# Management of Haemoglobin Disorders

**Report of Joint WHO-TIF Meeting**

*Nicosia, Cyprus,*
*16-18 November 2007*

World Health Organization

# MANAGEMENT OF HAEMOGLOBIN DISORDERS

REPORT OF A JOINT

WHO-TIF MEETING

Nicosia, Cyprus, 16-18 November 2007


**WHO-TIF MEETING ON THE MANAGEMENT OF HAEMOGLOBIN DISORDERS**

WHO Library Cataloguing-in-Publication Data

Joint WHO-TIF Meeting on Management of Haemoglobin Disorders (2nd : 2008 : Nicosia, Cyprus)

Management of haemoglobin disorders: report of a joint WHO-TIF meeting, Nicosia, Cyprus, 16-18 November 2007.

1.Abnormalities – prevention and control. 2.Abnormalities – therapy. 3.Abnormalities - classification. 4.Genetics, Medical. 5.Prenatal diagnosis. 6.Developing countries. I. World Health Organization. II. Thalassaemia International Federation. III. Title.

ISBN 978 92 4 159712 8 (NLM classification: WH 190)



**Printed by the WHO Document Production Services, Geneva, Switzerland**

**WHO-TIF MEETING ON THE MANAGEMENT OF HAEMOGLOBIN DISORDERS**

CONTENTS

# EXECUTIVE SUMMARY

On 16-18 November 2007, the World Health Organization (WHO) and the Thalassaemia International Federation (T.I.F.) held a joint meeting in Nicosia Cyprus, entitled: 'The Management of Haemoglobin Disorders'. The meeting was convened at the request of the WHO's Human Genetics Programme (HGN) following the WHO Resolutions on May 2006 on Sickle Cell Disease (WHA59.20) and Thalassaemia (EB118.R1), respectively.

Meeting participants included 28 experts from developing and industrialized countries and 6 staff from TIF headquarters. The meeting had 10 areas for discussion;

(i) Reviewing the current status of epidemiology and control services for Haemoglobin (Hb) disorders globally;

(ii) Identification of local and regional problems, needs and priorities for improving control policies;

(iii) Preparation and publication of Guidelines for the control of Hb disorders;

(iv) Supporting the establishment of new and promoting the services of existing reference or expert centres;

(v) Promotion of the establishment of regional expert advisory groups;

(vi) Fundraising to support programmes of control of Hb disorders;

(vii) Cost-effective approaches and interventions for the control of Hb Disorders;

(viii) Promoting the establishment of a World Haemoglobinopathies Day;

(ix) Collaboration between potential stakeholders, and;

(x) Develop a 5-year plan of action for WHO, in collaboration with TIF and SCD organizations, to strengthen care and prevention of Hb disorders in low and middle-income countries.

The overall consensus of the group was to promote the WHO Resolutions on Sickle Cell Disease and Thalassaemia, through efforts to fulfill the objectives of this meeting. The following summarizes the meeting consensus for each of the goals listed above:

a. Participants reviewed and discussed the epidemiological and available control services data, as demonstrated within each of the presentations. They endorsed a consensus that efforts should be intensified on expanding the database on the epidemiology and available control services.

b. Participants reached a consensus as to the identification of local and regional problems, needs and priorities for improving control policies. In addition, participants recommended the implementation and strengthening of programmes, including:
   i. Community Awareness;
   ii. Training of Health Professionals;
   iii. Pilot studies;

iv. Research;
v. Cost-effectiveness in programme design, and;
vi. Strengthening of medical and genetic services in low- and middle-income countries.

c. Participants concluded that the preparation and publication of WHO Guidelines for the control of Haemoglobin disorders is to include both prevention and clinical management, with particular focus on local and regional needs.

d. Participants endorsed the notion that in order to effectively prevent, or treat haemoglobin disorders on a global scale, efforts would require the strengthening of existing medical and genetic services, in low- and middle-income countries. In this context, participants agreed that the promotion of existing expert centres and their services is very important, and the establishment of new reference centres, especially in highly affected regions of the world is pivotal for effectively controlling haemoglobinopathies. In addition, by activating and organizing these centres into 'networking groups' priorities such as (i) continued research for collection and refinement of data relevant for the control of haemoglobin disorders; (ii) provision of practical and technical advice and support to countries to develop medical services for care and prevention of the disorders; and (iii) development of human resource capacity and technology transfer through training and education of clinicians, scientists, nurses and the evolution of patient-driven organizations, could be addressed.

e. Participants reached a consensus for the creation of regional expert advisory groups, under the 'umbrella' of WHO, which are most knowledgeable on the local/regional requirements for the control of haemoglobinopathies and thus could tailor guidance and expertise to individual countries within their region, for more effective outcomes.

f. Participants sanctioned that funds should be secured for the development and initiation of services for care, and successful implementation of control programmes, and agreed that any lobbying for funds should be preceded by adequate, updated and reliable information, and that collaboration or twinning with (i) patients' driven organizations, for patients' education, government lobbying and fund-raising, and (ii) reference centres for improving diagnosis and transfer of expertise, should be sought.

g. Participants agreed that efforts should focus on the identification and the promotion of affordable interventions. These included among others community education, training of health professionals, newborn screening for early diagnosis sickle cell disease, thus reducing or minimizing morbidity and mortality among patients with SCD, carrier identification, genetic counseling and prenatal diagnosis to minimize new affected births and sensitization of health authorities through provision of epidemiological data and the public resources burden imposed by these disorders.

h. Participants also endorsed the idea of officially declaring a 'World Haemoglobinopathy Day' during which activities for raising public awareness about these disorders, would be undertaken. Such activities, governments and policy makers are significantly sensitized towards developing, adopting and implementing policies for the control of these disorders. Participants agreed to collaborate and request from the WHO to adopt such a day.

i. Participants agreed that involving other potential stakeholders, such as patients/parents organizations and other national and international health related agencies could significantly contribute towards efforts relating to advocacy, technology transfer and capacity building.

j. Participants reached a consensus of a 5-year plan of action, for achieving the above goals (see page 24).

k. Participants agreed to recommend the establishment of an International SCD Federation, bringing together all groups dealing with SCD in a similar collaboration as that of the thalassaemia organizations who grouped under the umbrella of TIF. The two federal groupings could join forces in promoting the policies for haemoglobin disorders and advocacy to international and national agencies.

# 1. INTRODUCTION

Since the 1980s the World Health Organization (WHO) and the Thalassaemia International Federation (TIF) have recognized the need to support and facilitate the development and implementation of national policies for the management of thalassaemia and other haemoglobinopathies, mainly sickle cell disease. Moreover, since the late 1980s, the WHO, TIF and several sickle cell centres and organizations independently made an effort to promote the hereditary haemoglobin disorders as priorities on the health agenda of Member States, mainly as a consequence of the improvements achieved in the health infrastructure, public health services and the reduction in the annual infant mortality in affected countries of the developing world. Governmental and nongovernmental support was sought for educational activities, treatment services and research.

These disorders occur widely across the world, and both their natural history and prevalence varies considerably between the different regions of the world. Their prevalence may also vary (i) between countries of the same region; (ii) between different areas within a country and (iii) even between different medical centres within the same area. Despite the laboratory and clinical advancements towards their effective prevention and clinical management, increased numbers of annual affected births and high rates of mortality and morbidity are still observed in the majority of affected countries of the developing world (WHO, 2006a):

- Around 7% of the global population carries an abnormal haemoglobin gene;
- 300,000- 500,000 children are born with clinically significant haemoglobin disorders annually;
- About 80% of affected children are born in developing countries;
- About 70% are born with Sickle Cell Disease (SCD) and the rest with Thalassaemia Syndromes;
- 50-80% of children with SCD die each year in low and middle income countries;
- 50,000-100,000 children with thalassaemia major die each year in low and middle income countries.

Haemoglobin disorders constitute a major burden of disease, originally believed to be geographically restricted, mainly to malaria endemic or previously endemic regions of the world (see Figure, WHO, 1996). However migration has imported the condition to low prevalence areas, so that the problem is now global.

WHO, TIF and groups concerned with SCD, are deeply concerned with the growing impact of these diseases on the public health systems, across the globe, as well as by the poor quality of life and the diverse medical complications of those affected by these disorders. The present joint WHO-TIF meeting was organized in view of the recently adopted WHA Resolutions WHA59.20 and EB118.R1 (see Appendix A) regarding sickle cell anaemia and thalassaemia, respectively, aiming to review the current situation in all the WHO regions of the world, and to investigate ways for implementing these resolutions in countries.

## 1.1 The Role of the World Health Organization (WHO)

Genetic diseases and haemoglobinopathies, in particular, such as thalassaemia and sickle cell disease, have a tremendous impact on global mortality and morbidity (WHO, 1996). Due to insufficient epidemiological data, it is difficult to establish effective and equitable management programmes for these diseases, to include prenatal screening without catering for practices that are sensitive to specific cultural, legal, ethical practices, which are extremely important to different societies. Taking this into account and recognizing the current inequality of access to safe and appropriate genetic services throughout the world, WHO recognized the role of genetic services in improving health globally and in reducing the global health divide. The WHO report on Genomics and Health (WHO, 2002) stressed the importance of the haemoglobin disorders and the value of introducing simple molecular technology for their control and recommended the North/South and South/South partnerships for the control of genetic disease. These recommendations were accepted as the basis for the resolution WHA 57.13 on genomics and world health (WHO, 2004) and the discussion of the Executive Board at its 116th session on the control of genetic diseases (WHO, 2005). Moreover, having considered the secretariat reports on sickle cell anaemia and thalassaemia and other haemoglobinopathies in the course of its 59th World Health Assembly and the 118th session of its Executive Board, respectively, the Resolutions WHA59.20 (WHO, 2006b) and EB118.R1 (WHO, 2006c) were discussed and adopted.

Both of these Resolutions urge Member States to develop, implement and reinforce comprehensive national, integrated programmes for the prevention and management of HDs. They also urge to develop and strengthen medical genetics services, and to promote community education and training. The resolutions also request the Director-General of WHO to provide technical support to countries, to establish regional groups of experts, to improve training and education (see Appendix A).

Thus, WHO has been supporting and raising the haemoglobinopathies at the high international level with the hope to maximize the benefits of this and to promote networking and involvement of country experts, governments and non-governmental organizations in the future work.

## 1.2 The role of the Thalassaemia International Federation (TIF)

The TIF is a non-governmental, non-profit organization, established by parents and patients in 1987, specifically aiming:

- To strengthen the existing programmes of prevention and clinical management, and to promote research for further improving clinical care, and achieving the total cure;
- Support the establishment of new and the promotion of existing National Thalassaemia Associations across the world, for (i) safeguarding the rights of every patient for optimal treatment and satisfactory quality of life, and (ii) promoting national policies for the prevention of these disorders.

TIF's Mission is concerned with provision of equal access and quality health services for every patient with thalassaemia, across the world.

Towards these priorities TIF directs its activities, which include:

- The promotion of training and provision of awareness to patients and their families, to health professionals and the community at large, constitute one of the major activities of TIF towards achieving its mission.

- The educational programme constitutes the most important tool, through which TIF promotes its educational activities and this includes: (i) the preparation, publication, translation and free-of-charge distribution of educational material and (ii) the organization of local, national, regional and international workshops and conferences. A list of educational material is recorded in Appendix B.

- Today, TIF is an umbrella Federation with 98 member thalassaemia or thalassaemia-related organizations, from over 60 countries of the world. In addition, TIF is in official relations with the WHO since 1996, and collaborates closely with (i) National Thalassaemia Associations (NTAs); (ii) National Health Authorities (NHAs); (iii) Medical and Scientific communities, involved in the field; (iv) relevant pharmaceutical industries; (v) the European Commission; (vi) Council of Europe, other international Health Bodies, such as (i) the National Institute of Health (USA); (ii) The Federal Drug Administration (FDA), and the European Medical Evaluation Agency (EMEA), and patients/parents-directed organizations such as (i) European Organization of Rare Diseases (EURORDIS); (iii) The Pan-European Blood Safety Alliance (PBSA); (v) European Public Health Alliance (EPHA); (vi) The International Alliance of Patients' Organizations (IAPO) and other health related professional bodies or associations, such as (i) The International Society for Blood Transfusion (ISBT); (ii) The European Blood Alliance (EBA) and (iii) The European Platform for Patients' Organizations, Science and Industry (EPPOSI).

In addition, TIF co-ordinates or participates in international, European and national projects focused on improving epidemiology, prevention, management, cure and education of patients/parents, health professionals and the community.

- An international federation, similar to TIF, does not presently exist for sickle cell disease.

### 1.3. Scope and purpose of the meeting

As we see, there is a global concern on the impact of haemoglobin disorders, mainly sickle cell disease (SCD) and thalassaemia, on mortality and morbidity, especially in developing countries. Recognizing haemoglobin disorders as a global health burden and following recommendations of recently adopted WHO resolutions on sickle cell anaemia (WHA59.20) and thalassaemia (EB118.R1), WHO and TIF organized the joint meeting the main purpose of which was to investigate ways for implementing these resolutions in countries.

