



**2** PanEuropean Conference on Haemoglobinopathies  
13-14 MARCH 2010 – BERLIN

# 2<sup>nd</sup> Pan-European Conference on Haemoglobinopathies

13–14 March 2010, Berlin



Thalassaemia  
International  
Federation

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# 1. Executive summary

The 2<sup>nd</sup> Pan-European Conference on Haemoglobinopathies was held on 13-14 March 2010 in Berlin, with two pre-conference meetings taking place on Friday 12 March.

This was the first Europe-wide conference on haemoglobin disorders. A one-day workshop had been previously held in 2007, in the context of the 4<sup>th</sup> European Conference on Rare Diseases, which attracted 150 doctors and patients from across Europe and demonstrated a need for a larger-scale educational event addressing medical professionals, patients and national and EU policy-makers. In many EU Member States, the frequency and prevalence of haemoglobinopathies are steadily growing through immigration from affected regions. There is still a gap in awareness by health professionals of diagnosing and treating patients with Hb disorders, and in many EU member states national strategies for control are lacking and patients are not receiving adequate care.

The conference aimed to raise public awareness of Hb disorders in participating countries and at EU-level, and to empower patient groups through knowledge, support resources and networking. It also aimed to contribute towards sharing best practices and experiences at European level, between and among doctors and patients, in order to extend knowledge and capabilities to national and local levels, to promote optimal management and prevention of Hb disorders and therefore to control their public health burden. A wider aim was to highlight the inequalities that patients with haemoglobinopathies across the EU face in access to optimal care, and to address these inequalities through extending knowledge gained in experienced countries to other European states, promoting networks of medical and patients' communities.

A patients' perspective was given strong emphasis through the inclusion of patients into the scientific and organisation committees, inviting and supporting patients' participation from all affected countries, the inclusion of specific patients' issues in the conference programme, and importantly through promotion of dialogue between the patient and medical communities, due to the mixed audience format of the sessions.

As Hb disorders in Europe fall under the definition of rare diseases, affecting less than 1/2,000 people, rare diseases forms the wider policy context of the conference. The conference addressed the priorities of the 2<sup>nd</sup> Health Programme as specified in the Commission 2009 Work Programme, Art. 3.3.2.8, "Prevention of major and rare diseases" – "developing European cooperation on rare diseases, in particular regarding their recognition, shared information on them, and cross-border cooperation in diagnosis and treatment through European reference networks." It also referred indirectly to the objective of reducing health inequalities, as the dissemination and implementation of good practices for Hb disorders across Europe can be said to contribute to more equitable access to healthcare for patients with haemoglobin disorders across the EU.

EU added value was provided through dissemination of EU policy and project developments, as well as best practices on Hb disorders at European level, to an audience including representatives of all stakeholders primarily doctors, patients and parents, who are expected to share these with their national and local networks.

The conference also complemented the work of the Thalassaemia International Federation (TIF) with other international and European-level organisations and its projects, primarily the

EC co-funded ENERCA project (the European Network for Rare and Congenital Anaemias), in which TIF is a work package leader.

The 2<sup>nd</sup> Pan-European Conference on Haemoglobinopathies attracted participants from 19 EU member states and a total of 34 countries, including EU neighbouring countries Turkey, Albania and Morocco, which are the origin of many migrants entering Europe.

Target participants were patient representatives from all EU MS known to be affected by Hb disorders; health professionals involved in treating Hb disorders (mainly haematologists and paediatricians, but also other health professionals such as nurses); European and international bodies, organisations and agencies, as well as government and industry representatives.

The official language of the conference was English. In recognition to the diverse and multilingual audience, conference translation was available from English to German, Greek, Italian and French.

The conference was awarded with 13.75 CME Units from the European Haematology Association.

## 2. Purpose of the conference

The purpose of the conference was to bring together patients, medical professionals, and other stakeholders from across Europe in order to share best practices on patient care, prevention and patient empowerment and to encourage MS to recognise and address the public health burden of Hb disorders.

Hb disorders (thalassaemia and sickle cell disease) are genetic red cell disorders that lead to poor quality of life and death if not diagnosed early and managed appropriately. An estimated 7% of the global population carries an abnormal Hb gene. Successful control relies on nationally supported programmes for prevention and multidisciplinary management. Abnormal Hb genes are mainly prevalent in Africa, Asia, Middle East, South America, West Pacific and in Europe around the Mediterranean. In the rest of Europe, migration from affected regions has introduced the genes into the populations and prevalence continues to increase.

The status of Hb disorders varies between European countries, which can be broadly categorised into those with indigenous carrier rates of 6-19% where successful control programmes are long-established and serve as models (e.g., Cyprus); Those where Hb disorders occur at lower rates and national control services exist to varying degrees; Those where Hb disorders were introduced through migration and appropriate services either exist (e.g. UK) or must be developed (e.g. Germany). Even where services exist their take-up can be hampered by low awareness by patients and doctors, lacking data on numbers and location of patients, and cultural/language barriers.

In Europe Hb disorders fall under rare diseases. Sharing best practices and experiences at European level, and between countries, is crucial for reducing inequalities of patient access to appropriate care.

### 2.1. General and specific objectives

The general objective of the conference was to promote optimal management and prevention of Hb disorders in the context of European policies of rare diseases, to help reduce inequalities in access to optimal care, to disseminate good practices and share experiences between and among patients and doctors.

The specific objectives of the conference were defined as follows:

1. To gather together patient representatives as well as health professionals working in the field of Hb disorders from all affected European countries.
2. To extend the knowledge gained in experienced countries to other European countries through sharing experiences and best practices.
3. To update participating health professionals on state-of-the-art of clinical management and patients' needs.
4. To raise public awareness of Hb disorders among national authorities and medical communities at country and EU-level.
5. To inform patients and families about optimal care, available support resources and networks.

6. To gather patients' evidence of the status of Hb disorders, standards of care and patient-government relations in various European countries, as well as investigate patients' expectations regarding reference networks of centres of excellence.
7. To inform medical and patient communities and policymakers of the latest EU-level policies, projects and legislative developments in the fields of rare diseases, medicines, patients' rights and mobility, reference networks, etc.
8. To promote networking of patients' associations, sharing information and contacts, disseminate information on benefits of forming national associations and transnational networks.

## **2.2. Expected outcomes**

In the long term, these objectives should contribute to improvements in the standard of thalassaemia and sickle cell patient care across Europe, resulting in more equitable access to optimal care. Specifically, it is expected that:

1. Participating health professionals will gain an improved awareness of diagnosis and management of patients as well as prevention of Hb disorders.
2. National health policy-makers will have an improved awareness of the epidemiology and public health burden posed by Hb disorders, and of the requirements for optimal patient care.
3. Patients/parents will have better awareness of national and international networks.
4. Patients/parents will have better awareness about the condition and its optimal treatment, as well as relevant health policies.
5. TIF will have a better awareness of patients' needs and specific challenges faced in various EU MS, and will be able to focus its future activities accordingly.

### 3. Description of the conference

The conference programme ran over two days on 13-14 March 2010, with two pre-conference meetings held on the day prior to the conference, Friday 12 March. The full conference programme is attached in [Annex 1](#).

For maximum benefit to participants and other stakeholders, the detailed conference proceedings will be published in an extensive report (forthcoming) and disseminated to all participants, the patients' and medical communities, European-level patients' and relevant medical organisations and bodies, the European Commission and other appropriate EU-level decision-making bodies, WHO regional/country offices, and national health authorities in the 27 EU Member States and neighbouring countries.

#### 3.1. Day 1 (13 March 2010) – Plenary sessions and workshops

##### Opening Ceremony

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*Chairpersons:* Androulla Eleftheriou, Gerhard Gaedicke

*Speakers:* Panos Englezos, Gerhard Gaedicke, Günter Jonitz

The speakers welcomed the audience. In addition, a message of support was conveyed via telephone from the European Commissioner for Health and Consumers, **Mr John Dalli**, who was unable to participate in person due to a previous commitment.

