

Similar to other disease, the study of the genetic pattern in psoriasis can lead to the identification of novel pathophsyiological biochemical pathways and thus help to identify targets for novel therapeutics. In addition, a deeper understanding of the genetic background can also assist in disease prediction, prognosis, as well as in the pharmacogenomics of psoriasis. The latter could even lead to the creation of personalised therapies.

Drug	Group	Type	Structure	Action
Infliximab	3	MA	Anti-TNF-α	Neutralizes serum and membrane bound TNF-α
Etanercept	3	FP	Human IgG1 Fc + TNF-α receptor	Combines with TNF-α in serum (acts as receptor)
Efalizumab	2	MA	Human IgG + murine variable against CD11a subunit of LFA-1	Blocks interaction of LFA-1 with ICAM-1
Alefacept	1	FP	IgG Fc + LFA-3	Blocks T-cell activation by interfering with CD2/LFA-3 interaction

Figure 2: *Currently approved biologics for psoriasis (MA: Monoclonal Antibody; FP: Fusion Protein).*

Treatment aspects

As a chronic disease with exacerbations, remissions, and recurring lesions, the treatment options for Psoriasis depend on the extent and severity of the disease, safety aspects of systemic agents, economic issues, accessibility to phototherapy treatment centres and quality-of-life issues. Various treatments are available and are used either alone or in combination. The therapeutic mechanism of most traditional drugs can be explained through their action on T-cell function.

The Biologics

Biologic or 'Biologic response modifiers' is the generic term for a group of hormonal, neuroactive and immunoreactive compounds that act at the cellular level. Whilst derived from living material (human or non-human), they are produced through recombinant DNA techniques and possess pharmacological activity. Biologics include monoclonal antibodies, fusion proteins, cytokines, lymphokines, and other antiproliferative agents.

The biologics currently approved for psoriasis (Figure 2) are either fusion proteins or monoclonal antibodies and can be divided into three main groups based upon their modes of action:

- Group 1: Reduce the number of pathogenic T cells
- Group 2: Inhibit T-cell activation and migration
- Group 3: Block the activity of inflammatory cytokines

The Future

Psoriasis is a disorder of chronic T-cell stimulation with a genetic predisposition in which environmental triggers play a major role. With a greater knowledge of the molecular pathways responsible for both general as well as cutaneous immunology, new, highly specific, immune-targeting biologic modifiers can be developed. These would ideally have an excellent long term safety profile as well as being an effective treatment to ease most if not all problems associated with the disease.

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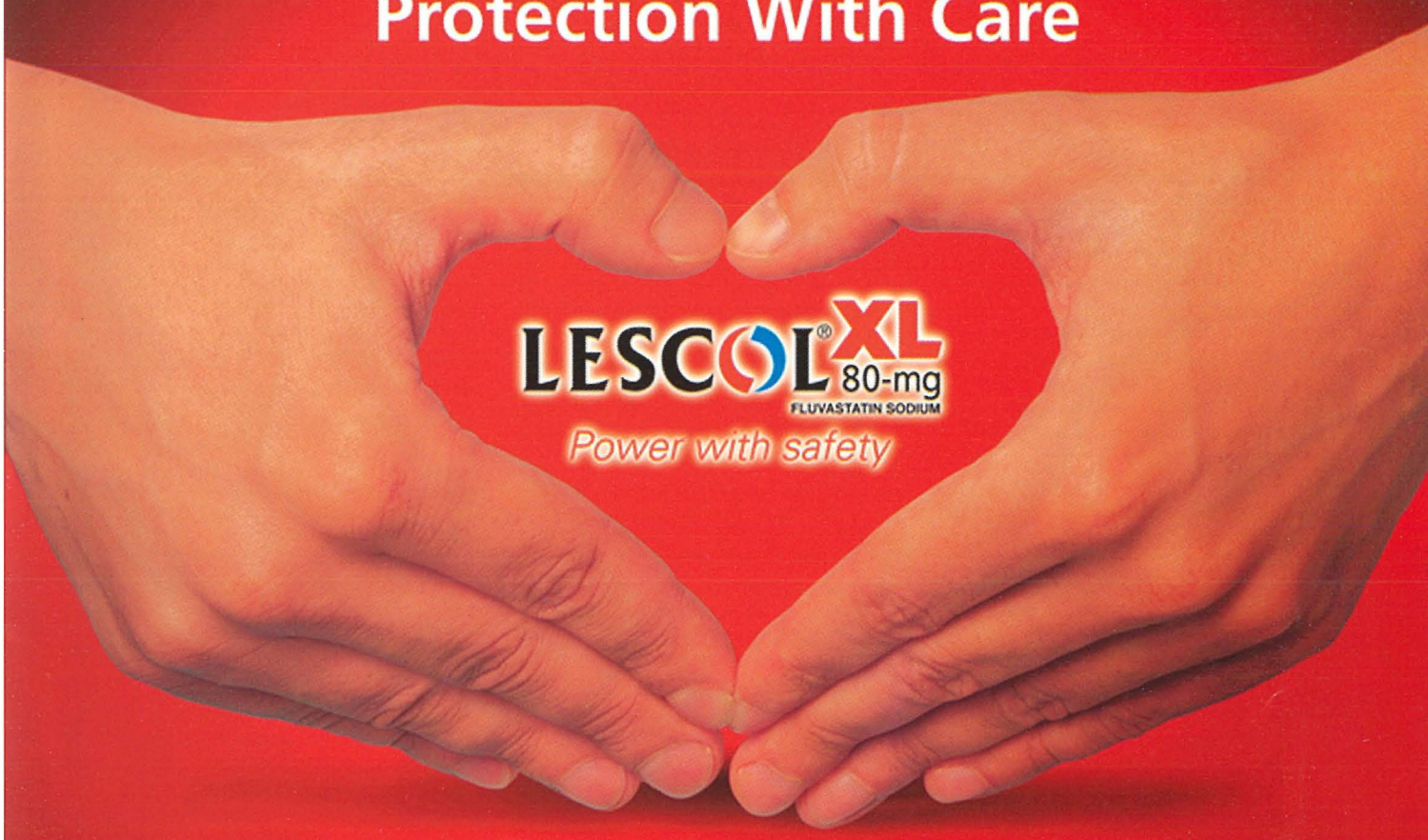
Protection With Care



- Lescol® XL provides effective lipid management in a wide range of high cardiovascular risk patients[1]
- Lescol® XL is one of the safest statins, especially in patients receiving multiple medications[1]

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

LESCOL®/LESCOL® XL

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

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Professor Basant K. Puri's Medical School Talk on Fatty Acids & Health – Part I

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

Basant Puri is a consultant psychiatrist holding a Personal Chair in the MRI Unit of the Medical Research Council's Clinical Sciences Centre at the Hammersmith Hospital, and is also Head of the Lipid Neuroscience Group at Imperial College, London.

Basant Puri was invited by our University departments of Family Medicine and of Psychiatry, and was duly introduced by Drs Philip Sciortino and David Cassar. Although his talk on 11th December was expected to focus on fatty acid research in depression, chronic fatigue syndrome/Myalgic Encephalomyelitis and attention deficit and hyperactivity disorder, he tackled a whole gamut of serious chronic diseases which might be ameliorated by dietary fatty acids and, in particular, by the omega-3 polyunsaturated fatty acid eicoapentaenoic acid (EPA).

He started off on cardiac health by going back to the Eskimo studies of the Oxford biochemist Dr Hugh Sinclair in 1944 and those of the Danish scientists Drs Hans Bang and Jorn Dyerberg in 1976. Sinclair had first noted a possible association between eating plenty of fish and virtually no heart attacks, psoriasis, asthma, diabetes, immune disorders, gallstones, diverticular disease or ulcerative colitis in Eskimos, although they did suffer from some cancers, peptic ulcers and cerebral haemorrhage. The reason for this different disease pattern from Westerners was not genetic, because Eskimos who had emigrated from Greenland to Canada, and adopted a Western lifestyle, suffered heart attacks and other Western disease patterns within a time span of a single generation.