The main goals of the meeting include: reviewing the current status of epidemiology and control services for Haemoglobin (Hb) disorders globally; identification of local and regional problems, needs and priorities for improving control policies; preparation and publication of Guidelines for the control of Hb disorders; supporting the establishment of new and promoting the services of existing reference or expert centres; promotion of the establishment of regional expert advisory groups; fundraising to support programmes of control of Hb disorders; cost-effective approaches and interventions for the control of Hb disorders; promoting the establishment of a World

Haemoglobinopathies Day; collaboration between potential stakeholders; and develop a 5-year plan of action for WHO, in collaboration with TIF and SCD organizations to strengthen care and prevention of Hb disorders in low and middle-income countries.

# 2. MEETING GOALS

For the purpose of reaching a consensus on the ways to achieve the set goals of this meeting (1-10, as above) and after presenting the state of affairs in the countries grouped according to the WHO regions (see Appendices C and D) **-** Information on the country profiles and problems faced regarding Hb disorders in developing regions was obtained from the participants' reports), the participants were separated into two working groups. Each discussed the problems identified and the priorities needed to be addressed, with one group focusing on thalassaemia while the other focusing on Sickle Cell Disease.

The major issue to be addressed in the course of these discussions, in the context of a 5-year plan, was the identification of ways to assist countries in their efforts to control thalassaemia and sickle cell disease, according to the WHO Resolutions EB118.R1 and WHA59.20, May 2006, respectively.

## 2.1 Reviewing the current status of epidemiology and control services for Haemoglobin (Hb) disorders globally

After reviewing the country reports (see Appendix C and D), the participants recognized that the current status of thalassaemia and SCD is greatly heterogeneous between the different regions and countries of the world as described below. Analysis of this data confirms WHO's and TIF's concerns relating to the urgent needs to strengthen and expand existing and instigate new initiatives and efforts towards the promotion of control programmes for Hb disorders, according to the relevant recent WHO Resolutions. The need for developing a 5 year plan of activities and of setting up regional groups of experts to support and coordinate the implementation of these two resolutions were among the two most important priority goals that could not be underscored enough.

It was agreed that currently countries were divided into four (4) broad groups according to the levels of services, they provided and on which the future priorities and control programmes could be based:

I. Developed countries in which services are well established and most of which have developed national or regional control programmes;

II. Developed countries in which services are available across, but considerable efforts are needed to (i) improve access of the community and patients to the services and (ii) to raise awareness to patients, health professionals and the community at large (iii) to establish national networks of expert centres (iv) to initiate funding streams that incorporate the costs of advances in patient management;

III. Developing countries, some with resources, which have developed considerable expertise in the control, prevention and management of Hb disorders, but which need political commitment and recognition by their respective Governments in order to move forward, and;

IV. Developing countries where limited or no relevant services are available.

### 2.2 Identification of local and regional problems, needs and priorities for improving control policies

The particular problems relating to the developing societies included:

- The lack of updated reliable epidemiological data including incidence, carrier and prevalence rates as well as the clinical spectrum, across regions and countries;
- The diseases occur against a background of many other health challenges and priorities including malaria, other infections, infestation, malnutrition and others;
- The health infrastructure in the majority of these countries is often poorly developed to enable promotion of effective control policies which particularly in the case of Hb disorders involve multifaceted efforts and activities;
- Religious and cultural beliefs, and in many countries, literacy problems are seriously hindering promotion of significant aspects of the control programme including spreading of community awareness and clear understanding of the nature of these diseases, their prevention and management;
- Low resources in the majority of the developing countries coupled with unavailability of reliable epidemiological information to support political decisions and commitments, considerably hamper progress in the development and implementation of control programmes;
- The lack of recognition of the haemoglobin disorders by governments and also by international health agencies and funding bodies, is a situation sadly, equally relevant to both developed and developing countries;
- Absence of local, national, regional and international collaboration to support professional and patient-family oriented organizations, and;
- Poor local infrastructures in other areas apart from health pose additional difficulties, including patients' transportation to reach health care facilities for treatment or prevention services, even where these services exist.

For industrialized countries, the major problems were:

- Still lack of recognition by Governments on the contribution of haemoglobin disorders to the public health burden;
- Needs for strengthening community and health professional awareness and access to existing, available services, and;
- Need for the promotion of a network of collaboration between existing Centres of Excellence for Hb Disorders and the need for core funding for such centres and networks.

In many industrialized countries patients with Hb disorders are immigrants, coming from high prevalence areas of the world widely dispersed throughout their new countries of residence, with significant cultural, religious, moral and linguistic barriers in the uptake of appropriate health services which do exist (even with the need to expand), in the majority if not all of the industrialized countries.

*2.2.1 Needs and Priorities:*

The procurement of *political commitment* is the first and most important priority.

*Community Awareness, Health Education and Genetic Counseling*. Emphasis was given to the need for increasing community awareness and that funding for such activities should be raised. Working with local Thalassaemia and Sickle Cell Patients/Family Associations is important as these can reach the general public and the patients and their families in a local or lay language. The means suggested by the participants to address this issue included:

- The use of Mass Media which can reach much of the population, so that awareness and openness can help to remove the 'shame' or 'stigma' often associated with having either sickle cell disease or thalassaemia – issues that often led to the isolation of patients and their families, and the loss of motivation to seek health care. Such prejudices still persist in many societies;

- Inclusion of genetics and basic information concerning haemoglobin disorders in the teaching of Biology in the secondary school curriculum; In addition more hours should be dedicated to haemoglobin disorders in the Medical school undergraduate courses. Training of health professionals at various levels and in particular primary health professionals and nursing staff. Public health officials and policy makers also need information concerning these disorders;

- The adoption of a 'World Haemoglobinopathy Day'. In more than 60 (sixty) countries of the world, TIF member National thalassaemia Associations have adopted and celebrated, since 1993, the 8$^{TH}$ of May, as the World Thalassaemia Day. In the UK, the 4$^{TH}$ of July has been adopted as the 'Sickle Cell Day', while UNESCO has adopted the 19$^{TH}$ of June for the same topic. In the USA, September is 'SCD month' and in Africa May 10$^{th}$ is Africa Sickle Cell Day. An internationally agreed day should be adopted with specific promotional activities in each country, to be proposed for endorsement by the WHO. On such days worldwide activities are organized, contributing significantly to the spreading of awareness and sensitization of governments and policy-makers;

- Creation and constant updating of websites, on both disorders, separately and together, can be used more extensively to spread news and information on all aspects of prevention, managements and cure;

- The involvement of the Ministry of Health, health education units, market promotion agencies and advertising is essential for carefully designed campaigns. Collaborating with official health NGOs – local, regional and international such as the WHO, UNESCO, European Public Health Alliance (EPHA), Agencies of the US Department of Health and Human Services, International Sickle Cell Organizations, EU Commission and other

international health related bodies which have experience in such educational and dissemination activities will also significantly contribute.

These suggestions should be preceded by "market" research to take local conditions and culture into account. Their implementation should also be followed by research and evaluation to assess their impact.

Community education is of primary importance in both thalassaemia and SCD. However, some differences stand out including the following: Whereas in SCD the emphasis is on neonatal screening and early diagnosis followed by the institution of preventive therapy, in Thalassaemia more emphasis is given to prevention, because of the need to limit new births consequent to the heavy burden of treatments which constitute a drain on resources, such as blood supplies and essential drugs, and very importantly chelating agents. Ineffective prevention leading to increasing numbers of new affected births will over the years make the availability of optimum treatment almost impossible, even in high resource areas. Prevention must also be considered for SCD since the burden it bears is considerable for both families and the health system.

The population should therefore be aware of the need for screening to identify carriers, the risk of bearing affected children and the choices available to avoid such pregnancies. Equally important though is that the public should be aware of the needs of total patient care. An existence of informed community is of great contribution to the country's efforts in promoting control programmes for any disease.

The educational programme of patients/parents NGOs such as TIF, for example, and its member associations is an excellent example of a valuable contribution towards this cause among other areas.

*Training of Health Professionals.* A programme of manpower development needs to be implemented in many parts of the world, to increase knowledge and expertise of the various disciplines involved in the comprehensive management of Thalassaemia and Sickle Cell Disease. These include medical and paramedical personnel such as health educators, counselors, social workers, psychologists and primary care workers, all of whom need to become familiar with the strategies used in the management programme. Health administrators of all levels, including regional health officers and hospital administrators, are other key partners that need to receive adequate and reliable information from the Ministry of Health.

Seminars, workshops, conferences such as those organized by TIF, on an annual basis, should be organized in each region with emphasis on the local clinical, public health and administrative problems.

*Potential pilot studies in selected countries.* As part of a control policy for Hb disorders preventive services depend primarily on population screening, counseling and more in the case of thalassaemia on prenatal diagnosis. Care of Hb disorders which is more complicated and requires life-long multidisciplinary approach is significantly expensive. Policy makers, thus, require appropriate epidemiological data and cost-effective approaches, to support and base their decision to develop, to implement and sustain control policies.

Hence, Pilot Studies in many countries, where such information is lacking or inadequate, is urgently needed to: promote control policies, and develop and direct appropriate services across

the country. Such pilot studies may require collaboration with international centres where technology and expertise are available underscoring the need for networking on an international level. Such studies should include an analysis of the most cost-effective way of carrying out micro-mapping of the frequencies of these disorders with adequate quality control. Health economists should be more involved so that governments can be advised on the increasing health burden that will be caused by these conditions in the future.

Without information on the burden of genetic disease including Hb disorders on public health and their financial implications in general, it will be difficult for any progress to be achieved in the establishment of effective control. Better knowledge of the problems and the economic aspects of Hb disorders are essential.

In planning for example for thalassaemia control, the genetic and clinical heterogeneity of the thalassaemia syndromes must be taken into consideration. In various geographical regions the spectrum of severity of the disorder differs. It is therefore important to obtain, mainly through micro-mapping, high quality data, especially from low resource countries, including genetic information, prevalence and birth incidence of carriers and clinical information with local data, which will help in directing services. The type and extent of services will depend on such data.

Due to diversity, socio-economic and cultural differences, adoption of a universal plan for thalassaemia and sickle cell disease control may be difficult and policies, thus adopted in one area may not be relevant or may be very difficult to apply elsewhere.

*Research.* Research is regarded as an integral part of a service, especially by expert centres and public health authorities. Therefore, support for continued research for the collection and refinement of data relevant for the control of haemoglobin disorders is pivotal to the management of this diseases.

*Cost-effective consideration.* Specifically, the development of simple research programmes into important aspects of the haemoglobin disorders is required. Low- and middle-income countries in which the haemoglobin disorders are common need considerably more information to be able to develop the structure and the economic requirements for their care and prevention services. Carrier frequency determination requires micro-surveys that are the analysis of a few hundred people from every region of a particular country. The screening methods for all haemoglobin disorders are simple and cheap, and a programme of this type simply requires adequate organization and training in the technology required. The importance of obtaining this information cannot be overemphasized (WHO, 1994; Weatherall et al, 2006). In many developing countries with multi-ethnic populations, use of Thalassaemia and Sickle Cell disease Registries to collect clinical and laboratory data on severe forms of thalassaemia and sickle cell anaemia can provide useful information on the needs for long-term care of these diseases and result in the development of cost-effective preventive strategies (Setianingsih et al, 1998; Thong et al, 2005).

A recent preliminary cost-benefit analysis of service issues related to the haemoglobin disorders concluded that specialized treatment centres and neonatal screening programmes are cost-effective approaches towards the control of sickle cell disease and thalassaemia (Weatherall et al, 2006). Further economic data of this kind are urgently required.

Information is also required on local environmental influences on mortality and morbidity of these disorders, and how best to combat these. Numerous questions on best practices in the care and prevention of the haemoglobin disorders need answering. For example, it has been shown unequivocally that neonatal screening and the initiation of prophylactic penicillin can save the lives of many children with sickle cell disease in some countries, but what is the pattern of death due to infection in children with this condition in Africa? Would prophylactic penicillin save a similar number of lives in Africa or India? What is the effect of malaria on sickle cell disease in Africa or on thalassaemia in Asia?

Recent examples of such research that can inform policy development are available from two haemoglobin disorder programmes: the significant reduction of mortality and morbidity from sickle cell disease in Lagos-Nigeria, by the implementation of basic primary health care interventions and the development and effectiveness of thalassaemia services in Iran (WHO 2000; Samavat and Modell, 2004; Akinyanju et al, 2005).

*Strengthening of health services.* As in both cases of SCD and thalassaemia, it is acknowledged that patient care is best provided by centres where large numbers of patients can be managed with continuity by multidisciplinary group of professional experts in the field. These reference centres must comply with certain standards which may be set by health administration or which may be adopted from international agencies. An example is the standards set for centres of reference for rare diseases of the European Commission – SANCO – Rare Diseases Task Force. Selected centres may be designated as WHO Collaborating Centres, and so acquire an international role as well as being national focal points for expert care. The criteria include:

- The capacity to provide expert diagnosis or confirmation of diagnosis;
- The capacity to provide expert management;
- Implementation of outcome measures and quality control;
- Sufficient activity and capacity to provide relevant services at a sustained level of quality;
- Staff Expertise;
- Involvement in epidemiological surveillance;
- Close links with other expert national and international centres with the capacity to network, and;
- Close links with patient associations.

In many countries, services for Thalassaemia and Sickle Cell Disease are catered for at the same centre, so that the roles of training, public education, developing protocols, research etc are shared.

