NEWSPAPER POST

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MEDICAL IMAGING

Imaging Pyelonephritis - Part II

by **Pierre Vassallo**
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Consultant Radiologist

The last article introduced the clinical and radiological features of uncomplicated pyelonephritis, where the superior accuracy and efficiency of Computed Tomography (CT) over other imaging modalities was stressed. This article will briefly summarise the imaging findings of uncomplicated pyelonephritis and will discuss complicated and less common types of pyelonephritis including xanthogranulomatous pyelonephritis, and tuberculosis, where CT is of even greater value.

The recommended protocol for CT evaluation of pyelonephritis (or any other CT pathology) includes a three phase examination starting with a non-contrast-enhanced scan, followed by an contrast-enhanced scan performed 50-90 seconds after contrast injection and a delayed scan performed about 5 minutes after injection.

On unenhanced CT, regions of the kidney involved with pyelophritis may have lower density related to oedema and the kidney may be enlarged; less frequently, pockets of higher density may be present that are thought to represent hemorrhage. However, unenhanced CT may appear normal in pyelonephritis. Unenhanced CT is excellent for identifying urinary tract gas, calculi, hemorrhage and obstruction.

It is only after contrast material is administered that the diagnostic features of acute bacterial nephritis are revealed. After administration of contrast material, acute bacterial nephritis most commonly manifests as one or more wedge-shaped areas or streaky zones of lesser enhancement that extend from the papilla to the renal cortex. This pattern of differential enhancement reflects the underlying pathophysiology of tubular obstruction caused by inflammatory debris within the lumen, interstitial oedema, and vasospasm (figure 1).

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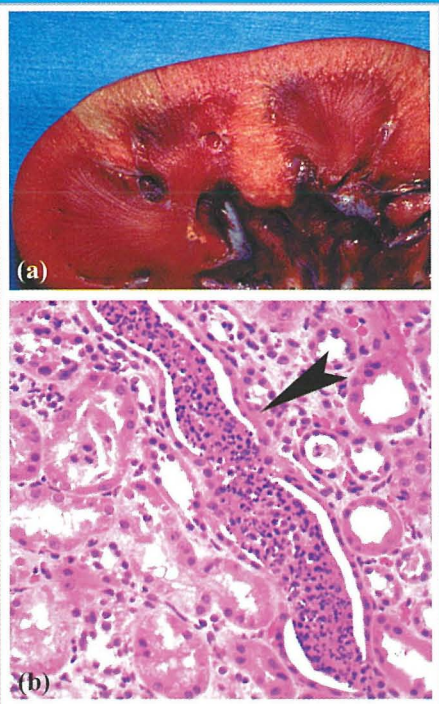

Figure 1. *(a) Acute bacterial nephritis seen in a resected kidney shows a wedge-shaped, lighter region of renal cortex that represents acute bacterial nephritis. (b) Photomicrograph (original magnification, x400; hematoxylineosin stain) shows a collecting duct (arrowhead) filled with a cast of polymorphonuclear leukocytes.*

Editor's Word

Dear Friends and Colleagues,

Welcome to the third issue of the magazine for this year.

This issue marks the seventh anniversary of the publication of this magazine which has managed to establish itself as one of the leading regular medical publications in the Maltese islands.

This could only be made possible through the constant support of our contributors, readers, advertisers and our hard working team. Your feedback has also been very important for us.

In this issue we bring you a number of very interesting articles on a vast range of topics – we want to ensure that you always find articles of interest to you.

We would also like to wish you a relaxing summer.

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Imaging Pyelor

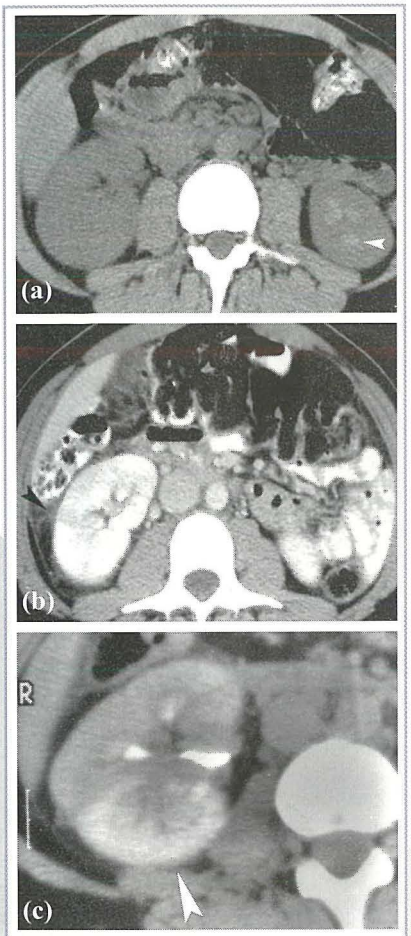

Figure 2. *(a) Unenhanced CT scan showing enlargement of the infected right kidney and loss of medullary pyramids (note pyramids on normal left kidney (arrowhead)). (b) Early enhanced CT scan showing area of diminished perfusion (arrow). (c) Delayed scan (note contrast material is already in the renal calyces) showing an area of persistent contrast enhancement (arrowhead).*

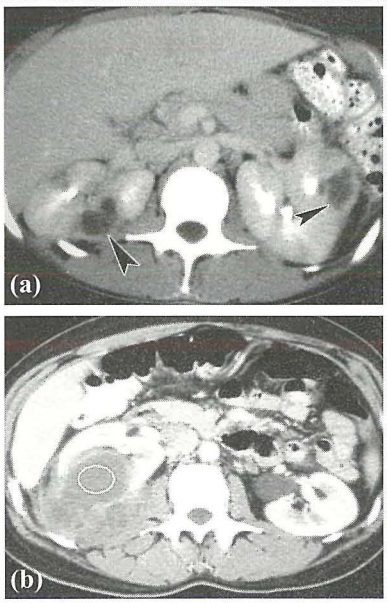

Figure 3. *(a) Enhanced CT showing multiple renal lesions with central fluid density representing abscesses. (b) CT scan demonstrates an abscess cavity with a peripheral enhancing rim extending outside the right kidney and into the perinephric fat and psoas muscle.*

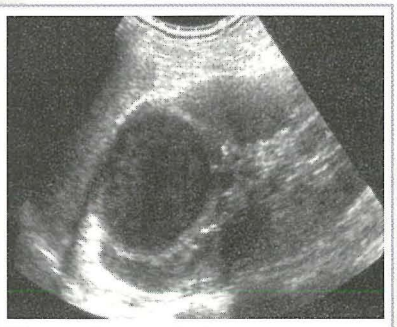

Figure 4. *Renal abscess cavity on ultrasound.*

All three of these pathophysiologic disturbances tend to decrease the flow of contrast agent through the tubule. This explains why enhancement of the inflamed parenchymal areas is delayed and once contrast agent is delivered to the area the enhancement persists 3–6 hours after injection (figure 2). These foci of infection demonstrate reduced density during the early phase enhanced CT followed by increased density due to delayed clearance of the contrast agent as it slowly passes through the compromised tubules and collecting ducts.

With more severe inflammatory disease, necrosis of renal parenchyma may occur with resulting abscess formation (figure 3). Abscesses may extend through the renal capsule outside the kidney to involve adjacent structures, most classically the psoas muscle. A renal abscess should be suspected when appropriate therapy does not lead to clinical response. Diabetic patients are predisposed to abscess formation, with 75% of all renal abscesses occurring in this patient population. Interestingly, up to 15%–20% of patients with an abscess have negative urine cultures. Abscess cavities may be visible on ultrasound (figure 4).

Infection is only one cause of interstitial nephritis. The inflammation can be induced by drugs, granulomatous diseases, metabolic disorders, and immunologically mediated mechanisms. These other entities are much less common than acute bacterial nephritis; thus, in the appropriate clinical setting, it is reasonable to assume that the characteristic findings of interstitial nephritis are caused by infection.

nephritis - Part II

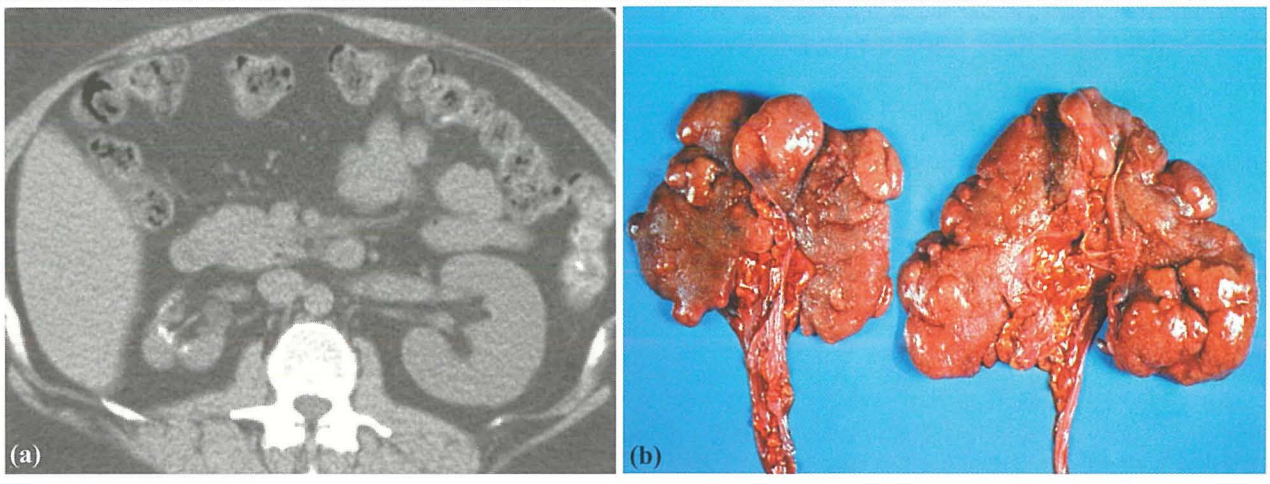

Figure 5. *(a) Chronic pyelonephritis involving the right kidney, which is small, deformed right kidney with multiple deep scars and contains dystrophic calcifications. (b) Photograph of the resected kidneys demonstrates extensive bilateral scar formation.*

Chronic pyelonephritis is a somewhat controversial disease from a pathogenetic standpoint, as we are uncertain whether it represents an active chronic infection, multiple recurrent infections, or stable changes from a remote single infection; however whatever the pathogenesis, its radiologic appearance is the same. The imaging findings are characterized by renal scarring, atrophy and cortical thinning, hypertrophy of residual normal tissue (which may mimic a mass lesion), calyceal dilatation or clubbing secondary to retraction of the papilla from overlying scar, thickening and dilatation of the calyceal system, and overall renal asymmetry (figure 5). Hypertension is frequently a long-term sequela of chronic pyelonephritis.

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Thalassaemia - A review

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Although reference to a disease causing anaemia in children can be found in ancient Greek and Italian writings[1], the first clinical description of thalassaemia as a separate entity, was done by Cooley and Lee in 1925.[2] Since then b-thalassaemia has also been known as Cooley's anaemia. The term 'thalassaemia' was in fact coined by Whipple and Bradford[3] in 1932, in their paper on the pathology of the disease. Thalassaemia is derived from the Greek word Qalassa (Thalassa) meaning 'the sea'.