##### Keynote lectures

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*Speakers:* Béatrice Gulbis, Paul Telfer

The programme was opened by two keynote lectures. The first was by **Dr Beatrice Gulbis** of the Erasme Academic Hospital in Brussels. She pointed out that despite World Health Assembly resolutions urging member states to establish national programmes for prevention and patient care of haemoglobin disorders, this has not yet materialised in many European states. This is partly because of the rarity of the disease in many parts of Europe, and also since it is a relatively new importation from immigrants who came from high prevalence areas. With the adoption of policies for rare diseases across the EU now, there are more opportunities to improve services for these disorders. In these efforts, both through the Commission's policies and the efforts of national and international patients' groups, the patient has been placed at the forefront of comprehensive care and there is increased spread of information promoting patient empowerment.

**Dr Paul Telfer** of the St. Bartholomew's and the London Hospitals in the UK, touched on another important and emerging challenge in haemoglobinopathy care, that of improved care life expectancy with many patients now over the age of 40 years. The expected complications, the kind and frequency of monitoring and the treatment in this age group are still under consideration since long term complications such as liver disease, bone disease, infections, malignancy, thrombotic disease, pulmonary hypertension, chronic renal impairment and others, are still being identified and long-term follow-up is sparse. Dr Telfer also emphasised the need for networking of haemoglobinopathy centres with long-term

follow-up data being acquired for research, audit and training, including the development of protocols and guidelines for this relatively new group of patients.

## **Plenary 1 – Screening of Haemoglobinopathies**

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*Chairpersons:* Antonio Cao, Michael Angastiniotis

*Speakers:* Allison Streetly, Antonio Cao, Piero Giordano

The first plenary session was dedicated to prevention practices for haemoglobin disorders. The first speaker was **Dr Allison Streetly**, Programme Director of the NHS Sickle Cell and Thalassaemia Screening Programme of the U.K. She described the advisory role of the UK National Screening Committee in developing government policies such as the linked newborn and antenatal programme. Developing a screening programme requires policy development and endorsement, data and standards, funding, implementation plans which include laboratory facilities, information technology, counselling, education, training, quality assurance, monitoring and evaluation. In a multi-cultural population, acceptability of the programme by each community is of key importance. There is also a wide variation in prevalence across the country so that different screening algorithms must be adopted for high and low prevalence areas. Community awareness and engagement are essential not only for the adoption of screening but also for prenatal diagnosis and sensitivity to each community's needs is required (including language).

**Professor Antonio Cao** of the University of Cagliari, Sardinia, with long experience in prevention of thalassaemia in a high prevalence population, also emphasised the organisational aspects of a prevention programme, including the need for adequate facilities, education campaigns, liaison with doctors as well as the patient associations and the need for reference centres with satellite units. All this must be incorporated in the National Health System. In the Northern European setting there is lack of awareness among policy makers, health professionals and the immigrant groups at risk. In some groups consanguineous marriage is customary. It is important to emphasize the voluntary nature of the programme and to avoid discrimination. General ethical principles such as respect of person, autonomy and beneficence must be adhered to. Suggested European policies for prevention are: guidelines for laboratory services; counselling; education (both for health professionals and the general population); electronic information system.

**Dr Piero C Giordano**, director of the Haemoglobinopathy laboratory of Leiden University Medical Centre in the Netherlands, described the neonatal and other screening policies in Holland. He demonstrated mainly the laboratory techniques used in screening, such as HPLC for the neonatal screening programme and compared it with capillary electrophoresis. The latter is a relatively new introduction which gives good resolution and quantifications.

## **Plenary 2 – Clinical Management of Thalassaemia**

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*Chairpersons:* Aurelio Maggio, Renzo Galanello, Antonio Piga, Holger Cario, Loizos Pericleous

*Speakers:* John Porter, Aurelio Maggio, Maria Domenica Cappellini, Renzo Galanello, Antonio Piga, Chris Sotirelis, Michael Angastiniotis, Ali Taher, Paul Telfer

The second plenary session was devoted to clinical management and was initiated by **Professor John Porter** of the University College Hospital, London. He reviewed transfusion therapy, including the goals of transfusion, donor selection, blood storage, compatibility

testing and adverse reactions. He described the recommended transfusion regime in order to optimise oxygen carriage and minimise iron loading. After following TIF guidelines for most aspects of blood transfusion, Prof Porter described some newer developments. These included:

1. Pathogen reduction by various treatments, especially those that may be effective in red cell concentrates, such as Riboflavin light treatments.
2. Embryonic Stem Cells – may be used to produce mature, viable red cells in sufficient numbers for transfusion. Also, induced pluripotential stem cells (IPS) from skin fibroblasts or other somatic stem cells, may also be a source, according to recent studies. This means that functional oxygen-carrying red cells may be produced on a large scale with oxygen equilibrium curves comparable to normal red cells.

**Dr Aurelio Maggio** of the University of Palermo, Sicily, gave an overview of iron overload and its effects. He described the mechanisms involved in transfusional iron load and its assessment using serum ferritin, transferrin saturation, liver biopsy, MRI and SQUID. He reviewed the role of genetic modifiers such as the C282Y HFE (haemochromatosis gene mutation), in increasing the severity of iron loading. He also reviewed the role of iron overload in organ complications, such as the heart, the gonads, the liver, the pancreas (diabetes) and the effect on survival. Dr Maggio concluded that the available MRI methodologies, which quantify iron overload in different organs, should make possible the tailoring of chelation treatment to specific organ involvement, further improving clinical outcomes, including survival.

**Professor Maria D Cappellini** of the University of Milano, Italy, reviewed the iron chelation history and proceeded with a more detailed analysis of the development, efficacy trials and other assessment of two chelating agents, Desferrioxamine and Deferasirox.

**Professor Renzo Galanello** of the 2<sup>nd</sup> Paediatric Clinic and the Thalassaemia Paediatric Unit of the University of Cagliari, reviewed the clinical use, safety and efficacy of Deferiprone, used as monotherapy or in combination with Desferrioxamine. Data on the cardioprotective effect of Deferiprone were present and also the effect on survival.

**Dr Ali Taher** of the American University of Beirut Medical Centre, gave an overview of total body chelation emphasising the goals of iron chelation which are to prevent accumulation, by matching transfused iron with chelated (excreted) iron, removing excess iron and detoxification of labile, unbound iron, particularly when Deferasirox is used. He made special mention of the control of iron loading in Thalassaemia Intermedia patients.

One important aspect of patient care is the adherence to prescribed therapies by patients. The health professional's perspective was presented by **Dr Antonio Piga** of the University of Torino Thalassaemia Centre. Dr Piga felt that the terms compliance, adherence and concordance referred to the voluntary cooperation of the patient in following a prescribed regimen, including timing, dosage and frequency. Compliance, especially to iron chelation is crucial to survival. He reviewed methods for assessing compliance and emphasised the obstacles to optimal compliance, both emotional and physical. According to modern thinking, the patient's view takes precedence. This raises challenging questions about choice and responsibility because if the patient's choice falls substantially short of "safe" levels of treatment according to evidence based guidelines, then the doctor may be left with a burden of responsibility that is hard to manage emotionally, ethically and legally. A change in the culture of the doctor-patient encounter is needed but this does not mean just improving communication skills but must involve mutual respect for both the doctor's professional opinion and the patient's personal decisions (see [www.medicines-partnership.org](http://www.medicines-partnership.org)).

Compliance is a function of trust, of the quality of health professional – patient relationship, which considers the emotional as well as the physical obstacles to chelation, and is a well-balanced and close one.

The patient's perspective was presented by **Dr Chris Sotirelis**, a transfusion dependent thalassaemia patient and an aeronautical engineer by profession. He pointed out that adherence to medication has been a big problem since the time of Hippocrates. He felt however that terminology describing the phenomenon of not taking medication had a significant effect on patients' attitudes. Compliance, the term traditionally used, refers to conformity, "complying or else...", in which patient beliefs are not interacting or are seen as an obstacle to treatment. It implies passivity on the part of the patient, who, if not complying is seen as a rebel, incompetent or a nuisance. The term "adherence" on the other hand, has the quality of clinging or being closely attached to a set regimen, following the rules, guidelines or standards. Adherence implies a more active role, a collaboration with the physician and a self-motivated decision to adhere to advice. In this model, patient acceptance is based on trust. The patient should convey his/her health beliefs to the doctor and the doctor should assist the patient to make an informed choice. In this way, an alliance is formed, in which the most important determinations are agreed to be those made by the patient. This leads to the concept of concordance which is not synonymous with either compliance or adherence.