Accessibility to such centres may not be possible for all patients, either because of distance or lack of resources - networking with peripheral hospitals or health units and primary care facilities, so that referrals may be accepted or the provision of advisory services or ‘shared-care’ situation. It must be noted that patients and families often suffer miserably from ignorance, misunderstanding and malpractice on the part of non-specialized personnel, including physicians,

nurses and auxiliaries working in the communities. Support from reference centres, is, therefore, essential along with increased efforts in education of these health workers.

A striking example of the value of expert centres is provided by the United Kingdom, where the survival estimates of such a centre (University College London Hospital – UCH) are significantly better (78% survival at 40 years) compared to the national survival data which show that 50% of thalassaemia major patients die before the age of 35 years (Modell et al.,, 2000).

In conclusion, for a more comprehensive approach to controlling the haemoglobinopathies, several key issues need to be studied:

- Epidemiological information through screening surveys, which include regional frequencies for the purpose of micro-mapping the distribution of haemoglobin disorders. Such information is essential so that services may be directed to the areas where they are most needed including the size of the required services.
- Studies on methods of case capturing following Neonatal screening in SCD, so that universal follow-up and comprehensive care can be offered. For example, based on country presentation, currently, a minority of around 30% actually benefit from the screening programmes implemented in African countries.
- The use of limited 'demonstrating' programmes to study the effectiveness of interventions.
- Studies to compare survival and complication rates between different models of care, such as care in expert reference centres compared to care in general hospital units or the primary care setting.
- Study of the environmental effects on the natural history of SCD such as Malaria, humidity, lifestyle and socioeconomic factors.
- Health Related Quality of Life Studies.
- Social integration and scholarship.
- Population attitudes to methods of prevention.

Successful programmes of prevention that have been ongoing in several countries for many years are based on carrier screening, genetic counseling and availability of prenatal or pre-implementation diagnosis. There are various approaches in the implementation of these interventions. Carrier screening for example can be carried out in antenatal clinics, in schools, pre-maritally or by focusing on the extended family of homozygotes.

Recommendations as to the best methods cannot be offered. Rather descriptions of the available interventions should be made available (as in the TIF's publications on the prevention of haemoglobinopathies), allowing for discussion on the ethical issues and the implications of each methodology, so that each society may choose the policies and strategies, it wished to follow.

The acceptability of each intervention has been shown to vary in different societies. An example is the different level of acceptance of prenatal diagnosis by Cypriot immigrants in the UK, compared to the immigrants from Pakistan (Modell et al, 2000). In Ghana, 75% of families accept prenatal diagnosis, but 60% were hesitant about termination of pregnancy. Identifying community resources in this way will help to plan services, although availability of a spectrum of choices will allow individual choice and ensure autonomy of couples.

Selective screening based on ethnic background is a strategy which may be necessary (cost-effective) in countries where haemoglobin disorders are rare in the indigenous population and

frequent in immigrant minorities. In policy planning by health authorities, it must be reminded that prevention of new affected births is one aspect of a total control programme which is developed in parallel and in order to support the establishment of the best possible services for patient care.

Haemoglobinopathy control programmes based on WHO approaches and recommendations have been established in different countries and in each WHO Region. Appropriate thalassaemia programmes are established in Cyprus, Greece, Italy, United Kingdom, the Islamic Republic of Iran, and are currently being developed in Brazil, China, India, Myanmar, Pakistan, Thailand, Tunisia, Egypt, Maldives and the Kingdom of Saudi Arabia. Further, appropriate sickle cell control programmes have been established in the Kingdom of Bahrain, which includes prevention since 1985, Cuba and Jamaica, while similar programmes are being initiated in Nigeria and Ghana.

In many countries, there are national support associations for thalassaemia which are linked internationally through the Thalassaemia International Federation (TIF). TIF organizes international meetings, bringing together patients and doctors, and providing information, encouragement and support in developing appropriate services in countries (TIF, 2003). Similarly there are national SCD organizations in many countries performing similar functions. The WHO, its collaborating centres, TIF and other SCD non-governmental organizations could explore ways to increase public knowledge of haemoglobin disorders and contribute to a global public dialogue about improving of medical genetic services.

Regional WHO offices and the WHO Collaborating Centres could play a major role in monitoring the progress of the networks and reporting back to individual governments. Suggestions for strengthening existing and creating new WHO Collaborating Centres were made. This support could also include the drafting of regional guidelines on care and prevention of birth defects and the advocating of research. The regional offices for Africa, South-East Asia and the Eastern Mediterranean have included haemoglobin disorders among their planned activities.

Implementation and strengthening of programmes, including medical genetics services in low- and middle-income countries, requires both professional education and training and funding for the laboratory and other services necessary in support. This is a recognized function of the WHO. Meeting participants agreed that there is considerable potential in the WHO to provide impetus to technology transfer and capacity building through coordination of these resources via the structures and influence of its Regional Offices. The process of technology transfer could begin with the accurate preparation of pedigree, interpretation of the mode of inheritance, decision-making about the best molecular investigations to perform and on whom in the family, and then progress to evidence-based therapeutic measures.

The basic requirements for the development of programmes for the control of the haemoglobin disorders have been described in detail in several publications (TIF, 2003; W.H.O., 1994, 2000; Alwan and Modell, 1997; Weatherall and Clegg, 2001; Weatherall et al, 2006). They involve the combination of intensive education programmes combined with the development of clinical and diagnostic services, which must be established simultaneously.

The education programmes include clinicians, scientists, nurses, counselors, outreach workers for rural areas and the inclusion of parent associations. The basic clinical services involve education

about the diagnosis and treatment of the disorders backed up by laboratory services for screening and heterozygote identification, the diagnosis of the major haemoglobin disorders and, in countries in which it is acceptable, facilities for prenatal diagnosis and bone-marrow transplantation.

The curricula and experience necessary to undertake such education and training programmes and to integrate this into the programmes for the establishment of haemoglobin disorder services in low- and middle-income nations is available. All that is required is reasonable financial sponsorship and collaboration between the WHO/HQ, the WHO Regional Offices, national governments and individuals and organizations committed to achieving control of haemoglobin disorders.

Regional expert working groups; further partnerships at national, regional and global levels; and high-level advocacy are needed to ensure that governments of the most affected countries and international aid agencies are fully aware of the extent of the problem and pay close attention to thalassaemia and sickle cell disease.

In some countries, programmes for the care of haemoglobin disorders can also be the prototype of the genetic management of other, non-haematological disorders. Therefore, the paediatric neurologist or immunologist in developing countries will benefit from awareness of the blood disorder care networks.

### 2.3 Preparation and publication of Guidelines for the control of Hb disorders

There is an urgent need to develop protocols or guidelines for the control of Hb disorders in an effort to provide consistent, appropriate care to every patient with an Hb disorder across the world. In addition there is need to provide consistent guidelines and recommendations to policymakers on the development of national prevention and medical care programmes. Such publications as the 'Guidelines to the Clinical Management of Haemoglobin Disorders' (TIF, 2007) and the 'Prevention of thalassaemia and other haemoglobin disorders' (TIF, 2003, 2005 - Volumes I & II)are examples which are based on existing information and evidence. Such guidelines and others that exist for SCD, include advances taken from High Resource countries that may need to be adapted to conditions in Low Resource countries.

There are local conditions whose effect on the natural history of the disease and consequently on clinical management requires considerable further research, such as the need for malaria prophylaxis for children with SCD.

For example, the role of malaria in various complications in patients with Hb disorders needs considerably more investigating, with regard to its effect on the incidence of splenomegaly, acute splenic sequestration and chronic hypersplenism. The role of pneumococcal prophylaxis, also, in an African environment and whether protection from other microbial or environmental hazards is warranted, is also an issue where more research should be focused.

While such questions are being researched by experts, guidelines for early diagnosis, and prevention and management of complications, based on existing evidence-based information should be prepared by the WHO in collaboration with international experts and directed at all levels of health care personnel: doctors, nurses and social workers.

Guidelines should also be accessible to patients, in an as simplified a text as possible, so that patient/parent empowerment and self-management is promoted. TIF for example has published "About Thalassaemia" - a book, translated in more than 13 languages, focused particularly on the needs of the patients and parents and extended for the needs of high school students and the community at large provides detailed information on all aspects of prevention and clinical management of Thalassaemia (TIF, 2003, updated in 2007). Likewise there are several publications for patients with SCD and their families. Such publications are typically of local relevance but some have been codified for international use.

### 2.4 Supporting and promoting the services of reference or centres of excellence

The requirement for patients to be managed in centres specialized in the management of complications is well recognized, both in high resource countries, as well as in low resource areas. The experience of staff in managing many cases as opposed to few and in following evidence-based guidelines and protocols is the main advantage and leads to decreased morbidity, mortality and improved quality of life.

Reference centres of expertise with large numbers of patients and dedicated multidisciplinary staff have a significant role to play, in the training of health workers, diffusion of expertise to secondary centres, and for developing local protocols based on local needs and priorities. Such centres also have a significant role in promoting national education and prevention programmes, including genetic counseling.

Such centres are also engaged in research and require large and sustained funding which is a major problem in many countries. In this respect, these centres of excellence, should be fully recognized by governments, an issue to which WHO can contribute by advising or recommending to National Health Authorities (NHAs) the criteria and benefits of developing Expert Centre, the number of which, in a country, should be determined by the needs of a country, based on the local and regional incidence and prevalence of these disorders.

Centres of excellence must have links with local treatment centres, patients' support groups, and with international professional health organizations and non-governmental organizations like TIF and SCD associations. This partnership with non-governmental organizations is emphasized in the WHO resolutions and is relevant and important to the effective dissemination of information, public education, fund-raising and advocacy.

A network of centres of excellence will greatly facilitate exchange of knowledge, experiences and expertise. In this context the need to define and set criteria for the development of such centres was discussed. Several sources can provide valuable information on which to base WHO criteria for the development of such centres. These include EU funded projects, such as ENERCA (European Network for Rare and Congenital Anaemias) as well as the EU created and supported task force developed in collaboration with major European patients led organizations, notably EURODIS (European Organisation for Rare Diseases). Similarly SCD centres supported by agencies of the Department of Health and Human Resources in the USA can also serve as sources of valuable information for the creation of WHO – recognized centres. The consensus of the participants was that the Hb expert group (to be formed as an outcome of this meeting) would have the responsibility to address this issue.

### 2.5 Promotion of the establishment of regional expert advisory groups

The consensus of the discussion regarding the above issue was the formation of an international advisory panel and regional groups, with the commitment to materialize the recommendations and plan of action of this meeting and through those, the implementation of WHO resolutions on thalassaemia and SCD.

The effective functioning of these regional expert groups relies on adequate funding and so this aspect was extensively discussed. This may require the formation of a fund-raising committee, clearly defined projects and an appropriate business plan. Four networks of regional expert groups, already existing were mentioned including the South Asian, South East Asian, the Middle East Opinion Leaders and the Arab Networks, and which, despite their commitments to promote efforts towards improved control policies for Hb disorders, their work is limited considerably by inadequate funding.. Proposals for funding are described below.

### 2.6 Fund raising to support programmes of control of Hb disorders

Fund-raising constitutes a major component of effective promotion of control programmes and this is not confined to developing societies, only. To assist the development of strategies for fund-raising, a business plan is to be developed with the following features: clear objectives and evaluable end-points, and benefit to the patient population; education/training/dissemination and will present methods of achieving the objectives and maintaining sustainability of programmes.

Fund-raising may take the form of grants which require carefully presented proposals in which sustainability of activities following the grant period is addressed. Grant funding may be a major advantage as it may attract and motivate governments to take over or develop permanent programmes.

Lobbying for funds (particularly from Governments and public health authorities) must be preceded by adequate, updated and reliable information, especially epidemiological data. WHO has its own mechanism for negotiation for fund-raising and for priorities. It was therefore recommended by the participants of this meeting that a proposal should be made to WHO through the Human Genetics (HGN) programme of the Chronic Diseases and Health Promotion Division, as well as the government of each country, for including Hb disorders among the priorities on their health agenda.

Collaboration with and sponsorship from patient and community based organizations can also provide funding support for specific research topics focused on improving clinical management and on developing a cure for thalassaemia or SCD.

The promotion of a twinning programme was also put forward in the course of this discussion, whereby funding can be secured in two ways:

a) Treatment/Prevention Centres, Twinning programmes which can assist emerging treatment and/or prevention centres to develop partnerships with well established expert centres. Twinning can help to improve diagnosis and clinical care through coaching, training and transfer of expertise, ultimately leading to improved quality of life for patients. Twinning can enhance the profile and recognition of treatment centres in developing or other countries and can also be valuable in raising awareness among politicians and the media. Some of the principal types of

twinning activities include providing medical advice; training of health workers; donation of laboratory equipment and reagents; and working together on special projects, such as creation of a computerized patient registry, organization of workshops or conferences and numerous other activities.

b) Non-governmental support and community based organizations twinning programmes focusing on strengthening; patients' education, governmental relations and fund-raising. Such programmes allow expansion of collaboration, beyond historical, linguistic, cultural and/or political limits.