Bang, Dyerberg and Sinclair found that Eskimos' bleeding time was about twice that of Europeans and, although they had similar average total cholesterol levels, Eskimos had higher high-density lipoprotein cholesterol (HDL-C) and far lower blood triglycerides. The blood lipid differences were not fully understood at the time, but the longer bleeding time due to diminished platelet aggregation in Eskimos was clear enough. In 1979 Sinclair put himself and other volunteers at Oxford on a 3-month fish and seafood-only diet. He found that although their total blood cholesterol was slightly higher, their HDL-C had risen, their triglycerides had fallen sharply, and their bleeding time had roughly doubled. This Eskimo pattern of blood findings was therefore not genetically determined, but was diet-related. Something in fish diminished platelet aggregation and was probably responsible, via this mechanism, for the rarity of coronary thrombosis in Eskimos.

"Good" Eicosanoids	"Bad" Eicosanoids
Prevent blood clots caused by platelet aggregation	Promote blood clots caused by platelet aggregation
Cause vasodilatation	Cause vasoconstriction
Reduce pain	Promote pain
Decrease cell division	Promote cell division
Enhance the immune system	Depress the immune system
Improve brain function	Depress brain function

Figure 1

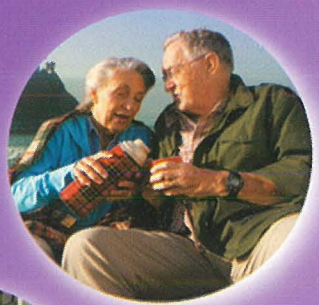
In 1982 the Nobel Price for Medicine went to John Vane, Sune Bergstrom and Bengt Samuelsson for their work on eicosanoids and elucidation of how the 20th century wonder drug, acetylsalicylic acid (aspirin), worked. Eicosanoids are a large family of fast-acting, very short-lived autocrine hormones acting locally in all cell membranes, and not at distant sites via blood transport. They include *prostaglandins, thromboxanes, leukotrienes and lipoxins*. Although they control every physiological function, they are almost undetectable within blood and have largely remained mysterious to most members of the medical and pharmaceutical professions. Different eicosanoids have diametrically opposite physiological actions, and biological equilibrium is maintained by a balance of these opposing actions. For simplicity, eicosanoids can therefore be broadly divided into 'good' and 'bad' according to the physiological changes they encourage (Figure 1).

The author has included an eicosanoid pathophysiology outline to enhance understanding of Basant Puri's delivery on the omega-6 essential fatty acids metabolism cascade (Figure 2). The metabolism of arachidonic acid is controlled by the cyclo-oxygenase enzymes COX-1 and COX-2. Aspirin and other NSAIDs inhibit both COX-1 and COX-2. Aspirin's analgesic, anti-inflammatory, anti-thrombotic and tumour-inhibiting actions are delivered via this mechanism. When pharmaceutical companies thought they had developed drugs that selectively inhibited COX-2 for anti-inflammatory action only, they did not realise that some of these new drugs might eventually cause thrombotic complications due to encouragement of platelet-aggregating eicosanoids. The complicated biochemistry of eicosanoids is still poorly understood.

The omega-3 fatty acid EPA is thought to exert its various claimed beneficial functions, including anti-thrombotic and ant-inflammatory actions, by inhibiting the arachidonic acid pathway (Figure 2), thus encouraging the 'good eicosanoids'. Its anti-thrombotic action probably explains the Eskimo and Japanese cardiovascular disease patterns. Japanese ischaemic heart disease prevalence is low compared to Western countries, and Japan maintains the world's highest longevity figures. This is claimed to be largely due to their mainly vegetarian and fish diet with little or no animal-origin foods.

continues on page 14

THE *FIRST AND ONLY* PATCH THERAPY FOR MILD TO MODERATE ALZHEIMER'S DISEASE



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Exelon 4.6 mg/24h Transdermal patch
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Presentation: Exelon Patch 4.6 mg/24h contains 9 mg rivastigmine. The release rate is 4.6 mg/24h. Exelon Patch 9.5 mg/24h contains 18 mg rivastigmine. The release rate is 9.5mg /24h. Indication: Symptomatic treatment of mild to moderately severe Alzheimer's dementia. **Dosage and Administration:** Treatment should be initiated and supervised by a physician experienced in the diagnosis and treatment of Alzheimer's dementia. A caregiver should be available to regularly administer and monitor the treatment. Initiation and re-initiation of therapy should start with one Exelon Patch 4.6 mg/24h. It may be increased after a minimum of 4 weeks to one Exelon Patch 9.5 mg/24h each day. Patients treated by Exelon capsules or oral suspension with a maintenance dose of 3 mg /day or 6 mg/day may be switched to Exelon Patch 4.6 mg/24h . Patients on a dose of 9 mg/day or higher may be switched to 9.5 mg/24h transdermal patch. A minimum of 4 weeks of treatment and good tolerability with the previous dose should be observed before titrating up to higher doses. Transdermal patches should be applied once a day to clean, dry, hairless, intact healthy skin on the upper or lower back, upper arm or chest, in a place which will not be rubbed by tight clothing. It is not recommended to apply the transdermal patch to the thigh or to the abdomen. The transdermal patch should not be applied to skin that is red, irritated or cut. Reapplication to the exact same skin location within 14 days should be avoided. The transdermal patch should be pressed down firmly until the edges stick well. It can be used in everyday situations, including bathing and during hot weather. No dose adjustment is necessary for patients with renal impairment. **Contraindications:** Known hypersensitivity to rivastigmine, other carbamate derivatives, or other excipients used in the formulation. **Precautions/Warnings:** If treatment is interrupted for longer than several days, treatment should be re-initiated with Exelon 4.6 mg/24h. Gastrointestinal adverse effects such as nausea and vomiting can occur at initiation of therapy and shortly after dose increase. Patient's weight should be monitored during therapy with Exelon Patch as they may lose weight. As with other cholinomimetics, caution is recommended in patients with sick sinus syndrome or conduction defects (sino-atrial block, atrio-ventricular block), with gastroduodenal ulcerative conditions or patients predisposed to these conditions, with a history of asthma or pulmonary disease, patients predisposed to urinary obstruction and seizures. Caution in patients with clinically significant hepatic impairment and in patients with body weight below 50 kg. The safety of Exelon Patch is not established in pregnant and lactating women. Not recommended in children. Contact with the eyes should be avoided after handling Exelon transdermal patches. **Interactions:** Caution in case of concomitant use with cholinomimetic drugs, anticholinergic medications, succinylcholine-type muscle relaxants during anaesthesia. **Adverse reactions:** Common: vomiting, nausea, anorexia, urinary tract infection, decreased appetite, anxiety, depression, insomnia, delirium, syncope, rash, headache, diarrhoea, dyspepsia, abdominal pain, fatigue, asthenia, weight decrease, pyrexia, application site reactions i.e. erythema, pruritus, irritation, oedema, dermatitis. Uncommon: Bradycardia, gastric ulcers, extrapyramidal symptoms. **Pack sizes:** Cartons containing 30 sachets and each sachet contains one transdermal patch. **Legal category:** POM. **Marketing Authorisation Numbers:** EU/1/98/066/019-022, EU/1/98/066/023-026. MARKETING AUTHORISATION HOLDER: Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. Consult full Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available upon request from: Novartis Pharma, P.O. Box 124, Valletta CMR 01, Malta. Tel +356 22983217.

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A Brand New Look for The Synapse

The Synapse is changing again and it's got a great new look and feel to it that should make it more user-friendly than ever before. As from January 1, 2009 in fact, The Synapse has intensified its determination to be the perfect one-stop entry point for medical professionals, providing a variety of new services to complement its existing ones.

