USA thalassaemia patients celebrate the licensing of the oral chelator deferiprone

The 14th of October 2011 was a truly momentous day for the thalassaemia patients of America. On that day, the U.S. Food and Drug Administration (FDA) approved deferiprone (also known as L1 or Ferriprox) to treat patients with iron overload due to blood transfusions in patients with thalassaemia.

Despite being licensed for use in 61 other countries worldwide, including of course the UK, until now patients in North America and Canada have had to rely on desferrioxamine (Desferal) and, more recently, deferasirox (Exjade) as their only options for chelation. This was despite strong evidence that deferiprone is very effective in removing iron from the heart.

According to information collected by our sister organisation in the USA, the Cooley’s Anemia Foundation (CAF), cardiac disease remains the commonest cause of death among thalassaemia patients in the USA. This is starkly illustrated by an observation of the Thalassaemia International Federation conference in Palermo in 2003. From the USA, 20 adults with thalassaemia attended the conference. Of these 20 only 2 are still alive, the other 18 having all been lost due to cardiac disease. Contrast this situation with the UK, which also had 20 adult thalassaemics attending – of those 20, 18 patients are still alive; and cardiac disease was not a factor in the deaths of the 2 patients who are sadly no longer with us.

At the request of our colleagues at the CAF, UKTS conducted its own campaign in favour of the FDA licensing of deferiprone. Our President wrote to the FDA in his official capacity and we sent out emails encouraging all our members, parents, patients and health professionals to write to the FDA backing the licensing of the drug. We were immensely heartened by the response, as many of you did indeed write to the FDA with your own experiences. Thank you to everyone who took the time to write.

Mr Tony Viola, President of CAF, wrote to us after the decision; “Thank you for the support of the UKTS. We could not have accomplished our goal of allowing our patients the freely available use of deferiprone in our country without it. The thalassemia community is substantially united in the fight to give our patients the best treatment options available.”

Gina Cioffi, the National Executive Director of CAF says; “The Cooley’s Anemia Foundation is thrilled that U.S. patients will now have access to another chelating option. We are so thankful to the UKTS for being our “partner across the pond” and for letting the FDA know about your support and your experiences using Ferriprox. Your friendship is deeply valued by the Foundation and by the U.S. thalassemia community.”

It was UKTS which funded the research into the development of deferiprone when no oral chelators existed; and we are grateful that we can still play our part in working towards improvements in treatment, life expectancy and quality of life for thalassaemia patients.
Dear friends

Back in the 1980s, the life of a thalassaemia patient was fairly grim. Although we had Desferal, undoubtedly a lifesaver for many, there were many more who simply could not face a lifetime inextricably tied to a Desferal pump. In the UKTS office we have archived issues of “Thalassaemia Matters” going back to this time; and they are sobering to read as virtually every issue contains at least one report of someone who was lost to iron overload. The older patients have many sad stories to tell of these years, of how they lost friends and in some cases family members, who simply could not cope with the demands of Desferal treatment. At that time, very few people other than patients and families seemed to see quality of life as a priority. The attitude of many scientists and doctors seemed to be that we should be grateful that we had any treatment at all – you have transfusions, you have Desferal, what do you expect, a normal life????

But we did expect a normal life. And that is why, for almost fifteen years from 1980 onwards the UK Thalassaemia Society worked tirelessly to raise £750,000 which provided the funds to develop the world’s first oral chelator, known in those days as L1. The leaders of this fund raising work were Avraam Demetriou and Phedias Soteriou, who were the joint recipients of the first UKTS award for outstanding contribution to the work of the Society at our conference in Nottingham 2003. We funded the research ourselves because no pharma companies were interested at the time. The money raised by the Society enabled Professor George Kontoghiorges to continue to develop the drug, working under Professor Victor Hoffbrand in his laboratory at the Royal Free Hospital. With the cooperation of clinicians Bernadette Modell and Beatrix Wonke, the Whittington Hospital in North London became a world leader in ground breaking thalassaemia treatment.

Like many of you, I am too young to remember those early, difficult days; or the subsequent tangled story of L1 and why it has taken so long for the USA to license the drug. We who came along later have benefited from many improvements in treatment and most of us enjoy a quality of life that our predecessors could only dream of. It is easy to take what we have for granted; but despite the many challenges we still face, we are indeed fortunate compared to the patients of 30 years ago. As we celebrate with the patients of the USA who now, finally, have access to all three chelating drugs, it is a time to look back and remember what we owe to those early pioneers of treatment, Hoffbrand, Kontoghiorges, Modell and Wonke. At the same time we applaud the patients and members of the UKTS like the indefatigable Demetriou and Soteriou, who dreamed of a better quality of life for thalassaemia patients and worked to achieve it. We who are living and building on their dream will be eternally grateful.

My very best wishes to all of you.

Gabriel Theophanous
President, UK Thalassaemia Society

A word from our President

Our Mission Statement

■ To be the definitive source of information, education and research for those affected by, or working with thalassaemia.

The UKTS Management Committee

President
Gabriel Theophanous

Vice-President
Andy Charalambous

Secretary
George Constantinou

Treasurer
Romaine Maharaj

Assistant Treasurer
Nina Demetriou

Committee Members
Adam Christodoulou
Pany Garibaldinos
Tanya Yucel
The Thalassaemia International Federation is delighted to announce the organisation of the 3rd Pan-European Conference continuing the success of the events of Lisbon (2007) and Berlin (2010). Held under the auspices of the Cyprus Presidency and in close collaboration with the Cyprus Ministry of Health the conference will bring together stakeholders from 27 Member States to discuss avenues of action to tackle the growing public health burden of chronic and rare diseases in Member States and the EU.

The two-day conference aims to:

• Set the scene for the implementation of national prevention and management programmes in all EU Member States
• Address the issue of health inequalities across the EU
• Motivate patients to claim their rights for access to quality healthcare
• Stress the benefits of multidisciplinary care
• Promote active and healthy ageing
• Convey information regarding cardiac, endocrine and liver complications
• Explore the new advancements in the care and cure of haemoglobin disorders and rare anaemias
• Debate on methods of best practice
• Emphasize the importance of patient-centred healthcare systems
• Discuss EU health policies, directives, strategies, programmes as they relate to chronic and rare diseases

Who should attend?

• Patients and Patient Organisations
• Healthcare professionals
• Academics
• Policy-makers at national, regional and EU level
• Industry

A detailed programme and registration/accommodation details will be sent in January 2012.

For further information about TIF, please visit www.thalassaemia.org.cy

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THANK YOU FOR YOUR SUPPORT!
The UK Thalassaemia Society Annual General Meeting took place on 4th October 2011 at the Society’s premises in North London. 22 members were present. As there were only 8 nominees to the Management Committee, no vote took place and all 8 nominees were automatically elected. Lyons Leonidou were re-appointed as Accountants/Auditors. We are grateful to Dr Josu de la Fuente, Consultant Paediatric Haematologist from St Mary’s Hospital/Imperial College for his very interesting presentation on new developments in bone marrow transplantation.

Meet the Committee

Andy Charalambous (Vice President)
Andy is a 52 year old beta thalassaemia major patient. He is a founder member of UKTS and has served on the Management Committee for several terms in the past. Andy has always been a regular attendee at both national and international thalassaemia events and conferences. Andy is a retail shop manager by profession. He is married with a son and daughter. This will be his second consecutive term as Vice-President.

Adam Christodoulou
Adam is a 43 year old beta thalassaemia major patient. His experience as a patient is further informed by the fact that his wife’s family is also affected by thalassaemia major. He has been a life member of UKTS since 1991. I look forward to another year working with the other members of the Management Committee to take the Society forward. Adam is a project manager for a mechanical/electrical company by profession and is married with a son.

George Constantinou (Secretary)
George is a beta thalassaemia major patient. He is a founder member of the UKTS, having served on the Management Committee from 1976-1985 and again from 1999 to the present day. George has been a tireless campaigner on behalf of thalassaemia all his adult life and has conceived and been involved with many UKTS projects including conferences and awareness projects. He was involved in producing the revised version of the UK National Standards for thalassaemia treatment (published October 2008) and with the finance committee of the Society. He has served UKTS in the office of Treasurer in the past, and this will be his second consecutive term as Secretary. George is a hotel manager by profession and is married and has a daughter.