### 2.7 Cost-effective approaches and interventions for the control of Hb Disorders

A number of cost-effective approaches to the intervention for the control of haemoglobin disorders were suggested through the presentations and discussion, in an effort to promote control policies in low resource countries in an as affordable manner as possible. These interventions are expected to produce tangible results without expensive preparation or the use of high and expensive technology:

- Sensitization of health authorities through the provision of information prepared by the local expert group with support, where necessary, from W.H.O. or other international exports. The information should include epidemiological data to convince public health authorities of the impact of Hb disorders. The outcomes of this sensitization process are the formation of an advisory body at Ministry level and the formulation of national policies and strategies to include the following:

- Community education and sensitization, including the hereditary nature of Hb disorders, the possibility of prevention, the benefits of early diagnosis, teaching on the subject in schools and the production of educational materials, the use of mass media etc.

- Parental education programme, necessary both for SCD and thalassaemia and important both for case management and prevention.

- Training of health professionals, especially nurses and local health care personnel.

- Limiting new births through carrier identification, especially pre-marital screening.

- Genetic counseling by trained health workers.

- The creation and use of national guidelines and protocols, adapted from already existing international, evidence-based guidelines.

- Adequate, safe blood transfusions, derived from voluntary donations, to prevent blood born infections.

- Health insurance to cover free medical treatment for patients as part of National policy. Providing free treatment will ensure not only survival but also low complication rates and so will reduce costs in the long run.

- Organization of follow-up visits or part of the minimization of complication rates.

- Manpower planning to improve the staff/patient ratio.

- Enhancing the role of primary care workers in psychosocial support along with community based resources.

- Involving the community by encouraging the creation of patient-support organizations whose functions should include public education, advocacy and fund-raising.

- The promotion of vaccination programmes, especially pneumococcal, *haemophilus influenzae* and hepatitis B.

- The use of Hydroxyurea to reduce acute complications in SCD and to postpone transfusion dependency in thalassaemia Intermedia.

- The use of appropriate technology to prevent complications e.g. trans-cranial Doppler ultrasonography followed by chronic transfusion therapy for primary stroke prevention.

- The support of stem cell transplantation especially in countries where customary consanguineous marriage increases the chance of having matched sibling donors. This is a cost effective intervention compared to lifelong conventional treatment in thalassaemia.

- The creation of centres of excellence which are of proven benefit to patient care.

- Encouraging networking and twinning between centres of various countries for the benefit of exchanging experiences, transfer of knowledge and technical expertise, case management support and research collaboration. The use of electronic infrastructures for these activities (such as Ithanet see appendix D) is more cost effective than traveling between centres to share experiences and to conduct multi-centre research.

### 2.8 Promoting the establishment of a World Haemoglobinopathies Day

Efforts should be made to establish collaboration between all patient-driven Associations (Thalassaemia and Sickle Cell Disease), including Thalassaemia International Federation, the Sickle Cell Disease Association of America (SCDAA), the Sickle Cell Disease International Organization (SCDIO/OILD), the Federation des Associations de Lutte contre la Drepanocytose en Afrique (FALDA), the Caribbean Organisation of Sickle Cell Associations, and other disease-related international and European organizations and projects such as the European Organisation for Rare Diseases (EURORDIS), IAPO, IthaNet, the European Network for Rare and Congenital Anaemias (ENERCA), and others to establish a consensus on the most appropriate world- wide symbolic day for all haemoglobin disorders. The participants agreed to promote such collaboration and suggest to WHO to adopt it. Moreover, this was an item that was discussed and contained within both aforementioned WHO Resolutions (see Appendix A).

### 2.9 Collaboration between potential stakeholders

The roles and responsibilities of a consortium of stakeholders including the WHO Regional offices, WHO Collaborating Centres, International and National government agencies, Foundations and other Non-governmental organizations - patients/family support groups, the private sector and donor organizations, could contribute significantly towards efforts relating to funding, advocacy, technology transfer and capacity building, research and, the promotion of

ethics and human rights in research. An international Sickle Cell federation of local groups, with a constitution and governing body, with representatives from member countries/organizations across the globe has not yet been formed. Although, no plan of action was formulated, TIF through its president expressed willingness to give assistance to the formation of an international Sickle Cell Federation as an independent NGO. Collaboration of the two bodies will then provide a powerful body for fund-raising and advocacy.

Several misperceptions help to explain why care and prevention of birth defects, including haemoglobin disorders, have received little attention from international donors and health agencies. These include a lack of awareness of the high global toll of birth defects; the erroneous belief that effective care and prevention require costly, high-technology interventions that are beyond the health budgets of low- and middle-income countries; and concern that attention to haemoglobin disorders will draw funding away from other high priority maternal, newborn and child health priorities.

Meeting participants agreed, therefore, that it is vitally important that the nature and benefits of medical genetics services be promoted to WHO Regional Offices, national Ministries of Health, policy-makers and senior public health, primary health care, obstetric and paediatric practitioners. Ideally, this could be accomplished through in-depth courses in community Genetics held under the auspices of WHO Regional Offices and targeted to specific audiences and population needs. For example, special attention would be given to haemoglobin disorders in those regions or countries in which they are common.

There is a need for improved data on the global toll of haemoglobin disorders, particularly thalassaemia and sickle cell disease, including birth prevalence, mortality and disability. The WHO and its partners such as March of Dimes, TIF and SCD organizations and other involved stakeholders such as the National Institutes of Health of the US and the European Union can play a very important role in identifying, quantifying and incorporating data on haemoglobin disorders including prevalence, mortality, disability, and the economic costs of action versus inaction.

**2.10 Develop a 5-year plan of action for WHO, TIF and SCD organizations to strengthen the care and prevention of Hb disorders globally with significant focus on low and middle-income countries.**

The table below summarizes the time–frames by which the various goals are expected to be fulfilled:

| 5- YEAR PLAN OF ACTION | | | | | |
|---|---|---|---|---|---|
| **GOAL** | **2008** | **2009** | **2010** | **2011** | **2012** |
| 1: Reviewing the current status of epidemiology and control services for Haemoglobin (Hb) disorders globally | √ | | | | |
| 2: Identification of local and regional problems, needs and priorities for improving control policies | √ | √ | | | |
| 3: Preparation and publication of Guidelines for the control of Hb disorders | √ | √ | | | |

| | | | | | |
|---|---|---|---|---|---|
| 4: Supporting the establishment of new and promoting the services of existing expert centres - Ongoing | √ | √ | √ | √ | √ |
| 5: Promotion of the establishment of regional expert advisory groups | √ | √ | | | |
| 6: Fundraising to support programmes of control of Hb disorders - Ongoing | √ | √ | √ | √ | √ |
| 7: Development of cost-effective approaches and interventions for the control of Hb disorders:<br>a) Ongoing:<br>b) Publication of a Scientific Paper: | <br>√<br>√ | <br>√<br>√ | <br>√<br>- | <br>√<br>- | <br>√<br>- |
| 8: Promotion of the establishment of a World Day for Haemoglobin Disorders | √ | √ | - | | |
| 9: Collaboration between potential stakeholders - Ongoing | √ | √ | √ | √ | √ |

More detailed information using time-frames, wherever possible, for achieving each goal is given below, although, it is recognized by all participants that most goals need lifelong efforts to develop and be sustained:

1. Reviewing the current status of epidemiology and control services for Haemoglobin (Hb) disorders globally:
   Reviewed in the course of these proceedings – (November 2007);
   Complete this through published data and include more countries, by the end of 2008.

2. Identification of local and regional problems, needs and priorities for improving control policies:
   Already identified in the course of the WHO-TIF joint meeting of Experts on Haemoglobinopathies (November 2007, Nicosia, Cyprus), and the WHO and March of Dimes 2006 Report on the 'Management of Birth Defects and Haemoglobin disorders;
   Review published data for additional information from participating and other countries, by March 2009;

3. Preparation and publication of Guidelines for the control of Hb disorders:
   Plan of Action:
   a) Selection and official invitation of potential authors;
   b) WHO Endorsement;
   c) Scheduling of Meetings between Authors:
      (i) First Meeting between Authors:
         a) Setting Priorities;
         b) Division of responsibilities;
         c) Dissemination of information;

d) Setting a time-frame

TIME-LINE: Within 2008.

(ii) Interim Progress meeting of Authors:

a) Updating on the progress of the write up;
b) Preliminary drafts should be exchanged;
c) Identify weaknesses and their solutions;

TIME – LINE: By April 2009

(iii) Final Meeting of Authors, before finalization, editing and publishing:

a) Final drafts should be revised and approved by Authors;
b) Forward to WHO for endorsement.

TIME-LINE: August 2009

(iv) Publication – End of 2009

**4.** Supporting the establishment of new and promoting the services of existing centres of excellence:

(i) Information on the available services provided by these centres should be provided;
(ii) Identification of potentially new centres within highly affected regions world;
(iii) Promotion of twinning of established centres with new or less well resourced centres in different countries.
(iv) Utilize information on criteria from Europe, the US and other areas to develop standards and guidelines with the collaboration of the proposed WHO group of experts.

TIME-LINE: Ongoing throughout the 5 year period.

**5.** Promotion of the establishment of regional expert advisory groups:

This should be established by the end of 2008.

Discussion on the role and activities of these groups could be the objective of a WHO-TIF-SCD organizations meeting in Singapore (7-11 October 2008) in the course of the $11^{TH}$ International Conference on thalassaemia for Health Professionals and the $13^{TH}$ International TIF Conference for patients and parents.

**6.** Fundraising to support programmes of control of Hb disorders:

Ongoing throughout the 5 year period, and well beyond:

Twinning programmes:

(i) Between patients/family driven organizations;
(ii) Between centres of excellence and other centres, and;
(iii) Between other health-related national and international institutions.

Application for EU and other International, Regional or National Bodies' funded projects or grants.

**7.** Development of cost-effective approaches and interventions for the control of Hb disorders:

Ongoing throughout the 5 year period and well beyond;

Publication of a scientific paper, by end of 2009.

**8.** Promotion of the establishment of a World Sickle Cell Disease and Thalassaemia Day: Participating patients' organizations should work to forward and officially propose to the WHO to adopt a symbolic day for commemoration. This should be accomplished within the next 2 years – by the end of 2009.

**9.** Collaboration between potential stakeholders, established by the end of 2009, but continue to expand and strengthen throughout the 5-year period and beyond.

# 3. CONCLUSION

Based on the analysis of the information and data, obtained through country reports of the participants of this meeting, problems, needs and priorities were identified. As a consequence, a 5 year plan of activities was proposed, through which the following issues are anticipated to be addressed:

1) The level of magnitude of the problem, across the world, through epidemiological work;

2) The spread of awareness and training of health professionals in every affected country;

3) The preparation of Guidelines for the control (prevention and case management) of haemoglobin disorders, including cost-effective intervention, evidence-based information and best practices focusing on establishing protocols for the consistent medical and other care for patients and for the prevention of Hb disorders;

4) The establishment and promotion of centres of excellence and a network of collaboration between them, between WHO regional and collaborating centres, patients' driven and community- based organizations and other interested stakeholders;

5) The preparation of a scientific paper on cost–effective interventions and the economic, moral, social and cultural implications of effective prevention policies in the provision of quality health services to patients with Hb disorders, and;

6) Adoption of a World Haemoglobinopathy Day

There is a need for improved data on the global toll of haemoglobin disorders, particularly thalassaemia and sickle cell disease, including birth incidence, prevalence, mortality and disability. The WHO and its partners such as TIF and SCD organizations and other stakeholders such as the National Institutes of Health of the US or the European Union can play a very important role in identifying, quantifying and incorporating data on haemoglobin disorders prevalence, mortality, disability, and the economic costs of action versus inaction.

It is hoped that through the materialization of the above 6 major goals, this meeting will contribute significantly to the promotion of the WHO Resolutions WHA59.20 and EB118.R1 for sickle cell disease and thalassaemia, respectively.