Thalassaemia patients are asked to comply with many treatments and this reduces life to "getting treatment". There is need to respect the patients' "normal life" priorities and the patients' time to fulfil them. The patient expects the doctor to share in the battles and be an ally, helping to reduce the burdens of the condition and the treatment.

The theme of quality of care and of quality of services was taken up by **Dr Michael Angastiniotis**, a medical advisor to TIF. He pointed to the improved survival of birth cohorts as treatment improved over the years, yet quality of life is an equal priority for service providers. Quality of life depends on many factors in thalassaemia such as the patient being in a good clinical condition with minimal complications, including the endocrine ones which affect appearance and sexual development and the experience of pain. The quality of psychological support will allow the patient to fulfil life expectations, such as education, employment, marriage and having children. To achieve this quality of life, quality of care is an essential principle, yet this is unevenly provided and equity of care has not been achieved throughout Europe. Both quality and equity of care require services planned at central level. Planning is often poor because there is often a lack of awareness among both health planners and the public. The needs are many and include multidisciplinary care and psychological support in treatment centres of excellence. Chronic disorders demand comprehensive care, treating the whole person and the family, considering physical, emotional, educational, financial and vocational factors. Centres of Excellence have been defined by the EU Rare Disease Task Force in their report of 2006. The criteria include comprehensive care, the capacity to provide expert diagnosis by experienced and well qualified staff, supporting self-management and networking with secondary centres and other expert centres. Another set of criteria was formulated in the USA by EH Wagner and associates as the Chronic Care Model. This includes good healthcare organisation with a delivery system design, promoting self-management support. The community resources in this model are recruited to support the patient while for the care team decision support and clinical information systems are provided. A recognised need in treatment centres is decision support, such as evidence-based guidelines. The availability of an Electronic Health Record, which reflects the multidisciplinary nature of care is a valuable tool .

The plenary session was completed by an update on survival in thalassaemia by **Dr Paul Telfer**. He pointed out that survival analysis gives information on prognosis, changes in

trends, especially comparing different treatments and providing predictive data for planning of health service needs. Information is provided on the causes of premature death, the main cause of which is heart disease. Good life expectancy has been shown to depend very much on adherence to chelation therapy. Cardiac mortality is decreasing with the introduction of early detection of iron overload by cardiac MRI and the early use of Deferiprone and combination treatment. Globally, survival depends on availability and accessibility of treatment which very much depends on the economic status of the country. In low income countries, treatment is available only to a small minority who can afford it.

### **Joint Workshop – Addressing patients’ concerns**

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*Chairpersons:* Panos Englezos, George Constantinou

*Panel:* Vincenzo de Sanctis, Anna Meo, Soroya Beacher, Roswitha Dickerhoff, Marco Bianchi, Yameen Rasul, Loizos Pericleous, Ofrah Muflani, Michael Michael, Edith Aimiuwu

*Speakers:* Soroya Beacher, Yameen Rasul, Loizos Pericleous, Ofrah Muflani, Michael Michael, Anton Skafi

The role of the national and international patients’ associations in the quality of care provided to the patients, was developed by **Dr Roswitha Dickerhoff** of the University of Düsseldorf. There are 450-500 Thalassaemia major patients in Germany and 1000-1500 Sickle Cell patients, who are distributed widely across the country. This means that often there is only one patient per institution. National Associations have a task of bringing these isolated patients into contact with other patients and families and of providing information about the available services. It helps to establish contacts of migrant patients with their country of origin and obtaining information concerning the disease in their own language. In Germany so far, the needs of the specific health issues of the migrant population, (9 million inhabitants from countries at risk for haemoglobin disorders), have not been met. Specifically, there is no screening in early pregnancy and no neonatal screening. For this reason, patient associations will have to become active in health politics.

A major issue during the conference was patient-centred healthcare. This theme was initiated by a patient, **Mr Yameen Rasul**, of the North of England Bone Marrow and Thalassaemia Association. He posed the question “What is being treated, the patient or the illness?” It is easy to forget the patient who wants to live a normal life, and not just to be alive. In practical terms it means being able to fit treatment around the person’s life, such as arranging flexible appointment and transfusion times and taking the patient’s point of view in the decisions about treatment policy and in running hospitals. This requires patients who are well informed and experienced health professionals and good communication between them.

**Mr Loizos Pericleous**, President of the Cyprus Association and TIF board member, explained the “Reach the Patient” project, whose main aim is to provide quality information to every patient across the world. Disseminating such information is by means of the associations, the TIF magazine, electronic communication (such as an e-newsletter in various languages), through networking (regionally and globally) and through the development of an expert patient group in each country, able to communicate with other patients who can benefit from their experience. Patients who have such knowledge feel empowered in their relationship with healthcare professionals, have a higher self-esteem to cope and achieve goals. They have better health outcomes and quality of life. A national Patient Registry should be created

The next theme concerned the role of the haemoglobinopathy nurse, presented by **Ms Ofrah Muflahi** from the National Health Service, West Midlands, UK. She described the key competencies required for a specialist nurse. These are:

- A patient-centred approach which includes understanding of culture, religion, family dynamics and language.
- Knowledge of legislation and patients' rights.
- The importance of compliance to medical treatment.
- Having the skills of a counsellor but also recognising the need to refer at-risk couples to a genetic counsellor.
- Being up to date in clinical skills
- Being involved in partnership with community activities, locally and nationally, especially in parent and patient forums and educational activities.

**Mr Michael Michael**, president of the UK Thalassaemia Society, discussed the subject of social integration. He pointed out that in many countries around the world, social integration cannot even be discussed since a thalassaemia patient's life is measured by the financial burden on the family and survival is only for the rich few. Social integration cannot even be discussed until the community reaches a stage where new births are limited, clean, safe and adequate treatment is provided and survival rate is increased. Social integration basically means that if you have friends, enjoy life and achieve the same as everybody else in society, you will be happy, healthy, wise and integrated. Most thalassaemia patients are already integrated but do not always realise it. Above all is Love, love of friends and family.

Another member of TIF Board of Directors, thalassaemia patient **Mr Anton Skafi**, discussed the role of national and international patient associations. To be effective associations need members who are well motivated. Their more general functions include education and the dissemination of information, such as the production of books, guidelines and other publications in local languages. In addition associations strengthen local and assist health authorities in the development of policies.

National associations are usually established by motivated individuals such as parents and doctors, and work mainly with volunteers. They act as a pressure group and as a support group. They also have a mission to increase awareness in the community, promote prevention and research, considering ethical, legal and cultural issues in the community.

### **Joint Workshop – European Developments in the areas of Expert Centres and Registries**

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*Panel: Joan Lluís Vives Corrons, Antonio Piga, George Constantinou, Patricia Aguilar Martínez, Isabelle Thuret*

*Speakers: Isabelle Thuret, Michele Lipucci di Paola, Joan Lluís Vives Corrons, George Constantinou*

The subject was introduced by **Dr Patricia Aguilar Martínez** of CHU de Montpellier, France, and group leader in the Enerca project.

The first speaker was **Dr Isabelle Thuret** of the rare Disease Centre for Thalassaemia in France. As in other northern European countries, beta-thalassaemia is a rare disease in France and so, until recently, no national data on this condition were available. In 2004,

France adopted a national plan for rare diseases and one centre was dedicated to develop a National Registry of beta-thalassaemia patients, to characterise demographic and clinical features of patients. A total of 437 patients were included on the register from 2005 to 2009, from 65 different paediatric or haematology departments. The majority of these departments treat less than 5 patients each, while 6 centres follow more than 15 cases. 71% of these patients were born in France. The geographical location of patients has been mapped and so reference centres chosen are located where the majority of patients are located i.e. Marseille and Lyon. The register has allowed the recording of clinical characteristics of patients, showing for example that the median age of thalassaemia major is 19 years, 20.6% are HCV positive, 6.4% have diabetes and 10.6% are in heart failure.