It has been generally accepted that the high incidence of thalassaemia and the common haemoglobin variants, Hb S, Hb E and HB C, in certain areas of the world is the result of selective pressures of *Plasmodium falciparum* malaria.[4,5] As can be seen in figure 1, the distribution of these disorders follow quite closely the distribution of *P. falciparum.* There is good evidence to believe that carriers of one mutated gene had a higher reproductive fitness in malarial areas as compared to normal individuals, possibly due to an inability of the intracellular parasite to complete its life cycle.

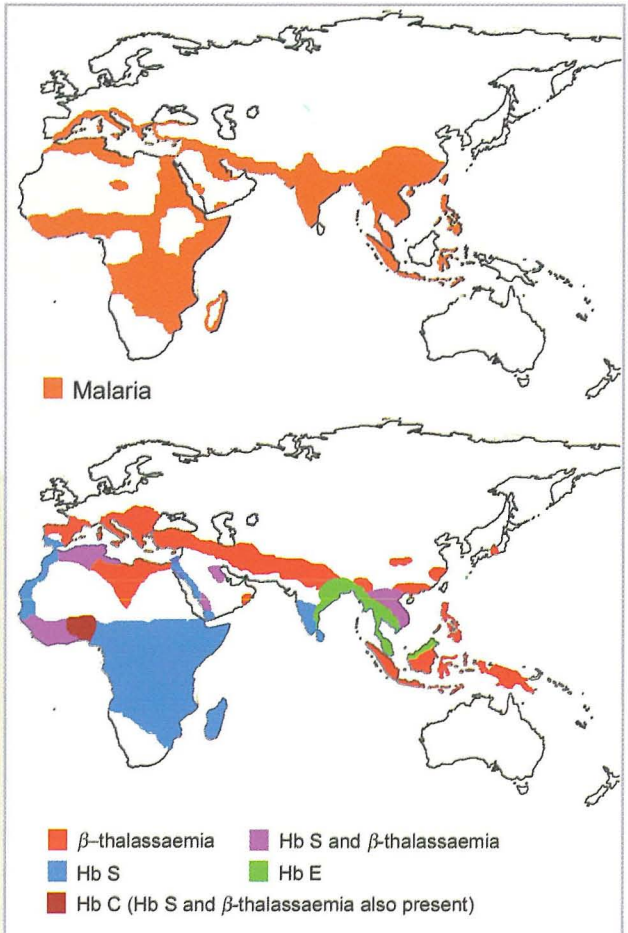

Figure 1. *Distribution of malaria and β-thalassaemia, Hb S, Hb C and Hb E*

Human Haemoglobins – Structure

Human haemoglobins are tetramers of two a-globins, i.e. ζ or α, and two non-a-globins, i.e. ε, $^{G}\gamma$, $^{A}\gamma$, δ, or β each associated with a haem group. The haem group is formed by an iron atom surrounded by a porphyrin ring. The genes that encode for the globins are arranged 5' to 3' in the same order in which they are sequentially expressed during development. Thus the a-globin gene cluster, spanning a region of around 50 kilobases (Kb) on the short arm of chromosome 16, contains the embryonic ζ gene and two α genes - α2 and α1, together with a number of non-functional pseudo-genes.

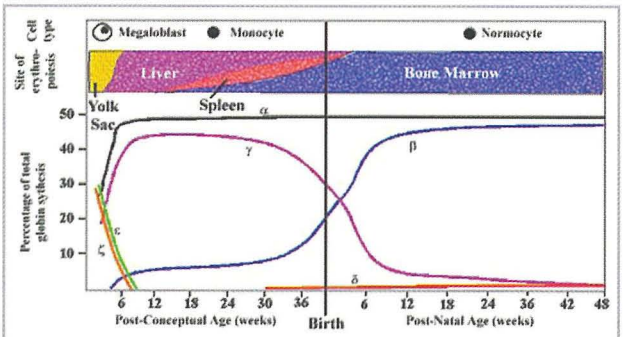

Figure 2. Globin chain synthesis at different stages of foetal maturation (Source: Weatherall DJ and Clegg JB, The Thalassaemia Syndromes[2])

The non-α-gene cluster, spanning a region of around 90Kb on the short arm of chromosomes 11, comprises, from 5' to 3', the embryonic ε-gene, two foetal genes, $^{G}\gamma$ and $^{A}\gamma$, and the adult δ and β genes.

Molecular structure of globin genes

Being only around 2 Kb long, globin genes are relatively small, in contrast to other genes (blood coagulation Factor VII gene ~13Kb; human dystrophin gene ~2 megabases Mb). The relatively small size facilitated the identification and characterisation of mutations leading to thalassaemia and other haemoglobin variants.

In thalassaemia, there is a reduction of one of the globin chains due to mutations or deletions affecting DNA transcription or translation. α-thalassaemia (affecting α-chain production) and β-thalassaemia (affecting β-chain production) are common and clinically important.

Whilst the majority of β-thalassaemia conditions are due to point mutations involving one or two nucleotides, α-thalassaemia is commonly due to large deletions involving the whole gene. Thalassemia mutations and deletions are relatively population specific and Malta is no exception.

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References:
1. Philipp T. et al. Clin Therapeutics 2007; 29 (4): online 1-18
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Thalassaemia - A review

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Around 72% of the β-thalassaemia cases are due to the relatively mild IVS1-6T->C mutation (i.e. a Cytosine to Thymine substitution in the 6th nucleotide of the first intron sequencing).[6] This mutation decreases the efficiency of normal splicing (to about 30% of normal), resulting in an increase in the utilisation of the alternative splice sites and a prematurely terminated protein.

Three other mutations, codon 39 C->T (insertion of a premature stop codon), the IVS-I-110 G->A (production of a new acceptor splice site in the first intron) and the IVS-II-1 G->A (abolition of the splice site), make up the remaining 28%. In the case of ·-thalassaemia, a 3.7 Kb deletion (basically this deletion reduces the number of α gene copies to 1 from the normal 2 genes per chromosome 16), is the only α gene deletion discovered amongst the Maltese population.

From the knowledge of the molecular pathology, it is clear that the major problem in thalassaemia is a disbalance between the α and β globins that are an integral part of the heamoglobin molecule. Thus in β-thalassaemia, there is a relatively higher level of α globin in relationship to β-globin and vice versa in α-thalassaemia. The unpaired, excess globin chains either form unstable tetramers (β chains - HbH and γ chains - HbBarts) or else the α chains bind to the erythrocyte membranes causing membrane damage. In both cases, apart from inefficient erythropoiesis there is also increased intra-medullary haemolysis.

Whilst thalassaemia carriers (i.e. carrying one mutated allele in the case of β-thalassaemia and up to 2 mutated/deleted alleles in the case of α-thalassaemia) are usually asymptomatic, they have a slightly lowered haemoglobin level (10-12g/dl) and microcytosis (a MCV lower than 80fl and a MCH lower than 26pg) with a high Hb A2 (higher than 3.5%) in the case of β thalassaemia carriers. The identification of thalassaemia carriers is further complicated by concurrent presence of iron deficiency. In the case of β-thalassaemia, the presence of mutations causing mild disease, or concurrent presence of α-thalassaemia or δ-β, thalassaemia (deleterious mutations in both the δ and β genes) can further complicate its diagnosis.

Thalassaemia Major

Thalassaemia major can be divided into α^0 or β^0 and α^+ or β^+ depending on the amount of the respective residual globin chain production. Whilst α^0 and β^0 thalassaemias are present with very severe anaemia, in α^+ and β^+ thalassaemias the picture is more varied. α^+ thalassaemia can be divided into two distinct groups:

1. Individuals that inherit Thalassemia 3 normal α-genes (-α/αα). These individuals are referred to clinically as silent carriers of α-thalassemia or α-thalassemia-2 trait. The affected individuals exhibit no clinical abnormality and usually have mild reductions in red cell mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH).

2. The inheritance of 2 normal alpha genes either due to heterozygosity for alpha (0) thalassemia (αα/--) or homozygosity for alpha (+) thalassemia (-α/-α) results in the development of α-thalassemia minor or α-thalassemia-1 trait. Similarly to α-thalassemia-2, the affected individuals are clinically normal with minimal anaemia and reduced MCV and MCH.

3. HbH disease or the inheritance of one normal alpha gene (-α/--), is the result of abundant formation of hemoglobin H composed of tetramers of excess beta chains. The affected individuals have moderate to severe lifelong haemolytic anemia, modest degrees of ineffective erythropoiesis, splenomegaly and variable bony changes.

The clinical picture of β^+ thalassaemia is more varied as it depends on the inherited mutation and other genetic (and probably environmental) factors. The clinical picture can range from a severe to moderate anaemia (Hb levels of 5 to 8 g/dl) to very mild anaemia (9-10g/dl).

Clinical Management of Thalassaemia

The classical management of thalassemia is based on an adequate transfusion regime and proper iron chelation. The transfusion regime (usually every 4-6 weeks) is aimed at ensuring that the mean haemoglobin level is around 9-10g/dl, thus reducing the lifelong complications associated with severe, chronic anaemia. Coupled with the transfusions, these individuals require adequate iron chelation, to reduce iron overload. Up to now, this was achieved through the daily, subcutaneous injection of deferoxamine administered through a syringe pump but newer, oral chelators have been developed and are presently being introduced into the market. These oral chelators are offering both a reduction in the discomfort from the subcutaneous injection as well as generally improving the compliance and thus reducing iron overload complications.

In addition to transfusion and chelation, splenectomy has the potential of reducing the transfusion requirement and is usually performed just before puberty. Furthermore, bone marrow transplant, when appropriate and where a donor is available, offers a cure, as opposed to treatment, for thalassaemia major individuals.