Launched on October 18, 1996, Dr Wilfred Galea's brainchild has developed steadily over the years, constantly incorporating new features that refine not merely its appearance as a portal, but also its efficiency.

Several new features have been introduced and can be accessed simply by clicking on *www.thesynapse.net* and joining up. In The Synapse portal one can find:

- **Events Diary** – this diary provides an information service about conferences and medical-related events in Malta. Dr Galea expands on this, "The idea is to offer an opportunity to organizing bodies by which they can easily and effectively inform the people that count. We offer free listings on The Synapse and the listing is shown for one month after the actual event takes place. We added on another adjacent service which should surely come in handy for busy professionals. An *I-attended* button is available on the Events Diary page. By clicking on this, The Synapse members can access their personal profile which they can routinely update to keep records of events attended and thus keep their accreditation status constantly on track. This should surely go some way towards helping doctors keep track of the events they attend during the year, making it simpler for them to eventually notch up their final credit status at the end of it."

- **E-library** – this is an archive of articles published in The Synapse magazine.

- **Videos** – a selection of medical-related video clips.

- **Medical images** – a series of case-related observational tools in the form of images that can help medical professionals distinguish ailments.

- **Case-studies in radiology** – case-related observational tools in the form of images related to radiology (currently under construction).

- **Poll** – this is a bi-weekly poll asking members for their opinion on specific topics. A great tool for anybody interested in starting a new area of research or complementing an already existing line of research.

These are in addition to the already existing features:

- **News from the medical world** – a round-up of all the medical news received by The Synapse in its capacity as a news service provider. The five-strong IT team behind The Synapse portal is constantly filtering information and selecting the most relevant information for medics on Malta.

- **The Synapse Direct** – instead of waiting for test results for days or having to collect them from

laboratories, this allows doctors to securely download results from their clinic, directly onto one's practice record system. The Synapse Direct also offers a safe, simple and secure method of on line notification of vaccinations and notifiable infectious diseases.

- **Corporate news on new products by medical companies & financial news**

- **Network announcements** – including exhibitions & leisure events organized by fellow colleagues, campaigns, etc.

- **Job opportunities**

Presently The Synapse network boasts more than 3,000 members including local and foreign healthcare professionals. And as always, this medical media company is already eyeing its plans in the pipeline. "We plan to add on to the already well-established range of services. We are constantly encouraged by the regular use of The Synapse website, which together with positive feedback is particularly rewarding for us. As always, we stick to our motto – If it's relevant, it's on The Synapse. I believe the portal's success so far means we're probably doing things right."

If you are experiencing technical problems to view or access certain features on *www.thesynapse.net*. Kindly contact us on *editor@thesynapse.net* or 21453973 and we will be glad to assist you.

'GRAPE EXPECTATIONS'

Continuing our Introduction to Wine Enjoyment

Albert Cilia-Vincenti

The previous introductory article laid down some basic rules on how to approach wine to understand and enjoy it, and why one needs to learn how to taste. We shall continue expanding on this theme. I shall keep emphasizing that you should be guided by two basic questions: how much do I like what's in the glass? – how do I know how much I like it? The answer to these questions should not be that you have seen the label and know the price. You learn how to taste so that you can appreciate the wine's aromatic and flavour characteristics even before you've looked at its label.

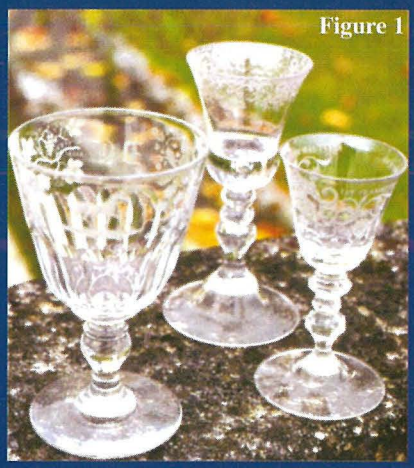

Figure 1

The right glasses are important because they definitely enhance your wine enjoyment. Funnel-shaped glasses, however beautiful and valuable they might be, such as those in figure 1 (which belong to Comtesse de Lalande of ChĞeau Pichon-Longueville in Bordeaux), do not transmit the wine's aromas to your nose as efficiently as the more modern tulip-shaped clear glasses, such as the ones in figure 2. The glass rim should be thin enough for close sensual contact between wine and lip, and its bowl should be big enough to hold a proper ration without being filled to the brim. The glass should, in fact, not be filled more than a third to half full, so that you can swirl the wine in the glass to wet all the inside of the glass, thus increasing evaporation and aromatic pick-up by your olfactory senses.

One frequently forgotten precaution is to make sure the glass is clean. Foul smells from cupboards or dirty dish-cloths linger on the glass surfaces and can ruin your enjoyment of a quality wine, because the first thing you smell is not the wine's bouquet but that unpleasant smell. Each time a wine glass comes out of a cupboard, it should be rinsed under a hot water tap and dried with a clean dish-cloth. If you think this is ridiculously obsessional, I can assure you that I have been treated to this annoying ruining of wine several times. On these occasions I wonder why the hosts haven't noticed the foul smell in the glass – the reason is they don't smell wine – they drink it like water without knowing that wine tasting starts with lingering on the wine's bouquet – betraying an indifference and ignorance of wine irrespective of their culinary education.