The subject of networking, especially of expert centres, was developed by **Professor J L Vives Corrons** of the Hospital Clinic, University of Barcelona and the Head of the Enerca consortium (European reference Network of Expert Centres in Rare Anaemias). He explained the main purpose of Enerca, which is to increase the efficacy of diagnosis, treatment and follow-up of patients with Rare Anaemias and to improve the quality of their life. To achieve these aims, the Enerca consortium is promoting programmes to increase awareness, provide training, harmonisation of protocols, to collect epidemiological information, to facilitate networking and to promote research. The project is promoting the creation of a European Registry of Rare Anaemias. There is need to identify centres of Expertise for rare anaemias, which meet European criteria and satisfy patient expectations.

The patients' view and expectations from expert centres was expressed by **Mr George Constantinou**, a TIF and UKTS Board Member. He expressed patients' expectations with these words: "It is essential that patients feel that the unit is their 'own place' and that the medical staff have the patient's best interest as their priority. Long-term management implies collaboration of the patient and the family with the well organised treatment unit to ensure continuous, appropriate treatment for a long and productive life for the patient".

In order to have patient-friendly services, more was needed and he gave the following examples:

- Staff willing to spend time and listen to patients with respect for privacy and confidentiality
- There is need for convenient appointment times with due consideration of school and working hours.
- Consideration of the family as well as the patient's feelings
- Developing a partnership relationship between professionals and patients.
- Empowerment requires knowledge so that time must be devoted to patient education

### **3.2. Day 2 (14 March 2010) – Plenary sessions and workshops**

#### **Key Presentation Dr Karl Freese, European Commission DG Health and Consumers**

This was a presentation by Dr Karl Freese of the EU Commission, DG, SANCO, and concerned the EU policies on rare diseases. Legal basis for the developments of the EU Public Health Policy, was based on Article 168 (former 152) of the EU Treaty. For the period 2008-2013 the Commission has adopted the White Paper "Together for Health: A Strategic Approach for the EU 2008-2013". Actions under Objective 1 of this EU Strategy cover a Communication on European Action in the Field of Rare Diseases. As a consequence Rare diseases are now one of the priorities in the Second EU Health Programme 2008-2013. The Member States are invited to establish national or regional action plans for rare diseases before 2013

### Plenary 3 – Clinical Management of Thalassaemia and Sickle Cell Disease

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*Chairpersons:* Dora Bachir and Maria Domenica Cappellini

*Speakers:* Frederick Galacteros, Marianne de Montalembert, Holger Cario, Vito Di Marco, Alastair Kent

**Dr Frederic Galacteros** of the Red Cell Genetic Disease Unit, Henri Mondor University Hospital, Creteil France, reviewed the pathophysiology of sickle cell disease. He described the different pathophysiological levels, which include: Haemoglobin S polymerisation in vitro, intracellular HbS polymerisation, red cell sickling, red cell adhesion to the endothelial border, the sickle vascular disease, intravascular haemolysis, the vaso-occlusive crisis, the acute chest syndrome, and specific organ damage. These complications have an environmental as well as a genetic background. The percentage of fetal haemoglobin (HbF) influences the natural history. When elevated complications such as episodic pain, acute chest syndrome, and leg ulcers are reduced and so the drug, hydroxyurea is helpful since it increases the HbF level. Most deaths are caused by vaso-occlusive accidents (44%), while severe sepsis causes 16% of deaths and chronic organ complications (hepatic, renal, cardiac) are responsible for another 16%.

**Dr Marianne de Montalembert** of the Necker Enfant Malade Hospital in Paris discussed the management of sickle cell disease in children. In children sepsis is the main cause of death. If the disease is diagnosed early in the neonatal period, then survival is much improved – 98-99% at 10 years - because of the prophylactic measures against infection. On contrary, if diagnosed later survival falls to 92% over the first 10 years. With proper early protection against pneumococcal sepsis, the survival at 16 years in the UK is 99%. Neonatal screening is not universal across Europe and is mainly practiced in 5 countries. Preventive care is necessary with early immunisation and penicillin prophylaxis, parent and patient education, and monitoring by annual transcranial Doppler ultrasound and, from the age of 5-10 years, annual echocardiography, hepatic ultrasound, ophthalmologic evaluation and pulmonary function tests.

The severity of sickle cell disease varies widely between patients. Stroke may occur at an early age – around 1% per year between 2-5 years of age. By the age of 20 there is evidence of stroke in 11% of patients. Those who develop serious complications such as hyperhaemolysis, splenic sequestration, aplastic crises, stroke, acute chest syndrome, organ failure and priapism are recommended to commence regular blood transfusion therapy. This necessitates monitoring for transfusion complications such as alloimmunisation and iron overload. Hydroxyurea may also be used in children and long term benefits have been demonstrated such as protection from acute chest syndrome and stroke. Also a better life expectancy is achieved. Bone marrow transplantation is recommended if there is an HLA compatible donor in the family, in severe forms of the disease where stroke and other complications occur and before severe organ damage has occurred.

**Dr Holger Cario** of the Children's Hospital, University of Ulm, Germany, described the difficulties of transition of patients with thalassaemia and sickle cell disease, from paediatric to adult medical care. Difficulties arise because of abrupt transfer with little preparation, lack of communication between paediatric and adult medical care providers, lack of familiarity of the adult provider and a lack of transmission programmes, which include education, discussion and support. Transition is recognised as a challenging, complex and multisided process. Common treatment standard are needed, with close collaboration of the multidisciplinary team, but also of training of health professionals as well as patients and

integration of the patient into decision making . It is desirable to initially have joint appointments with both the paediatric and the adult physician.

**Dr Vito Di Marco** of the Gastroenterology and hepatology department of the University of Palermo, Italy, described the chronic liver disease of thalassaemia. The causes of liver damage in thalassaemia are both iron overload and viral infections. These can lead to chronic hepatitis, cirrhosis and liver cancer. The common viruses are Hepatitis B (now reduced due to general vaccination) and hepatitis C (HCV) which affects 20-80% of the thalassaemia population. In investigating the condition liver biopsy is an important tool although non-invasive markers can be used to evaluate fibrosis, especially transient elastography (Fibroscan) and MRI. The goals of treatment are to eradicate the virus and to control liver inflammation and fibrosis. Current treatment is by a combination of Pegylated Interferon and Ribavarin. Response is influenced by the viral genotype. The need for blood transfusions can increase due to the Ribavarin- associated haemolysis.

**Mr Alastair Kent** of the Genetic Interest Group discussed the value of networking which adds value through critical mass, cooperation, communication, efficiency, effectiveness and expertise.

#### **Plenary 4 – New Scientific Developments**

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*Chairpersons:* Gerhard Gaedicke and John Porter

*Speakers:* Emanuele Angelucci, Stefano Rivella, Giuliana Ferrari, Roberto Gambari

The 4<sup>th</sup> plenary session was concerned with other approaches to treatment. The session was initiated by **Dr Emanuele Angelucci** of the Cagliari “A. Businco” Oncology Centre, who gave an update on stem cell transplantation in thalassaemia. Allogenic haemopoietic stem cell transplantation is now used in increasing numbers. The European Group for Blood and Marrow Transplantation (EBMT) has a registry of over 3000 transplants, ranging from 133-197 per year in the last 15 years. The classical approach is to use marrow derived haemopoietic stem cells from an HLA identical sibling. With this approach, the overall survival of 1086 patients from the EBMT registry was in the region of 90% and the disease-free survival 80% over a period of 12 years. Best results are achieved in younger patients with less iron related tissue damage. In adult thalassaemia patients, the risks are higher, giving a thalassaemia-free survival of 67% and a transplant-related mortality of 27%. Since approximately 1 in 3 of patients has an HLA identical sibling, the use of matched unrelated donors has been offered. Results are now similar to those obtained from sibling donors, as reported by an Italian multicentre study involving patients 2-17 years old. The thalassaemia-free survival is 88%. The results are poor when class 3 patients are involved with a 30% non-rejection mortality.