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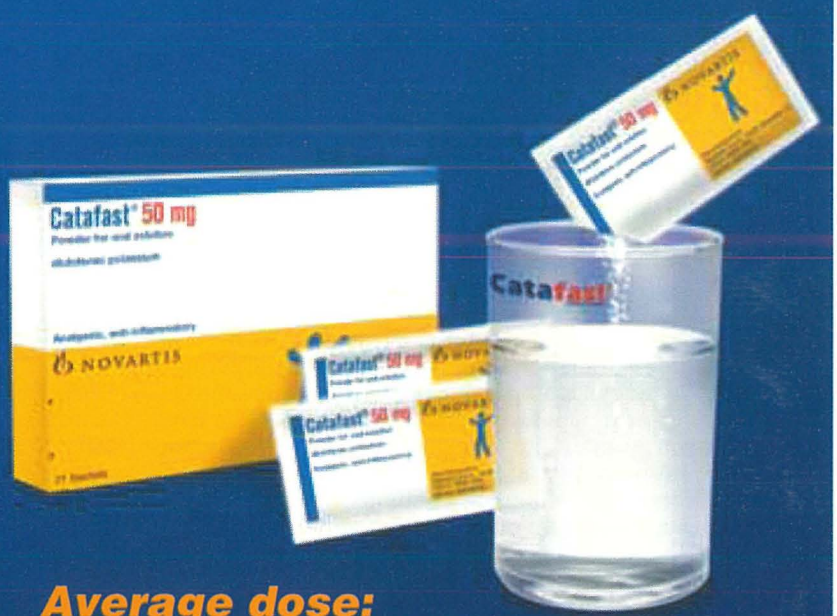

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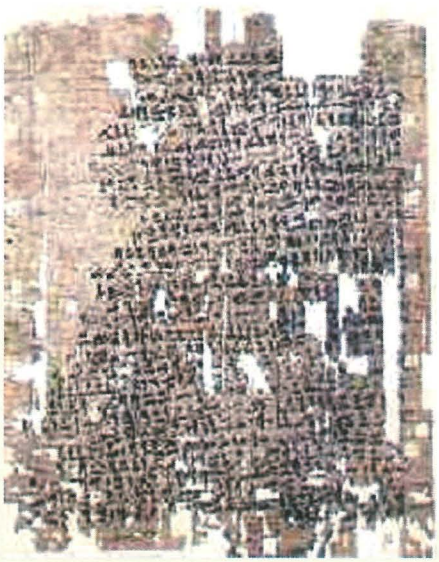
Ancient Egyptian Medicine

Part IV [2] – Medical Papyri

by **Charles Savona-Ventura** *MD DScMed FRCOG AccrCOG MRCPI*
Professor of Obstetrics & Gynaecology, Faculty of Medicine & Surgery, University of Malta

The Kahun Papyrus was discovered by Flinders Petrie in 1889 at the Fayum site of Lahun and was eventually deposited in the London University College. The papyrus is dated to this period by a note on the recto which states the date as being the 29th year of the reign of Amenenhat III (c. 1825 BC). The text was published in facsimile, with hieroglyphic transcription and translation into English, by Griffith in 1898. It is badly fragmented. The textual material is similar in style to the Edwin Smith Papyrus but deals mainly with gynaecological matters and other problems affecting women. The gynecological text can be divided into thirty-four paragraphs, of which the first seventeen have a common format. The first seventeen start with a title and are followed by a brief description of the symptoms, usually, though not always, dealing with the reproductive organs. The second section begins on the third page, and comprises eight paragraphs which, because of both the state of the extant copy and the language, are almost unintelligible. Despite this, there are some paragraphs that have a sufficiently clear level of language as well as being intact which can be understood. Paragraph 19 is concerned with the recognition of who will give birth, paragraph 20 is concerned with the fumigation procedure which causes conception to occur and paragraphs 20-22 are concerned with contraception. Among those materials prescribed for contraception are crocodile dung, 45ml of honey and sour milk. The third section (paragraphs 26-32) is concerned with the testing for pregnancy. These include the placing of an onion bulb deep in the patient's flesh, with the positive outcome being determined by the odor appearing to the patient's nose. The fourth and final section contains two paragraphs which do not fall into any of the previous categories. The first prescribes treatment for toothaches during pregnancy. The second describes what appears to be a fistula between bladder and vagina with incontinence of urine "in an irksome place." [The transcribed text at *http://www.reshafim.org.il/ad/egypt/timelines/topics/kahunpapyrus.htm*].



The Hearst Papyrus was given in 1901 to the expedition carried out by the University of California in Egypt by a peasant, in exchange for some waste soil he required as fertilizer. It is named after William Randolph Hearst, who funded much of the work of the expedition. The papyrus dates from the reign of Tuthmosis III in the 18th Dynasty in the first half of the second millennium BC. It consists of 18 pages with 260 paragraphs with hieratic Egyptian writing (a cursive form of hieroglyphic writing). Eighteen columns deal with medical prescriptions which concentrate on ailments of the urinary system, blood and hair, and bites. The ailments for which cures are offered range from "*a tooth which falls out*" (Col. I, l. 7) and "*remedy for treatment of the lung*" (Col. IV, l. 8) to bites by human beings (Col. II, ll. 6–7) pigs and hippopotami (Col. XVI, ll. 5–7). [The *transcribed text can be seen at http://www.reshafim.org.il/ad/egypt/timelines/topics/hearstpapyrus.htm*].

The Chester Beatty Papyri was one of a series of 19 papyri donated to the British Museum by the millionaire industrialist Sir Alfred Chester Beatty. These papyri were found in the workers village at Deir el-Medina in 1928. These papyri, together with many others now dispersed in various libraries were the private collection of the scribe Qen-her-khepeshef who lived in the 19th Dynasty and which were passed on down through his family until they were placed in a tomb. These papyri have undergone extensive reconstruction and translated into English by Gardiner in 1935. Their content comprises many magical incantations against headaches, but there is much space given over to vague rectal ailments with various remedies and incantations.

The Berlin Papyrus was acquired by Giuseppe Passalacqua in Sakkara and was sold on to Friedrich Wilhelm IV of Prussia with other objects in 1827 for the Berlin Museum. It was originally translated into German by Wreszinski in 1909. The style suggests a 19th Dynasty origin. It is made up of 24 pages - 21 verso and 3 retro – and its content is similar to the Ebers papyrus.

The London Medical Papyrus was passed on to the British Museum in 1860 having been in the possession of the Royal Institute of London prior to that. Its style dates it to the reign of Tutankhamun. It comprises 19 pages but is in very poor condition. It concentrates mostly on magical spells.

The Ramesseum Papyri was discovered in the great temple of the Ramesseum. This group of 17 papyri are believed to date to the 13th Dynasty (Early Second Intermediate Period). The main medical content is concentrated in Parts III, IV and V, all written in vertical columns. These sections discuss diseases of the eyes, gynaecological conditions, diseases affecting children and those affecting muscles and tendons.

continues on page 15

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Ethics in Psychiatry

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

Psychiatrists in the UK have recently lamented the need for a code of ethics for psychiatry.[1-3] There is a clear difference between a code of ethics and a code of practice (such as the non-statutory one of the UK Mental Health Act of 1983) or indeed a code of conduct. Sarkar and Adshead (2003) argue for the need to protect the patient in a world which is becoming more and more contractarian and utilitarian. Indeed the public often views psychiatrists as having to protect it from psychiatric patients and because of this the latter are put at a higher risk for detention. Codes of conduct and practice are therefore not sufficient for psychiatrists[1] as patients put trust in these professionals to "protect their interests when they are not well enough to protect themselves".

There are a number of issues in which psychiatric ethics differs from mainstream clinical ethics, mostly having to do with the vulnerability of this group of patients and indeed their mental incapacity. Indeed Sarkar and Adshead argue that the relative incapacity of patients to make decisions for themselves puts them in an especially vulnerable situation because they depend on others. In the UK this translates often into a 'complete loss of autonomy' and even patients' competent refusal may, under British law, be over-ridden, even though psychiatric patients, even in-patients, may be perfectly capable of taking some decisions and participating in one's choice for treatment.[2] Even in forensic psychiatry it has been noted that for public interests, the interests of the patient may not be fully observed and that a code of ethics which trumps justice over other principles needs to be addressed in these specific areas.[3]

A common point raised is the vulnerability of patients, which may lead to sexual abuse – an exploitation of the vulnerability. This has been raised frequently in the United States, but certainly, according to General Medical Council data and information from voluntary groups, Sarkar and Adshead point out that the problem is not uncommon in the UK. In point of fact it seems to be entirely legal in the UK to have sexual relationships with a psychiatric patient 'so long as the patient is not detained'.[3]

Thirdly, the Royal College of Psychiatrists[4] points out the need for psychiatrists to ensure that the risk of detaining patients more than necessary is reduced. Psychiatry risks harming people by treating them unjustly and in fact those patients who commit offences may actually be kept in psychiatric detention for longer periods than they would actually have spent in prison for the same offence.[1]

Current legislative frameworks in the UK seem to protect third parties more than they protect the mentally ill patient. It sees the professional role of psychiatrists as having an obligation to protect the public from these people. This conflicts with the altruistic role of psychiatrists and indeed, the profession complains that such attitude is in conflict with the Declaration of Madrid[5] which puts values towards patients and altruism as the defining intention of the profession.

These problems therefore frequently put psychiatrists at odds with the principle of nonmaleficence[6] and the current western view of the relationship between a doctor and a patient being a contract is at odds with Hippocratic ideals. It also risks making the psychiatric encounter too utilitarian, that is, based on the value of a person balanced against his or her value/risk to society.[7] This risk/benefit analysis on patients is perhaps a morally repugnant reflective equilibrium, which justifies the plea of modern psychiatrists. This, apart from the fact that patients may in the long run loose trust in the profession.

Michele Foucault[A] has noted how 'madness' was not always seen as a responsibility of the medical profession. Indeed mental patients were often detained with criminals in France. In time they fell under the care of doctors and eventually the field of psychiatry came to be. Moreover treatment in psychiatry was often unorthodox, especially those preceding current Electro-convulsive therapy. Certainly hitting someone in the head with a stick is not normal. Detaining people in cages and boxes seems repulsive today, yet we still occasionally detain people in strait jackets and others locked up in small rooms without proper facilities; and if nursing staff are unavailable patients may not get their daily walk outside. This is more often the responsibility of the state than the institution itself. But the vulnerabilities of mental patients remain. Unfortunately, locally, only patients who suffer from more severe mental illness are entitled to free medication, through the Schedule V (Yellow Card) scheme.

One has to acknowledge that if the field is not to recede back to a state where psychiatric patients are locked away (at least for longer periods than they should) then society must certainly listen to the psychiatrists themselves, who are the people entrusted by society to look after, in the best possible manner, our mentally ill. They are the profession who can see what kind of treatment and/or action is justified and what is not. Societies' feelings should not trump, because of fear, over the limited autonomy of mentally ill patients. For this reason alone it is imperative that the all-important field of biomedical and clinical ethics is not left only to legislators and other professionals who are not medical people and certainly cannot share the same encounter with patients.

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[A] French philosopher renowned for his book 'Madness and Civilisation'