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Figure 2

Professor Basant K. Puri's Medical School Talk on Fatty Acids & Health – Part I

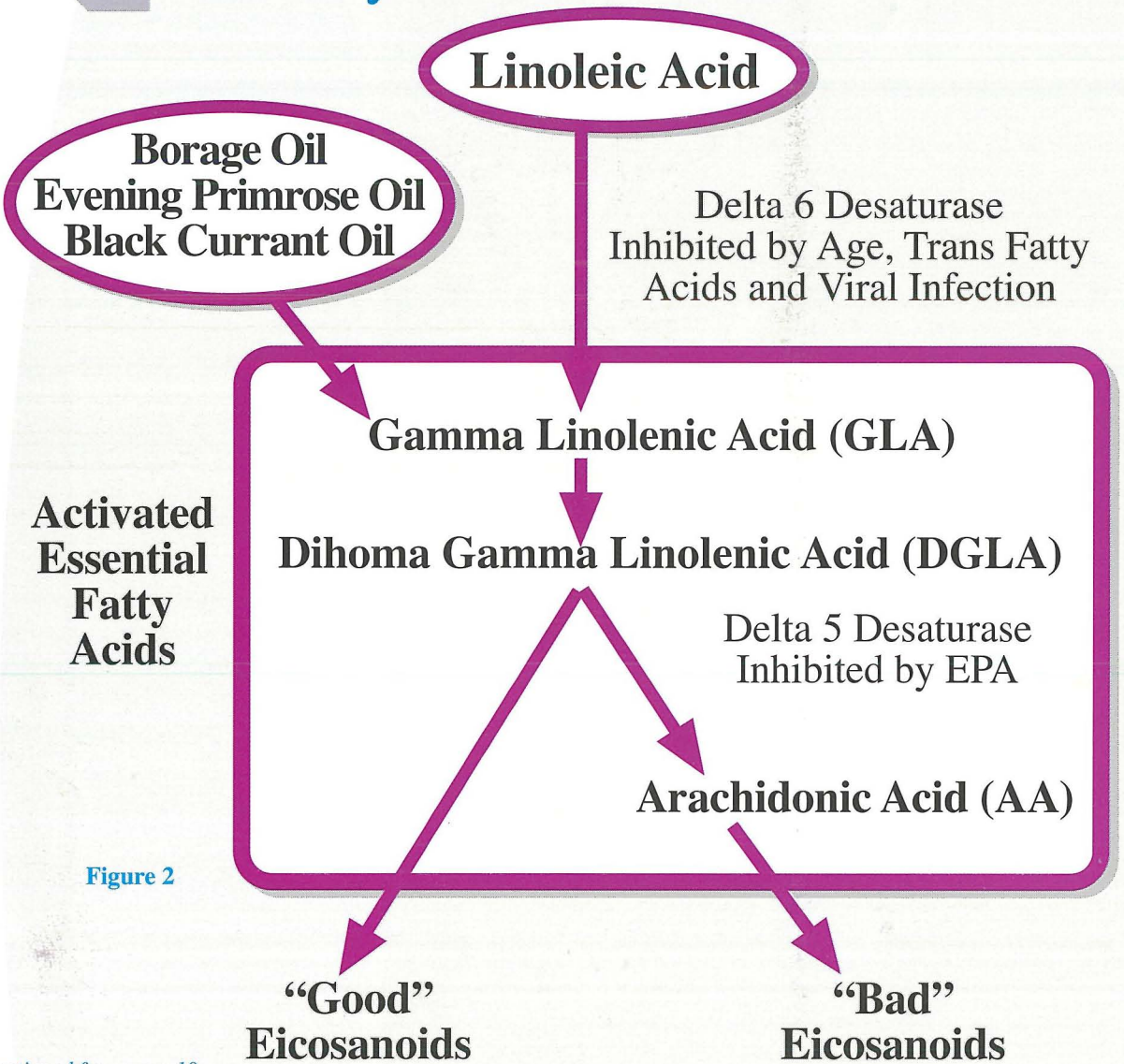

Figure 2

continued from page 10

Furthermore, a recently published Japan EPA lipid intervention study (JELIS) demonstrates that addition of EPA to statins has beneficial effects on lipid profiles of patients with mixed type hypercholesterolaemia and reduces further their major coronary events.[1] Purified EPA is already approved by Japan's Ministry of Health, Labour and Welfare as a treatment for hyperlipidaemia and peripheral artery disease.

The JELIS study also focused on risk factors for coronary disease other than low-density lipoprotein cholesterol (LDL-C).[2] In the higher risk group with high triglyceride and low HDL C, commonly seen in the metabolic syndrome, pure EPA suppressed the risk of coronary artery disease by 53%, suggesting that EPA is particularly beneficial in this group of patients.

Furthermore, *The Lancet* comment on a recently published Italian study3 states, "supplementation with omega-3 fatty acids should join the short list of evidence-based life-prolonging therapies for heart failure".

A further article on the part of Basant Puri's talk dealing with EPA and brain function will appear in the next issue.

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Prof Cilia-Vincenti is a former London University Recognised Teacher at Charing Cross and The Middlesex Hospital Medical Schools, and a former teacher at Malta's University Medical School. He maintains a longstanding interest in nutrition, health and longevity.

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Update on Avian Influenza

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

Five years have passed since the avian influenza strain H5N1 started killing poultry and humans in Southeast Asia, but still researchers know little about how influenza viruses emerge and spread from one species to another.

2008 has seen the least number of human avian cases since 2003. During December there were two cases in Indonesia, one in Egypt and one in Cambodia. Total human avian cases in 2008 were 42 with 31 deaths. Cases occurred in Indonesia, Vietnam, China, Cambodia, Bangladesh and Egypt. Re-emergence of Avian influenza outbreaks amongst poultry in December occurred in India, Hong Kong, Cambodia and Egypt.

There are 100 strains of avian influenza but only 4 types H5N1, H7N3, H7N7 and H9N2 are known to cause human infections. Hong Kong had a human case infected with H9N2 in December. To date it has recorded 4 human cases with this virus. H9N2 possesses the same threat to humanity as H5N1.

Seasonal Influenza

There is concern presently that this influenza season might be more severe than in previous years and in fact may result in an influenza epidemic. Over the Christmas period, a number of Western and Southern European countries like Portugal, Spain, England, Ireland and Bulgaria have seen above-threshold levels of Influenza-like illnesses. It is expected that influenza will continue to spread in central, eastern and northern European countries. A substantial increased rate of acute bronchitis has been noted especially in the over-65 age groups. It is being recommended to vaccinate health care workers, elderly patients and those suffering from chronic diseases who have not as yet taken the seasonal vaccine.

Most of the viruses identified so far are influenza A (H3N1). This subtype was associated with moderately severe epidemics last season (2007/8) in Northern America and in parts of the Southern Hemisphere Winter. According to European Centre for Disease Prevention and Control experts, the influenza A (H3N1) virus variant represented by the A/Brisbane/10 /2007 is a drift variant virus to which most of Europe has not previously been exposed to.

So far specimens obtained from Influenza A H3 subtype were found to be sensitive to both oseltamivir and zanamivir but resistant to amantadine while almost all Influenza A H1 specimens were found to be resistant to oseltamivir but sensitive to zanamivir and amantadine.

Based on the antigenic and genetic characterisation data available so far, the WHO collaborating Centre in Europe considers that 98% of the viruses tested, match the recommended strains in the current influenza vaccine and so immunised subjects would have good protection against the circulating influenza viruses.

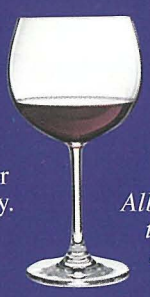
'GRAPE EXPECTATIONS'

Continuing our Introduction to Wine Enjoyment

Albert Cilia-Vincenti

continues on page 13

One particular Austrian manufacturer of very high quality (and price) modern wine glasses claims the precise shape of the bowl and rim has a significant effect on your tasting perception. This is true, and the right shape of glass for red Bordeaux should be different from that for red Burgundy, and the glass for Riesling should be different from that for Chardonnay. However, it is difficult to accept these glass manufacturers' claims that the glasses for Syrah and



Sangiovese should be different, which sound very much like marketing ploys to drain your pocket. A range of glasses similar to those in figure 2 is more than enough.

Albert Cilia-Vincenti is a long-standing member of the UK's Wine Society (1874), and founding committee member of Il-Qatra Wine Club (1999).

Effective relief from cold and flu symptoms.

Panadol Cold & Flu is highly effective on...

Runny Nose • Blocked Nose • Sneezing
Headache • Itchy Eyes • Fever

Dosage - Adults and children of 12 years and over:
Two caplets up to four times a day

Panadol Cold & Flu Caplets Product Information

Description:
Each tablet contains: Paracetamol 500mg
Pseudoephedrine Hydrochloride 30mg
Chlorpheniramine Maleate 2mg

Pharmacology:
Paracetamol is clinically proven analgesic and antipyretic. Pseudoephedrine is a sympathomimetic agent, for symptomatic relief from nasal congestion. Chlorpheniramine maleate is an antihistamine.

Indications:
PANADOL Cold & Flu caplets are indicated for the relief of symptoms of the common cold and influenza such as: fever, nasal congestion, sinus congestion, headache and sinus pain, sneezing, itchy and watery eyes.

Dosage and administration:
PANADOL Cold & Flu caplets are suitable for adults and children of 12 years of age and over.
Adults and children of 12 years and over: two caplets up to four times a day. If necessary the dose may be repeated every four to six hours but do not take more than four doses (8 caplets) in 24 hours.

Contraindications:
PANADOL Cold & Flu caplets are contra-indicated in patients with known hypersensitivity to paracetamol, pseudoephedrine hydrochloride or chlorpheniramine maleate or related compounds. Not to be used by patients taking monoamine oxidase inhibitor antidepressants or within two weeks of stopping such treatment.