Stem cells, derived from cord blood of HLA identical sibling are increasingly being used. According to the Eurocord study, reported in 2008, neutrophil recovery is shown in the first 40 days than marrow derived transplants but the incidence of acute & chronic GVHD is much less and survival is the same. Experimental approaches include the use of less toxic, non-myeloablative conditioning regimes. Experience from 11 cases where a minimal toxicity regime was used (Walters ASH 2005) showed that stable engraftment is not achieved in the majority of cases, possibly due to the expanded erythropoietic tissue.

Another experimental approach is the use of unrelated cord blood. Disease-free survival in a small published series was only 65% and mortality was 20%. A third experimental approach

is to use a related haploidentical donor. Results recently published indicate a good survival rate resulting in a thalassaemia-free survival of only 61%.

#### The Gene Therapy lectures

Two lectures were presented at the conference by well-known researchers in the field. The first was given by **Dr Giuliana Ferrari** of the SR-Telethon Institute for Gene Therapy in Milano. Gene transfer aimed to correct a genetic defect has long been under investigation. In recent years some clinical trials have been initiated.

The proposed process is to retrieve and purify stem cells (CD 34<sup>+</sup> cells) from the patient and to transduce them with a viral vector in which the functional  $\beta$ -globin gene has been introduced. These stem cells now have a gene able to produce  $\beta$ -globin, they are genetically corrected and so are infused back to the patient. Success of gene therapy depends on efficient gene transfer to the target stem cells, adequate and persistent production of  $\beta$ -globin (gene expression) and safety. At the San Raffaele Telethon Institute for Gene Therapy (HSR-TIGET) in Milan, for  $\beta$ -thalassaemia, a clinical trial is scheduled for 2012. In preclinical research, a lentiviral vector has been developed at the Institute termed GLOBE-LV, whose therapeutic potential has been validated using thalassaemic mice as well as human thalassaemic stem cells.

**Dr Stefano Rivella** of the Weill Cornell Medical College in New York, using a different lentiviral vector – the TN59, also demonstrated therapeutic levels of haemoglobin in thalassaemic mice. Experimental work has demonstrated that genotype influences the outcome of gene transfer so that in  $\beta^0$  mutations  $\beta$ -globin chains are produced, since the mutated  $\beta$ -globin in RNA is unstable and rapidly degraded while in  $\beta^+$  mutations the RNA is more stable so limited  $\beta$ -globin chains are made. By using an additional sequence at the 3' of the TN59 vector sequence, named the Ankyrin Sequence, there is improvement in the phenotype of mice, affected by  $\beta$ -thal. intermedia.

The final lecture in this plenary concerned the search for molecules with the property of inducing fetal haemoglobin. The presentation was by **Dr Roberto Gambari** of the Department of Biochemistry and Molecular Biology of Ferrara University. The purpose is to modify the clinical picture of homozygous  $\beta$ -thalassaemia. Some of the substances that have been screened so far include Rapamycin, Angelicin, Bergamot, and Resveratrol. Clinical validation through trials is still required for these substances. They are, however, natural products, freely available in the market and of low cost.

#### **Parallel Workshop 1: Aspects of Holistic Management – Thalassaemia**

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*Chairpersons: Vincenzo De Sanctis, Malcolm Walker, Vasilios Demos*

*Speakers: Ersi Voskaridou, Vincenzo De Sanctis, Ali Taher, Athanasios Aessopos,  
John Malcolm Walker, John Porter*

The first subject was bone disease in thalassaemia, presented by **Dr Ersi Voskaridou** (Laikon Hospital, Athens). Bone disease in thalassaemia includes abnormalities of bone metabolism that lead to enlargement of the cranial and facial bones, osteopenia or osteoporosis, spinal deformities and spontaneous fractures. The pathogenesis of bone destruction in this condition is very complicated and differs from classical osteoporosis. Osteoporosis results from an imbalance in bone remodelling. It results in decreased bone mineral density (BMD), deterioration in the micro-architecture of bone, decreased bone strength and increased fracture risk. Bone mineral density, is measured by dual-energy X-ray absorptiometry (DEXA). The prevalence of osteoporosis in adolescent and adult

thalassaemia patients is very high, 89% in lumbar spine, 62% in hip and 73% in distal radius. Apart from bone marrow expansion, multiple endocrine imbalances can alter bone metabolism in thalassaemia, including hypogonadism and defects in growth hormone/insulin-like growth factor. Iron overload and iron deposition in bone causes impaired maturation of bone cells and reduces local mineralisation. Iron chelation on the other hand, with desferrioxamine reduces collagen formation. Other factors in thalassaemia include vitamin D deficiency, zinc deficiency, and genetic factors such as polymorphisms in collagen type I gene, transforming growth factor  $\beta$ 1, calcitonin receptor, oestrogen receptor and interleukin 6. Markers of bone metabolism have been identified which give further information concerning bone formation, such as bone specific alkaline phosphatase, collagen type I polypeptides. There are also markers of bone resorption which are significantly increased. A protein which is crucial to bone formation, Dickkopf-1 (DKK1), is increased in thalassaemia patients with osteoporosis and also correlates with BMD. These increased levels may be at least partially responsible for osteoblast dysfunction. Diverse treatment strategies are currently in use, which include preventive measures and general lifestyle adaptations, hormonal replacement therapy, and pharmaceutical approaches. Every thalassaemia patient should have an annual check of BMD, starting from adolescence. Hormonal replacement seems to be the most effective way of preventing osteoporosis in thalassaemia major. Biphosphonates are a group of drugs which are potent inhibitors of osteoclast function which have been extensively used in the treatment of osteoporosis in thalassaemia. There are still outstanding questions regarding the use of these substances which include the optimal dose, the frequency and the duration of therapy. Newer approaches include the use of novel antiresorptive agents such as denosumab (anti-RANKL).

The subject of Thalassaemia intermedia was covered by **Dr Ali Taher** of the American University of Beirut. Beta thalassaemia has a wide spectrum of clinical severity. The molecular basis of Thalassaemia intermedia includes the inheritance of mild  $\beta^+$  mutations, the presence of a polymorphism in the Gy promoting region which is associated with increased HbF, co-inheritance of  $\alpha$ -thalassaemia and increased production of  $\alpha$ -globin chains by the triplicated  $\alpha$ -genotype associated with  $\beta$ -thalassaemia heterozygosity, and increased HbF production in association with  $\delta\beta$ -thalassaemia. Environmental factors may also modify the clinical picture such as social conditions, nutrition and the availability of medical care. Clinically, there are significant differences in the prevalence of common complications between the intermedia (TI) and the major (TM) forms of thalassaemia. For example, cholelithiasis, extramedullary haemopoiesis leg ulcers, thrombotic events, and pulmonary hypertension are more common in TI. Cardiomyopathy, hypogonadism, diabetes and hypothyroidism are more common in TM.

One important complication of TI is venous thromboembolism and hypercoagulability in splenectomised patients. Iron overload occurs even in TI patients who are not transfused at a much lower rate than transfused patients. The mechanism of iron overload depends on iron absorption by the gut via a pathway which is caused by chronic anaemia and hypoxia. It is for these reasons that assessment of iron overload is important in TI. One important finding is that serum ferritin levels in TI patients are significantly lower than in TM patients, despite similar LIC. The patients with TI seem to be protected from cardiac siderosis despite significant iron loading in the liver. Indications for initiating blood transfusions in TI, include: failure to thrive in childhood, increasing anaemia, delayed or poor pubertal spurt, progressive splenic enlargement, bone deformities, tendency to thrombosis, leg ulcers, extramedullary haemopoiesis, and pulmonary hypertension. Indications for initiating iron chelation therapy in TI patients include the rate of accumulation and duration of exposure to excess iron. Iron chelation therapy was protective for hypogonadism, pulmonary hypertension, cholelithiasis and osteoporosis. Hydroxyurea treatment was protective for extramedullary haemopoiesis, pulmonary hypertension, leg ulcers, hypothyroidism and osteoporosis. The conclusion of

several studies is that the roles of blood transfusion, iron chelation therapy and fetal haemoglobin induction, merit large prospective evaluation.