Katerina (Nina) Demetriou (Assistant Treasurer)
Nina has previously served on the UKTS Management Committee for several terms as the Treasurer. She has also been involved in the sub-committees organising conferences and workshops and is always willing to help where possible. Nina’s involvement with the UKTS has included the management of the accounts and she is keen to see that funds received through hard work are used efficiently to meet the objectives of the Society. Nina held the post of Assistant Secretary in 2009/2010. She is a senior finance officer by profession.

Pany Garibaldinos
Pany is a 54 year old beta thalassaemia major patient. He was a founder member of UKTS in 1976 and served on the Management Committee for many terms in the early years of the Society. He is now keen to return to add his experience to the Management Committee. As one of the older patients, he has experienced the progression of thalassaemia treatment from the bare minimum of blood transfusions to the sophisticated treatment regimes of the present day. Pany feels that his experiences will enable him to make a valuable contribution to the work of the Society. Pany is married with a son, and he is a driving test examiner by profession.

Gabriel Theophanous (President)
(In Gabriel’s own words) – I am 39 years old with beta thalassaemia major. I work in accounts and am currently studying towards an ACCA qualification. I would like to be a member of the committee of UKTS because I admire all the hard work the Society has done in the past and would now like to contribute as much as I can. It would be an honour and a privilege to help those less fortunate than myself. Having become close friends with the current Committee members after attending meetings and conferences, I realise just how much I (as well as all that patients) have benefited from the hard work the UKTS has done over the past 30 years so this is an opportunity to give something back. This will be Gabriel’s second consecutive term as UKTS President.

Tanya Yucel
I am 39 years old with beta thalassaemia major. I am a retail Manager and currently working for Clinic. I would like to be a member of the committee of UKTS because I would like to contribute some of my time to this worth while society. I have organised 2 fund raising events and feel that I can bring a lot more to the Society, I feel that I have benefited from the amazing work that the UKTS has done.

Romaine Maharaj (Treasurer)
Romaine’s daughter Roanna is a beta thalassaemia major patient. Prior to moving to the United Kingdom in 2004, Romaine served as the President of the Society of Severe and Inherited Blood Disorders, Trinidad and Tobago, one of the founding members of TIF. She was attached as a Patient Advocate with ApoPharma for a year. She was also the Head of a mortgage division for one of the major banks in the Caribbean, her financial background spanning a period of twenty-three years. Currently she is working as an Assistant Attaché at the Trinidad and Tobago High Commission, London. This will be her first term as UKTS Treasurer.
The All Party Parliamentary Group (APPG) on Sickle Cell and Thalassaemia held a special reception at Portcullis House on 21 June 2011 to mark the 10th anniversary of the NHS Sickle Cell and Thalassaemia (SC+T) Screening Programme. The event, attended by the Right Honourable and Most Reverend Dr John Sentamu, Archbishop of York, also honours World Sickle Cell Day (19 June).

Launched in 2001, the SC+T Screening Programme is the first national genetic screening programme in the NHS and the first in the world to link antenatal and newborn screening. It offers antenatal screening to all pregnant women in England and to fathers-to-be where the mother is identified as a genetic carrier. It also offers screening to all newborn babies in England.

In a statement, Anne Milton, Minister for Public Health, congratulated the Programme Director, Dr Allison Streetly OBE, for her vision and leadership and noted that the Programme, “has not only played a major role in early identification of disease - leading to prompt treatment - but has also helped reduce the stigma so often attached to these conditions.”

Dianne Abbott, Chair of the APPG said, “In the last 10 years sickle cell and thalassaemia have successfully come from the margins of the NHS into the mainstream. Today sickle cell is the most common serious inherited condition in England and it is essential that we continue to invest to deliver high quality and accessible screening and care.”

Congratulating the Programme, The Archbishop of York particularly highlighted the exceptionally close working with service users, carers and the voluntary sector. “This was a programme developed in response to lobbying from patients and in which users have played a vital role in shaping both strategy and implementation.

“It is a tremendous achievement to have delivered universal screening within 10 years and to be acknowledged as a national and international leader. But we have to keep our feet on the ground – there is still a very long way to go – particularly around building awareness and understanding, offering screening earlier in pregnancy, engaging fathers and delivering quality care across England.”

Gabriel Theophanous, president of the UK Thalassemia Society also spoke at the meeting, as follows: “I would like to congratulate Dr Allison Streetly and the staff of the Screening Programme for their ground breaking work over the last ten years. One of the greatest achievements of the Screening Programme is the raising of the profile of thalassaemia and sickle cell within the National Health Service. Ten years ago most doctors, nurses and midwives had never heard of thalassaemia. Although work remains to be done there is a lot more awareness today within the medical professions and for that we have to thank the Screening Programme. I would also like to commend Dr Streetly for her forward thinking in recognising that it is unethical to promote a screening programme without simultaneously considering the quality of care given to children who are born with the disorders. As a thalassaemia patient who is fortunate enough to enjoy excellent medical care, I know many other patients who are not so lucky. We will continue to work with the APPG and the Screening Programme towards the development of effective networks of care which will give everyone access to top quality treatment. We also need to persevere with our demands for more resources for the haemoglobinopathies. We have some of the best doctors and nurses in the world (many of them are with us tonight) but too many of them are operating at the absolute limit of their capacity. Patient care suffers when staff are overworked, stressed and burnt out and it is unacceptable. For too long the haemoglobinopathies have been the “poor relation” of white cell haematology. It is we, the patients, who need to stand up and let our voices be heard. We are not second class citizens and we are not settling for a second class service.”
Osteoporosis represents a prominent cause of morbidity in patients with thalassemia. The delay in sexual maturation, the presence of diabetes and hypothyroidism, the parathyroid gland dysfunction, the progressive marrow expansion, the iron toxicity on osteoblasts, the iron chelators, and the deficiency of growth hormone or insulin growth factors have been identified as major causes of osteoporosis in thalassemia. Adequate hormonal replacement, effective iron chelation, improvement of hemoglobin levels, calcium and vitamin D administration, physical activity, and smoking cessation are the main to-date measures for the management of the disease. During the last decade, novel pathogenetic data suggest that the reduced osteoblastic activity, which is believed to be the basic mechanism of bone loss in thalassemia, is accompanied by a comparable or even greater increase in bone resorption. Therefore, the role of bisphosphonates, potent inhibitors of osteoclast activation, arises as a major factor in the management of osteoporosis in thalassemia patients.

Keywords: thalassemia; osteoporosis; bisphosphonates; therapy; pathogenesis

Pathogenesis of osteoporosis in thalassemia

According to the World Health Organization, osteoporosis is a disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequential increase in fracture risk. The cut-off of 2.5 standard deviations below the normal mean in BMD for the respective age is used for the definition of osteoporosis, whereas the decrease of BMD between 1.5 and 2.5 standard deviations below the normal mean for the respective age is defined as osteopenia. The most important factors that are implicated in the pathogenesis of bone loss in thalassemia patients are described later.

Genetic factors

Genetic factors seem to play a role in the development of low bone mass and osteoporotic fractures. These factors have been implicated in the pathogenesis of postmenopausal osteoporosis, as regulator genes of BMD, but have not been studied thoroughly in thalassemia-induced
osteoporosis. The polymorphism at the Sp1 site of the collagen type la1 (COLIA 1) gene (collagen type I is the major bone matrix protein) was studied by Wonke and colleagues, who found that approximately 30% of the TM patients were heterozygotes (Ss) and 4% were homozygotes (SS) for the Sp1 polymorphism. The authors have concluded that male patients with TM carrying the Sp1 mutation may develop severe osteoporosis of the spine and the hip more frequently than patients who do not carry this mutation. The COLIA 1 polymorphism has been associated with reduced BMD in postmenopausal osteoporosis, and predisposes women to osteoporotic fractures.11 The genes encoding collagen types la1 and la2 (COLIA 1 and COLIA 2, respectively) are also important candidates for the genetic regulation of BMD, as mutations that affect the coding regimens of these genes are implicated in the pathogenesis of osteogenesis imperfecta and osteoarthritis.12 The study of COLIA 1 polymorphism may help in identifying thalassemia patients who are at higher risk to develop osteoporosis and pathologic fractures.13

Other genetic factors that have been reported to correlate with bone mineral damage in adult patients with thalassemia include the vitamin D receptor (VDR) BsmI BB polymorphism, the loss-of-function mutations in the gene of the vitamin D receptor, the sequence variation of 713-8delC of the calcitonin (CT) receptor gene, estrogen receptor and interleukin-6 gene loci.1,13 Although further studies are needed to exact final conclusion for the association between gene polymorphisms and bone mass in TM patients, COLIA 1 gene polymorphisms seem to be of importance in the pathogenesis of thalassemia-induced osteoporosis.