Precautions:
Keep out of reach of children.
This preparation contains paracetamol. Do not exceed the stated dose.
Do not take other paracetamol, containing medications, nasal decongestants, or antihistamines at the same time as PANADOL Cold & Flu caplets.
PANADOL Cold & Flu caplets should be administered with caution to patients with hepatic or renal dysfunction, severe hypertension, cardiac or peripheral vascular disease, hyperthyroidism or on antihypersensitive or antidepressant therapy. Pseudoephedrine should be given with care to patients with diabetes mellitus, closed-angle glaucoma, or prostrate enlargement. Anginal pain may be precipitated in angina pectoris. Antihistamines should be used with caution in conditions such as epilepsy, prostatic enlargement, urinaryretention, glaucoma, severe cardiovascular disorders or pyloroduodenal obstruction.
Do not take this product for more than 10 days or for fever more than 3 days unless directed by a doctor. If pain persists or gets worse, if new symptoms occur, or if redness and swelling is present consult a doctor because these could be signs of serious condition. If nervousness, dizziness or insomnia occur, if a sore throat is severe and persists for more than two days and is accompanied by fever, headache, rash, nausea or vomiting, consult a doctor promptly.
Use in Pregnancy and Lactation:
Although there are no known risks associated with the use of these active ingredients during pregnancy, as with all medicines, medical advice should be sought before using this product. PANADOL Cold & Flu should not be used during breast feeding as there may be risks associated with the use of antihistamines in infants.

Use in Children:
Do not give to children below 12 of age.

Driving and Operating Machinery:
Since PANADOL Cold & Flu caplets contain an antihistamine, sedation may occur impairing the ability to drive or operate machinery.

Side Effects:
Paracetamol: When taken in recommended doses, paracetamol is usually free from side effects. However skin reactions such as urticaria have been reported rarely.
Pseudoephedrine: May occasionally cause anxiety, tremor, dizziness, cardiovascular effects including tachycardia and hypertension, insomnia reported rarely.
Chlorpheniramine: The antihistamine may cause sedation, gastrointestinal disturbances and antimuscarinic effects.

Drug Interactions:
Paracetamol: PANADOL Cold & Flu caplets may interact with anticoagulant agents on prothrombin time. The liver effects of PANADOL Cold & Flu caplets may be increased by the use of alcohol and the concomitant use of certain drugs which enhance the metabolism of paracetamol in the liver (i.e. barbiturates, tricyclic antidepressants).
Co-administration of pseudoephedrine and MAOI's may lead to hypertensive crisis. The effect may persist for up to 2 weeks after discontinuation of MAOI's.
Enhanced sedative effects of chlorpheniramine can occur with simultaneous administration of alcohol, anxiolytics and hypnotics. Tricyclic antidepressants and antimuscarinic can increase antimuscarinic side effects.

Overdosage:
In massive paracetamol over dosage, Panadol Cold & Flu caplets may cause liver damage. Early symptoms may include pallor, nausea, vomiting, (diaphoresis) and general malaise.
Clinical and laboratory evidence of liver damage may not be apparent for 48 hours to 72 hours post-ingestion. Overdose should be promptly treated by gastric lavage followed by intravenous N-acetylcysteine or methionine without waiting for the results of plasma paracetamol levels.
Additional antidote therapy is normally considered in light of further plasma paracetamol levels and the time elapsed since ingestion. In all cases of suspected overdose, prompt medical attention is critical for adults as well as for children, even if you do not notice any signs or symptoms.
Pseudoephedrine overdose is likely to result in effects similar to those listed as adverse effects, and may also produce excess sympathetic stimulation. 7-8 caplets have been shown to cause hypertension in normotensive subjects. Treatment of pseudoephedrine overdose is mainly symptomatic. Measures should be taken to support respiration and control hypertension. Convulsions should be supported with an anticonvulsant if required. Elimination of pseudoephedrine can be accelerated by acidification of the urine. Antihistamine over dosage may cause sedation and central nervous system depression.

Pharmaceutical precautions
Store below 25°C. Store in a well sealed container.

Legal Category: OTC
Market Authorisation Number: MA575/00101

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For further information please contact GlaxoSmithKline (Malta) Ltd, Consumer Healthcare 13/11 Vincenti Buildings, Strait Street, Valletta. Tel: 21234044

Ethics Matrices – Part II

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

The first part of this article has tackled the issue of separating the main moral argument at hand from other moral pragmatic issues. It was seen that when negotiating moral problems it is sometimes clear what the main argument is – such as, 'Should we have InVitro Fertilization?' or 'Should we sell organs?. On the other hand, other moral arguments, called pragmatic, may not be the main argument but can still have weight on the final acceptance of the moral issue at hand.

Pragmatic arguments are those which may be resolved in time, with advancing technology. On the other hand, ethical arguments are other moral issues which may not be resolved but which in themselves present another moral argument for discussion. In the previous argument, autostimulation to produce a sample of sperm for IVF was considered an ethical issue. It is not pragmatic as this cannot be resolved in time. Yet it is legitimately another moral argument. It should be made clear that this was not the main argument being discussed, if what was being deliberated was IVF. It may merit a separate discussion and within that context be put into the category (or box) labelled 'moral'. But that would then be another argument.

Another example is freezing of embryos. This again is considered immoral by many. However it cannot be the main argument against the use of IVF, as it may be bypassed. Conversely it is another ethical issue and may merit discussion on its own, being *then* put in the category of 'moral'. It is not a pragmatic issue however as it is not a technology which can be improved, other than its omission.

Sometimes we can be unclear as to whether an argument is simply pragmatic or ethical and therefore we have the convenient category labelled 'unknown'. We can come to it later without sidelining the arguments at hand. For example, one argument often brought into the case for IVF is that couples should not be encouraged to go through extreme sacrifices like selling a house; for others, having a baby may be more important than owning a large, nice house.

Principles Matrix

Another ethics matrix convenient for use is that developed by Ben Mepham which considers a principles approach. Mepham uses three principles: well-being, autonomy and Fairness. It is basically an attempt to move away from the four-principled approach developed by Beauchamp and Childress which have been discussed in this column in previous articles, ie autonomy, beneficence, non-maleficence, and justice. He applies this matrix, an example of which is given here, in various parts of his book, dealing with many areas of bioethics.

Respect for:	Well-being	Autonomy	Fairness
Farmers	Satisfactory income	Managerial freedom	Fair trade laws and practices
Consumers	Food Safety	Informed choice	Affordable food
The Biota	Conservation	Biodiversity	Sustainability
Genetically Modified Crop	Flourishment	Adaptability	Intrinsic value

In the case of Terri Schiavo ... one may apply the four principles to all parties concerned: the patient, the husband & parents, the religious community at large, and the medical team making the decision

The above matrix deals with genetically modified crops. In reality fairness is a principle used in justice. Justice has fairness and equality as two principles usually defined within it. However one may separate justice into 'equality', and 'fairness' or put beneficence and non-maleficence in one category for convenience, according to the topic being discussed. One should keep in mind that the four principles proposed by Beauchamp and Childress do not resolve moral problems. They simply allow a framework for discussion and allow one to formulate a path for arriving to a conclusion. This conclusion however is usually based on separate issues than the four principles alone, such as respect for life, which can be used therefore to arrive at quite opposite conclusions. They nevertheless are the main principles discussed in moral discourse.

	Autonomy	Beneficence	Non-maleficence	Justice
Patient	Can/cannot make a choice	Treatment	Side effects	What is in his/her best interest?
Relatives	Who is to act as proxy?	Information	Giving (bad) news	Any right to knowledge
Medical team	Explaining/taking medical choices	Is treatment futile?	Balance benefits with side effects	Cost/benefit ratio
Community	Does it have a say?	Can others benefit?	Slippery slope arguments	Justice to the community

In the case of Terri Schiavo – the American brain-injured woman who died nearly four years ago, after doctors removed the feeding tube that had sustained her for more than a decade – one may apply the four principles to all parties concerned: the patient, the husband & parents, the religious community at large, and the medical team making the decision. We usually balance between principles and specify them to the situation; but arriving at a moral conclusion is usually an a priori affair. One uses the matrix simply to put one's arguments in a clear, understandable, and common ethical language. Not all boxes need be 'filled'.