The cardiovascular involvement in thalassaemia major and intermedia was reviewed by **Professor Athanasios Aessopos** of the University of Athens Medical School. He pointed out that the heart failure remains the most frequent cause of death. Concerning the mechanism of heart injury in thalassaemia, major and intermedia, there are two competing factors – high cardiac output and myocardial iron deposition. The high output state is due to the chronic anaemia, the shunt development due to bone marrow expansion and extramedullary haemopoiesis, hepatic injury and vascular elastic tissue disorder which result in vessel dilatation. An important advance has been the correlation of the T2\* cardiac MRI measurement with the left ventricular ejection fraction (LVEF) in thalassaemia major (7) which has made the T2\* an important predictor of deterioration of heart function. Patients with a T2\* less than 20ms are at risk for myocardial dysfunction and heart failure, especially those with measurements below 10ms. Pulmonary hypertension is present in thalassaemia major patients who were poorly treated, but it is the major cause of congestive heart failure in thalassaemia intermedia

Discussion of cardiac complications was continued by **Dr J Malcolm Walker**, consultant cardiologist of the University College Hospital in London. He concentrated on the methods of early identification of patients at-risk, before the onset of obvious heart failure. In the past many patients who needed intensive treatment were missed, since we relied on indices such as high ferritin averages to indicate those at-risk. This situation changed with the advent of the CMR T2\* technique. With application of this technique it was established that while in some patients both cardiac and hepatic tissues can be iron loaded, there are many where there is accumulation in the liver and not the heart, and others with iron loaded hearts in the absence of significant liver iron. Cardiac T2\* is highly predictive for the development of heart failure and arrhythmia and that the inclusion of this assessment in the routine assessment of multi transfused patients is mandatory. CMR T2\* assessment should start in adolescence and repeated annually, unless there is any change in functional status or a change in chelation regime. If there is an episode of heart failure, the progress should be monitored after 6 months (it is not necessary too soon, e.g. less than 3 months after change in treatment). Monitoring with CMR T2\* has already had an impact on survival of patients in the UK.

Monitoring of liver iron with R2 magnetic imaging was explained by **Professor John Porter**. In multi-transfused patients, liver iron concentration (LIC) is an essential measurement, since LIC predicts total body iron stores, and can show changes with chelation therapy. LIC also predicts the risk of both hepatic and extra-hepatic complications.

Serum ferritin cannot be used also to quantify body iron since it can be affected by other factors such as inflammation, tissue damage and vitamin C deficiency. Liver iron may be measured directly by liver biopsy. Another method of measurement is SQUID which gives a linear relationship to iron by biopsy. There are, however, only 4 operating machines in the world and it is an expensive method. The most currently used method is magnetic resonance imaging. An R2 image and distribution, producing axial images with a multiple spin-echo pulse sequence (Ferriscan), is now available. The LIC values obtained by Ferriscan correlate with T2\* values but there is no equivalence so that the two methods are not currently interchangeable.

## **Parallel Workshop 1: Aspects of Holistic Management – Sickle Cell Disease**

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*Chairpersons:* Marianne de Montalembert, Soroya Beacher, Frederick Galacteros

*Speakers:* Paul Telfer, Marianne de Montalembert, Dora Bachir, Soroya Beacher  
Dora Bachir, Ersi Voskaridou

The subject of emergencies in adults with Sickle Cell Disease was introduced by **Dr Dora Bachir** of the Sickle Cell Referral Centre of the Henri Mondor Hospital in Creteil, France. Dr Bachir described the pathophysiology of the disease leading to chronic haemolytic anaemia, vaso-occlusion and infections. There is great heterogeneity in the natural history of the condition which becomes more apparent as life expectancy increases. Two specific high-risk situations are pregnancy and when surgery is needed. In an analysis of the causes of death in adults with SCD, published in 2002 vaso-occlusive events leading to multi-organ failure, acute chest syndrome and cerebrovascular accidents, are the main causes. Infection, chronic organ failure, suicide or refusal of care, are other identified causes. Pain is the main symptom for these patients and it is the reason for 90% of hospitalisations. Pain is associated with vaso-occlusive complications including priapism, leg ulcers, osteonecrosis, and chronic bone pain. Acute chest syndrome is a form of acute lung injury, which leads to acute respiratory distress and has a 5% mortality. Stroke is another serious vaso-occlusive complication. Infection is a rare event in adults with SCD compared to children. However, septicaemia does occur, often secondary to bone or joint infections and carries 11% mortality. Priapism a major cause of impotence.

Abdominal pain is a very frequent complaint in SCD which may lead to hypoventilation and in acute chest syndrome. Multidisciplinary approaches and prompt identification of patients needing intensive care are warranted. Top up transfusions or exchange transfusions are always required in the management of severe vaso-occlusive or septic complications. Education of families and patients is essential for early management. Patients experiencing frequent vaso-occlusive episodes or acute chest syndrome should be offered long term hydroxyurea treatment.

Dr Bachir continued with a second talk on the risk of severe haemolytic reactions in SCD and strategies to address them. Blood transfusion is a major element in the treatment of SCD, including acute complications such as the acute chest syndrome, but also as a lifelong treatment to prevent stroke and in adult organ failure (such as pulmonary hypertension). This treatment brings with it possible complications such as alloimmunisation,

**Dr Marianne de Montalembert** spoke on the prevention and treatment of strokes in Sickle Cell Disease. Stroke may be infarctive or haemorrhagic, with the infarctive type being more common in patients under 20 years, while the incidence of haemorrhagic is highest over the age of 20 years. By the age of 20 years, 11% of patients have clinical evidence of stroke. 20-30% of children present also with silent infarcts which are associated with cognitive defects and the risk of overt strokes. Risk factors for overt strokes have been identified. For infarctive stroke these are prior transient ischaemic attack, a low steady state haemoglobin concentration, a recent episode of acute chest syndrome, genetic factors, and silent infarcts. For haemorrhagic stroke, low steady state haemoglobin and a high leukocyte count.

Other factors include a past history of bacterial meningitis and nocturnal hypoxaemia. In the pathophysiology of stroke, the main changes are seen in the endothelium of large intracranial arteries. The arterial blood flow, is measured by transcranial Doppler ultrasound (TCD). Children on long term transfusions are stroke free for longer than those on standard care. Iron overload is an inevitable consequence of chronic transfusions. It is for this reason

that hydroxyurea has been proposed for cerebral vasculopathy. Stem cell transplantation is a plausible standard for those children with cerebral vasculopathy and a high risk of stroke.

**Dr Paul Telfer** continued the discussion on Sickle Cell Disease care with a talk on pain management. The most frequent complication of East London neonatal cohort was pain crisis. The painful episodes present with dactylitis before the age of 3 years, with swelling of joints or limbs (between 3-6 years) and single or multiple other sites (eg. back, limbs, abdomen etc) and may change location during the crisis. Management of pain includes relaxation, rest, reassurance, distraction, massage and analgesia at home but then hospital care of pain is not settling or additional symptoms appear, such as fever, pallor, lethargy, chest pain, dyspnoea, enlarging of spleen, severe headache or priapism, it is advisable to admit to hospital. Analgesia is escalated according to pain. Treatment may be given in the Emergency room, or the haematology day care clinic, but patient should be admitted if the pain continues. Long term management depends on education, life style management, psychosocial support, pain management skill training, and if necessary, hydroxyurea.