Acquired factors

Endocrine complications. Hypothyroidism, hypoparathyroidism, diabetes mellitus, and mainly hypogonadism (as delayed puberty and/or secondary hypogonadism) are considered as major causes of osteopenia/osteoporosis in TM.1,3,5 Hemosiderosis of the pituitary gonadotrophic cells and iron deposition in the testes and ovaries are involved in the pathogenesis of endocrine complications in TM.14 Hypogonadism is a well-recognized cause of osteoporosis and osteopenia not only in patients with TM but also in the general population and is characterized by high bone turnover with enhanced resorptive phase.15 Estrogen and progesterone appear to inhibit osteoclast activity and promote bone formation, whereas testosterone has a direct stimulatory effect on osteoblast proliferation and differentiation.3 IGFs play also an important role in bone remodeling. Low-serum IGF levels decrease osteoblast proliferation and bone matrix formation and reduce the activation of osteoclasts.16 Several studies have demonstrated a positive correlation between the BMD of the lumbar spine and the IGF-I concentration.17 It is well documented that the GH–IGF axis is defective in TM. Thalassemia patients have significantly lower circulating levels of IGF-I and the corresponding binding protein (IGFBP-III) than normal individuals; thus, leading to increased bone resorption, decreased bone formation, and finally to bone loss.18,19

Iron overload and desferrioxamine.

Iron deposition in the bone impairs osteoid maturation and inhibits mineralization locally, resulting in focal osteomalacia. The mechanism by which iron overload interferes in osteoid maturation and mineralization includes the incorporation of iron into crystals of calcium hydroxyapatite, which consequently affects the growth of hydroxyapatite crystals and reduces the bone metabolism unit tensile strength.20 Furthermore, desferrioxamine inhibits DNA synthesis, osteoblast, and fibroblast proliferation, osteoblast precursors differentiation, and collagen formation, although enhances osteoblast apoptosis, especially in patients who receive inappropriately high doses of desferrioxamine.21

Bone marrow expansion.

Bone marrow expansion, which is a typical finding in patients with TM, has been considered as a major cause of bone destruction.20 Transferrin receptor studies have demonstrated increased bone marrow activity even in patients with low reticulocyte count or marrow hypoplasia.22 However, there was found no direct correlation between serum levels of soluble transferrin receptor and the severity of osteoporosis.10

Vitamin deficiencies. Vitamin C deficiency in iron-overload patients with low levels of serum ascorbic acid induces the risk of osteoporotic fractures.23 Vitamin D deficiency is also implicated in the pathogenesis of osteoporosis in TM patients due to the regulatory effect of vitamin D in both osteoclasts and osteoblasts. Adequate calcium intake and small amounts of vitamin D administration during skeleton development can increase bone mass in adolescents and decrease bone loss in adult life. However, most studies have failed to show reduced serum levels of 25-hydroxyvitamin D in TM patients.

Physical activity. Patients with TM have reduced physical activity due to the complications of the disease and the overprotection by their parents who do not encourage muscle activity. Thus, the lack of physical activity is another predisposing factor for osteoporosis in TM patients and muscle activity has to be encouraged in these patients.1–3 These factors can lead to the destruction of bone in thalassemia patients by increasing the osteoclast function and/or reducing the osteoblast activity.

Increased osteoclast function in thalassemic patients with osteoporosis.

During the last decade, there was sufficient data supporting that increased osteoclast activation is present in TM patients. Patients with TM and osteoporosis have elevated markers of bone resorption, such as N-terminal cross-linking telopeptide of collagen type-I (NTX) and tartrate-resistant acid phosphatase type 5b (TRACP-5b)4,25 that correlated with BMD of the lumbar spine in these patients.25,26 This increased osteoclast activity seems to be at least partially due to an imbalance in the receptor–activator of nuclear factor-kappa B ligand (RANKL)/osteoprotegerin (OPG) system and the overproduction of cytokines that are involved in the osteoclast differentiation and function.4 The RANK/RANKL/OPG pathway is of great importance for the activation and proliferation of osteoclast precursors. We and others have shown that the ratio

Continues on page 9 ➪
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of sRANKL/OPG in the serum was increased in thalassemia patients with osteopenia/osteoporosis, providing evidence for the role of RANKL/OPG system in the pathogenesis of osteoporosis in thalassemia. Serum levels of IL-1e, TNF-e, IL-6, and TGF-, that are able to increase osteoclast function, were elevated in TM and correlated with bone resorption and lumbar BMD, suggesting their involvement in the pathogenesis of TM osteoporosis and supporting the role of the immune system in the bone loss of TM.

### Reduced osteoblast function in thalassemic patients with osteoporosis.

There is evidence of reduced osteoblast thickness, increased osteoid maturation and mineralization lag time, which indicate impaired bone matrix maturation, and defective mineralization is present in children and adolescents with TM. In addition, iron deposits appeared along mineralization fronts and osteoid surfaces, whereas focal thickened osteoid seams were found together with focal iron deposits. Finally, dynamic bone formation histomorphometry studies established reduced bone formation rate in TM patients. This reduced bone formation is thought to-date to be mainly the result of iron poisoning in osteoblasts and/or the result of reduced function of GH and IGF-1 axis in TM patients. However, novel molecules seem to be implicated in osteoblast dysfunction in TM. Dickkopf-1 (Dkk-1) is a Wnt signaling inhibitor, which inhibits the osteoblast differentiation and function. We have recently shown that serum levels of Dkk-1 were increased in TM patients with osteoporosis and correlated with lumbar spine and wrist BMD. Interestingly, when zoledronic acid (ZA) was given in these patients there was a reduction in Dkk-1 levels, which was not observed in the placebo group of this randomized trial.

### Management of thalassemia-associated osteoporosis

#### Prevention and general principles.

Prevention and treatment of early bone loss make the best policy. Annual checking of BMD starting in adolescence is considered indispensable. Physical activity must always be encouraged. Moderate and high impact activities are to be supported. Exercise has additional benefits: it improves cardiovascular system, reduces the risk of diabetes, and prevents depression. Smoking should be discouraged. Adequate calcium intake during skeleton development can increase bone mass in adult life and in combination with administration of low doses of vitamin D may prevent bone loss and fractures. Early diagnosis and treatment of diabetes mellitus is also important, as the association between diabetes and low bone mass in TM patients has been well documented. Furthermore, adequate iron chelation may prevent iron toxicity in the bone and sufficient blood transfusions may inhibit uncontrolled bone marrow expansion.

#### Hormonal replacement.

Prevention of hypogonadism seems to be the most effective way for preventing osteoporosis and other bone deformities in thalassemia patients. Anapliotou and colleagues recommended that continuous hormonal replacement therapy with transdermal estrogen for females or human chorionic gonadotrophin for males improves bone density parameters. However, despite hormonal replacement, calcium and vitamin D administration, effective iron chelation, and normalization of hemoglobin levels, patients with TM continue to lose bone mass.

#### Calcitonin.

Canatan and colleagues have evaluated the effect of calcitonin (CT), a potent inhibitor of osteoclasts, on bone mass in 14 patients with TM. One hundred IU of CT were administered, three times a week, for 1 year in combination with daily administration of 250 mg of calcium. At the end of treatment period, bone pain had disappeared, radiological findings of osteoporosis had been improved, and the number of fractures had been decreased in the treatment group but not in controls. CT had no important side effects. Both parenteral and intranasal instillations are available.

#### Hydroxyurea.

Ten patients with TM were given hydroxyurea (HU), at a dose of 1.5 g p.o. daily, in an attempt to reduce marrow hyperplasia diagnosed by MRI. HU improved bone pain and MRI findings. However, in another study, the administration of HU for at least 2 years did not manage to show any improvement of the BMD compared with patients who did not receive HU.