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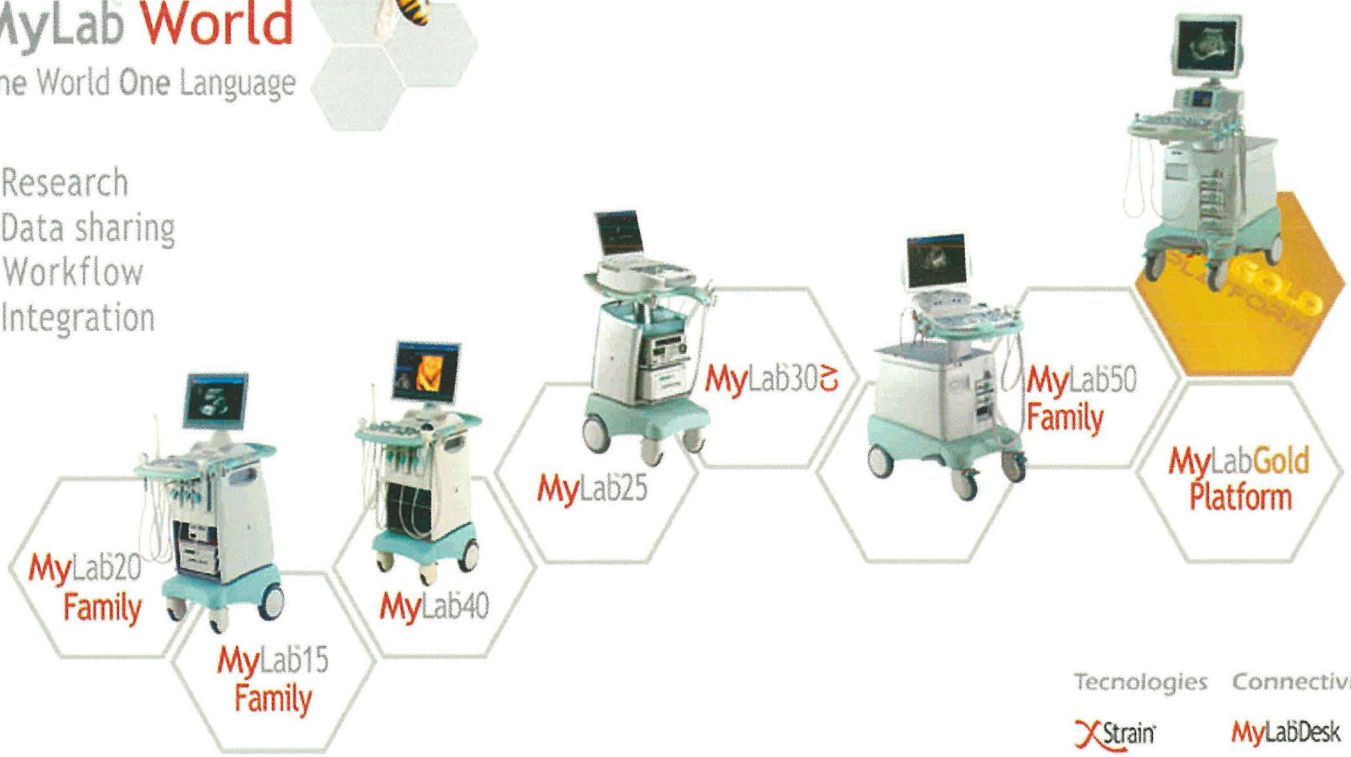

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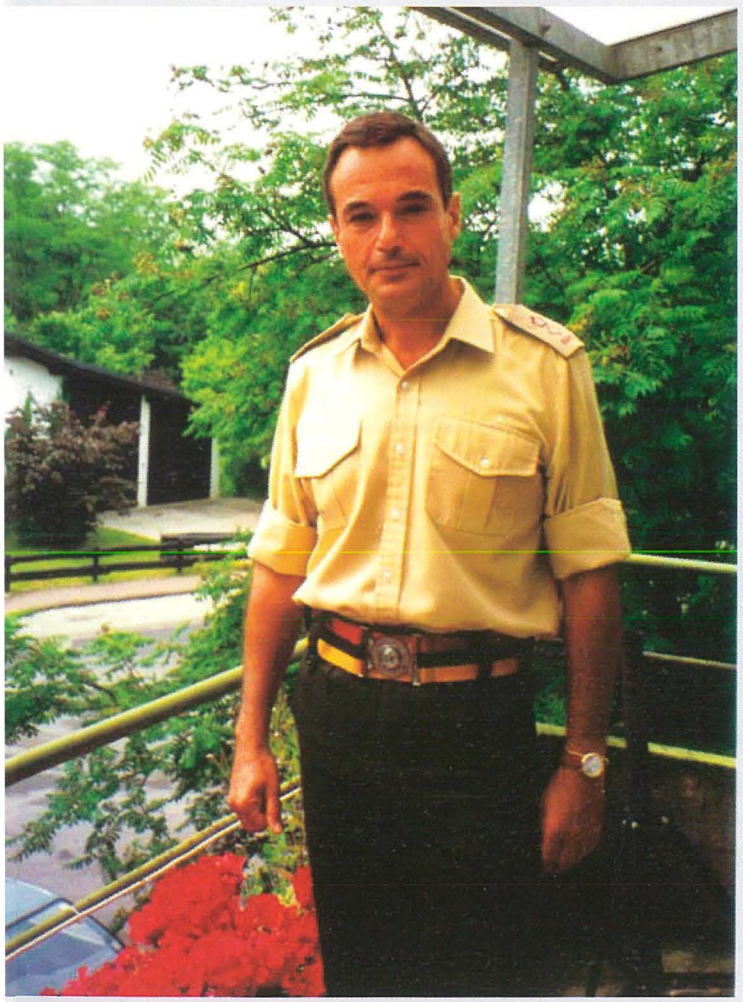
Of Spandau, KGB & STDs

by **Marika Azzopardi**

Sitting in the waiting room to the Genito-Urinary Clinic at Boffa Hospital, I wonder what trepidation patients sitting in my seat feel. As one patient emerges with an embarrassed smile on his face and an empty plastic bottle, only to return after a short while, gingerly trying to keep the full bottle out of my line of vision, I try to stifle a smile.

Of course, there is nothing to smile about in such places, and once inside a GU Clinic, I have to ask the obvious question – are sexually transmitted diseases on the increase?

Dr Philip Carabot, consultant in charge, is emphatic, "Of course – terribly so. We have a problem. There is still not enough awareness and this sheds serious doubts on what's being taught to young people in schools. I am sure PSD teachers are doing their utmost on the whole, but I feel most parents are simply relying squarely on the goodwill of teachers to teach their children the facts of life. When in reality, it should be parents who are the prime teachers of their children in this regard."



Dr Carabot is alarmed for varied reasons. He speaks of our country as acquiring the lifestyle of western developed countries in too short a time span and not being prepared for the full onslaught of such a reality. "I worry about the attitude of people who come here. We see younger and younger patients – 13 year olds having sex with no inhibitions whatsoever, no condoms and a devil-may-care attitude that is especially troubling. The girls aren't even bothered about landing an unwanted pregnancy anymore and having to raise a child single-handed!" One of the key culprits is the free consumption of drugs and alcohol which remove all inhibitions and lead to uninhibited sex. Then again, drug users are more likely to barter sex for drugs which makes things even worse. Dr Carabot also highlights the importance of adequate inspections and enforcement when it comes to alcohol consumption by minors.

The prime concern is still AIDS. After the 'apparent' onset of AIDS in the early eighties, people were initially terrified of the disease especially as there was much media attention to it and no known cure or treatment. People seemed to stay put for a while, behaving well and trying to steer clear of risky situations. Eventually when information fatigue set in and a somewhat effective treatment became available, people began to loosen their wariness. But as Dr Carabot indicates, treatment for HIV and AIDS is not 100% effective, and whilst it does keep an infected person in relatively good health, the treatment itself is fraught with particularly nasty side effects.