**Ms Soroya Beacher**, chairperson of Oscar Netherlands, then discussed self-management by sickle cell patients. This depends on knowledge about the condition, the ability to manage pain, the acceptance of the condition, good communication, and working together with the different disciplines concerned with patient care. Ways to increase patient knowledge include speaking to other patients in the context of the patient organisation and speaking to members of the multi-disciplinary team. Patients should be aware of the complications of the disease and of their medication. Patients should have access to the records of all their tests, such as the MRI, blood tests etc. Where the multi-disciplinary approach is missing, patients should request it, since Sickle Cell Disease is a multi-organ condition. Concerning pain management, it is important for the patient to be able to communicate concisely and clearly what they are experiencing. Of the various forms of pain management, patients may have preferences such as continuous infusions or patient control pump and some still prefer two hourly injections. These alternatives are discussed with the specialist, who must know how the patient intends to cope with pain, how long to continue with high medication and when to start reducing the dosage. Also, for pain control at home, there needs to be liaison between patient, general practitioner and the specialist. The patient needs to accept the fact that Sickle Cell Disease is part of his/her life and by acceptance, anger subsides, fear falls into proportion and stigmatisation and disruption in life are reduced. The patient needs to be "an empowered client with excellent self management skills who receives support and advice from family, carers and medical staff".

The effect of prolonged administration of Hydroxyurea was explained by **Dr Ersi Voskaridou** of the Thalassaemia Centre of the Laikon General Hospital in Athens. She pointed out that as recently as 1970, 10% of children with SCD died before their 10<sup>th</sup> birthday, while 50% died before their 21<sup>st</sup>. Now life expectancy is much improved. Perhaps the most important parameter influencing clinical severity is the percentage of fetal haemoglobin (HbF). HbF interferes with the polymerisation of HbS and decreases sickling, and severity of vaso-occlusive crises declines. There is a decrease in chronic pain. No serious toxicity was found to be associated with hydroxyurea over periods of more than five years in three published studies. The drug was also shown to decrease elevated transcranial Doppler velocities. In a recently published study the long-term effects of hydroxyurea over a period of up to 17 years, were investigated. The trial showed a dramatic reduction (95%) in the median annual rate of painful crises. The death rate in patients who received the drug for a long period of time was significantly lower than that observed among patients who were conventionally treated.

## **Final plenary – Conclusions, Outcomes and the Way Forward**

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*Speakers:* Panos Englezos, Androulla Eleftheriou, Michael Angastiniotis, John Porter

At the end of the conference, conclusions and the way forward were presented by the four speakers.

There is a clear need to continue to provide capacity-building to patients' organisations, particularly national associations, and to ensure they are aware of the European policies in the field of rare diseases and other relevant areas, such as patient safety, cross-border healthcare and information to patients.

It is necessary to improve the existing services, and there is a particular need for the designation of reference centres in every EU Member State, as well as networking between existing reference or expert centres.

The Thalassaemia Federation commits itself strongly to advocating for free access to the necessary medicines, primarily iron chelation drugs for thalassaemia patients but also other multi-care aspects of the treatment of Hb disorders. There is a greater need for networking between the patients' and medical communities.

Regarding prevention, there is still a general absence of national integrated prevention programmes. Only a few southern European countries have to date managed to establish prevention programmes at national level – Cyprus, Greece, and to a certain extent Italy, although some considerable improvements have been achieved for example in France and the Netherlands. It is important that such national programmes are planned and implemented, possibly in the context of national plans for rare diseases.

### **3.3. Pre-conference meetings**

Two pre-conference meetings were held on the day prior to the 2<sup>nd</sup> Pan-European Conference – Friday 12 March 2010. The objectives of these meetings complemented and augmented the objectives of the Conference. The meetings concerned specific projects undertaken by the Thalassaemia International Federation, and their organisational costs were undertaken by the Federation, with the exception of the specific costs detailed in the conference budget financial statement (venue and catering costs).

#### **1. First meeting of TIF's Expert Patient Programme**

The first pre-conference meeting concerned a major initiative within TIF's "Reach the Patient" project: the inaugural meeting of the Expert Patient Programme. The Programme aims to extend quality information to patients with thalassaemia across the world on their disease, its medical care and other forms of care – the core objective being to empower patients to take meaningful and timely decisions concerning their healthcare and quality of life.

Twelve participants took part in the meeting. The objectives, mission and vision of the project were presented by George Constantinou, one of the coordinators. The detailed methodology was explained by Louis Pericleous, the second coordinator. A thorough discussion took place and all enquiries, concerns and questions were addressed. Two patient representatives from

Italy presented their successful stories, underscoring the instrumental role and contribution a well-structured, active patient association can achieve.

The methodology of the Expert Patient Programme was agreed as follows:

- i. A group of 6 patients fulfilling the agreed criteria (10+ years active involvement at national association level; involvement at global level in TIF's activities; excellent English; interest and commitment to spend the necessary time and effort; at least secondary education) will form the "Core Expert Patient Group". The core group will be presented to the TIF Board at its next meeting for final approval.
- ii. The core group will review and comment on the educational materials already prepared by TIF, intended for use by the core group only. They will also be involved in writing or updating patient education material; monitoring and assessing the progress of the programme; establishing collaborations with other expert patient programmes.
- iii. A group of 6 medical experts will be selected by the coordinators of the project to support and advise in the preparation of educational materials.
- iv. A workshop will be organised for a final review of the educational material, at the end of which each core group member will have an in-depth understanding of its contents and is able to educate other patients using the material.
- v. The core group will identify new patients each year to undergo the training programme, starting with two patients each from 10 countries in the first year and aiming to train 80 patients from 40 countries within three years. Countries will be prioritised in terms of prevalence/incidence.
- vi. An annual 3-day workshop will take place in Cyprus each year for training new expert patients using the patient-friendly educational materials. A certificate will be issued to the patients at the completion of the workshop. The certified patients will be able to organise national workshops in their countries and train groups of patients. Members of the core group will oversee the national training activities, assessing their quality and impact.
- vii. Expert patients, both from the core group and those newly trained, will also take up responsibilities for close collaboration with health professionals and health authorities at national level.

## **2. First meeting of TIF's European Network of Medical Specialists and Patients' Organisations in Haemoglobin Disorders**

The second pre-conference meeting was the official launch of TIF's European Network of Medical Specialists and Patients' Organisations in Haemoglobin Disorders. The Network is the first of TIF's regional networking initiatives, aiming to bring together patients' and medical communities in the field of haemoglobin disorders, while addressing the lack of awareness and lack of unity between the relatively few and unevenly dispersed patients in European countries.

The Network will function as a platform for sharing information, exchanging experiences and contributing to TIF's European policy work. It will help to form an accurate picture of the services available to patients in different EU countries; problems and challenges faced by patients. It will also be involved in preparing reports to national governments, EU bodies and WHO to support TIF's advocacy and policy work, as well as planning TIF's future activities.

The first meeting was very well attended, with 60 participants from 12 European countries: Belgium, Bulgaria, Cyprus, France, Germany, Italy, the Netherlands, Portugal, Romania, Spain, Sweden, and the United Kingdom. Of these, 20 were patients representing 12 thalassaemia and sickle cell associations, and 35 were doctors and nurses. The European Commission was represented through Dr Karl Freese of DG SANCO (Directorate-General for Health and Consumers), who attended the meeting as an observer.

The vision, mission and scope of the Network on behalf of patients were presented by the Executive Director of TIF, Dr Androulla Eleftheriou, while Professor John Porter from the UK gave the medical specialist's perspective. A lively discussion then followed, during which several issues of importance emerged. A major concern in Europe concerns the transition from paediatric to adult care, as well as the need for smooth coordination among the health team to secure continuation of care. Patients expressed a strong wish to collaborate with medical professionals and take an active part in decisions concerning their care. Health professionals, in turn, highlighted the importance of electronic health records to gather evidence about the status of treatment and prevention, as well as epidemiological data for targeting services.

Awareness of health professionals also emerged as an important concern. In this context the recently launched e-MSc course in Haemoglobinopathies at University College London was presented. This unique course, created by UCL in close partnership with TIF, offers an opportunity for health professionals from all over the world to specialise in Hb disorders online. The ENERCA project also includes training packages for health professionals and patients.

It was concluded that the European Network was now established and would proceed to form a Steering Committee and plan its next meeting and activities.

### **3.4. Conference participation**

#### **Target participants**

The target participants of the conference included, first and foremost, patients with Hb disorders – sickle cell and thalassaemia. This group included also parents, as many patients with Hb disorders are under the age of 18. A number of travel bursaries were made available through its "Patient Sponsorship Programme" to facilitate the attendance of patients and to ensure balanced attendance. Applicants were assessed on the basis of balanced geographical representation and need (e.g. previous attendance).