# 4. LIST OF PARTICIPANTS

Professor O. O. Akinyanju
College of Medicine, University of Lagos, P.M.B. 12003,
Lagos, Nigéria
Tel/Fax: 002341 263 2888;
Tel: 002341 482 0517
oluphysic@cyberspace.net.ng

Dr Shaikha Al-Arrayed
Chief, Genetics Unit, P.O. Box 12
Manama, Bahrain
Tel.: 00973 (279) 717
ssarayed@batelco.com.bh

Professor Amal El-Beshlawy
Paediatric Hospital of Cairo University,
Haematology Department,
1 Ali Imbrahim Street El-Mounira,
El-Sayeda-Zeinab
Cairo, Egypt
Tel: 00202 531 4533;
Fax: 00202 7962140;
Mob: 0020123124674
amalelbshlawy@yahoo.com

Dr Marina Boussiou
Geniko Laiko Nosokomion Athinon,
Thalassaemia Unit.
16 Sevastoupoleos Street
11526 Athens, Greece
Tel: 00302-1074-56138;
Fax: 00302-1077-57442
m.boussiou@gmail.com

Dr Silvia Regina Brandalise
Rua Dr Gabriel Porto, 1270
Cidade Univ. - Campinas SP
Cep.13083-210
Boldrini, Brazil
Tel: 0055 19 3787 5001
silvia@boldrini.org.br

Dr Maria Domenica Cappellini
Centro Anemie Congenite,
Ospedale Maggiore Policlinico,
Dipartimento di Medicina Interna

Universita Degli studi Milano
20122 Milan, Italy
Tel: 00390255033752;
Fax: 00390255180421;
Mob: 00393477885455
Maria.Cappellini@unimi.it

Dr Roshan B. Colah
Deputy Director
Institute of Immunohaematology (ICMR),
13th Floor, MS Building,
K.E.M. Hospital Campus, Parel
400012 Bombay, India
Tel: 009122 24138518
Fax: 009122 24138521
colahrb@icmr.org.in or colahrd@gmail.com

Professor Suthat Fucharoen
Thalassaemia Research Centre,
Institute of Science & Technology for Research,
Mahidol University, Salaya Campus, 25/25 M. 3,
Puttamonthon 4 Rd,
Puttamonthon
73170 Nakarnpathom,
Bangkok, Thailand
Tel: 00662 8892557;
Fax: 00662 889 2559;
Mob: 00662 1 8896112
grsfc@mucc.mahidol.ac.th

Professor Renzo Galanello
2a Clinica Pediatrica,
Ospedale Regionale Microcitemie,
Dipartmenento di Scienze Biomediche e Biotechnologie,
Universita di Cagliari, Via Jenner
09121 – Cagliari, Italy
Tel: 00390706095508;
Fax: 00390706095509
renzo.galanello@mcweb.unica.it

Professor Dora Mbanya
Chief of Service, Haematology & Transfusion Service,
C.H.U - Yaounde, B.P. 8046,
Yaounde, Cameroon
Tel: +237 760 7037/42;
Fax: +237 231 4039
dmbanya1@yahoo.co.uk

Professor Kwaku Ohene-Frempong
Professor of Pediatrics,
University of Pennsylvania School of Medicine Director
Comprehensive Sickle Cell Center,
The Children's Hospital of Philadelphia, USA
Tel: + 215-590-3423;
Fax: 215-590-3992
ohene-frempong@email.chop.edu

Dr Antonio Piga
Department of Paediatric Haematology – Oncology,
University of Torino,
Piazza Polonia 94
10126 Torino, Italy
Tel: 00390113134771;
Fax: 00390113134590;
Mob: 00393281506782
antonio.piga@unito.it

Professor John B. Porter
Head of the Thalassaemia and Sickle Cell Unit,
Haematology Department,
University College London- Medical School,
Paul O'Gorman Building
72 Huntley Street
London WC1E 6BT
United Kingdom
TEL: 0044 207 679 6224;
Fax: 0044 207 679 6222
Mob: 0044 7760263470
j.porter@ucl.ac.uk

Dr Anuja Premawardhena
Faculty of Medicine, University of Kelaniya,
PO Box 6, Talagolla Rd
Ragama, Sri Lanka
Mobile: 0094 716 80 3559
premawa@hotmail.com

Professor Mohamed Cherif-Deen Rahimi
Director, National SCD Centre, Univ. Abomey-Calavi,
PO 01 Box 2640
RP Cotonou,
Republic of Benin
Tel/Fax - 00229 213 072 42
mrahimy@bj.refer.org

Professor Graham R Serjeant **(Co-Chairperson)**
14 Milverton Crescent, Kingston 6,
Jamaica
Tel: 00 (876) 927 2300, (876) 970 0077;
Fax: 00 (876) 970 0074
grserjeant@cwjamaica.com

Professor Ali Taher
American University of Beirut, Medical Centre-
Department of Internal Medicine, Haematology – Oncology,
P.O.Box 11-0236, Riad El Solh
1107 2020 Beirut, Lebanon
Tel: 009611749230 Ext: 538; Fax: 009611755669
ataher@aub.edu.lb

Dr Leon Tshilolo
Medical Director,
Centre Hospitalier Monkole-Hopital,
Centre de Formation et d'Appui Sanitaire,
Kinshasa, Democratic Republic of the Congo
Tel: 00243 892 60 00/813 051 446;
Fax: 00243 812 610 005
leon.tshilolo@gb-solution.cd

Professor Mohsen A. F. El-Hazmi (Not able to attend)
Department of Medical Biochemistry
College of Medicine & King Saud University Hospital
P.O.Box 2925
Riyadh 11461
Kingdom of Saudi Arabia
Tel : 00966 1 467 1523 ;
Fax : 00966 1 467 1320
hazmigene1@hotmail.com

Professor Ishwar C. Verma
Snr. Consultant & Head of Dept. of Genetic Medicine,
Sir Ganga Ram Hospital,
Poorvi Marg.
Rajinder Nagar
110060 New Dehli,
India
Tel: 0091 11 25821767;
Fax: 0091 11 26589434;
Mob: 0091 98101 09629
icverma@vsnl.com

Professor Sir David Weatherall **(Co-Chairperson)**
Weatherall Institute of Molecular Medicine,
John Ratcliff Hospital,
Oxford OX3 9DS,
United Kingdom
Tel: 0044 1865 222 398;
Fax: 0044 1865 222 424
liz.rose@imm.ox.ac.uk

**Representatives of International Groups and Institutions:**

Ms Edwige Ebakisse-Badassou
Présidente de l'OILD
Dr Raymondo Didier
Director de l'OILD
SCD International Organization,
21 rue Godefroy,
92800 Puteaux, France
Tel: 00 33 1 49 01 13 54;
Fax: 0033 1 47 74 69 31
eebakisse@hotmail.com
didier.raymondo@drepanetworld.org

Dr Asa'ah Nkohkwo FRSH
Chairman, London Focus SCA,
Sickle Cell Society,
54 Station Road,
London NW10 4UA
United Kingdom
Tel: 0044 208 974 2737 (H);
0044 7921 049 570 (M)
nkohkwo@btinternet.com

Dr Patricia Aguilar-Martinez
ENERCA - The European Network of Rare Anaemias
Member of the WHO Panel on Human Genetics
Laboratoire d'hématologie,
Hôpital Saint Eloi,
34295 Montpellier CEDEX 5
France
Tél: 33 4 67 33 70 31;
Fax: 33 4 67 33 70 36
e-mail:p-martinez@chu-montpellier.fr

Dr Michael Angastiniotis **(Co-Rapporteur)**
Ithanet Portal (International network for thalassaemia research)
P.O.Box 28807,
2083 Nicosia - Cyprus
Tel: 00357 22 319 129;
Fax: 00357 22 314 552
m.angastiniotis@cytanet.com.cy

Dr Willarda Edwards (Not able to attend)
President and Chief Operating Officer
Sickle Cell Disease Association of America,
Inc., 231 East Baltimore Street,
STE 800 Baltimore,
Maryland 21202,
USA
Tel: 001 410.528.1555;
Fax:001 410.528.1495
wvedwards@comcast.net

Professor Brad Therrell
Director, National Newborn Screening and Genetics Resource Center (NNSGRC)
Dept. of Pediatrics, UTHSCSA,
1912 W. Anderson Lane #210
Austin, Texas 78757, USA
Tel: 001 512-454-6419;
Fax: 001 512-454-6509
therrell@uthscsa.edu

Dr Greg Evans
National Institutes Health (NIH) - NHLBI (U.S.)
Chief, Hemoglobinopathies and Genetics Section,
Blood Diseases Branch
National Heart, Lung, and Blood Institute,
6701 Rockledge Dr, MSC 7950,
Room 9156
Bethesda, MD 20892-7950, USA
Tel: 001 301-435-0050;
Fax: 001 301-480-0868
evansgl@mail.nih.gov

**Observers:**

Dr. Soteroulla Christou
WHO Thalassaemia Collaborating Centre
Thalassaemia Clinic
Makarios III Hospital
Nicosia – Cyprus
Tel: +357 22 40 5409

Dr. Androulla Kyrri
WHO Thalassaemia Collaborating Centre
Thalassaemia Diagnostic Laboratory
Makarios III Hospital
Nicosia – Cyprus
Tel: +357 22 40 5482

Dr. Marina Kleanthous
Thalassaemia Research Unit
Cyprus Institute of Neurology and Genetics
P.O.Box 23462
6 Diethnous Aerodromiou Ave
Ag. Dometios
2376 Nicosia
Cyprus
Tel: + 357 22358600
Fax: + 357 22358238/22358237
marinakl@cing.ac.cy

**TIF**

Mr Panos Englezos
President
P.O.Box 28807,
2083 Nicosia
Cyprus
Tel: 00357 22 319 129;
Fax: 00357 22 314 552
thalassaemia@cytanet.com.cy

Dr Androulla Eleftheriou (**Co-Rapporteur**)
Executive Director
P.O.Box 28807,
2083 Nicosia
Cyprus
Tel: 00357 22 319 129;
Fax: 00357 22 314 552
thalassaemia@cytanet.com.cy

Dr Matheos Demetriades
Projects' Coordinator
P.O.Box 28807,
2083 Nicosia
Cyprus
Tel: 00357 22 319 129;
Fax: 00357 22 314 552
thalassaemia@cytanet.com.cy

**WHO/HQ**

Dr Victor Boulyjenkov (**Secretary**)
Human Genetics, Chronic Diseases and Health Promotion,
World Health Organization
20, Avenue Appia,
CH-1211 Geneva 27,
Switzerland
Tel: 0041 22 791 3442;
Fax: 0041 22 791 4769
boulyjenkovV@who.int

Dr Neelam Dhingra (Not able to attend)
Blood Transfusion Safety (BTS) & Injection Safety,
Essential Health Technologies,
World Health Organization,
20, Avenue Appia,
CH-1211 Geneva 27,
Switzerland
Tel: + 41 22 791 4660;
Fax: + 41 22 791 4836
dhingran@who.int

**WHO/ROs**

**AFRO**

Dr B.H. Sambo (Not able to attend)
STP/CDP/Prevention Primaire,
P.O. Box 06 OMS,
Brazzaville,
Congo
Tel: +47 241 39330;
Fax: +47 241 39514
Boureima-samboh@afro.who.int

## 5. REFERENCES

Akinyanju OO, Otaigbe AI, Ibidapo MO., 2005 Outcome of holistic care in Nigerian patients with sickle cell anaemia. Clin. Lab. Haematol., 27(3): 195-9.

Alwan A, Modell B., 1997. Community control of genetic and congenital disorders. Eastern Mediterranean Regional Office Technical Publication Series 24. WHO: Regional Office of the Eastern Mediterranean, Alexandria, Egypt.

Angastiniotis MA, Kyriakidou S, Hadjiminas M., 1986. How thalassaemia was controlled in Cyprus. World Health Forum 7: 291-297.

Badens C, North ML, Lena-Russo D., 2003 Beta –thalassaemia in Metropolitan France. Presse Med., 32(22): 1016-21.

Bryce RJ, Li Z, Erickson JD, Li S, Moore CA, Wang H, Mulinare J, Zhao P, Wong L-YC, Gindler J, Hong S-x, Correa A., 1999. Prevention of neural-tube defects with folic acid in China. New England Journal of Medicine 341: 1485-1490.

Calvo JM et al., 2006. Prevalence on hemoglobinopathies in pregnant women in the Lanzarote health sanitary level". Anales de Medicina Interna, 23.

Christianson AL and Modell B., 2004. Medical Genetics in Developing Countries. Annual Reviews in Genomics and human Genetics 5: 219-265.

Christianson AL, Howson CP and Modell B., 2006. March of Dimes Global report on Birth Defects: the hidden toll of dying and disabled children. March of Dimes Birth Defects Foundation, White Plains, New York, USA.

Colah R, Surve R, Nadkarni A, Gorakshakar A, Phanasgaonkar S, Satoskar P, Mohanty D. Prenatal diagnosis of sickle syndromes in India: Dilemmas in Counseling. Prenat. Diagn. 2005: 25; 345-349.

Dickerhoff R., 2006. Sickle Cell disease in Germany – Disease Manifestations, therapeutic options and possibilities for improvement of care. Klin. Padiatr., 218(3): 165-9.

Dulin E., 2007. Evaluación del tercer año de implantación del cribado neonatal universal de anemia falciforme en la Comunidad de Madrid. Anales de pediatría, 66 (4): 382-6

Gulbis B et al, Hemoglobin, In press

Gulbis B, Ferster A, Cotton F, Lebouchard MP, Cochaux P, Vertongen F., 2006. Neonatal haemoglobinopathy screening: review of a 10-year programme in Brussels. J Med Screen.13(2):76-8.

Jamison & e. al) pp 663-680. Oxford University Press and the World Bank, New York Washington.

Kladny B, Getting EA, Krishnamurti L., 2005. Systematic follow-up and case management of the abnormal newborn screen can improve acceptance of genetic counseling for sickle cell or other haemoglobinopathy trait. Genet. Med., 7(2):139-42

Mañu M. y cols., 2006. Cribado neonatal de hemoglobinopatías y déficit de glucosa-6-fosfato deshidrogenasa (g6pd) en Cataluña. I- estudio piloto en población anónima no relacionada". Medicina Clínica, 126 (8): 281-5

Mañu M. et al., 2007. Cribado neonatal de hemoglobinopatías y déficit de glucosa-6-fosfato deshidrogenasa (g6pd) en Cataluña. Estudio molecular de la anemia falciforme asociada a alfa talasemia y déficit de G6PD.Medicina Clínica, 129 (5 )º:161-4

Modell B, Darlison M, Birgens H, Cario H, Faustino P, Giordano PC, Gulbis B, Hopmeier P, Lena-Russo D, Romao L, Theodorsson E., 2007. Epidemiology of haemoglobin disorders in Europe: an overview. Scand J Clin Lab Invest., 67(1):39-69. Review.