The GU Clinic which opened in 2000, has seen a continuous increase in its patient numbers over the years and Philip Carabot is pleased with its success but is quick to point out that the ones who do turn up at the clinic are just the tip of an iceberg. With casual sex being so rampant, diseases like gonorrhoea have increased in Malta and become even more virulent than ever before. "We try to trace the links because for each single case of gonorrhoea there are usually several other cases out there – it is a whole network of infected people who carry the disease around with them unknowingly. It is very rare for a patient to come ahead with names and contacts, so we cannot trace who got infected and ask them to get themselves checked out. That worries us

because each infected person out there is a walking time bomb and when one considers how many diseases are initially symptom-free and how women are especially likely to remain symptom-free for many years, the repercussions are enormous."

He points out that women have the very erroneous impression that when a smear test gives the all-clear, it covers everything and includes STD screening as well. "A smear test can only screen abnormalities linked to cancer in the cervix or uterus. It cannot screen STDs. Women need to be told this, and referred to the GU Clinic if there is a slight suspicion of infection. This is where things are done properly in this regard."

[Doctors] are the first contacts with infected patients and need to have a very high index of suspicion ... [they] must stop treating blindly and they must refer more patients to this clinic. It is the only way to try and stall the wave of STDs that is hitting the country

We pause to talk about the man himself and his past career as an army man. Having qualified as a doctor in 1975, he left Malta for the UK and worked for the NHS between 1976 and 1982. "I did various jobs within the NHS including GU medicine which was of great interest to me. Then in 1982 I decided to enter the British Army. It was a lifelong desire and I had reached an age when army entry was the last port of call and if I missed the boat then, it would never have happened. Coincidentally the British army required a GU doctor and following my standard training at Sandhurst, I was sent out to my first posting. It was a baptism of fire – Belfast at the height of the worst periods of its fighting history. My next posting was in Germany and there I visited several different places. But the highlight of my German experience was during 1984-86."

Philip Carabot was assigned a rare task indeed – taking care of Hitler's deputy Rudolph Hoess, a prisoner of war in West Berlin when the segmented city was in the hands of the foreign powers. The west was controlled by the British, the Americans and the French, whilst the east was in the hands of the Russians. "Hoess was living in Spandau prison which was an eerie place, the kind you see in horror movies. It was a gigantic place being used for one single prisoner – Hoess himself; the other prisoners of war had all been released but for mysterious reasons, Hoess was kept detained until his death, after which Spandau was demolished. But in the meantime he lived a long life even in such grim isolation."

Dr Carabot describes Hoess as a strong man albeit his old age, with piercing bright blue eyes under straggly bushy eyebrows. As a doctor of the British army, the Maltese doctor was responsible for Hoess' health but on meeting Hoess for the first time, he was to be scrutinised at close quarters. "He came up to me and looked me over from head to toe like I was the one to be examined. He was extremely diffident of strangers but once he conceded my presence, it was ok. We never had one private conversation because he was constantly supervised at close range by the KGB. They never even addressed him with his name – he was merely prisoner no.7."

No.7's health issues were discussed at a round table including Carabot, the KGB, the CIA and others. A trip to the British Military Hospital needed the organisation of a state visit and the Germans would close West Berlin's main thoroughfare just to transfer the man to the Military Hospital and back. Hoess is said to have committed suicide in what were extremely dubious circumstances. Luckily for Dr Carabot, he was away at the time, and that spared him interrogations and questioning.

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Spiral CT: The Gold Standard fo

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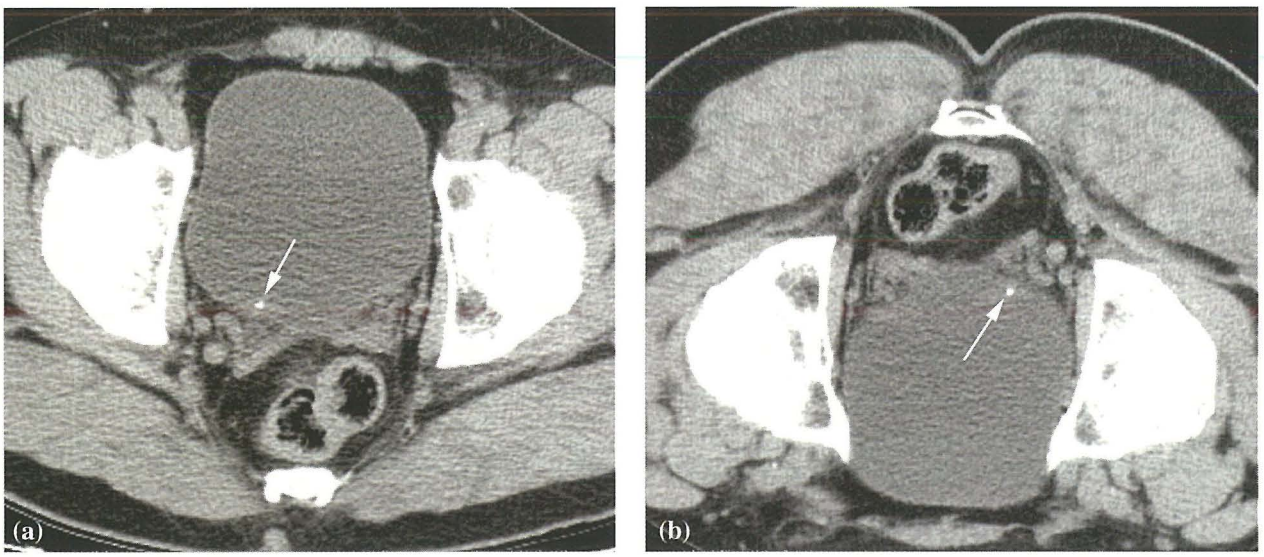

Figure 6.*(a) Axial CT scan of a patient with right flank pain, obtained with the patient supine, shows a stone adjacent to the right posterior bladder wall. (b) On a scan obtained with the patient placed prone, the stone does not fall anteriorly, indicating the stone is still within the ureterovesical junction.*

Numerous diseases may manifest as acute flank pain and mimic urolithiasis. Up to one-third of unenhanced CT examinations performed because of flank pain may reveal unsuspected findings unrelated to stone disease, many of which can help explain the patient's condition. Alternative diagnoses are most commonly related to gynaecologic conditions (especially adnexal masses) and nonstone genitourinary disease (example, pyelonephritis, renal neoplasm), closely followed by gastrointestinal disease (especially appendicitis and diverticulitis). Hepatobiliary, vascular, and musculoskeletal conditions may also be encountered. Vascular causes of acute flank pain (dissecting or leaking aortic aneurysm) must always be considered, since these constitute life-threatening emergencies that may require the intravenous administration of contrast material for diagnosis. Radiologists should be familiar with the typical findings of urinary stone disease at unenhanced CT, as well as the spectrum of alternative diagnoses that may be detected with this modality, to accurately diagnose the source of flank pain.

Of Spandau, KGB & STDs

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When Carabot left the British army in 1999, he was approached by Professor Joe Pace then Chairman of Dermatology at Boffa Hospital, who suggested he start off the GU Clinic from scratch. Nine years down the line, Dr Carabot has a new project at hand "We have reached a point where we are presently working on a National Sexual Health Policy. There is an urgent need for a drastic re-look at how we handle the sex issue in Malta and it is a national issue which concerns us all. There is an urgent need for prevalence studies to better assess the situation and monitor trends."

As a final word, Dr Carabot addresses family doctors and other specialists who might see patients with a potential STD, "Doctors need to adopt a uniform approach in screening and treating STDs. They are the first contacts with infected patients and need to have a very high index of suspicion. The truth is that the GU Clinic gets very few referrals from doctors and what reaches us are mostly self-referrals. Doctors must stop treating blindly and they must refer more patients to this clinic. It is the only way to try and stall the wave of STDs that is hitting the country."