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ABBREVIATED PRESCRIBING INFORMATION NAME OF THE MEDICINAL PRODUCT Actonel Plus Ca & D 35 mg film-coated tablets + 1000mg / 880 i.u. effervescent granules. COMPOSITION Each film-coated tablet contains 35 mg risedronate sodium, (equivalent to 32.5 mg risedronic acid). Each sachet of effervescent granules contains 2500 mg calcium carbonate equivalent to 1000 mg calcium and 22 micrograms (880 IU) colecalciferol (vitamin D_3). Indications: Treatment of postmenopausal osteoporosis, to reduce the risk of vertebral fractures and to reduce the risk of hip fractures. Actonel Plus Ca & D is only intended for used in assessed patients for whom the amount of calcium and vitamin D_3 included is considered to provide adequate supplementation. DOSE & ADMINISTRATION Take one Actonel 35mg tablet on the first day followed on the next day by one sachet of effervescent granules daily for 6 days. The 7 day sequence is then repeated each week. The contents of the sachet should be poured into a glass of plain water stirred and drunk immediately once the fizzing has subsided. Children: Safety and efficacy has not been established in children and adolescents.. Contraindications Hypersensitivity to r colecalciferol or to any of the excipients (in particular soya-bean oil); hypocalcaemia; hypercalcaemia; hypercalciuria; diseases and/or conditions (such as prolonged immobilization) associated with hypercalcaemia and/or hypercalciuria; nephrolithiasis; pregnancy and lactation; severe renal impairment (creatinine clearance <30ml/min); hypervitaminosis D. Precautions:Caution should be used in patients who have a history of oesophageal disorders which delay oesophageal transit or emptying (e.g. stricture or achalasia) or who are unable to stay in the upright position for at least 30 minutes after taking the Actonel tabletHypocalcaemia should be treated before starting therapy. Other disturbances of bone and mineral metabolism should be treated at the time of starting therapy. This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product. Foods, drinks (other than plain water) and medicinal products containing polyvalent cations (such as calcium, magnesium, iron and aluminium) may interfere with risedronate. Strict adherence to dosing recommendations is necessary. Osteonecrosis of the jaw has also been reported in patients with osteoporosis receiving oral bisphosphonates. A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors (e.g. cancer, chemotherapy, radiotherapy, corticosteroids, poor oral hygiene). While on treatment, these patients should avoid invasive dental procedures if possible. Limited evidence to support the efficacy of Actonel in very elderly women (>80 years) Vitamin D_3 should be used with caution in patients with impairment of renal function and the effect on calcium and phosphate levels should be monitored. In patients with severe renal insufficiency, vitamin D in the form of colecalciferol is not metabolised normally and another form of vitamin D should be used. During long-term treatment, serum and urinary calcium levels should be followed and renal function should be monitored through measurement of serum creatinine. In case of hypercalcaemia or signs of impaired renal function, treatment with calcium/vitamin D_3 sachets should be discontinued. The dose of vitamin D_3 in the sachets should be considered when prescribing other drugs containing vitamin D. Calcium/vitamin D_3 sachets should be used with caution in patients suffering from sarcoidosis because of the risk of increased metabolism of vitamin D to its active metabolite. In these patients, serum calcium levels and urinary calcium excretion must be monitored. Calcium/vitamin D_3 sachets should be used with caution in immobilised patients with osteoporosis due to the increased risk of hypercalcaemia. The calcium/vitamin D_3 treatment might be discontinued in prolonged immobilization and should only be resumed once the patient becomes mobile again. This medicinal product contains sorbitol and sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicinal product. Interaction with other medicinal products and other forms of interaction Risedronate sodium: No formal interaction studies have been performed with risedronate sodium, however no clinically relevant interactions with other medicinal products were found during clinical trials. 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The following additional adverse reactions have been reported during post-marketing use (frequency unknown): osteonecrosis of the jaw iritis, uveitis, hypersensitivity and skin reactions, including angioedema, generalised rash, and bullous skin reactions, some severe. Pruritus, rash and urticaria Muskuloskeletal and connective tissues disorders:. MARKETING AUTHORISATION HOLDER Sanofi-Aventis Malta Ltd., Triq Kan. K. Pirotta, B'Kara. BKR 1114 Malta. MARKETING AUTHORISATION NUMBER MA082/00105 For further information please contact Sanofi-aventis Malta Tel: 21493022. Reference Number MT-RIS-08-04-02.

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Pharmacy of Your Choice

Change and Innovation in Community Pharmacy – Phased National Implementation of the POYC scheme and Educational Opportunities

by **Mary Ann Sant Fournier** *BPharm MPhil*
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The national implementation of the POYC continues to roll-out with patient registration being extended in a further 10 localities (Pieta, Lija, Balzan, Fleur-de-Lys, B'Kara, Floriana, Valletta, Iklin, Siggiewi and Qormi during the period of 17 March till May 2008). To date, more than 22,500 patients have registered for the scheme in 29 localities.

Patients in Rabat were able to accede to the POYC service at the end of April. This brings the number of patients being served by the pharmacists in the pharmacy of their choice to 2390.

The service was extended gradually during May to Swieqi, St Andrews, Ta' Giorni (which forms part of St Julians), Pembroke, Paceville, Dingli, Bahrija, Mtarfa, Ta' Xbiex and Msida. In June, the rest of the pharmacies in St. Julian's, together with those in Attard, San Gwann and Gzira are expected to start serving registered patients.

During April, several POYC meetings were held. The Standing Advisory Committee met on 10th April with the main item on the agenda being the pressing need to enhance the human resources at the central processing unit.

Two meetings were held at the Professional Centre, Gzira, for pharmacists practicing in the pharmacies, and owners. These consisted of a 'brainstorming' session (10th April), and an information meeting for those pharmacists and owners in localities which were at patient registration or implementation stages of the national roll-out, as explained above (29th April).

With the conclusion of the pilot stage and the introduction of the phased roll-out of the national implementation, several lessons are being learnt, particularly from the pharmacists themselves who have and are experiencing the registration and implementation stages.

Discussions have focused on specific emerging issues, such as the information which should be given by the Department of Health to patients about changes to their entitlement, where there is a perceived clinically unjustifiable usage. This would be an effective supportive tool to the pharmacists' interventions. In this regard, a structured educational campaign using all the communications media possible and targeting the public on the registration and service delivery phases is also envisaged. It is recommended that such a campaign should be designed and implemented on the successful model of the recent Malta Euro Changeover campaign.

Educational initiatives at community pharmacists are in the pipeline. These shall have a strong information communication technology component and will range from the upgrading of computer skills to full e-learning initiatives. Indeed the Chamber is expecting the outcome of a recent application[A] for a grant to the UNESCO Participation Programme 2008-9 for the implementation of a project on "Pharmacy *e*-Learning".

EU Leonardo Project supported training visit to independent pharmacies which are NHS Contractors in the UK

Meanwhile, 6 community pharmacists and a pharmacy owner have already had the unique opportunity to participate in a training visit to independent pharmacies which are NHS contractors in the UK. The visit (5-21 November 2007) was partly supported by the EU Leonardo Projects and was organized by the Malta Chamber of Pharmacists (MCOP) in collaboration with the Pharmacy Section of the Chamber for Small and Medium Enterprises, and with the then Parliamentary Secretary for Small and Medium Enterprises in the Ministry for Competitiveness and Communications.

The visit included a one day training seminar with representatives of the UK National Pharmaceutical Association (NPA) and the Pharmaceutical Services Negotiating Committee (PSNC), with which the MCOP has longstanding professional relations. This was followed by structured visits to independent pharmacies which are NHS contractors in the UK.

The Chamber was supported in the coordination of the visit by Colette McCreedy, Director of Pharmacy Practice, NPA. The NPA training seminar consisted of an intensive meeting with McCreedy, who was accompanied by Raj Patel (the NPAs new EU representative), a member of the NPA Board of Management, and a key member of the PSNCs Negotiating Committee. The PSNC represents community pharmacy on NHS matters.

The Chamber delegation presented and explained the principles and provisions of the Memorandum of Understanding (2007) and the new Pharmacy regulations and the POYC scheme, giving a picture of the realities and vision for community pharmacy in Malta. The delegates had the opportunity to participate proactively.

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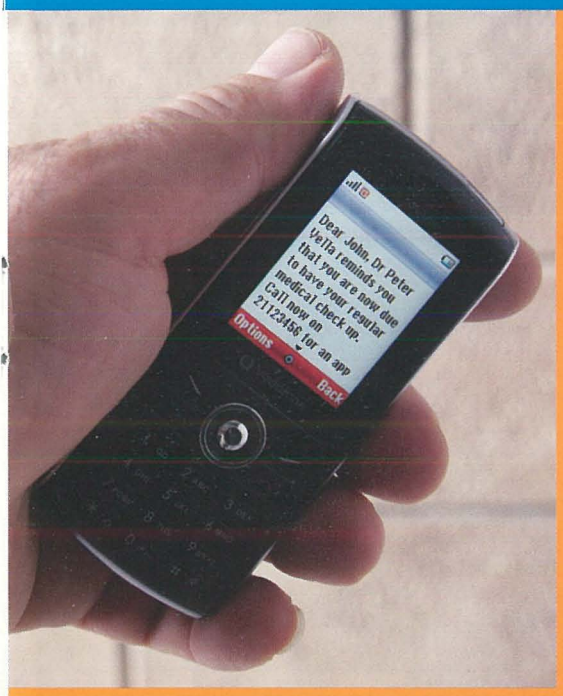

New SMS4Health facilities launched

Developers at SMS4Health have recently announced the launch of new facilities for this innovative service. These facilities enable a broader range of professionals to use the recall facilities provided. SMS4Health facilities can now be provided to family doctors as well as paediatricians, gynaecologists, dentists, radiology clinics, laboratories as well as hospitals.

The very large mobile penetration in Malta makes it an ideal vehicle for medical professionals to remind their patients when they are due for some health intervention or repeat investigation, through their mobile phones. Users of the system note a very high response rate when compared to paper based recalls.

SMS4Health software is very easy and intuitive to use. Once the patient data is entered into the software, the whole process is fully automated according to pre-determined protocols. Patients receive a personalized reminder message on behalf of their medical services provider on their mobile phone.

Commenting on the launch of this service, Dr Wilfred Galea stated that *"This is another tool which helps medical professionals provide a better service to their patients. It is a well known fact that patients appreciate when their doctor is proactive and takes the opportunity to remind them when they are due for their tests or interventions. SMS4Health is proving to be particularly useful in ensuring that patients remember to comply with doctors' advice. We are all aware that when disease is managed at an early stage, this leads to less mortality and morbidity. SMS4Health bridges the communication gap between doctors and patients by offering an efficient recall tool."*

Launched in 2007, SMS4Health has three main functions:

- **SMS4Health Remind** where subscribers receive health recalls based on advice given by their doctor. Presently there are over 45 different templates that can be used ranging from childhood vaccinations, well-person checks, cervical smears as well as chronic disease follow-up.

- Another facility is **SMS4Health Inform** where subscribers receive regular health tips and is a very useful health promotion tool.

- **SMS4Health Alert** is another service whereby subscribers can be informed immediately should there be some item of information that is urgent and important such as a drug withdrawal or some similarly important news.

All health professionals may provide SMS4Health services from their practice. Medical professionals interested in introducing SMS4Health services in their practice are invited to contact Medical Portals Ltd by email admin@sms4health.com or telephone 21453973.

Health News

Vitamin supplements - more harmful than healthy?

Dr Joanne Lunn

Senior Nutrition Scientist at the British Nutrition Foundation

Taking vitamin pills may not prolong your life, and some may even increase your risk of dying early, according to a new review of the evidence. To investigate this, authors from the Cochrane Collaboration (an independent not-for-profit organisation) reviewed the current evidence on the effect of antioxidant vitamin supplements on death rates.

They analysed 67 high quality studies looking at vitamin supplements and number of deaths. The analysis found no evidence to support the use of vitamin supplements, either by healthy people or those with an illness. Vitamin supplements didn't seem to decrease the number of deaths. Some supplements - vitamins A, E and beta carotene - even seemed to increase death rates. The findings for vitamin C and selenium were not conclusive.

From an initial search of the evidence, they found a large number of research studies looking at vitamin supplements. They narrowed their search to include only studies on vitamin supplements and death rates. The 67 studies included a total of 232,550 people, both healthy people and those with an illness. They compared antioxidant vitamin supplements, placebo (dummy) pills or taking no supplements at all on the number of deaths in these people.

Dr Joanne Lunn, Senior Nutrition Scientist at the British Nutrition Foundation said: "This review has assessed all the relevant studies and has concluded that people who take these supplements don't live longer lives. By eating a healthy balanced diet with plenty of fruit and vegetable you will be able to get all the vitamins and minerals you need. Your body will only absorb the vitamins it needs and will excrete anything extra. By taking high doses of individual vitamins, you may end up just producing very expensive urine."