Modell B, Harris R, Lane B, Khan M, Darlison M, Petrou M, Old J, Layton M, Varnavides. Informed choice in genetic screening for thalassaemia during pregnancy: audit from a national confidential inquiry. Brit. Med. Jour. 2000, 320: 337-341.

Modell B, Khan M, Darlison M., 2000. Survival in beta-thalassaemia major in the UK: data from the UK Thalassaemia Register. Lancet, 355 (9220): 2051-2.

Moreno Miralles I., 1999. Alteraciones moleculares de las talasemias en España. Revisión de los estudios existentes. Medicina Clinica, 113: 789-794

Rahimy MC, Gangbo A, et al., 2000. Effect of active prenatal management on pregnancy outcome in sickle cell disease in an African setting. Blood, 96: 1685-9.

Rahimy MC, Gangbo A, et al., 2003. Effect of a comprehensive clinical care programme on disease course in severely ill children with sickle cell anaemia in a Sub-Saharn Afircan setting. Blood, 102(3):834-8.

Samavat A, Modell B. 2004. Iranian national thalassaemia screening programme. BMJ 329:1134-1137.

Serjeant GR, Serjeant BE, Forbes M, Hayes RJ, Higgs DR, Lehmann H., 1986. Haemoglobin gene frequencies in the Jamaican population: a study of 100,000 newborns'. Br J Haematol, 6; 64:253-62.

Setianingsih I, Williamson R, Marzuki S et al., 1998. Molecular basis of β-thalassaemia in Indonesia: application to prenatal diagnosis. Molecular Diagnosis 3: 11-20.

Thong MK, Tan JAMA, Tan KL, Yap SF. 2005. Characterisation of β-globin gene mutations in Malaysian children: A strategy for the control of β-thalassaemia in a developing country. Journal of Tropical Paediatrics 51(6): 328-33.

TIF, 2000. Guidelines to the Clinical Management of Haemoglobin Disorders.

TIF, 2003. Prevention of Thalassaemia and other haemoglobin disorders. Volume I. Nicosia, Cyprus, pp 1-188.

TIF, 2003. About Thalassaemia

Tshilolo L, Mukendi K, Wembonyama O., 2007. Blood transfusion rate in Congolese patients with Sickle Cell Anaemia. Indian J. of Paediatr., 74: 735-8.

Vichinsky E., 2005. Changes in the epidemiology of thalassaemia in North America: a new minority disease. Paediatrics, 116(6): 818 – 25.

Weatherall DJ, Clegg JB. 2001. The Thalassaemia Syndromes. 4Th Edition. Blackwell Science. Oxford, United Kingdom.

Weatherall DJ, Akinyanju O, Fucharoen S., Olivieri N. and Musgrove P. 2006. Inherited Disorders of Haemoglobin. In: Disease control Priorities in Developing countries (ed. By D.

WHO, 1994. Guidelines for the control of Haemoglobin Disorders. WHO, Geneva, Switzerland (WHO/HDP/HB/GL/94.1)

WHO, 2000. Primary Health Care Approaches for Prevention and Control of Congenital and Genetic Disorders. WHO. Geneva, Switzerland (WHO/HGN/WG/00.1)

WHO, 2002. Report of the Advisory Committee on Health Research. Genomics and World Health. WHO, Geneva, Switzerland (ISBN 92 4 154554 2).

WHO, 1996. Control of Hereditary Diseases. WHO Technical Report Series 865. WHO, Geneva, Switzerland.

WHO, 2004. World Health Assembly Resolution on Genomics and World Health. WHA57.13. WHO, Geneva, Switzerland [ www.who.int/gb ]

WHO, 2005. Report to Executive Board: Control of Genetic Diseases. EB116/3. WHO, Geneva, Switzerland [ www.who.int/gb ]

WHO, 2006a. World Health Assembly Resolution on Sickle Cell Anaemia. WHA59.20. WHO, Geneva, Switzerland [ www.who.int/gb ]

WHO, 2006b. Executive Board Resolution on Thalassaemia and Other Haemoglobinopathies. EB118.R1. WHO, Geneva, Switzerland [ www.who.int/gb ]

WHO, 2006c. Management of Birth Defects and Haemoglobin Disorders – Report of a Joint WHO-March of Dimes Meeting, 17-19 May 2006.

World Bank, 2006. Priorities in Health. Eds by Jamison DT et al. The World Bank, Washington, D.C., pp 106-110.

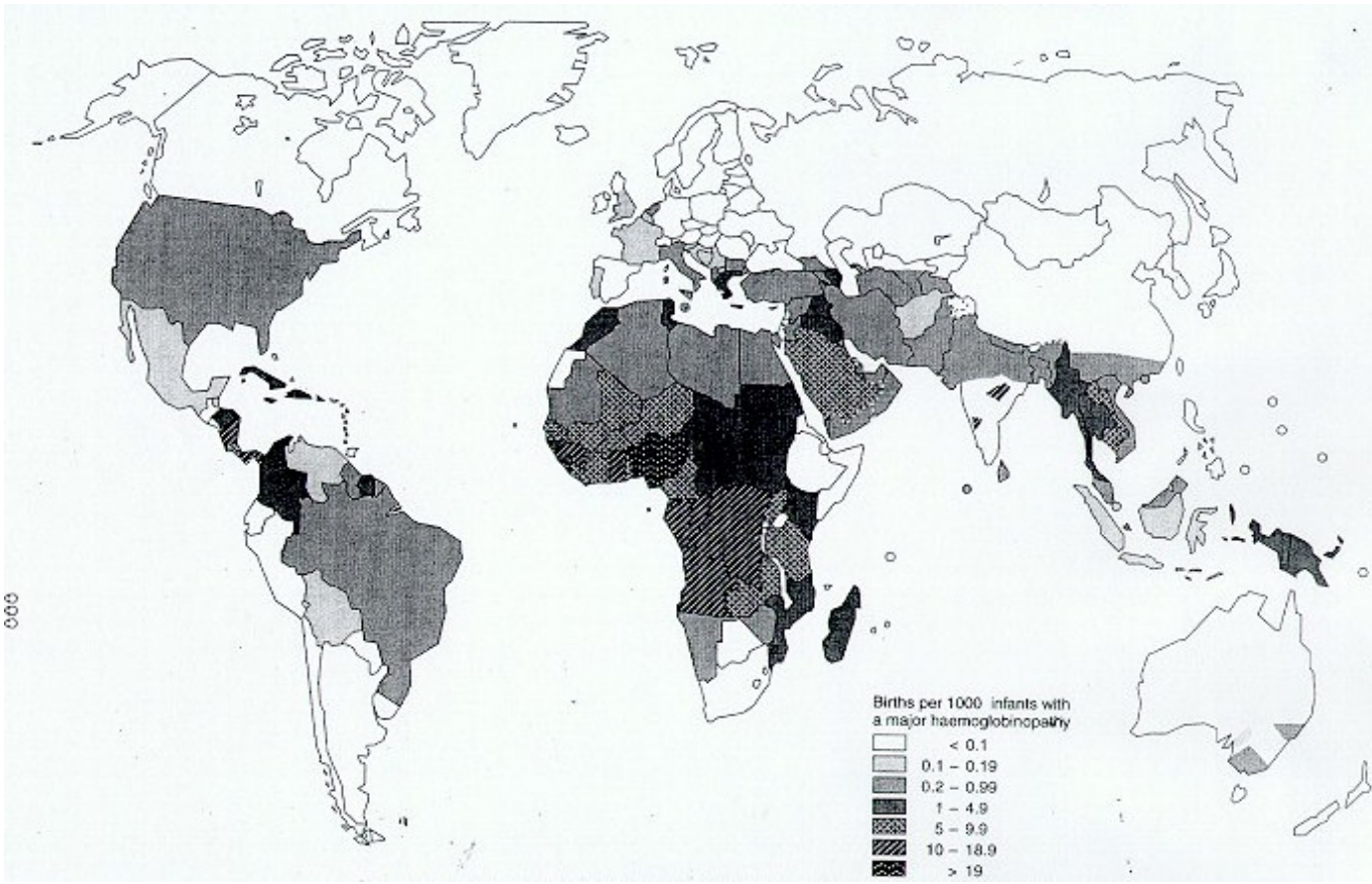



Figure: Global distribution of haemoglobin disorders,

In terms of births of affected infants per 1000 births (WHO, 1996)

## INFORMATION PROVIDED THROUGH THE PRESENTATIONS – AT A GLANCE

### Table 1a: For sickle cell disease

| PREVALENCE | EURO | EMRO | SEARO | AMRO | AFRO | WPRO |
|---|---|---|---|---|---|---|
| **In Indigenous populations:** | | | | | | |
| HIGH | | | √ | | √ | |
| MEDIUM | | √ | | | | √ |
| LOW | √ | | | √ | | |
| **In Immigrant populations:** | | | | | | |
| HIGH | √ | **Not applicable** | **Not applicable** | √ | **Not applicable** | **Not applicable** |
| MEDIUM | | | | | | |
| LOW | | | | | | |
| **AVAILABILITY OF PREVENTION SERVICES: Population, Antenatal, Newborn Screening, Prenatal Diagnosis, Genetic Counseling, Community Awareness etc** | **EURO** | **EMRO** | **SEARO** | **AMRO** | **AFRO** | **WPRO** |
| **Limited in parts of a country/region** | √ | - | √ | √ | √* | √ |
| **Available across a country** | √ | - | - | √ | - | - |
| **As part of a National Health System** | √* | √* | - | √ | - | - |
| **AVAILABILITY OF SERVICES FOR CLINICAL MANAGEMENT: Diagnosis, Treatment, Follow-up, Training etc** | **EURO** | **EMRO** | **SEARO** | **AMRO** | **AFRO** | **WPRO** |
| **Services available across a country** | √ | - | | √ | | |
| **Limited in parts of a country/region** | - | √ | √ | - | √ | √ |

***- In some countries or States**

## Table 1b: For thalassaemia

| PREVALENCE | EURO | EMRO | SEARO | AMRO | AFRO | WPRO |
|---|---|---|---|---|---|---|
| **In Indigenous populations:** | | | | | | |
| HIGH | | √ | √ | | | √ |
| MEDIUM | | | | | | |
| LOW | √ | | | √ | √ | |
| **In Immigrant populations:** | | | | | | |
| HIGH | √ | **Not applicable** | **Not applicable** | | **Not applicable** | **Not applicable** |
| MEDIUM | | | | √ | | |
| LOW | | | | | | |
| **AVAILABILITY OF PREVENTION SERVICES: Population, Antenatal, Newborn Screening, Prenatal Diagnosis, Genetic Counseling, Community Awareness etc** | **EURO** | **EMRO** | **SEARO** | **AMRO** | **AFRO** | **WPRO** |
| **Limited to parts of a country/region** | √ | √ | √ | √ | √ | √ |
| **As part of a National Health System** | √* | √* | √* | √* | - | - |
| **AVAILABILITY OF SERVICES FOR CLINICAL MANAGEMENT: Diagnosis, Treatment, Follow-up, Training etc** | **EURO** | **EMRO** | **SEARO** | **AMRO** | **AFRO** | **WPRO** |
| **Services available across a country** | √ | | | √ | - | - |
| **Limited in parts of a country/region** | - | √ | √ | - | √ | √ |

***- In some countries or States**

**APPENDIX A: WHO RESOLUTIONS ON HAEMOGLOBINOPATHIES**

**FIFTY-NINTH WORLD HEALTH ASSEMBLY** **WHA59.20**

**Agenda item 11.4** **27 May 2006**

# Sickle-cell anaemia

Having examined the report on sickle-cell anaemia;[1]

Recalling resolution WHA57.13 on genomics and world health, and the discussion of the Executive Board at its 116th session on control of genetic diseases, which recognized the role of genetic services in improving health globally and in reducing the global health divide;[2]

Recalling decision Assembly/AU/Dec.81 (V) of the Assembly of the African Union at its Fifth Ordinary Session;

Noting the conclusions of the 4th International African American Symposium on sickle-cell anaemia (Accra, 26-28 July 2000), and the results of the first and second international congresses of the International Organization to Combat Sickle-Cell Anaemia (respectively, Paris, 25-26 January 2002 and Cotonou, 20-23 January 2003);

Concerned at the impact of genetic diseases, and of sickle-cell anaemia in particular, on global mortality and morbidity, especially in developing countries, and by the suffering of patients and families affected by the disease;

Recognizing that the prevalence of sickle-cell anaemia varies between communities, and that insufficiency of relevant epidemiological data may present a challenge to effective and equitable management;

Deeply concerned at the absence of official recognition of sickle-cell anaemia as a priority in public health;
Recognizing the current inequality of access to safe and appropriate genetic services throughout the world;

Recognizing that effective programmes for sickle-cell anaemia must be sensitive to cultural practices, and appropriate for the given social context;

[1] Document A59/9.

[2] See document EB116/2005/REC/1, Summary record of the first meeting, section 4.