Another important target group were health professionals involved in the treatment of patients with Hb disorders. These are mainly paediatricians and haematologists, but could also be geneticists, specialist nurses and other health professionals, as well as scientists involved in diagnosis. A limited number of bursaries was made available for health professionals to facilitate their participation, with the aim of ensuring participation from lower-resource countries especially the new EU MS.

The conference aimed to attract representative from the national health authorities from Germany, and if possible from other countries where Hb disorders pose a growing public health problem. Finally, the conference aimed to include representatives of non-governmental and decision-making bodies of the EU, as well as WHO.

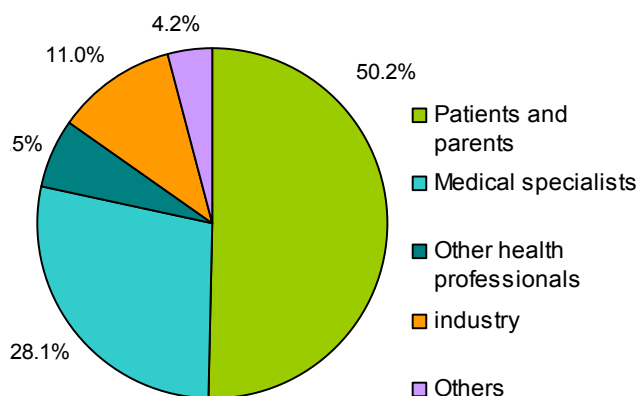
## Actual participation

The total number of participants was **512**, exceeding by a very wide margin the number that had been expected based on previous experience. The number of participants clearly demonstrates that there is a need for this kind of large-scale educational conference on Hb disorders in Europe.

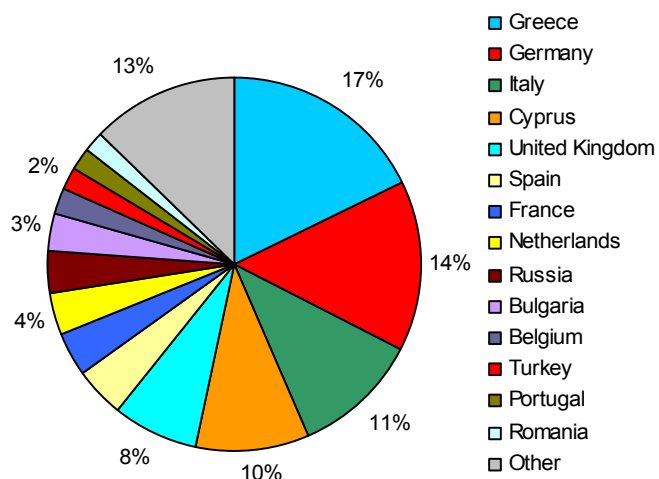
The 512 conference delegates included 264 patients/parents, 182 medical specialists and other health professionals, and 66 others (including industry representatives). Delegates hailed from 34 countries, including 19 EU member states.

<u>List of participating countries</u>		
Albania	Germany	Portugal
Austria	Greece	Romania
Azerbaijan	India	Russia
Belgium	Indonesia	Spain
Brazil	Israel	Sweden
Bulgaria	Italy	Switzerland
Canada	Lebanon	Thailand
Cyprus	Luxembourg	Turkey
Denmark	Malta	United Kingdom
Finland	Morocco	United States of America
France	Netherlands	
Fyrom	Poland	

**Graph 1: Participation by delegate category**



**Graph 2: Participation by country**



## 4. Technical implementation of the project

### 4.1. The Conference Secretariat

Administration and management of the conference was undertaken by the Conference Leader (TIF Executive Director) and her team at the conference secretariat (TIF office), in close consultation with the Steering and Scientific Committees. A Project Officer undertook all daily correspondence, registration of delegates, organisation of meetings and liaison with the public. She also managed the sponsorship (travel grants) programme for patients and health professionals, under close supervision by the Executive Director. A Projects Manager provided support in communications and PR, preparation of conference materials, exhibition and liaison with commercial sponsors. In addition, a Medical Advisor was responsible for day-to-day liaison with the Scientific Committee. Administrative support was provided by the TIF Secretary.

The following staff members of the Thalassaemia International Federation were involved in the materialisation of the conference:

*Project Leader and Financial Manager: Dr Androulla Eleftheriou, TIF Executive Director*  
BSc, MSc, PhD Biochemistry, Microbiology and Virology. Awarded a number of scholarships by the WHO and Fulbright Commission. Postdoctoral fellowship completed at Center for Disease Control, Atlanta, GA, USA. Diploma in Management from the University of Leicester. Head of Virus Reference Centre of the Cyprus Ministry of Health, 1990-2006. She regularly acts as a WHO consultant on issues related to her field of expertise.

*Project Coordinator: Eliana Iliofotou, European Project Officer*  
MSc, MA Economics and European Studies, MBA. Plans and implements TIF's country activities in the European region, as well as tasks in the areas of membership, events coordination and fundraising.

Other staff involved:

*Kaisa Immonen-Charalambous, Projects Manager*  
MA International Relations. Responsible for external and international relations, communications and European policy.

*Michael Angastiniotis, Medical Advisor*  
MD (Paediatrics). Board member of the Cyprus Institute of Neurology & Genetics, member of the WHO Advisory Panel on Human Genetics. Former Director, Paediatric Dept., Archbishop Makarios III Hospital, and Cyprus Thalassaemia Centre. WHO consultant, member of the Committee for Control of Hereditary Anaemias.

*Subcontracting, assistance, outsourcing.* Mrs Panayiota Xenofontos (Expert Panel) was contracted to support venue and organisational arrangements between November 2009 and March 2010. Kongdredi company were subcontracted to support venue and local arrangements between April and December 2009. A local medical student service team of four was subcontracted to provide support and assistance during the conference.

## 4.2. Steering and Scientific Committees

The organisation of the conference was overseen by a Steering Committee chaired by the Executive Director Dr Eleftheriou, the designated Conference Leader. Dr Eleftheriou had the overall responsibility for the implementation of the work plan and financial aspects of the conference.

A Scientific Committee was set up to formulate the programme and select the expert speakers, consisting of a number of internationally recognised high-level experts in the field of Hb disorders. For the inclusion of a patients' perspective, patient representatives were included in both committees.

A Local organising committee consisting of German members was set up from among the two official committees, primarily to support the Conference leader in communications and arrangements with German stakeholders, as well as to help with local marketing.

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### Scientific Committee

**Panos Englezos (Honorary Chair)**

President, Thalassaemia International Federation, Cyprus

**Sir David Weatherall (Chair)**

Founder of the "Weatherall Institute of Molecular Medicine" in the John Ratcliff Hospital in Oxford, UK

**Athanasios Aessopos**

Professor of Internal Medicine, Laikon Hospital, University of Athens, Medical School a WHO Collaborating Centre for Community Control of Hereditary Anaemias, Greece

**Renzo Galanello**

Professor of Paediatrics, Director WHO Collaborating Center for Community Control of Hereditary Diseases, Università degli Studi di Cagliari, Italy

**Patricia Aguilar Martinez**

Director of the Laboratoire d'hématologie, Hôpital Saint Eloi, France

**Beatrice Gulbis**

Head Clinical Chemistry, Hôpital Erasme Université Libre de Bruxelles, Belgium  
Hermann Heimpel

**Michael Angastiniotis**

Medical Advisor, Thalassaemia International Federation, Cyprus

Prof. Emerit. German Registry on Congenital Dyserythropoietic anaemias, Medizinische Universitätsklinik Ulm, Germany

**Dora Bachir**

Director Red Blood Cell Genetic Disease Unit for Adults, Henri-Mondor Hospital, Paris, France

**Gisela Janssen**

Paediatric Haematologist, University Hospital Düsseldorf, Germany

**Holger Cario**

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Roswitha Dickerhoff – Paediatric Haematologist/Oncologist, University of Dusseldorf; Chair, Interessengemeinschaft Sichelzellkrankheit und Thalassämie e.V., Germany

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