The authors say that more research is needed to look at the effects of vitamin C and selenium, and the effects of vitamin treatments taken by groups of patients who are specifically prescribed them.

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I need a pain reliever that's less likely to affect my asthma

- A systematic review in the British Medical Journal has determined that up to 21% of adult asthmatics are sensitive to aspirin.[1]
- It is widely recognised that asthmatics who are sensitive to aspirin are also highly crosssensitive to other non-steroidal anti-inflammatory drugs (NSAIDs), including ibuprofen, naproxen sodium and diclofenac.[1]
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[†]Less than 2% of asthmatics are cross-sensitive to paracetamol, but reactions tend to be less severe[1,4] and of shorter duration.[6]

References: 1. Jenkins C et al. BMJ 2004. Vol. 328; Issue 7437. 2. Szczeklik A et al. Am J Ther 2002;9:233-43 3. MIMS Panadol Prescribing Information. 2003. 4. Jenkins C. Am J Ther 2000; 7:55-61. 5. Lamb C et al. The Pharmaceutical Journal 1995;254:802-4. 6. Settipane RA et al. J Allergy Clin Immunol 1995;96:480-5.

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Pharmacy of Your Choice

Change and Innovation in Community Pharmacy – Phased National Implementation of the POYC scheme and Educational Opportunities

continued from page 12

McCreedy gave a presentation[B] on community pharmacy in the UK, which essentially addressed the pharmaceutical demographic and regulatory background, together with the new NHS contract (2005).

The local management of the NHS in the UK is undertaken by 10 Strategic Health Authorities and 152 Primary Care Trusts (PCTs), with each PCT serving on average 350,000 people (approximately Malta's total population) though the geographical size varies considerably. There is an average of 70 pharmacies within each PCT area. The higher accessibility of patients to pharmacists' services in Malta is immediately evident when the demographic ratios are compared (Malta – 400,000 population: 209 pharmacies i.e., approx 1914:1). There are an average of 40 GP clinics within each PCT area.

The new NHS pharmacy contract was introduced in 2005. It was expected to bring about a fundamental change in community pharmacy practice with more focus on quality and less focus on prescription volume. The new contract framework is represented by Essential, Advanced (which include medicines use review (MUR)), and Enhanced services.

The NPA considers the following as challenges faced by pharmacists in the UK: the uncertainty about pharmacy opening legislation; the difficulty to achieve the MUR targets; and NHS reforms are making it difficult for local health economies to commission enhanced services.

New opportunities include the increasing recognition by the Government of the value of the community pharmacy services and the emerging roles for pharmacists in prescribing, public health and as special interest practitioners. And there is a high level of public confidence in the community pharmacy service.

On-site experience of the implementation of the above was later possible for the Maltese delegation through the visits to several pharmacies, chosen for logistical reasons in or close to London. A visit to a large single-owner pharmacy, incidentally managed by a Maltese colleague, situated in central London offered the right 'control' in that its practice and financing does not depend on NHS prescriptions; in fact, this does not reflect the rest of UK, where in the majority, 80% of practice and pharmacy financing is NHS centred. The other independent pharmacies which were visited were single-owner and situated in South-West and West London, in Hertfordshire and Bedfordshire respectively. The delegation could thus see the different levels of development of services to patients and of IT applications.

Importantly, the Maltese contract was considered by our UK counterparts as "unique and forward-looking" in that service payment is patient based and not related to the number of items dispensed or prescription volume. The immediate computerization of the scheme introducing patient mediation records at pilot stage was also commended.

This was a unique opportunity to gain an insight, observe and learn from and exchange views with community pharmacists delivering an NHS service in the UK. Other opportunities in other EU countries will be announced shortly.

[A] '*Pharmacy e-Learning - The setting up, implementation, evaluation and accreditation of an On-Line Continuing Professional Development Programme for Pharmacists*' Grant Application to the UNESCO Participation Programme 2008-9. Archives of the Malta Chamber of Pharmacists. 2008.

[B] McCreedy Colette. *Community Pharmacy in the UK.* Presentation to the Malta Chamber of Pharmacists and the Chamber for Small and Medium Enterprises. National Pharmaceutical Association, United Kingdom. Archives of the Malta Chamber of Pharmacists. 2007.

Ancient Egyptian Medicine

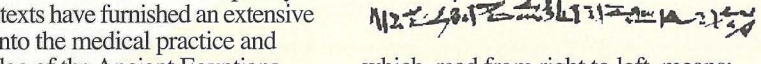
Part IV [2] – Medical Papyri

continued from page 8

The Carlsberg Papyrus is the property of the Carlsberg Foundation and is housed in the Egyptological Institute of the University of Copenhagen. Its style dates it to the 19th/20th Dynasties. It deals mainly with eye disease and pregnancy; and bears similarities to the Kahun and Berlin papyri.

The Brooklyn Papyrus is housed in the Brooklyn Museum. The style relates this to the Ebers Papyrus and has been dated to the 30th Dynasty or Early Ptolemic Period. It discusses various remedies to drive out the poison from snakes, scorpions and tarantulas.

The above-mentioned contemporary medical texts have furnished an extensive insight into the medical practice and knowledge of the Ancient Egyptians. Other textual information has also been gleaned from inscribed text found on sculptured reliefs and on pieces of pottery and ostraca, particularly from those dating from the Amarna Period to the time of Roman occupation. An example of such fragmentary textual sources is a little pink pot bears the following hieratic inscription:



which, read from right to left, means: "*Saw dust, acacia leaves, galena, goose fat. Bandage with it.*"

Prediction of falls among the elderly at risk – Part II

by **Melanie Ng** *BSc Physiotherapy, SRP Physiotherapist*

Further investigation

Further investigation entails a close examination by a specialist to reassess and review medications, such as supplementation of Vitamin D, and psychotropic or anxiolytic medications, as well as carry out necessary tests to rule out any chronic medical conditions that may be contributing to the occurrence of falls. However one must not forget to asses and look closely to the physical conditions that may be further contributing to this scenario, with the help of a physiotherapist.

A specific physiological assessment needs to be carried out. This will provide the physiotherapist with objective measures indicating the changes in vision secondary to cataracts or diabetic neuropathy, proprioception, reaction time, postural sway (balance) and muscle strength which may also be playing a major role. According to Lord et al[1] these 5 physiological components are the main factors that cause falls among the elderly.

This assessment provides the physiotherapist with the following tools:

- An indication of the individual's overall falls risk score
- An indication of the individual's test performance in relation to age matched norms (Figure 1)
- A profile of the individual's test performance with clear indication of the physiological strengths and weaknesses.

This allows for effective and efficient intervention on a physical level.

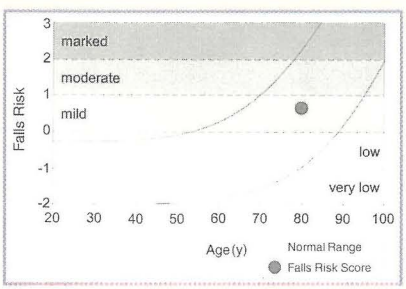


Figure 1. A patient's test performance in relation to age matched norms
Source: http://www.ptjournal.org/cgi/reprint/83/3/237

Interventions

Assessment is also valuable to determine what sort of intervention is deemed most appropriate for each patient. Furthermore the clinician must realize that different risk factors exist for different populations.

Hospital In-patients and Nursing Home Residents

Risk factors within such different environments are very different to those of the community dweller. Acute illness and a new environment are among some of the risk factors that are unique to these settings. The intervention which is deemed effective would be entirely different to that of a community dweller, example, more staff supervision, alarm calls, door magnets, more lighting, cubicle ergonomics, etc. Individuals suffering from dementia are also a risk population. This latter population is cognitively and physically frailer and therefore appropriate intervention may include the use of hip protectors.

The physiological assessment may be still used for individuals who may show signs of dementia. Therapists in the UK use the assessment to determine whether the patient is able to follow through, and from their performance determine the best intervention for the patient.

However the role of exercise as a means of reducing falls has been clearly stated in various studies.[2] Walking as an exercise implementation to counteract falls, is not beneficial but rather places the individual more at risk of sustaining a fall. In fact falls in balance impaired individuals occur during walking and simultaneously performing a secondary task.[3] Specific validated exercises focusing on balance and muscle strength of lower limbs have been found to minimize falls, and only then may be followed by a walking program.[4]

Falls Prevention Program which encourages behavioral changes to minimize the risk of falls is also beneficial. These programs are currently being set up in various hospitals and day centers in Australia and UK to meet this demand. I personally had the pleasure to set one of these programs up whilst working at the Prince of Wales Hospital in Sydney in 2006.

Locally, the Live Life Wellness Centre for Active Adults, is currently running varied sorts of exercise classes to promote active aging amongst our older population. Clients ranging up to 88 years of age are engaging in water and land activities focusing on balance and strength, as well as Pilates to promote back and abdominal strength. Live Life has recently also started organizing monthly walking groups for those who fear outdoor mobility. The aim is to encourage outdoor mobility, whilst socializing in a safe environment with supervision and promoting quality of life. Falls Risk assessments are carried out and there are plans for the near future to set up educational falls prevention programs, that will go hand in hand with the already running strength and balance exercise classes on land and in water.

There is a need for all health providers to increase local awareness on the importance of preventing falls and to change mind-sets that falls are inevitable at this age, by implementing behavioral changes.

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- Most adverse events were transient and mild to moderate[1,2]
- Patient-preferred over weekly oral alendronate[3,4]

*Relative to placebo.[1]

**Nonvertebral fracture includes wrist, rib, arm, shoulder, or hip fracture; excludes finger, toe, or craniofacial fracture.[1]

Aclasta 5 mg Solution for Infusion BSS

PRESENTATION: Zoledronic acid. 100 mL solution bottle contains 5 mg zoledronic acid (anhydrous), corresponding to 5.330 mg zoledronic acid monohydrate.

INDICATIONS: Treatment of osteoporosis in post-menopausal women at increased risk of fracture. Treatment of Paget's disease of the bone.

DOSAGE AND ADMINISTRATION: Post-menopausal Osteoporosis: A single intravenous infusion of 5 mg Aclasta administered once a year. Paget's Disease: A single intravenous infusion of 5 mg Aclasta. Specific re-treatment data are not available for Paget's disease. Aclasta is administered via a vented infusion line and given at a constant infusion rate. The infusion time must not be less than 15 minutes. Patients must be appropriately hydrated prior to administration of Aclasta, especially important for the elderly and for patients receiving diuretic therapy. Adequate calcium and vitamin D are recommended in association with Aclasta administration. Not recommended for use in patients with severe renal impairment (creatinine clearance <40 ml/min). No dose adjustment in patients with creatinine clearance ≥40 mL/min, or in patients with hepatic impairment, or in elderly patients Aclasta should not be given to children or adolescents.

CONTRAINDICATIONS: Hypersensitivity to zoledronic acid or to any of the excipients or to any bisphosphonate; hypocalcaemia; pregnancy; lactation.