Recognizing that the pre-natal screening of sickle-cell anaemia raises specific ethical, legal and social issues that require appropriate consideration,

1. URGES Member States having sickle-cell anaemia as a public health problem:

(1) to develop, implement and reinforce in a systematic, equitable and effective manner, comprehensive national, integrated programmes for the prevention and management of sickle-cell anaemia, including surveillance, dissemination of information, awareness-raising, counselling and screening, such programmes being tailored to specific socioeconomic, health systems and cultural contexts and aimed at reducing the incidence, morbidity and mortality associated with this genetic disease;

(2) to work to ensure that adequate, appropriate and accessible emergency care is available to persons living with sickle-cell anaemia;

(3) to develop their capacity to evaluate the situation regarding sickle-cell anaemia and the impact of national programmes;

(4) to intensify the training of all health professionals and community volunteers in high-prevalence areas;

(5) to develop and strengthen systematic medical genetics services and holistic care, within existing primary health care systems, in partnership with national and local government agencies, and nongovernmental organizations**,** including parent/patient organizations;

(6) to promote community education, including health counselling, and associated ethical, legal and social issues;

(7) to promote effective international cooperation in combating sickle-cell anaemia;

(8) in collaboration with international organizations, to support basic and applied research on sickle-cell anaemia;

2. REQUESTS the Director-General:

(1) to increase awareness of the international community of the global burden of sickle-cell anaemia, and to promote equitable access to health services for prevention and management of the disease;

(2) to provide technical support and advice to national programmes of Member States through the framing of policies and strategies for prevention and management of sickle-cell anaemia;

(3) to promote and support:

(a) intercountry collaboration to develop training and expertise of personnel and to support the further transfer of advanced technologies and expertise to developing countries;

(b) the construction and equipment of referral centres for care, training and research;

(4) to continue WHO's normative functions in drafting guidelines, including good practices and practical models**,** on prevention and management of sickle-cell anaemia with a view to elaborating regional plans and fostering the establishment of regional groups of experts;

(5) to promote, support and coordinate the research needed on sickle-cell disorders in order to improve the duration and quality of life of those affected by such disorders.

Ninth plenary meeting, 27 May 2006
A59/VR/9

= = =

**118th Session** **EB118.R1**

**Agenda item 5.2** **29 May 2006**

# Thalassaemia and other haemoglobinopathies

The Executive Board,

Having considered the report on thalassaemia and other haemoglobinopathies;[3]

Recalling resolution WHA57.13 on genomics and world health, resolution EB117.R3 on sickle-cell anaemia and the recognition by the Executive Board at its 116th session of the role of genetic services in improving health globally and in reducing the global health divide;[4]

Concerned at the impact of genetic diseases, and of haemoglobinopathies (thalassaemia and sickle-cell anaemia) in particular, on global mortality and morbidity, especially in developing countries, and by the suffering of patients and families affected by the disease;

Recognizing that the prevalence of thalassaemia varies between communities, and that insufficient epidemiological data may hamper effective and equitable management;

Deeply concerned that thalassaemia and other haemoglobinopathies are not recognized as priorities in public health;

Deploring the current worldwide lack of access to safe and appropriate genetic services;
Aware that effective programmes for thalassaemia must be sensitive to cultural practices and appropriate for the given social context;

Recognizing that the management of haemoglobinopathies, particularly prenatal screening, raises specific ethical, legal and social issues that require appropriate consideration,

1. URGES Member States:

(1) to design, implement and reinforce in a systematic, equitable and effective manner, comprehensive national, integrated programmes for prevention and management of thalassaemia and other haemoglobinopathies, including surveillance, dissemination of information, awareness-raising and screening, such programmes being tailored to specific

[3] Document EB118/5.

[4] See document EB116/2005/REC/1, summary record of the first meeting, section 4.

socioeconomic and cultural contexts and aimed at reducing the incidence, morbidity and mortality associated with these diseases;

(2) to develop their capacity to monitor thalassaemia and other haemoglobinopathies and to evaluate the impact of national programmes;

(3) to intensify the training of all health professionals in high-prevalence areas;

(4) to develop and strengthen medical services, within existing primary health-care systems, in partnership with parent or patient organizations;

(5) to promote community education, including health counselling and ethical, legal and social issues associated with haemoglobinopathies;

(6) to promote international cooperation in combating haemoglobinopathies;

(7) to provide support for basic and applied research on thalassaemia in collaboration with international organizations;

2. REQUESTS the Director-General:

(1) to raise awareness of the international community of the global burden of thalassaemia and other haemoglobinopathies, and to promote equitable access to health services and drugs for prevention and management of these diseases;

(2) to provide technical support and advice to Member States in framing of national policies and strategies for prevention and management of thalassaemia and other haemoglobinopathies;

(3) to promote intercountry collaboration in order to expand the training and expertise of personnel, and to provide support for the further transfer of affordable technologies and expertise to developing countries;

(4) to continue WHO's normative functions by drafting guidelines on prevention and management of thalassaemia and other haemoglobinopathies;

(5) to promote research on thalassaemia and other haemoglobinopathies in order to improve the duration and quality of life of those affected by such disorders;

(6) to consider having a World Health Day on haemoglobinopathy diseases such as thalassaemia and sickle-cell anaemia in the near future.

Second meeting, 29 May 2006
EB118/SR/2

= = =

## APPENDIX B: TIF's educational materials

1"Blood Safety Kit" – (1999)

2. "Guidelines to the Clinical Management of Thalassaemia" – (2000)
3. "Compliance to Iron Chelation Therapy with Desferrioxamine" – (2000 – Reprinted 2005)
4. "About Thalassaemia" – 2003
5. "Prevention of Thalassaemias and Other Haemoglobinopathies" – Volume I – (2003)
6. "Prevention of Thalassaemias and Other Haemoglobinopathies" – Volume II – (2005)
7. "Patients' Rights" – (2007)
8. "A guide to establishing a non-profit patient support organisation" – 2007
9. "Guidelines o the Clinical Management of Thalassaemia"- Second Edition – (2007)
10. "Thalassaemia Major and Me" – children's Book – (2007)
11. "About β-thalassaemia" – (2007)
12. "About α-thalassaemia" – (2007)
13. "About Sickle Cell disease" – (2007)
14. Educational Folder – (2007)

## APPENDIX C: COUNTRY REPORTS

### WHO African Region

### BENIN: - Mohamed Cherif-Deen Rahimy

*Introduction*
Benin until 10 years ago had no specific care programme for sickle cell disease (SCD). The result was typical of many underdeveloped countries, where early childhood mortality is the rule. The common belief in Benin, as in most of Africa, was that the expensive care of patients is beyond the reach of national economies, and because of other factors, such as beliefs, traditions, poverty, malnutrition and poor infrastructure a fatalistic view was prevalent. Problems that had to be faced include poor prenatal follow-up, short period of stay in hospital after delivery, and difficulty in tracing diagnosed babies after discharge.

Because of these factors, a systematic approach to the control of SCD was initiated in 1993, through a 'demonstrating' programme, a pilot study in order to show the possibility of having a positive effect on mortality and morbidity.

*Epidemiology*
Frequency (carrier rate): About 25%

*Available Services*
The current services are still not nationwide, even though a National SCD programme was adopted in 2002. These services offered, include:

- A tailored newborn screening programme which is enhanced by the provision of information to mothers of diagnosed neonates to ensure compliance. This has ensured that 85% of the eligible babies are enrolled in the follow-up programme. It has been demonstrated that this has resulted in a fall in the under-5 mortality rate of these affected children to 15.5/1,000 live births (compared to an overall 'under-5 mortality rate' of 160/1,000 for the country as a whole);
- Comprehensive clinical care: This has resulted in a reduction of both morbidity and mortality rates;
- Sensitization and health education, mainly through the media, meetings, congresses and festivities, and;
- The creation of a National reference Centre inaugurated in 2003 as a separate building inside the hospital complex.

### CAMEROON: - DORA MBANYA

*Introduction*

There are no established policies concerning diagnosis, prevention or management. Thus, there is a need for developing and implementing a national policy to include prevention and control, capacity development, research, partnerships and collaborations, as well as resource allocation.

Currently, a few couples have prenuptial testing without any organized genetic counseling. There is no programme for health promotion to increase awareness, no disease surveillance.

*Epidemiology*

Frequency (carrier rate): 20-25%

Prevalence (number of known patients): 2-3% of 16 million (around 320,000)

*Available Services*

National policy/programme has been drafted, but has not been implemented. Clinical services exist in a few major cities especially in the capital city, Yaounde where there are about 4500 patients monitored in one centre. Several studies on clinical complications of SCD have been carried out.

Concerning prevention prenuptial testing in available, but few come forward for testing, since health promotion to increase awareness is still lacking.

There is no neonatal screening programme.

Support associations (non-governmental organizations) exist, but are in need of financial and other support.

## DEMOCRATIC REPUBLIC OF THE CONGO: - LÉON TSHILOLO

*Introduction*

In this Sub-Saharan country with a high frequency of sickle cell genes, until recently there was no national programme. By 2006, a pilot study was conducted in Kinshasa, the capital city with 6 million inhabitants to implement a network of services to include neonatal screening, early patient care and to promote educational and preventive programmes. Emphasis at the start of the programme was given to training of medical and nursing personnel. The various aspects of this programme will form the basis of a comprehensive national programme which will take into consideration the data provided by the pilot study.

*Epidemiology*

Frequency (carrier rate): 15.5% (from the screening survey pf 16,000 neonates)

Incidence (new cases per year): 2.1% of the total births (from the neonatal screening programme)

*Available services*

These are limited mainly to the capital city and one of the main challenges will be the implementation of these programmes to all areas, especially in the rural areas. The available services include:

- Mass education through public meetings, the media and leaflets. Emphasis is given to the education of mothers especially after neonatal screening;

- Training of health professionals;
- Neonatal screening using economic laboratory methods (IEF). Results are given before mother and baby are discharged from the maternity unit;
- Follow-up of babies at the immunization centres (MCH centres) with penicillin prophylaxis (only 30% of detected patients are currently benefiting) and vaccinations which include pneumococcal, and *Haemophilus influenzae* immunizations. New strategies are proposed to reduce the number of children lost to follow-up.

Supplementary economic resources are required to sustain the programme and expand it nationwide.

## GHANA: - KWAKU OHENE-FREMPONG

*Introduction*

In Ghana, there are no epidemiological data on SCD, no national policy or guidelines on clinical management. However, a National Programme is under development eight treatment centres have been established and are located in major hospitals. It is estimated that 2% of neonates are affected, leading to 14,000 new cases annually. The overwhelming majority of people with SCD are either not diagnosed or do not receive proper medical care. A task force within the non-communicable disease programme of the Ghana Health Service has been really established to develop policy guidelines for SCD management. A report has been finalized and submitted for adoption and implementation in October 2007. Key features of these policy guidelines include:

1) Strengthening of clinical management of SCD, so that it can be standardized and comprehensive;
2) Development of protocols and guidelines for training;
3) Promotion of regular and continuous capacity-building of healthcare workers (specialist and generalist);
4) Improving of laboratory and blood transfusion services;
5) Implementing of newborn screening and early diagnosis;
6) Expanding the package of insurance scheme for SCD patients;
7) Extending strong public education awareness;
8) Developing Research as an integral aspect of services;
9) Promoting of Genetic counseling and testing facilities, and;
10) Extending and expanding support groups and social services with emphasis on education and employment.

Newborn screening has been established in Kumasi area (Ashanti Province). Kumasi has a population of 800,000 with 26,000 annual births. From February 1995 to December 2006, a total of 225,315 neonates were tested.

*Epidemiology*

The data are derived from the Kumasi neonatal screening programme:

Frequency: 13.38% were carriers (FAS) of HbS

8.71% were carriers (FAC) of HbC

1.84% had SCD (SS or SC)

Incidence: 2%, so that 14,000 new cases are expected annually.

*Available Services*

Treatment centres exist located within major hospitals. These services do not extend to the whole of the country and especially there is no provision for rural areas.

Of the 4,142 babies diagnosed in Kumasi with the severe form of the disease, 538 (13.6%) have been lost to follow-up and finally 2,914 enrolled in clinics (87.4%).

The Sickle Cell association of Ghana, a patient/family organization, is more than 20 years old and provides psychosocial support for families. The Sickle Cell Foundation was established in 2004 to lead the effort in advocacy and fund-raising.

## NIGERIA: - OLU O. AKINYANJU

*Introduction*

Nigeria is a large country with a population of more than 160 million of which 25% are carriers of SCD (about 40 million people), and 150,000 affected babies are expected to be born annually.

In a country in which health care expenditure is only 43USD/person/year and over 70% of the population is very poor and receives little or no psychosocial or financial support, care of the majority of the patients is sub-optimal or totally lacking. Other factors which contribute to poor services include:

(i) the lack of a National Policy on SCD;

(ii) an overall adverse patient/doctor ratio, and;

(iii) only a few hospital centres are able to provide standard quality care.

Within the families, ignorance, frequent illness, high cost of treatment, an excess of premature deaths, social stigmatization are added to the lack of appropriate services to increase anxiety and despair. An additional problem is that due to the lack of appropriate services drug piracy thrives of unproven and unregistered medication add to the financial burden of the families.

*Epidemiology*

Frequency (carrier rate): 25%

Incidence (new cases per year): 20-30 per 1,000 births, estimated 150, 000 births

Prevalence (number of existing patients): estimated at 0.6% of the total population.