#### Bisphosphonates.

The increased bone resorption observed in patients with thalassemia-induced osteoporosis has led to the use of bisphosphonates in the management of osteoporosis in this cohort of patients. Bisphosphonates are potent inhibitors of osteoclastic bone resorption. They act by inhibiting osteoclastic recruitment and maturation, preventing the development of monocyte precursors into osteoclasts, inducing osteoclast apoptosis and interrupting their attachment to the bone. In thalassemia osteoporosis, almost all generations of bisphosphonates have been used in an attempt to increase the BMD and improve the abnormal bone remodeling. Morabito and colleagues scheduled a randomized, placebo-controlled trial to investigate the effects of 2 years daily oral administration of alendronate or intramuscular administration of clodronate on BMD, bone turnover markers, safety, and tolerability in 25 thalassemia patients with osteoporosis. Patients were randomized to receive placebo (eight patients) or 100 mg of clodronate, i.e., every 10 days (eight patients) or 10 mg of alendronate per os daily (nine patients). All patients also received 500 mg of elemental calcium and 400 IU cholecalciferol daily. After 2 years of follow-up, the lumbar spine and femoral neck BMD had decreased significantly in the placebo group. Alendronate reduced bone resorption markers, deoxypyridinoline, and pyridinoline, and inhibited bone loss but it was unable to increase BMD at all studied sites. Daily treatment with alendronate normalized the rate of bone turnover, and resulted in a rise in BMD of the spine and the hip. This increment was statistically significant at the femoral neck, whereas at the lumbar spine the gain was less marked. Alendronate caused few adverse effects, including upper gastrointestinal symptoms, but no patient discontinued the study. The ineffectiveness of clodronate was established in another randomized, placebo-controlled trial.

Pamidronate, a second-generation aminobisphosphonate, has been given intravenously in patients with TM and osteoporosis. First, Wonke evaluated...
the effect of 15 mg of pamidronate on BMD. Pamidronate was given in a 40 min infusion, at monthly intervals. A significant improvement in BMD was observed in most patients.\(^{10}\) Our group compared the effects of two different doses of pamidronate, 30 mg versus 60 mg, on BMD of the lumbar spine, femoral neck, and forearm and on markers of bone remodeling and osteoclast function in 26 patients with thalassemia and osteoporosis. Thirteen patients with TM and five patients with TI were given pamidronate at a dose of 30 mg in a 2 h i.v. infusion, once a month for 12 months; another eight patients (four with TM and four with TI) received a dose of 60 mg/month, in an attempt to explore whether increasing the dose of pamidronate might have any additional effect. Both groups included patients with comparable degrees of osteoporosis and hypogonadism. All patients were also receiving calcium and vitamin D supplement prior and during the 12-month follow-up period of the study. Administration of 30 mg of pamidronate resulted in a significant increase of the BMD of the lumbar spine in all patients, but not the BMD of the femoral neck and the forearm. The 60 mg of pamidronate group showed a similarly significant increase in the BMD of the lumbar spine in both transfusion-dependent and transfusion-independent patients. Administration of both doses of pamidronate was also followed by a clear decrease of markers of bone resorption (NTX and TRACP-5b), OPG, and osteocalcin that was similar in patients of both treatment groups. Furthermore, most patients complaining of severe bone pain at the onset of the study had a significant reduction of pain after treatment period. No severe adverse events were reported in this study.\(^{25}\)

Zoledronic acid is the most potent third generation bisphosphonate to-date and has been found to be extremely efficacious in increasing BMD in TM patients. We reported the results of a randomized, placebo-controlled trial of ZA in 66 thalassemia patients with osteoporosis. The patients were randomized to receive 4 mg ZA intravenously every 6 months (23 patients; group A) or every 3 months (21 patients; group B), or to receive placebo every 3 months (22 patients; group C), for a period of 1 year. Patients of group B had a significant increase in their lumbar spine BMD, which was accompanied by dramatic reductions in bone pain, and bone markers. Patients in placebo group showed no alteration in BMD of any studied site or in bone pain scores; on the contrary, they had an aggravation in bone resorption. Therefore, this study confirmed that ZA is an effective treatment for increasing BMD and reducing bone resorption in thalassemia-induced osteoporosis with no serious side effects.\(^{28}\) As the duration of ZA therapy had not been evaluated in any trial, we followed-up our patients for 24 months after discontinuation of ZA for groups A and B and for 12 months for group C (patients of group C received ZA, 4 mg every 3 months, i.v., for 12 months after their placebo 12-month administration). We found, interestingly, that at the 36th month, patients of group B continued to show an increase in the BMD of all studied sites despite the discontinuation of ZA. Furthermore, patients of groups A and C showed a dramatic increase in BMD of all studied sites compared with baseline values (\(P < 0.01\)). The increase of BMD observed in groups A and C was accompanied by a comparable reduction in bone resorption marker CTX at the 36th month, which had not reported at the 12th month; on the contrary in group C there was an increase in CTX at the 12th month. These observations suggest that ZA continues to act after its discontinuation.\(^{29}\)

In another recent study, we confirmed that the increase of erythropoietic activity in TI, which continues irrespectively of the improvement of BMD produced by ZA, seems to be a major cause of bone loss in this hemoglobinopathy. Soluble transferrin receptor (sTfR) and erythropoietin (Epo) serum levels are increased in TI but we showed for the first time in the literature that this elevation was further increased by time, although BMD was improved by ZA.\(^{40}\)

All described studies confirm the effectiveness of bisphosphonates in the treatment of thalassemia-induced osteoporosis. Alendronate, pamidronate, and ZA seem to have the greater efficacy. However, more trials must be conducted to clarify the exact role of each bisphosphonate, the long-term benefit and side effects as well as the effects of the combination of bisphosphonates with other effective agents, such as hormonal replacement, in thalassemia-induced osteoporosis.

**Conclusion and future perspectives**

Thalassemia-associated osteoporosis is multifactorial and, therefore, very difficult in its management. Osteoporosis is a progressive disease; thus, prevention and early diagnosis are very important. Adequate hormonal replacement, effective iron chelation, improvement of hemoglobin levels, calcium and vitamin D administration, physical activity, and smoking cessation are the main to-date measures for the management of the disease. However, novel pathogenetic data suggest that the reduced osteoblastic activity, which is believed to be the basic mechanism of bone loss in TM, is accompanied by a comparable or even greater increase in bone resorption. Therefore, the role of bisphosphonates arises as major in the management of osteoporosis in these patients. However, many aspects have to be clarified before the broad use of bisphosphonates in TM-induced osteoporosis: which one? how long? and at what dose? The combination of bisphosphonates with other effective agents has also to be evaluated in randomized trials. Other novel agents that stimulate bone formation such as teriparatide, a recombinant peptide fragment of parathyroid hormone, strontium ranelate, a second anabolic agent, that seem to prevent osteoporotic fractures in postmenopausal women, are being studied but their effects in TM-induced osteoporosis remains to be proven. Finally, antibodies against RANKL, such as denosumab, which has just been licensed by FDA for the treatment of postmenopausal osteoporosis, and antibodies against Dkk-1 or against sclerostin maybe future agents for the effective management of this difficult complication of thalassemia.

**Conflicts of interest**

The authors have received research support and honoraria from NOVARTIS.

**References**

A complete list of references for this article is available from UKTS.
Peer review of red cell disorder networks 2010-11 (paediatrics)

by Elaine Miller

Background

Acting on a Dept of Health secondment, from November 2008 – March 2009 Dr Phil Darbyshire (Consultant Paediatric Haematologist and then Chair of the UK Forum on Haemoglobin Disorders) conducted an informal review of clinical networks for haemoglobin (HbO) disorders in England.

The need for such a review had long been recognised by the UK Forum; given that HbO offers particular challenges in service design. The prevalence of the conditions is very variable (i.e. not evenly spread geographically throughout the population) and it predominantly affects people from minority communities who experience a reduction in access to medical and social services. There are various sociocultural reasons behind this issue, for example patients and carers may not speak English as their first language, they are often of low socioeconomic status and may be highly mobile within the population; e.g. asylum seekers. Care provision is inconsistent and often put together on an ad hoc basis; with no-one taking overall responsibility for the service.

In the last 10 years however, there have been a number of drivers for change in this attitude, largely led by the implementation in 2001 of the NHS Screening Programme for Sickle Cell and Thalassaemia. Since then care standards for adults and children have been introduced (UKTS children 2005, SCS children 2006, SCS adults 2008) and the DH published the Long Term Conditions National Service Framework in 2005. The NCEPOD (National Confidential Enquiry into patient Outcome and death) report into mortality in the haemoglobinopathies was published in 2008. This highlighted the poor understanding of red cell disorders; even among health professionals working in the field of haematology. Since 2010 haemoglobinopathies have been under the remit of specialised services commissioning (Specialised Services National Definition Set No. 38, 3rd edition 2010); and the National Haemoglobinopathy Registry was piloted in 2008 and set up in 2009. These developments have led to increased DH and political interest; with the setting up of the Clinical Services Development Group and the All Party Parliamentary Group on Sickle Cell and Thalassaemia in 2008. Furthermore the activities of the patient societies have led to higher expectations on behalf of the patients and carers.