PRECAUTIONS AND WARNINGS: Serum creatinine should be measured before giving Aclasta. Not recommended in patients with creatinine clearance <40 ml/min. Appropriate hydration prior to treatment, especially in the elderly and in combination with diuretics. Use with caution in conjunction with medicinal products that can significantly impact renal function (e.g. aminoglycosides or diuretics that may cause dehydration), Pre-existing hypocalcaemia and other disturbances of mineral metabolism must be treated by adequate intake of calcium and vitamin D before initiating therapy with Aclasta. It is strongly advised that patients with Paget's disease receive supplemental calcium and vitamin D. Measurement of serum calcium before infusion is recommended for patients with Paget's disease. Severe and occasionally incapacitating bone, joint and/or muscle pain have been infrequently reported with bisphosphonate therapy. A patient being treated with Zometa should not be treated with Aclasta. As a precaution against osteonecrosis of the jaw (ONJ) a dental examination with appropriate preventive dentistry should be considered prior to treatment in patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids, poor oral hygiene). While on treatment, these patients should avoid invasive dental procedures if possible. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk of osteonecrosis of the jaw.

INTERACTIONS: Specific drug-drug interaction studies have not been conducted with zoledronic acid. Caution is recommended when Aclasta is used concomitantly with drugs that can significantly impact renal function, such as aminoglycosides and diuretics that can cause dehydration.

ADVERSE REACTIONS: The incidence of post-dose symptoms (e.g. fever, myalgia, flu-like symptoms, arthralgia and headache) are greatest with the first infusion and decrease markedly with subsequent infusions. The majority of these symptoms occur within the first three days and were mild to moderate and resolved within three days of the event onset. The incidence of post-dose symptoms can be reduced with the administration of paracetamol or ibuprofen shortly following Aclasta administration. Very common: Fever Common: Flu-like symptoms, chills, fatigue, pain, asthenia, malaise, arthralgia, myalgia, bone pain, back pain, pain in extremity, diarrhoea, vomiting, nausea, headache, dizziness, atrial fibrillation, hypocalcaemia†, rigors† . Local reactions: redness, swelling and/or pain Others: renal dysfunction and osteonecrosis of the jaw. † Common in Paget's disease only.

PACK SIZE: Aclasta is supplied in packs containing one 100ml bottle

LEGAL CATEGORY: POM.

MARKETING AUTHORISATION NUMBER: EU/1/05/308/001.

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 VLT 1000, Malta. Tel +356 22983217.

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Update on Avian Influenza

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

Possible human to human transmission in China

An article in *The Lancet*, March 2008 states that a family cluster of confirmed cases of the highly pathogenic avian influenza virus H5N1 was possibly due to human to human transmission. Genetic sequencing confirmed the likelihood that a 24 year old who died of bird flu passed the virus directly to his father who was taking care of him while he was in hospital. The father recovered and was given Oseltamivir, Rimantadine as well as a serum from a woman who was inoculated with an experimental H5N1 vaccine.

According to WHO, the H5N1 virus has already killed 234 people out of 376 in 12 countries. since 2003. Most were due to direct infection by sick birds but in a few rare cases it appears that there was human to human transmission. This occurred among genetically related persons.

Factors favouring the continuous reoccurrence of the H5NI virus

Statistical risk modelling was carried out in Thailand and Vietnam to analyse the statistical association between the presence of H5N1 virus and 5 key environmental variables comprising altitude, human population, chicken numbers, duck numbers and rice cropping intensity, and consistent patterns emerged suggesting that the risk is associated with duck abundance, human population and rice cropping intensity.

Avian influenza H5N1 virus in mosquitoes collected from a Thai poultry farm

A paper published in last March's issue of *Vector-borne and Zoonotic Diseases* showed that mosquitoes collected from a poultry farm during an outbreak of H5N1, tested positive for the virus using Reverse Transcriptase-PCR.

Arthropod vectors were never previously implicated in the epidemiology and transmission of avian influenza viruses and this now leaves open the question whether the virus surviving in the insect vector will be competent in vertebrate cells and in a form that may be infectious to live susceptible poultry and/or mammals.

International symposium reports on the use of antivirals in patients with H5N1

Physicians' reports during last March's International Symposium on Respiratory Viral Infections in Singapore, support the approval of Tamiflu for both treatment and post exposure prevention of influenza in adults and children over 1 year of age. However the magnitude of effect of Tamiflu in treating and preventing novel strains of influenza cannot be predicted as it has not been studied.

The WHO has recommended that higher doses and longer treatment durations may be required to combat novel strains of influenza. In the most recent clinical management guidelines issued by the WHO, Tamiflu remains the primary antiviral agent of choice for the treatment of H5N1 virus infections.

Interesting Symposium findings

In Indonesia, out of 119 reported H5N1 human cases, 22 survived - an 18% survival rate. Of the 119 cases, 33 patients received no Tamiflu, all of whom died. Tamiflu was administered to the other 86 patients, with a 26% survival rate. Time from onset of illness to initiation of treatment appeared to influence survival. The 2 patients who received Tamiflu within 24 hours of illness onset survived.

When the drug was given within 4 days, 55% survived, and 35% survived when given Tamiflu within 6 days. The survival rate of those receiving it later than 6 days after illness onset was 18%.

Information about 8 Vietnamese patients infected with H5N1 was also presented. All 8 patients received Tamiflu, but all of them were admitted to hospital later than 5 days after onset of illness. Only 3 of the 8 patients survived, reinforcing the hypothesis that treatment benefit is reduced for patients that receive the drug later in the course of illness. In 2 patients who were unable to take the drug orally due to the severity of their illness, physicians administered the drug by nasogastric tube and found that it was well absorbed and there was a reduction in the patients' viral load.

Susceptibility of circulating H5N1 strains to Tamiflu

Clinical findings supported by animal data, also presented at the symposium, showed that oseltamivir treatment was effective against H5N1 influenza viruses representing different clades/subclades.

Data also confirmed the low level of resistance reported to date with Tamiflu to H5N1, as there were only 5 cases of published reports of H5N1 resistance or reduced susceptibility.

This compares to the 14% of the seasonal influenza A H1N1 virus isolates tested this year showing resistance to Tamiflu. It is important to note that these increased levels of resistance have only been reported in this year's H1N1 (Solomon Islands) seasonal strain and not in patients infected with H5N1 who were administered Tamiflu.

Complete change of flu vaccine strains for the northern Hemisphere

This is the first time in 20 years that the trivalent vaccine will be completely changed in a single year for 2008-2009 Northern hemisphere season. The current H3N2 will be changed to the Brisbance/10 strain currently circulating in the USA. Nevertheless, manufacturers are concerned that with 3 new strains, delays will occur, hindering the delivery of the vaccine in time for the start of the season.

US panel recommends wider paediatric use of influenza vaccines

The US Centre for Disease Control and Prevention's Advisory Committee on Immunization Practices has recommended that current immunization guidelines should be extended to include all children aged 18 months to 18 years. The panel recommends that this measure should be adopted as soon as possible.

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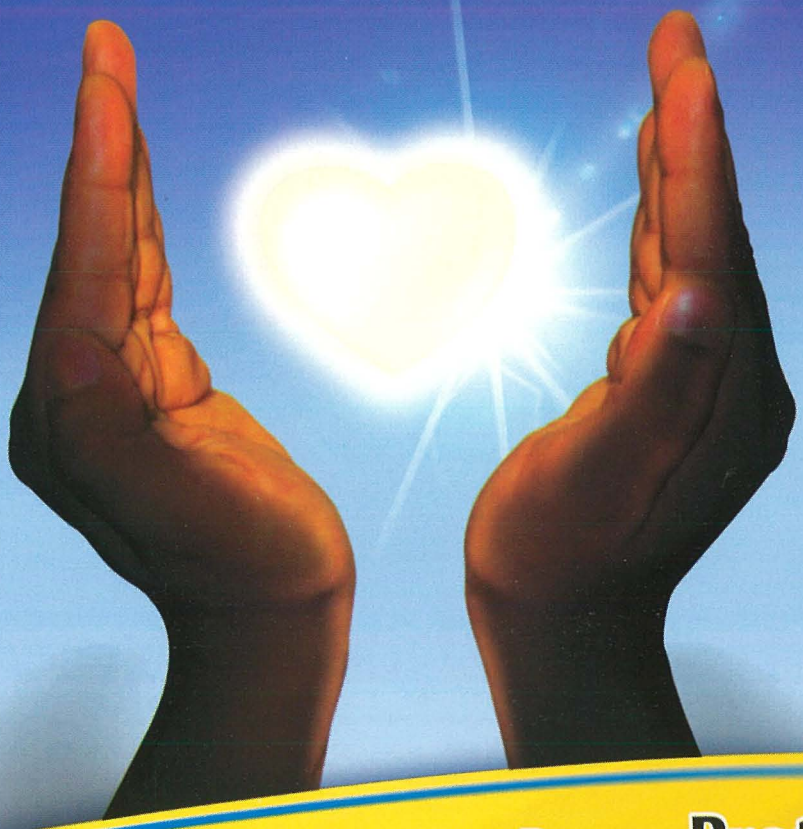

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More than Skin Deep

by **Marika Azzopardi**

I meet Professor Joseph Pace in between appointments, as he grabs time to talk to me, whilst eyeing a packed sandwich and drinking some coffee. Patients are waiting outside and he admits he is working too hard but only due to unusual circumstances. Specialised in Dermatology and Venerology, and the Foundation Chair of the Dermatology and Venereology Department at Boffa Hospital, he is presently Secretary-General of the European Academy of Dermatology & Venereology (EADV), whose appointment spans from 2004 through to 2010.

"EADV is a society that represents specialists throughout the geographical borders of Europe. Founded in 1988, its raison d'etre is to promote and make widely available excellence in continuing medical education in the specialty, and to endeavour to be the foremost advocate of patients with skin disorders. It is registered in Lugano but works mainly from its headquarters in Brussels which means it is easier to lobby the EU towards better recognition of crucial problems such as the increasing skin cancer incidence including the dreaded melanoma as well as equity of care for patients within Europe both regarding quality as well as access. Although travelling to the various meetings occurs regularly, these coming weeks will be exceptional, with six times in seven weeks! EADV meetings, the annual Spring Symposium due in Istanbul this year, and several important lecturing commitments have come together with a vengeance that makes even me wonder whether it is *slightly* too much. However with the backup of our wonderful staff in Malta and Brussels, lots of hard work, and a love of the job, we appear to pull through fairly successfully and ... start planning for our Congresses in 2011 and 2012 shortly."