Further information on the GU clinic may be accessed on www.sahha.gov.mt/pages.aspx?page=173. The contact numbers are 22987115 (clinic direct line) and 21227981 (for appointments).

or Urinary Tract Stone Detection

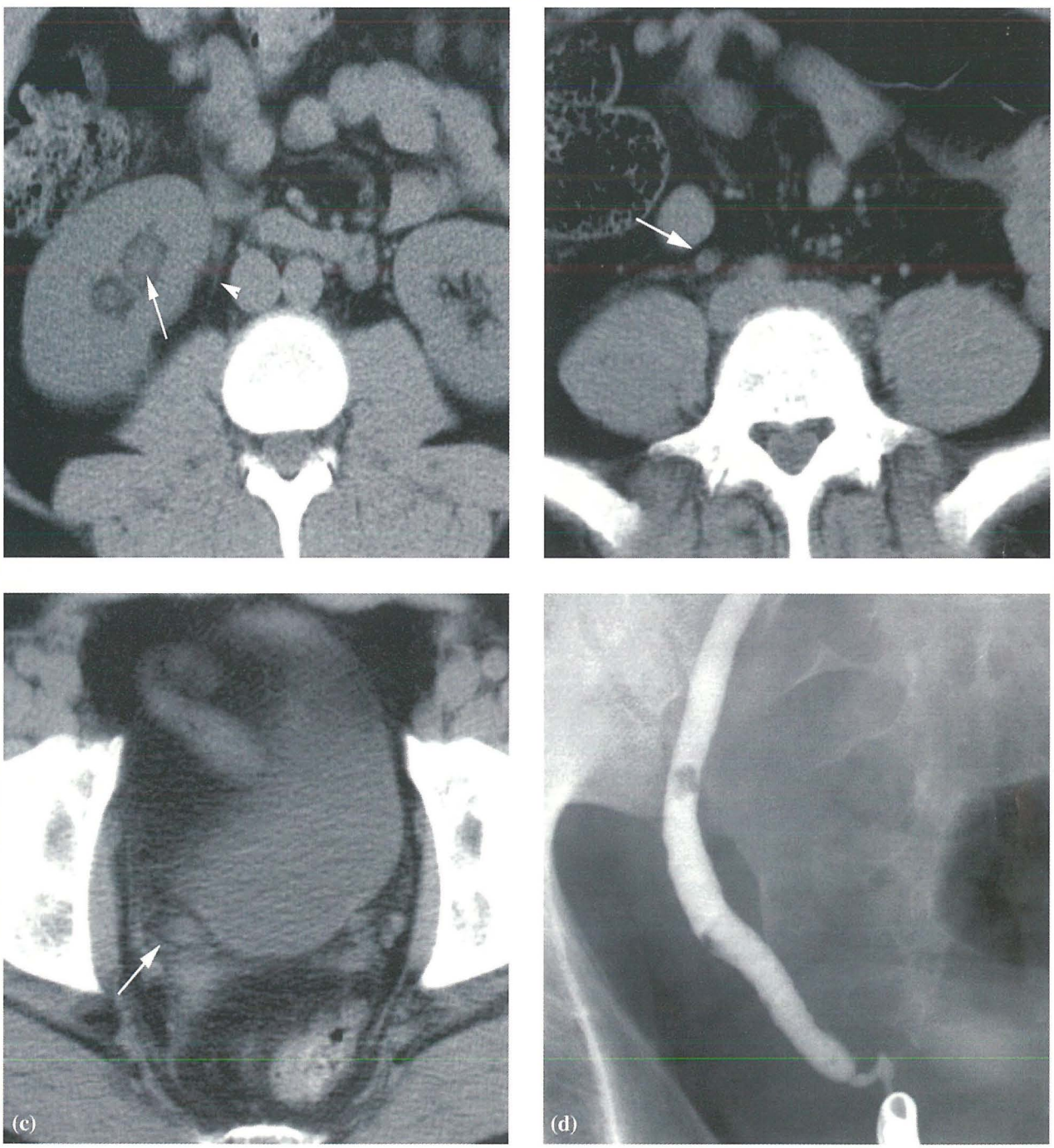

Figure 7. *Protease inhibitor deposition in a 35-year-old man with HIV disease taking indinavir who presented with right flank pain radiating to the right groin. (a) Axial CT scan of the kidneys shows dilatation of the right renal collecting system (arrow) and mild stranding of the perinephric fat (arrow head) medial to the lower pole of the right kidney. (b) A more inferior image shows dilatation of the right ureter (arrow). (c) Another more inferior scan shows that the right ureter remains dilated to the ureterovesical junction (arrow). No calcification was identified. (d) Subsequent retrograde ureterogram shows multiple filling defects in the distal right ureter. Stricture of the ureter distal to the indinavir fragments is likely caused by recent stone impaction near the ureterovesical junction.*

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

A practical and comprehensive overview of PET/CT – Part III

continued from page 4

4. Better staging and/or restaging: One example is yet another study in which the efficacy of ^{18}FDG-PET was evaluated and its impact in staging of patients with newly diagnosed breast cancer was assessed.[6] 271 patients with biopsy-proven primary breast cancer were examined. PET results were compared with the histopathology results. In this particular study the sensitivity of ^{18}FDG-PET for detecting axillary lymph node metastasis was 100% in pN3, and the specificity was 89% for pN0 stage. Detection of extra-axillary regional node or distant metastatic lesions revealed by PET scan in 22 of 24 patients resulted in a significant change in the TNM stage. Distant metastasis without axillary lymph node metastasis was noted in 21% (5/24) of patients. The results revealed that ^{18}FDG-PET upgraded TNM stage in 9.2% (22/240) of patients and 7.5% (18/240) of patients were diagnosed as having one or more distant metastases. ^{18}FDG-PET was able to identify extra-axillary regional nodal and distant lesions in newly diagnosed patients with breast cancer and altered the staging and management of therapy in patients with newly diagnosed breast cancer. There are numerous other examples in scientific literature which one may read about[7-10].

5. Use in patients allergic to contrast medium or in whom CT is contraindicated: Adverse reactions from contrast medium administration can occur and symptoms can range from mild to life-threatening. Serious side-effects include an anaphylaxis-like reaction and kidney damage which may occur because the contrast media are eliminated renally. There is no such risk in carrying out PET/CT since contrast media are not involved. Thus PET/CT can be carried out by patients who are allergic to contrast medium and by patients who cannot carry out a CT scan with contrast medium due to deranged creatinine levels or history of kidney problems.

Patient with lung cancer and bone metastases (vertebra). The bone lesion was not detected by CT. Sensibility for bone lesions is 90% in both PET/CT and bone scintigraphy, but specificity is much higher in PET/CT (98%) when compared to ^{99}Tc bone scan (61%).[11] A bone scan was avoided. Images courtesy of San Raffaele Hospital, Milan.

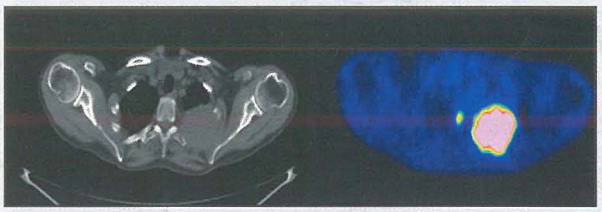

Figure 2. CT and PET image

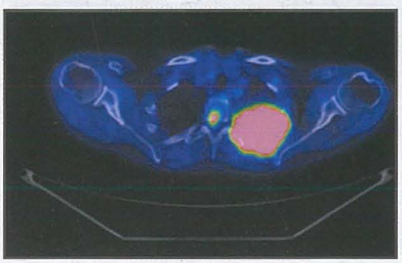

Figure 3. Superimposed PET-CT image showing both the lung and bone lesion in one scan.

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