The objectives of the network visits undertaken by Dr Darbyshire were:-
- To gather information about the services on behalf of the DH and to get an up to date picture of the operation of secondary and tertiary services
- To measure performance in key areas against the standards
- To establish the nature of the current clinical networks (see figures 2 and 3)
- To establish the nature of the current commissioning arrangements
- To identify perceived gaps in services and how to rectify these
- To inform medium to long term DH strategy

Although there were considerable variations between services, some common themes emerged from Dr Darbyshire’s review. The most striking of these were: inequalities both within individual networks and between networks, lack of specialist nursing support and community nursing support; and a lack of manpower and allocated time from health professionals at all levels (with particularly poor provision for psychology services). It was Dr Darbyshire’s perception that on an overall level, services for HbO operate as a “second string” to services for white cell haematology/malignancies. In some areas there is a lack of clarity and blurring of the responsibilities of acute and community services; which can lead to vulnerable patients falling through the gaps. In all areas, leadership is key to the development and standard of care given.

There is a notable lack of patient and carer involvement in service design throughout.

With reference to thalassaemia, it was clear from Dr Darbyshire’s work that the geographical distribution of thalassaemia is very different from that of sickle cell. Many centres with very large populations of sickle patients have very few thalassaemia patients (see figure 3). Medical staff, even those who have large numbers of sickle patients, are in the main receptive to their thalassaemia patients being regularly
medical news

reviewed by another centre which has greater expertise. This is very necessary as the few thalassaemia patients tend to be overwhelmed by the much greater number of sickle patients. Regular transfusions are usually carried out at the convenience of the hospital rather than the patient or family; with most units offering little flexibility. In some cases however, smaller units provided greater flexibility than larger units, having fewer patients to accommodate.

Peer review visits

What were we actually reviewing?

In November 2007 Dr Darbyshire put forward a proposal for a programme of peer review visits to services for children and young people with haemoglobinopathies. This initiative was endorsed and supported by the Department of Health in order to help the development of clinical networks. Standards for the clinical care of children and young people with thalassaemia and sickle cell disease were published in 2005 and 2006 respectively. Subsequently the UK Forum for Haemoglobin Disorders commissioned Jane Eminson, a management consultant with a long track record of undertaking such work, to draw from them a set of Quality Requirements against which service provision could be systematically reviewed (http://sct.screening.nhs.uk/getdata.php?id=10818). The Quality Requirements reflect the aims, standards and guidelines of both Standards documents. They clarify the arrangements that should be in place and provide the answer to the question: “For each service, how will I know that the ‘Standards and Guidelines for Clinical Care’ have been implemented?” The suitability of the Quality Requirements for use in peer review was tested in a pilot visit to the Royal London Hospital in January 2007. This visit also piloted the peer review process. Dr Anne Yardumian was asked to act as the Clinical Lead on the paediatric peer review process; with continued support from Jane Eminson and organisational and administrative support from the West Midlands Peer Review Team.

The purpose of the peer review programme was to:

• To ensure services are as safe as possible
• To improve the quality and effectiveness of care
• To improve children’s, young people’s and their families’ experience of care
• To undertake independent, fair reviews of services
• To provide development and learning for all involved
• To encourage the dissemination of good practice

The Quality Requirements are structured around Specialist and Local Haemoglobinopathy Teams and commissioners of these services. Specialist Haemoglobinopathy Teams (SHT) may currently be called ‘Centres’. Local Haemoglobinopathy Teams (LHT) provide shared care with a specific Specialist Team. Both types of team may care for patients with sickle cell disease and / or thalassaemia. Both types of team may be supported by a range of community-based services. The review visits covered the work of the Specialist Team, its commissioners and any linked Local Haemoglobinopathy Teams.

![Figure 1](current_network_links_as_at_april_2009_hbo_services_london_regions.png)

![Figure 2](current_network_links_as_at_april_2009_hbo_services_outside_london.png)

![Figure 3](patients_identified_adults__a__children__c_.png)
The visiting teams
Each visiting team consisted of:-

• Team Leader: A member of the Steering Group. (This was in fact Dr Anne Yardumian; who acted as Team Leader on all visits other than the review of the North Middlesex Hospital where she is Lead Consultant caring for haemoglobinopathy patients. In this case the role of Team Leader was undertaken by Dr Phil Darbyshire.)

• At least one medically qualified consultant who is a lead consultant / deputy in a Specialist Haemoglobinopathy Team (QR 9 / 10)

• At least one nurse who is a lead nurse from a Specialist Haemoglobinopathy Team (QR12)

• At least one representative of families who use services OR representative from the voluntary sector (UKTS Coordinator Elaine Miller attended 13 peer review visits; to ensure that as far as possible there would be a representative present whose primary concern was the care of thalassaemia patients).

• One lead consultant / lead nurse from a Local Haemoglobinopathy Team (if possible)

• One commissioner of services (if possible)

All review team members were required to attend a one-day training course.

What the teams saw
Each Specialist Team was expected to prepare folders of evidence of their compliance with the Quality Requirements. The visiting team reviewed this evidence, met members of the team, service users and their families, providers of community services, representatives of linked Local Teams and commissioners, viewed the facilities, drew their conclusions and then provided initial feedback. The visiting team also reviewed a number of case notes (N.B. Service users and representatives from the voluntary sector were not allowed to see case notes to maintain patient confidentiality.) Reviewers visited the main facilities where children and young people with haemoglobinopathies are cared for, including the in-patient ward, day unit and accident and emergency department. One very important part of the visit was a meeting with service users, which were in the main parents and carers, this being a review of paediatric services. The review teams regarded their feedback as vital; but were entirely dependent on the efforts of the local team to invite and motivate service users to attend. Thus the usefulness and relevance of these feedback sessions were highly variable (see individual reports below).

Reports
The reports from each visit identified:-

• Good practice

• Issues for further consideration

• Concerns

• Immediate risks to clinical safety or clinical outcomes

Draft reports of the visits were circulated to the visiting team and to the service that was reviewed for comments on factual accuracy prior to submission to the Steering Group for ‘sign off’. Trusts are expected to make reports publicly available and deal with any associated publicity through their usual mechanisms. Final reports were circulated to the Trust’s host PCT and to other service commissioners; with the intention that they will be published on the Trusts’ websites.

An Overview Report is being produced by Dr Anne Yardumian, summarising the findings and identifying common themes.

Follow Up
Trusts will be expected to address any issues identified by the peer review programme through their usual clinical and performance governance arrangements. Commissioners of haemoglobinopathy services should be involved if additional investment is required. Commissioners should also monitor that issues have been addressed. The Steering Group will maintain an overview of progress and will take action if progress is not satisfactory. The Steering Group may decide that a follow up visit is required in order to provide assurance of progress.

Dr Anne Yardumian, Clinical Lead of the paediatric peer reviews, felt strongly that the approach of the visits should be that of helping the local teams to improve standards rather than being there simply to criticise. It was felt that this would be more productive in gaining cooperation and transparency of communication from the local teams; especially in light of the fact that the peer review process can only highlight areas of good and poor performance; but has not the power to insist upon changes.

Evaluation
The visiting team and the service that was reviewed were asked to complete an evaluation form at the end of each visit. This information will be used for ongoing improvement of the programme.

All reviewers and services which have been reviewed were also asked to complete an evaluation form at the end of the programme. This will provide an internal evaluation of the changes that have been made and the programme’s impact.

The Department of Health may also wish to commission an external evaluation.

The future
Dr Anne Yardumian has prepared a final overview report on the paediatric peer review process; which have been disseminated to all the hospitals which took part and via the UK Forum on Haemoglobin Disorders. All the individual trusts who took part have received copies of the report relating to their own services and will this will be published on their websites. The UK Forum for Haemoglobin Disorders is currently considering the possibility of follow-up visits, possibly in 2013, but this is not yet confirmed.

An adult peer review process has been commissioned under the auspices of the UK Forum on Haemoglobin Disorders. The clinical leads are Dr Kate Ryan (Consultant Haematologist, Manchester Royal Infirmary) and Dr Joanne Howard (Consultant Haematologist, Guy’s & St Thomas’s Hospital) and the review will take place during 2012. UKTS Director Sema Kiamil and Coordinator Elaine Miller will take part as members of the review teams.