At an EADV board meeting

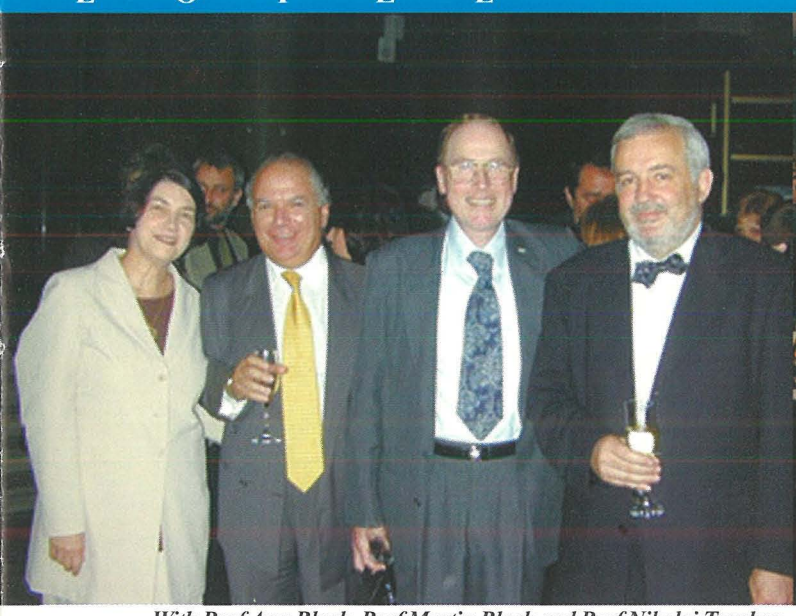
Lecturing in Sydney

But what does the post really involve apart from much travelling? The Academy looks into the standards of treatment and quality of care of skin disease patients within Europe as a geographical entity irrespective of EU membership. It strives to support specialists by providing regularly updated CME opportunities and guidelines of care. Our fast growing specialty has seen us move, within a very short time, from prescribing with serendipity to targeted medication resulting from huge advances in molecular biology. To this end we have two large annual academic events, one for 1,500 and one for 10,000 people. These are more successful than ever but have seen the need to go from the early DIY effort by doctors to a smoothly organised and professionally run event that is the envy of even larger Congresses outside Europe.

Apart from the Congresses, EADV also works on a very important programme entitled 'Fostering Dermatology'. This is mostly aimed at younger specialists and is funded to a level of €500,000 annually. In addition, the Journal of EADV, its EADV news, and its web site www.eadv.org all form important cogs in the effort to keep doctors up to date.

Prof Pace believes that Dermatology Research does not stop merely at treating skin diseases but also involves studying the quality of life of patients with these diseases. Prof Pace insists that skin disease can be as disruptive to a person's life as more serious diseases such as asthma or diabetes. In addition, most skin diseases are manifested for all to see and cannot be easily hidden away with resultant psychological effects on patients and their families.

As the founder and Honorary President of the Psoriasis Association of Malta, he is particularly keen and excited to point out the recent arrival of remarkable new psoriasis treatments (Biologic drugs), which could fulfil much-awaited hopes for psoriasis sufferers. "Unfortunately, treatment is still very expensive, costing in some cases close to €10,000 per annum per person. This sounds like plenty of money which it is, but when weighing the costs of providing this medication, the indirect costs of NOT



With Prof Ann Black, Prof Martin Black and Prof Nikolai Tsankov at an international meeting

Meeting His Majesty the King of Sweden when President of the World Medical Association

supplying it must also be underlined – society must financially sustain an adult sufferer and his family when he is obliged to quit a job, receive social security allowances, and not pay social security contributions and income tax. Furthermore, one should also consider other indirect effects such as when a spouse gives up work to look after the patient, resulting in similar financial results as above. Where scientific assessment has been carried out by respected academic institutions, the results have tended to favour supporting the expensive medication even on strict economic grounds alone!

Prof Pace has been active in public life with Past Presidency of the Medical Association of Malta, Past Presidency of the World Medical Association, and Chairman of the Foundation for Medical Services in Malta. He is Clinical Professor of Dermatology at the Jefferson Medical College of Thomas Jefferson University in Philadelphia and holds Honorary Memberships in several national Dermatological Societies. He has won the Saudi Medical Journal Gold Medal Prize for original Research, and was awarded the Certificate of Merit by the International League of Dermatological societies and the Avicenna medal by the Tunisian Medical Association for his contribution to Medicine.

At home Prof Pace is an ardent football fan of Juventus remembering with a smile his 50th Birthday when Juventus beat Ajax Amsterdam in Rome to win the European Cup and with much sadness the Heysel disaster in 1985 when he was also present.

Prof Pace has promised himself that the EADV position will close his public service and that come 2010 he will dedicate himself to his patients and his family in particular his grandchildren Luisa and Sam, and his superlatively understanding wife MaryAnn. Travel with friends to so many wonderful parts of the world not yet visited will be high on the agenda, as will learning Spanish and researching medical manuscripts of the physicians of the Order of Malta in relation to Dermatology!

At least those are the good intentions in May 2008...

The 4 Secretary-General of EADV to date

continued from page 3

Imaging Pyelon

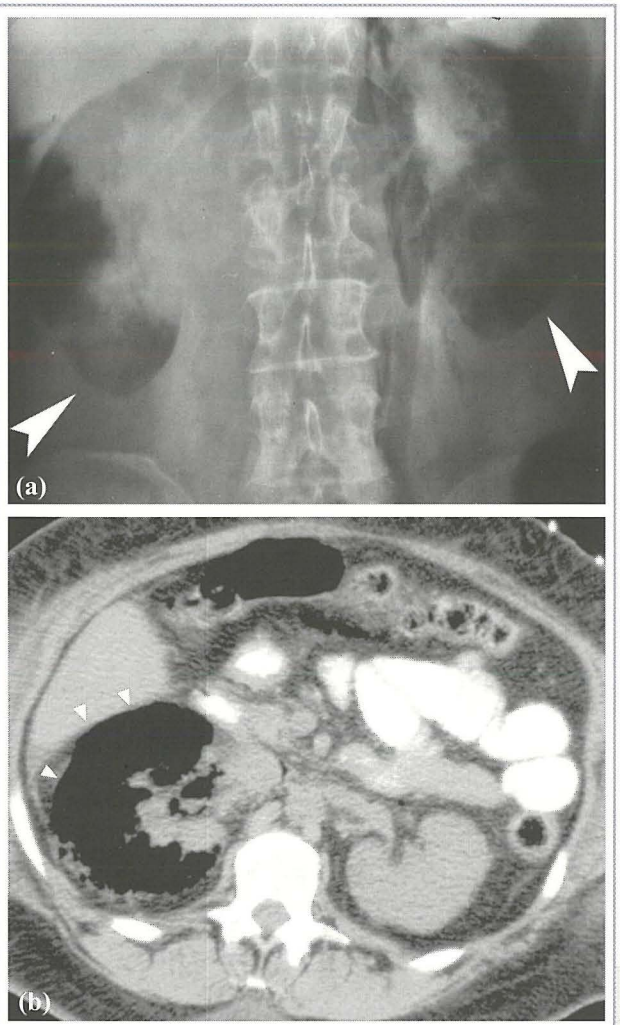


Figure 6. *(a) Emphysematous pyelonephritis seen on plain abdominal X-ray showing lucent air that outlines both kidneys (arrowheads). (b) Unenhanced CT showing gas bubbles (arrowheads) replacing the right kidney.*

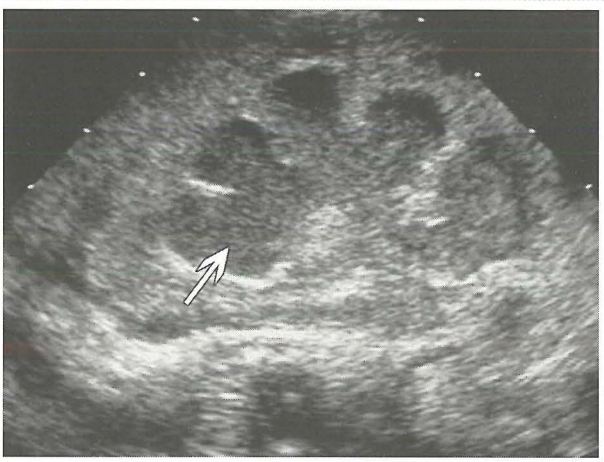


Figure 7. *Pyonephrosis on ultrasound showing a dilated collecting system that is filled with echogenic debris (arrow) in a patient with fever and flank pain*

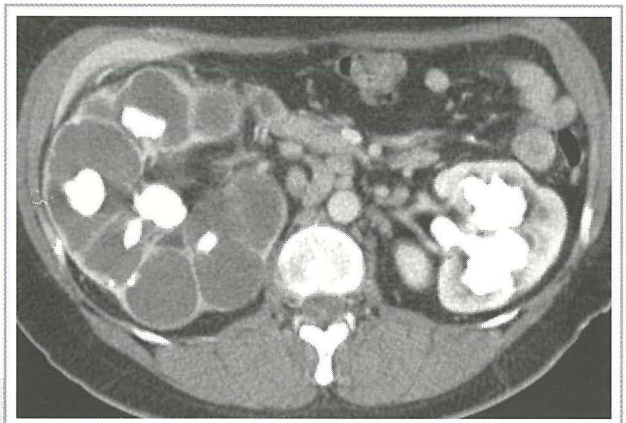


Figure 8. *Xanthogranulomatous pyelonephritis on contrast-enhanced CT with bilateral staghorn calculi, with distension of the right collecting system secondary to inflammatory debris.*

Emphysematous pyelonephritis is a life-threatening necrotizing infection of the kidneys characterized by gas formation within or surrounding the kidneys (figure 6). The majority (approximately 90%) of patients have poorly controlled diabetes.

Nondiabetic patients are typically either immunocompromised or have associated urinary tract obstruction secondary to stones, a neoplasm, or a sloughed papilla. The most commonly identified organisms are *E coli, Klebsiella,* and *Proteus mirabilis*. Without early therapeutic intervention, the condition rapidly progresses to fulminant sepsis, and carries a high mortality rate.

Emphysematous pyelitis is a less aggressive form of emphysematous infection of the upper urinary tract and is diagnosed when gas is localized to the renal collecting system (ie the ureter or renal pelvis). It is more common in women and is also associated with diabetes and urinary tract obstruction.

Pyonephrosis is simply an infected and obstructed collecting system, which frequently is be the result of calculi, tumors, complications from pyelonephritis (sloughed papilla), or strictures (figure 7). Early diagnosis is crucial because direct, immediate intervention is required with ultrasound guided nephrostomy to drain the obstructed renal pelvis and prevent decline in renal function and septic shock. Pyonephrosis should be suspected in any patient with a dilated renal collecting system and accompanying fever and flank pain.

Xanthogranulomatous pyelonephritis is a chronic destructive granulomatous process that is believed to result from an atypical, incomplete immune response to subacute bacterial infection. Most patients have no specific risk factors, although diabetes mellitus is seen in approximately 10% of patients. Female patients are more frequently affected than male patients in a ratio of 2:1, and the disease most commonly occurs in middle age. Symptoms are often nonspecific (low-grade fever and malaise), but flank

ephritis - Part II

pain and hematuria may help indicate a urinary tract problem. Pyuria and positive urine cultures are also frequently present.

In xanthogranulomatous pyelonephritis the renal parenchyma is ultimately replaced with lipid-laden (foamy) macrophages. Most cases occur in association with a renal pelvic calculus, and, consequently, hydronephrosis is thought to be a contributing factor. Ultimately, however, the loss of renal function and the destruction of the renal parenchyma are based on severe diffuse inflammation rather than obstruction. The most common organisms implicated are *P mirabilis* and *E coli*, but a variety of other bacteria may be found. The reason why in a small fraction of patients urinary tract infection progresses to xanthogranulomatous pyelonephritis is unknown. Without cross-sectional imaging, xanthogranulomatous pyelonephritis is difficult to detect. On plain X-rays, a large staghorn calculus may be seen, however this is not specific. Following contrast material injection, in an IVU, the affected kidney would show poor or no function which is also not specific. Ultrasound shows a dilated collecting system and calculi, which may be present in the absence of xanthogranulomatous pyelonephritis. CT contributes specific features that are diagnostic of this disease (figure 8); the affected kidney is enlarged, contains a large staghorn calculus and a collecting system distended with low attenuation material, which may have fat (rather than fluid) density. There is usually no renal parenchymal enhancement or function.

The increasing prevalence of tuberculosis in developed countries is well established and at least partly arises from both the spread of human immunodeficiency viral (HIV) infection and the continued emergence of mycobacterial strains with resistance to standard antibiotic therapy. The most common extrapulmonary site of tuberculosis is the urinary tract, with almost all cases resulting from hematogenous seeding. Despite the presumed route of spread from the lungs to the kidney, less than 50% of patients in whom urinary tract tuberculosis is ultimately diagnosed have abnormal results from chest radiography. Symptoms are often nonspecific (low-grade fever, malaise, or weakness). Hematuria and culture-negative pyuria may be seen at urinalysis.

After the tubercle bacilli reach the kidney, granulomas form and remain indolent for many years. If reactivation occurs, the infection spreads into the medulla, with direct involvement of the papillae. Further extension to the collecting system, with the potential for fibrosis, often occurs. Patients with untreated renal tuberculosis may totally lose renal function, and the disease may extend across retroperitoneal fascial planes to involve adjacent organs including the colon.

Imaging findings of renal tuberculosis result from the combination of papillary necrosis and parenchymal destruction. The latter typically involves the papillae initially, but cortical damage soon follows. The collecting system demonstrates thickening, ulceration, and fibrosis (often with stricture formation). The collecting system is distorted dilated calyces, strictures, sloughed or absent papillae and cavity formation, which arises from parenchymal necrosis, that may communicate with the collecting system (figure 9). In late stages, the whole kidney and ureter may be calcified.

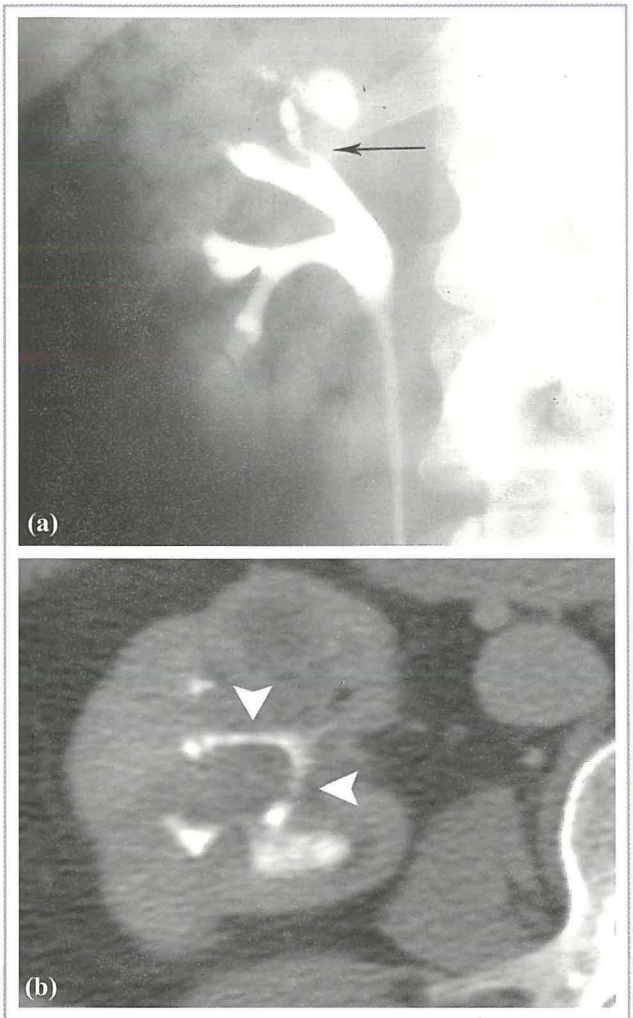


Figure 9. *(a) Retrograde pyelogram in renal tuberculosis shows stenosis of the upper pole calyx (arrow) with associated papillary necrosis. The adjacent calyx is fibrotic and distorted. (b) Contrast-enhanced CT scan shows dilated calyces and narrowing of the infundibula (arrowheads).*

This article has shortly reviewed uncomplicated pyelonephritis, which accounts for most cases of pyelonephritis. Complicated and less common forms of pyelonephritis have also been discussed. The importance of clinical data and frequently percutaneous imaging guided biopsy when interpreting CT images cannot be overstressed.

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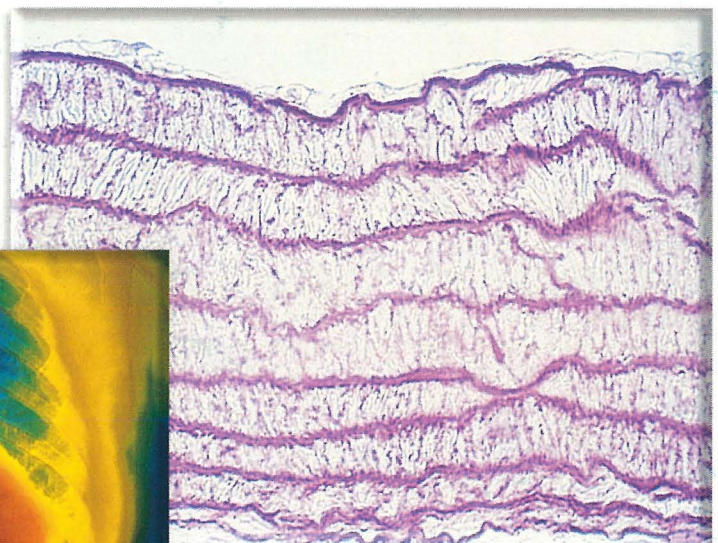
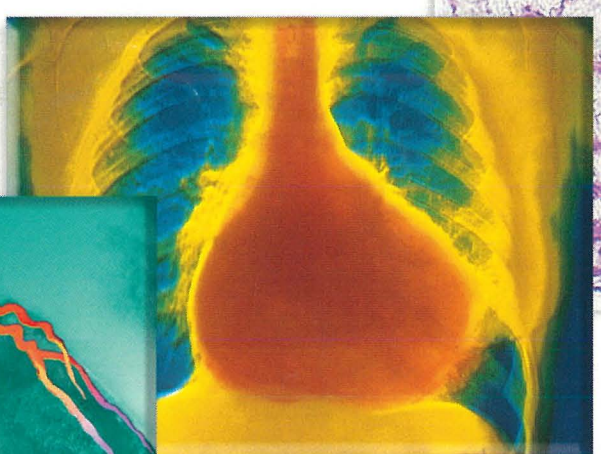
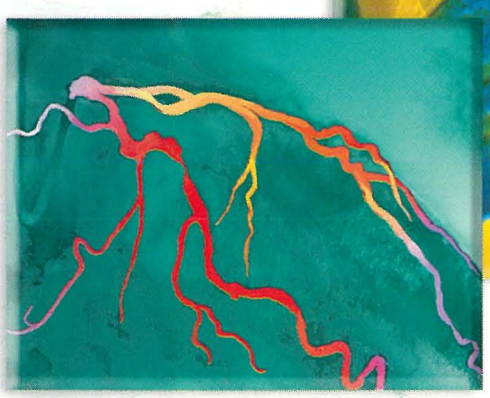


Hypertension [1,2]



Heart failure [3,4]



Stable coronary artery disease [5]

New indication

Stable coronary artery disease: reduction in risk of cardiac events in patients with history of myocardial infarction and/or revascularization

Coversyl is a long-acting ACE inhibitor. **International nonproprietary name:** Perindopril. **Indications:** Essential hypertension. Stable coronary artery disease: reduction in risk of cardiac events in patients with a history of myocardial infarction and/or revascularization. Treatment of symptomatic heart failure. **Dosage and administration:** Coversyl should be taken in the morning before food. **Hypertension:** 5 mg once daily then the dose may be increased to 10 mg after 1 month of treatment to improve blood pressure control or in case of concomitant stable coronary artery disease. **Stable coronary artery disease:** A starting dose of 5 mg for 2 weeks is recommended, then uptitration to 10 mg once daily, depending on acceptability. **Congestive heart failure:** Coversyl should be started under close medical supervision at a starting dose of 2.5 mg. This may be increased to 5 mg once blood pressure acceptability has been demonstrated. Elderly patients: start treatment at 2.5 mg daily. **Contraindications:** Children. Pregnancy. Lactation. Patients with a history of hypersensitivity to Coversyl. **Precautions:** Assess renal function before and during treatment where appropriate. Renovascular hypertension. Surgery/anesthesia. Renal failure: the dose should be cautiously adjusted in accordance with the creatinine clearance (refer to complete data sheet). Symptomatic hypotension is rarely seen, but is more likely in volume-depleted patients, those receiving diuretics, or with the first two doses. In diuretic-treated patients, stop the diuretic 3 days before starting Coversyl. A diuretic may later be given in combination if necessary; potassium-sparing diuretics are not recommended. Combination with neuroleptics or imipramine-type drugs may increase the hypotensive effect. Serum lithium concentrations may rise during lithium therapy. **Side effects:** Rare and mild, usually at the start of treatment. Cough, fatigue, asthenia, headache, disturbances of mood and/or sleep have been reported. Less often, taste impairment, epigastric discomfort, nausea, abdominal pain, and rash. Reversible increases in blood urea and creatinine may be observed. Proteinuria has occurred in some patients. Rarely, angioneurotic edema and decreases in hemoglobin, red cells, and platelets have been reported. **Composition:** Each tablet contains 5 mg or 10 mg of the arginine salt of perindopril. **Presentation:** Canister of 30 tablets of Coversyl 5 mg. Canister of 30 tablets of Coversyl 10 mg. *As prescribing information may vary from country to country, please refer to the complete data sheet supplied in your country.* Les Laboratoires Servier - France. Correspondent: **Servier International,** 22, rue Garnier 92578 Neuilly-sur-Seine Cedex, France. **www.servier.com**

1 tablet daily

Also available under the brand names Aceon®, Acertil®, Armix®, Coverene®, Coverex®, Coversum®, Prestarium®, Prexanil®, Prexum®, Procaptan®

1. Myers MG; Perindopril multicentre dose-response study group. A dose-response study of perindopril in hypertension: effects on blood pressure 6 and 24h after dosing. *Can J Cardiol.* 1996;12:1191-1196. **2.** Morgan T, Anderson A. Clinical efficacy of perindopril in hypertension. *Clin Exp Pharmacol Physiol.* 1992;19:61-65. **3.** Lechat P, Granham SP, Desche P, et al. Efficacy and acceptability of perindopril in mild-to-moderate chronic congestive heart failure. *Am Heart J.* 1993;126:798-806. **4.** Bounhoure JP, Bottineau G, Lechat P, et al. Value of perindopril in the treatment of chronic congestive heart failure: multicentre double-blind placebo-controlled study. *Clin Exp Hypertens.* 1989;A11(suppl 2):575-586. **5.** The EURopean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease Investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomized, double-blind, placebo controlled, multicentre trial (the EUROPA study). *Lancet.* 2003;362:782-788.

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For more information: www.coversyl.com