All the reports, including the final overview report, are available on the West Midlands Quality Review Service website at http://www.wmqrs.westmidlands.nhs.uk/wmqrs/publications/for-review-programme/52
Thalassaemia International Conference, Antalya, Turkey (11-15 May 2011)

By Noreen Khan from Coventry

When I booked to attend the 12th international conference in Turkey I wasn’t really sure what to expect as I had never been to one of the international conferences before. I had been told that the international thalassaemia conferences were really good but I didn’t know what happens there and if it was worth going. On the first day of the conference my mum and I went to register and got the conference pack. In the pack amongst other things it had the conference schedule, of what lectures were going on at what time and day and in what room. I scanned over the schedule and realised there was a lot going on over the four days of the conference, a lot of information. I saw quite a lot of lectures on the sheet that I was interested in and planned to go to. I managed to go to quite a lot of the lectures and gain a lot of knowledge. I remember thinking “Oh, I must remember that so that I can go back and tell my Doctor and other patients”.” I was really impressed with the layout of the conference, the structure and the smooth running of it all. I found it to be very well organised. It was really good seeing Elaine and others from UKTS there at the conference. I also got to see Dr Banu Kaya who was my doctor at the Royal London Hospital when I was living in London; it was great to see her as she is such a lovely person and a brilliant doctor. It was impressive to see doctors from around the world come and share information and present new research and findings. I think it is very important to further our understanding about thalassaemia and make it clear what it is, in order to cope with the illness better and not stop us thalassaemic patients from having a life and making the most out of it. When I wasn’t at one of the lectures I was glad to be just relaxing in the plush hotel, which had plenty to do, as there was a lot of information to take in and a lot of concentration required. What I enjoyed the most was meeting other thalassaemia patients, from the UK and from other countries. By talking to the patients and families from other countries it made me realise how hard it is for some people and how fortunate I am. I met a sister of one patient who was from India and she told me how worried she was for her brother’s health and how hard it is for him to get blood and to be able to afford it. As she was telling me she had tears in her eyes. Meeting other people really opens your eyes. I also met some lovely people from the UK and it was really good to speak to them and hear how they coped with the condition. On the last night of the conference there was a gala dinner which was really good and you could really feel the friendly and positive atmosphere. Most people have regularly been going to these conferences and it was nice to see the bond between people, it was like a family.

I can certainly say it was definitely worth going. You realise you are not alone and can feel more positive about thalassaemia. Meeting people from all walks of life was amazing and the advice and support you can get from them is inspirational. All in all I met some lovely people, learned and experienced a lot and stayed in a beautiful location. It was a rollercoaster of different emotions throughout the trip but at the end it was sad it was over. Can’t wait for the next conference!
patient news

Welcoming our latest arrivals

Our warmest congratulations to thalassaemia patient Mumta Walters and her husband Shane on the arrival of their twin daughters Sophie and Lola. The babies were born on 20th June 2011 at the Whittington Hospital, where Mumta is under the care of Dr Farrukh Shah.

Congratulations to Roanna Maharaj

Many congratulations to thalassaemia patient Roanna Maharaj, who has gained a BSc Honours degree in psychology from London Metropolitan University. Roanna is under the care of Dr Farrukh Shah at the Whittington Hospital, London.
This issue we bring you some very important news about a new appointment at UKTS – our first Director, Sema Kiamil! Sema joined the UKTS team at the beginning of April 2011. Here we introduce her

Can you tell us a little bit about your family and your background?

Born in Berlin in 1970 – seems so long ago – oh wait….it was a long time ago!! Now I have reached the mature age of 40, I feel that I need be a responsible adult with a responsible job – well I have achieved one out of two so that’s not a bad start! After leaving school without a clue of which path to go down, I decided to join a bunch of young people and join the student brigade in Brighton. After 3 exciting years at University I left with a degree in Social Policy and promptly found a job at Age Concern Haringey, working with Turkish Cypriot elders – this was very handy as I am Turkish Cypriot myself and was able to communicate with my clients which help! After landing a job, purchasing a property was the next chapter…..roll on 20 odd years and a few moves in jobs and homes and becoming a parent to the wonderful Leyla who is now 13, here I am at the UKTS.

What is your career/educational background?

My educational background is in social policy and social science with a bit of child psychology in the mix. I decided to further my academic studies and completed my Masters Degree 2 years ago. This was no mean feat and was a long haul journey for me, primarily because I have a 13 year old daughter who takes up most of my time outside work! I turned this to my advantage as she learnt to write by copying my essays from when she was 5 years old when I first embarked on this course! Not sure how useful this was to her in her first year at school, but she has very neat handwriting form all the practice! Work wise, I have always worked in the voluntary sector, focusing on vulnerable client groups including the elderly at Age Concern Haringey, victims of crime at Victim Support Brent, disabled children and their carers in Brent. Whilst at Brent Disabled Children’s Services, I worked closely with parents of disabled children and helped start up a new charity called 1 Voice which is run by parents. I also facilitated training sessions to professionals and carers on an assortment of topics including benefit awareness, assertiveness, public speaking, supporting victims of serious crimes and strategy planning to name but a few.

What attracted you to the idea of working with UKTS

My initial attraction to UKTS was not my overall interest in working within the charitable sector but also I had a personal interest in thalassaemia. Having been closely linked to thalassaemia all my adult life, I wanted to convert the knowledge and experience I had gained from my personal life to my professional life. The opportunity arose in February this year and I have been in post since April. I enjoy working in an environment where change can affect a client group, in this case patients and families of thalassaemia. The work that UKTS has achieved success in the past also made me want to be part of the team. The tireless work of the trustee’s also attracted me to the UKTS as their work underpins many successes achieved.

What do you see as the main challenges of working in a newly created, leading role in a small (but dynamic!!!!) charity?

As with all challenges within the charity sector, the primary one concerns finance and the stability of any organisation and UKTS is no different. A major part of my role is to fundraise in order to gain funds for future projects. Although this is a major external challenge that many organisations encounter, the internal challenges are more plausible to control and combat. For example, leading on new projects and working with the trustee’s is a challenge as my role has not been inherited. Being an entirely new role requires building relationships with the staff team that is key but so far there haven’t been any major challenges that could not have been worked out. I hope that the support of the trustee’s will continue so we can continue to thrive in this difficult climate. Leading the UKTS through these turbulent times is a challenge in itself, however what makes it easier is the support from members and trustee’s. The UKTS has strong foundations which have been laid so I can build on them and aim to transform challenges into advantages. Being the public figure, representing the UKTS at national conferences and at a later date, international conferences, will enable me to establish myself in the wider context of the world of thalassaemia. This is an area in which I particularly look forward to.
What would your goals for UKTS in the medium/long term?

Medium term goals for me at the UKTS would be to develop new projects and get a more diverse support base, including potential funders which have not been approached to date. Expansion of existing work is also a medium term goal as the ground work has already been completed, for example the work Elaine Miller is doing in the north of England.

Long term goals would be to develop a strategic plan to achieve sustainability. This is a massive challenge as these plans inevitably rely on funders. Being a long established charity, the UKTS is in a stronger position than some other charities to seek and apply for financial support. However, in line with the long term goals I envisage for the UKTS, I have to be realistic and expect this to be extremely challenging, difficult and time-consuming to pursue. In addition, I see working across communities as a long term goal. Our project in the north of England is spear heading this goal and in the long term, I hope to expand on this project with Elaine Miller. Building on existing work is not only a long term, but a short term goal as it is imperative for the UKTS to integrate with communities and produce effective working patterns and maintain strong relationships within such communities. Long term, expanding into areas where we have no presence, such as the north east, Wales and possibly Scotland would be a great achievement. These are long term goals; however, they are achievable with the commitment and dedication I aim to contribute to the UKTS.

What are your hobbies/interests?

This is a tricky question – I could reel off a whole bunch of interests and hobbies but I will keep it simple and say what I don’t like doing! Don’t like putting petrol in the car, sitting in traffic, queuing in shops, phoning call centres… all such a waste of time!

Seriously, I love to drink tea and catch up with family and friends. I enjoy going to the cinema, loved the King’s Speech and enjoy learning about history, especially the Tudor era. I am also very interested in travelling and discovering new parts of the globe.

Anything you particularly love / hate?

This is easier – love travelling to parts of the world that are a bit off the beaten track… Indonesia, Malaysia, Mexico, Egypt… I’m open to ideas as long as the sun is shining! However, have to negotiate with my daughter and come to an agreement, or compromise depending on the outcome. We can usually agree on many things but when it comes to travel destinations we tend to have heated debates! My daughter doesn’t want to India – I do, she doesn’t want to go to Sri Lanka – I do, she doesn’t want to go to the Maldives whereas I do – are you getting the picture? We haven’t done too badly so far and the next number one destination we are in agreement about is Cuba so maybe next year… however, if it was up to her we would go shopping in New York every holiday!

Apart from travelling, I love socialising and talking (maybe a bit too much!). Meeting friends/family or new contacts has always been appealing to me as I enjoy company and always find time to be sociable.

Any person you particularly admire?

I admire anyone who can make me laugh. There is too much doom and gloom at present so a good giggle does wonders for the body, mind and soul.

Are you a teenage thalassaemia patient?

If so, you could soon find yourself in the position of having to pay for your prescriptions. All children under the age of 16 and those aged 16-18 in full time education are exempt from prescription charges; however once you are 18 you will not automatically qualify for free prescriptions*. Many people are surprised to learn that all thalassaemia patients are not automatically exempt from charges, but sadly this is not the case. (Some of you may remember the Gilmore Report on prescription charges, which we reported on in issue 117 of Thalassaemia Matters.) If you approaching the age of 18, we advise you to speak to your doctor or specialist nurse to get advice about whether you will have to pay for your prescriptions in future. If you find out that you will have to pay for your prescriptions, and you have more than 14 prescriptions in 12 months, it is cheaper to buy a prescription prepayment certificate (see information below).

*You may continue to be entitled to free prescriptions under certain circumstances, for example if you suffer from another medical condition such as diabetes, which carries automatic exemption. Furthermore, those in receipt of certain benefits may be exempt from paying prescription charges (see below). If you are on a low income it may also be possible to obtain help with health costs.

Prescription prepayment certificates

A single prescription costs £7.40. If you have to pay for more than 14 items in 12 months, you may find it cheaper to buy a PPC (prescription prepayment certificate). A PPC for 12 months costs £104.00 and will cover ALL your prescription charges in the 12 month period. Furthermore you can spread the cost of the PPC by paying £10.40 per month for 10 months. You can buy or renew a PPC on-line and set up your direct debit by visiting the NHS Business Services Authority on http://www.nhsbsa.nhs.uk/1127.aspx.

There is also a telephone advice line and order line you can call 0845 850 0030.

Further information

- You must be a resident of England to purchase a PPC.
- You can also pay for a 3-month PPC which costs £29.10.
- Those receiving certain benefits (e.g. income support, tax credits) may be exempt from paying prescription charges.
- Some pharmacies are registered to sell PPCs. Your local pharmacist will be able to advise you if you need any more information about prescription charges.

For a comprehensive guide to free prescription help with healthcare costs please visit the following website: http://www.nhsbsa.nhs.uk/HelpWithHealthCosts.aspx.
Recent Events & Meetings

- 14 February 2011 – UK Forum on Haemoglobin Disorders Committee meeting, London – Attended by UKTS Coordinator Elaine Miller
- 23 February 2011 – NHS Sickle/Thalassaemia Screening Programme Steering Group, York – Attended by co-opted Committee member Dr Christos Sotirelis
- 04 March 2011 – meeting of protocol development group for care factors associated with positive mental health for sickle/thalassaemia patients, Edinburgh – Attended by UKTS Coordinator Elaine Miller
- Meeting of the DH Haemoglobinopathy Clinical Services Development Group, London – Attended by co-opted Committee member Dr Christos Sotirelis
- 15 March 2011 – meeting of the NHS Sickle/Thalassaemia Screening Programme Laboratory Subgroup, London – Attended by UKTS representative Martin Jarvis, Director, Pathology Laboratory, North Middlesex Hospital
- 21 March 2011 – (presentation) nurses meeting – Attended by UKTS Assistant Coordinator Katerina Loizi-Read
- 31 March 2011 – All Party Parliamentary Group on Sickle Cell and Thalassaemia, reception planning meeting, London – Attended by UKTS Coordinator Elaine Miller
- 08 April 2011 – meeting of the blood donor selection criteria steering group, advisory committee on Safety of Blood, Tissues and Organs, Dept of Health – Attended by UKTS Coordinator Elaine Miller
- 05 May 2011 – meeting with Sheffield Sickle Cell and Thalassaemia Foundation, Sheffield – Attended by UKTS Project Coordinator (North of England) Elaine Miller
- 11-15 May 2011 – Thalassaemia International Federation 12th International Conference, Antalya Turkey – Attended by UKTS President Gabriel Theophanous, Vice-President Andy Charalambous, Secretary George Constantinou, Assistant Secretary Romaine Maharaj, Assistant Treasurer Nina Demetriou, TIF representative Mike Michael, Project Coordinator (North of England), Assistant Coordinator Katerina Loizi-Read
- 24 May 2011 – UK Forum on Haemoglobin Disorders Academic Meeting, St Thomas’s Hospital, London – Attended by UKTS Director Sema Kiamil and Assistant Coordinator (North of England) Elaine Miller
- 07 June 2011 – NHS Sickle/Thalassaemia Screening Programme Public Outreach Steering Committee meeting – Attended by UKTS Director Sema Kiamil and Project Coordinator (North of England) Elaine Miller
- 09-12 June 2011 – European Haematology Association conference exhibition – Attended by UKTS Project Coordinator (North of England) Elaine Miller and Assistant Coordinator Katerina Loizi-Read
- 13 June 2011 – NHS Sickle/Thalassaemia Screening Programme newborn outcomes steering meeting, London – Attended by UKTS Director Sema Kiamil
- 21 June 2011 – All Party Parliamentary Group on Sickle cell and Thalassaemia Reception, House of Commons, London – Attended by UKTS President Gabriel Theophanous, Secretary George Constantinou, Director Sema Kiamil, Project Coordinator (North of England) Elaine Miller
- 01 July 2011 – meeting with Haemoglobinopathy Nurse Counsellor Janet Hall, Keighley West Yorkshire – UKTS Project Coordinator (North of England) Elaine Miller
- 16 July 2011 – UKTS Roadshow, Bradford – Attended by UKTS Vice-President Andy Charalambous, Director Sema Kiamil, Project Coordinator (North of England) Elaine Miller, Assistant Coordinator Katerina Loizi-Read
- 22 July 2011 – Manchester Sickle/Thalassaemia Awareness Day (presentation) – Attended by UKTS Project Coordinator (North of England) Elaine Miller
- 04 August 2011 – UKTS Project Coordinator (North of England) Elaine Miller attended the patient clinic held by Dr Christine Wright, Consultant Haematologist, Birmingham City Hospital
- 18 August 2011 – Meeting of UK Forum on Haemoglobin Disorders Committee – Attended by UKTS Project Coordinator (North of England) Elaine Miller
- 08 September 2011 - meeting of the NHS Sickle/Thalassaemia Screening Programme Laboratory Subgroup, London – Attended by UKTS representative Martin Jarvis, Director, Pathology Laboratory, North Middlesex Hospital
- 10 September 2011 – UKTS Roadshow, Leicester – Attended by UKTS President Gabriel Theophanous, Vice-President Andy Charalambous, Assistant Secretary Romaine Maharaj, Project Coordinator
15 September 2011 – NHS Sickle/Thalassaemia Screening Programme newborn outcomes steering meeting, London – Attended by UKTS Director Sema Kiamil

16 September 2011 – All Party Parliamentary Group on Sickle Cell and Thalassaemia planning meeting, London – Attended by UKTS Director Sema Kiamil

19 September 2011 – NHS Sickle/Thalassaemia Screening Programme 10th anniversary reception, London – Attended by UKTS Director Sema Kiamil

22 September 2011 – meeting with representatives of the Student Islamic Society, University of Birmingham – Attended by UKTS Project Coordinator (North of England) Elaine Miller

27 September 2011 – meeting with Engine Room Apps (smartphone applications) – Attended by UKTS Project Coordinator (North of England) Elaine Miller

29 September 2011 – meeting with Secretariat of All Party Parliamentary Group on Sickle Cell and Thalassaemia and representatives from Novartis Pharmaceuticals – Attended by UKTS Director Sema Kiamil and Project Coordinator (North of England) Elaine Miller

04 October 2011 – UK Thalassaemia Society Annual General Meeting, UKTS Head Office, Southgate, London

06 October 2011 - UKTS Project Coordinator (North of England) Elaine Miller attended the patient clinic held by Dr Jenny Welch, Consultant Paediatric Haematologist, Sheffield Children’s Hospital

08 October 2011 – All Scotland Managed Clinical Network for Haemoglobinopathies Service User Meeting, Kelvin Art Museum, Glasgow (presentation) – Attended by UKTS Project Coordinator (North of England) Elaine Miller

11 October 2011 – SaBTO (Advisory Committee on the Safety of Blood, Tissues and Organs) patient consent meeting – Attended by UKTS Director Sema Kiamil

12 October 2011 – Specialist Health Care Alliance meeting – Attended by UKTS Director Sema Kiamil

13 October 2011 – UKTS Project Coordinator (North of England) Elaine Miller attended a stakeholder meeting regarding the recommissioning of Sheffield community services for thalassaemia and sickle cell, at the Royal Hallamshire Hospital

26 October 2011 – Thalassaemia & Health Mela, Sangat Centre, Keighley (presentation) – Attended by UKTS Project Coordinator (North of England) Elaine Miller

27 October 2011 – Fund raising evening with UKTS Patron Peter Polycarpou, Theatre, Chichester – Attended by UKTS Director Sema Kiamil and Assistant Coordinator Katerina Loizi-Read

28 October 2011 – Meeting with NHSBT Director of External Affairs regarding NHSBT/UKTS cooperation on awareness/blood donor recruitment campaigns, London – Attended by UKTS Project Coordinator (North of England) Elaine Miller

31 October 2011 – “Mothers, babies and blood” education day for East Midlands health professionals, Royal Chesterfield Hospital (presentation) – Attended by UKTS Project Coordinator (North of England) Elaine Miller

02 November 2011 – British Society of Haematology meeting (presentation) – Attended by UKTS President Gabriel Theophanous and co-opted Committee member Dr Christos Sotirelis

04 November 2011 - UKTS Project Coordinator (North of England) Elaine Miller attended the transition clinic held by Dr Adrian Williams (Consultant Haematologist) and Dr Sally Pollard (Consultant Paediatrician), Bradford Royal Infirmary

09 November 2011 – NHS Sickle/Thalassaemia Screening Programme Steering Group, London – Attended by UKTS co-opted Committee member Dr Christos Sotirelis, Director Sema Kiamil and Project Coordinator (North of England) Elaine Miller

17 November 2011 – UK Forum on Haemoglobin Disorders/National Haemoglobinopathy Registry Academic Meeting, Manchester Royal Infirmary (presentation) – Attended by UKTS Director Sema Kiamil and Project Coordinator (North of England) Elaine Miller

19 November 2011 – UKTS Roadshow, Birmingham – Attended by UKTS President Gabriel Theophanous, Committee member Tanya Yucel, Director Sema Kiamil and Project Coordinator (North of England) Elaine Miller


24 November 2011 - NHS Sickle/Thalassaemia Screening Programme Public Outreach Steering Committee meeting – Attended by UKTS Director Sema Kiamil and Project Coordinator (North of England) Elaine Miller

26 November 2011 – UKTS annual dinner dance, Regency Banqueting Suite, London

27 November 2011 – NEBATA annual conference – Attended by UKTS Project Coordinator (North of England) Elaine Miller

28 November 2011 – NHS Sickle/Thalassaemia specialist nurses project service user workshop, SSCAT Centre, Sheffield – Attended by UKTS Project Coordinator (North of England) Elaine Miller

30 November 2011 – UKTS Project Coordinator (North of England) Elaine Miller attended the patient clinic held by Dr Kate Ryan, Consultant Haematologist, Manchester Royal Infirmary

30 November 2011 – National Association of Hospital Place Staff meeting (presentation) – Attended by UKTS President Gabriel Theophanous
We would like to inform all our members that Thalassaemia Matters will henceforth be issued twice per year. We are sure our members will understand that the rising costs of printing and postage make it impossible for us to produce more frequent issues. N.B. For those members who have an email address, it is possible for us to send Thalassaemia Matters to you as a pdf attachment. If you would prefer to receive the newsletter in this format, please contact the UKTS office office@ukts.org.

This year’s Virgin London Marathon took place on 17th April. Congratulations and thanks to all our brave runners who raised much-needed funds for UKTS; Denise Harding, Tony Lambrou, John Moran, Mike O’Sullivan, Naresh Trivedi and Marianna Vasiliou.
We provide valuable medicines to rare disease patients
July 2011 brought some very sad news to UKTS, with the passing of our dear friend and founder member Mario Sergides. Mario and his wife Tina, both thalassaemia patients, have always been extremely loyal supporters of the Society and Tina has served several terms on the Management Committee, finally becoming Vice-President in 2001 with Mario by her side. Unfortunately a few years ago Mario suffered a spinal stroke which rendered him paraplegic. He was thereafter cared for by Tina. He passed away in the University College Hospital on 27th July 2011. Mario's funeral was held on 3rd August at the Greek Orthodox Cathedral of the Holy Cross & St Michael in Golders Green, North London. We reproduce here words from his eulogy, which was spoken by his old friend (UKTS Secretary) George Constantinou.

In the very early days of the Society, a group of us thalassaemia patients used to have meetings in a room at the Royal Free Hospital. Mario was the youngest of the group, being only 12 or 13 at the time. I used to collect him and give him a lift to the meetings and I remember fondly how offended he got when I insisted on holding his hand when we crossed the road! He told me in no uncertain terms that he was not a child and didn't need to be treated like one. Mario was never shy of giving his opinion. Although he was by far the youngest, he was very outspoken in our group and he often kept us entertained. Mario always had a wicked sense of humour and he refused to let anything dampen his spirits, not even thalassaemia – he refused to let it dominate his life. In fact, in a gesture typical of Mario, he even poked fun at thalassaemia by having a large, bald vampire (complete with camera, as Mario was a keen photographer) tattooed on his arm. Nowadays everybody and their grandmothers seem to get tattoos but back then it was considered quite a daring thing to do – but that was Mario. He was his own person, a great character and a great friend.

He often used to help us out with his originality and creativity and his presence in meetings provided an alternative way of thinking about our work. He also introduced us to others that could help in our work. There was never a dull moment with Mario in a meeting and he ALWAYS had a knack of getting people to listen. Mario was an intelligent man and we remember fondly the debates that were had by many.

Words cannot really express what a beautiful couple Mario and Tina made. We could all see how much happiness they brought each other. You would never hear one name without the other and they faced everything unconditionally with each other. Tina was Mario’s rock and Mario was Tina’s rock, each bringing the other happiness, strength and above all true love. Their love made their houses in London and Cyprus into homes where many gathered; and they created very special memories for so many. The last few years had been very difficult ones for both Mario and Tina. It is always tragic when a young person suffers a stroke but it seemed particularly cruel that it should happen to Mario who was always so active and full of life. He coped as he had always coped, with courage and some humour. And no-one could have had better care than Tina gave to Mario. She cared for him devotedly and went to extraordinary lengths to make his life as easy and comfortable as possible. Tina, we hope you can take some comfort from the fact that you did everything you could possibly have done for Mario. On behalf of all your “thalassaemia family” at the UK Thalassaemia Society, we will always remember Mario with love and be grateful that we had the privilege of knowing him.
Our grateful thanks go to Paul Jarvis who raised over £350 for the UK Thalassemia Society by completing the Cowman Middle Distance Triathlon on 3rd July 2011. Paul’s employers, DHL, have kindly agreed to match the sponsorship funds, bringing the total raised to almost £700. Paul raised the money in memory of his friend, thalassaemia patient Ruby Saluja, who passed away in 2001.

Paul said afterwards “I’ve been competing in Triathlons for over five years and this was my toughest race, especially on the run as there was no shade and no wind so it got very, very hot. I was able to get through with support from a great crowd and the inspiration of raising funds for such a good cause. I was delighted with my time but more pleased to have raised a decent amount of money. When I found out that Ruby had passed away, I had to look up thalassaemia as it is a condition I’d never heard of. After talking to the UK Thalassemia Society and finding out about all the great work that they do in educating potential carriers and supporting sufferers, I was determined to try and do something to help them with this work.”

UKTS Welcomes NEW-MEMBERS

**Annual**

Meliz Toros
Sumara Jawad

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Charity Reg No. 275107

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- **Surname:** 
- **Address:**

If you are a patient or parent of a patient please complete the section below

- **Patient’s Name(s):** 
- **Date of Birth:**
- **Sex:**  □ Male  □ Female
- **Type of thalassaemia: (e.g. Major, Intermedia, Haemoglobin H etc)**

#### Contact Details
- **Telephone:**
  - **Home:**
  - **Work:**
- **Mobile:**
- **Fax:**
- **Email:**

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