*Available Services*

Regular training of health workers including a few from outside Nigeria, in Genetic Counselling and in setting up Parent/Patient organizations

Running and promoting the running of Sickle Cell Clinics and counseling services in different parts of the country

Sourcing donation of basic drugs including anti-malarial and antibiotics from pharmaceutical companies for indigent patients

Have involved Nigerian celebrities and the private sector in fund raising to develop a comprehensive National Sickle Cell Centre

Introduced 1st trimester prenatal diagnosis in 1993 and have run a client supported service by CVS since then'

Advocacy

Public enlightenment programmes delivered to interest groups or broadcast on radio or television

Annual seminars to school children on 'Understanding Sickle Cell Disorders'

Seminars to sensitize and educate journalists (print and electronic media)

Foundation membership of FALDA in 1996

Patient support groups, national or international, are not supported by governments. This includes the 'Federation des Associations de Lutte Centre la Drepanocytose en Afrique' (FALDA), which was founded in 1996 with members from 13 Central and Western African countries.

Identified needs include:

- Funding of service of key Sickle Centre personnel to drive and sustain programs
- Early diagnosis and equitable effective treatment of affected persons
- Education of health care personnel
- Adequate supply of safe blood for transfusion
- Adequate and reliable laboratory diagnostic facilities

- Initially build on local initiatives
- Adequate corps of trained counselors
- Funded prenatal diagnostic service
- Effective community information education and communication
- Support for research - molecular, clinical and operational
- Monitoring & Evaluation of Programmes

The importance of special dedicated centres (WHO, 1994) has been recognized and shown to increase survival. One positive achievement in Nigeria has been the training of counselors who are engaged in educational activities in schools, religious congregations, radio and TV. They have formed support and advocacy associations, dispelling ignorance and myths and supporting families to reduce guilt, despair and stigma, restore harmony in the family and increase self-esteem.

## SUMMARY:

The main characteristics of this region as they are expressed in reports from individual countries are the following:

1. Services (clinical or screening) for SCD are not universally available. These are confined to major cities (in most cases only the capital city) and related to universities or major hospitals mainly as 'demonstration' projects. Rural areas are especially lacking in services.
2. A major problem is recruiting cases for follow up, after identification by the neonatal screening programme. Neonatal screening is not available in all countries or regions.
3. Health information, both to the public and to specific groups, such as the mothers' of babies been screened, premarital couples and even health authorities is very limited.
4. National policies and health planning for haemoglobin disorders are lacking in most locations, even though local experts have drafted proposals.
5. Patient support and advocacy associations exist but suffer from lack of support.
6. Health professionals outside the few reference centres and hospitals require training both, in patient care or in preventive measures.
7. There is lack of epidemiological data.
8. Treatment costs are often born by the families.
9. Little support for research especially on how local environmental factors (e.g. Malaria and malnutrition) affect the natural history of the disease.

## WHO Region of the Americas

## BRAZIL: - SILVIA REGINA BRANDALISE

*Introduction*

The Sickle Cell Anaemia National Program was conceived and published by the Ministry of Health (Portaria MS No 951, May 10, 1996). Its main objective was to reduce the morbidity, lethality and to improve the Health Related Quality of Life (HRQL) of these affected patients. The strategies to establish a full dissemination and education program concerning SCD to the health professionals all over the country were defined. Emphasis was on early diagnosis, genetic counseling and public medications supply.

The first Neonatal Screening Program for SCD in Brazil was officially established in August 29, 1992 by the local Municipality of Campinas (São Paulo, Brazil), covering all the babies born in the city and surrounding areas.

*Epidemiology*

Frequency (carrier rate): 1 in 35

Incidence (new cases per year): 1 in every 1,000 live births (3,500 children)

Prevalence (number of existing patients): The numbers vary according to region e.g., in Bahia state 1 in 650 children has SCD

*Available Services*

Routine vaccinations, including Hepatitis, Pneumococcus and Haemophilus are supplied by the government, as well as the penicillin prophylaxis, pain medications including opioids and Hydroxyurea.

After the successful implementation of public policies directed for these patients in Campinas, other Neonatal Screening Programs for SCD were progressively established in the country, offered to every newborn and collecting data for the National Neonatal Screening Program.

Although improvements in the management of SCD have increased in Brazil, patient survival into adulthood, morbidity and mortality from end-organ damage remain major concerns. Nowadays, enormous differences concerning health care provided among different States/Cities represent a challenge in the country. Improved outcomes are obtained by the Comprehensive Sickle Cell Centers.

Determining the HRQL of patients with SCD provides insight into the impact of the disease on the child and family. When it is not possible to cure, suffering relief turns the goal of the interventions.

## JAMAICA: - GRAHAM R. SERJEANT

*Introduction*

Jamaica is a tropical island in the Caribbean measuring approximately 150 miles long and 60 miles wide with a population of 2.5M of almost entirely West African origin.

*Epidemiology*

Gene Frequency: The sickle cell trait occurs in 10%, the haemoglobin C trait in 3.5%, the beta$^+$ thalassaemia trait in 1% and the $\beta^o$ thalassaemia trait in 0.5%. It can be calculated that 15% carry genes which, when inherited with the sickle cell gene, cause births with sickle cell disease. Alpha thalassaemia of the mild $\alpha^+$ type occurs heterozygously ($\alpha$-/$\alpha\alpha$) in 32% and homozygously ($\alpha$-/$\alpha$-) in 2.4% of the population

Disease Frequency: In a study of 100,000 consecutive deliveries (1973-1981) at the main Government maternity hospital (Victoria Jubilee Hospital), the following frequencies of major genotypes of sickle cell disease occurred.

| | |
|---|---|
| Homozygous sickle cell (SS) disease | 1 in 300 births |
| Sickle cell-haemoglobin C (SC) disease | 1 in 500 births |
| Sickle cell-$\beta^+$ thalassaemia | 1 in 3,000 births |
| Sickle cell-$\beta^o$ thalassaemia | 1 in 7,000 births |

Combining these figures 1 in every 150 births had a significant form of sickle cell disease. In addition other abnormal haemoglobin genes were common, alpha chain variants occurring in 67 babies, beta chain variants in 114 babies, and gamma chain variants in 57 babies. Few of these interact with HbS to produce a disease but single cases of sickle cell-$HbD_{Punjab}$, sickle cell-$HbO_{Arab}$, and sickle cell-Hb Lepore-Boston were detected.

*Available Services*

Sickle Cell Disease Services: There has been a long history of interest in sickle cell disease at the University Hospital in Kingston, Jamaica where Dr. Paul Milner began a Sickle Cell Clinic in 1965. This work expanded with support from the Wellcome Trust to Dr. Milner and Dr. Graham Serjeant - between 1967-1971- when the population served by the Sickle Cell Clinic increased to 250 patients with SS disease. From 1972, sickle cell disease became a major component of the work of the MRC Laboratories at the University of the West Indies and Dr. Serjeant was appointed Unit Director in 1974.

Newborn screening for sickle cell disease commenced at Victoria Jubilee Hospital in June 1973 with a program to screen 100,000 consecutive deliveries in order to establish the Jamaican Cohort Study. This phase was completed in December 1981 by which time it was clear that newborn screening allowed major improvements in disease outcome. The Jamaican Government was persuaded to take over the program but this was not effective until the Sickle Cell Unit undertook supervision of the program in 1993. The program was gradually extended to include deliveries at the University Hospital and Spanish Town Hospital together accounting for approximately 40%

of all island deliveries. Jamaican services expanded when the Sickle Cell Trust was formed as a local charity in 1986 constructing a building for the Sickle Cell Clinic in 1988 and an Education Centre for Sickle Cell Disease in 1994. Specialist services at the Sickle Cell Unit expanded to include prenatal diagnosis, ultrasound and ophthalmological services.

Educational services with an educational coordinator delivering illustrated Power-point lectures to almost all of the islands 160 secondary schools, teacher training colleges and nursing schools. There has also been the development of educational materials including teaching slides, videos, DVD's, interactive CD-ROM tutorials (with the Wellcome Trust), posters, brochures, and various books and booklets.

The next project of the Trust will be a trial of the role of education in prevention of the disease. From 2008, free screening for the major genes causing sickle cell disease will be provided to the 4,000 students in senior classes of 16 secondary schools in the Parish of Manchester in central Jamaica.

After genotype identification, there will be targeted counseling explaining the significance of the carrier status and how to avoid having a child with sickle cell disease. To determine whether this program is effective, newborn screening, not currently available in central Jamaica will also be developed for the 6,000 neonates in the Parish each year. The program will continue for 5 years and seeks to empower Jamaican students to make informed reproductive decisions.

If successful, this study will provide a model for sub-Saharan Africa and other countries to use a similar approach to reduce the frequency of births with sickle cell disease.

It is to be hoped that the increased awareness and education of local health care personnel and the provision of suitable resources will soon allow this program to be spread island wide but emphasis must be placed on prevention of the disease where possible.

## UNITED STATES OF AMERICA: - KWAKU OHENE-FREMPONG

### For Sickle Cell Disease

*Epidemiology*

Frequency (carrier rate): Estimated 3 million carriers

Incidence (new cases per year): Approximately 2000 annually.

Prevalence (number of existing patients): 80,000- 100,000 cases.

*Available Services*

Clinical services in the USA: There are more than 60 well-organized comprehensive treatment centres, mostly in large urban communities. Even so a large number of patients are treated in small community hospitals and private physicians' offices.

State funding to support care coordination is available in some States. Psychosocial support is provided by both hospital-based social services and community-based services, such as the Sickle

Cell Association of America. Policies such as newborn screening, universal anti-pneumococcal vaccination of young children, supportive paediatric programmes, the wide application of trans-cranial Doppler for stroke prevention and hydroxyurea have all contributed to improved survival and quality of life.

Challenges in clinical care still remain: the services for adult patients are still regarded as inadequate and smooth transition from paediatric to adult care remains a problem. Emergency Department handling of cases needs improving. There are no uniform management standards.

**USA:**

**For Thalassaemia**

*Epidemiology*

Prevalence (number of existing patients): Estimated 2,000 patients cared for in 6 large treatment centres.

*Available Services*

Patients are cared for in 6 large treatment centres, although many are treated at local hospitals. Support is also provided.

**CANADA:**

**For Thalassaemia**

Around 70 new cases per year are expected. There are several treatment centres in urban areas with large African and Caribbean populations, mainly in Ontario and Quebec.

Newborn screening was initiated in Ontario in 2006. Community-based organizations exist in Ontario and Alberta.

**SUMMARY:**

The AMR countries represented at this meeting were Jamaica, Brazil and the USA. In these countries, adequate epidemiological information exists with local frequencies well documented. Neonatal screening is almost universal and services are created as a result of national or regional planning.

In this region, concerns about morbidity, mortality from end-organ damage and health related quality of life are being researched. The clinical services, especially for adult patients are still regarded as needing improvements in localized areas, especially since expert centres are limited in number and many cases are treated as isolated cases, living far from centres. This is especially true of Thalassaemia.

## WHO Eastern Mediterranean Region

### KINGDOM of BAHRAIN:- Shaikha Al Arrayed

The island Kingdom of Bahrain has a population of 0.6 million with a high frequency hereditary blood disorders.

*Epidemiology*

Thalassaemia frequency (carrier rate) 2%

Incidence 2 new cases per year.

Prevalence 0.09%

SCD frequency 11%

Prevalence 2.1%

*Available services*

The hereditary diseases programme of Bahrain started in 1984 when a genetic medical centre was opened to study the control of hereditary diseases in the country. In 1991 a national committee for prevention was formed by Ministerial order. The measures adopted included community education and screening programmes which focused on neonates of carrier mothers, schools and ante-natal clinics. Premarital counseling was offered to carriers detected and this was accompanied by a comprehensive health educational programme to increase public awareness of the diseases. Key opinion leaders were targeted for sensitization and the mass media, the schools, leaflets, booklets and public meetings were used to reach the population. Training courses were organized for all doctors in health centres. A specific risk assessment sheet was issued.

During the first few years only 20% of the couples attended premarital counseling so that by 2004 screening became mandatory but the autonomy of the couple at genetic counseling is fully respected. Pilot studies of newborn screening over the years have demonstrated a 60% decline in the incidence of SCD over the years (1985 – 2.1%, 2002 – 0.9%, 2007 – 0.8%).

Neonatal screening was adopted as a universal national programme in 2007

Consanguinity is also coming down as a social phenomenon and this will also have an effect on birth incidence. In 1995 consanguinity rate was 39.4% (with first cousin marriages at 21%) while in 2005 the rate fell to 20% (with first cousin marriages at 11.4%).

### EGYPT: - Amal El-Beshlawy

*Introduction*

Egypt is a country with a population of 72 million. β-thalassaemia is the most common chronic haemolytic anaemia in Egypt.

*Epidemiology*

Thalassaemia:

Frequency (carrier rate): 5.3%- < 9% - Gene Frequency 0.03

Incidence (new cases per year): 1,000 per 1.5 million live births (~ 2,000 in 2006)

Prevalence (number of existing patients): Registered cases 9,912.

*Epidemiology:*- Sickle Cell Anaemia

Frequency (carrier rate): 0.3% - In the Western Desert carrier rates of 9%-22% have been recorded

Prevalence (number of existing patients): 757 registered cases.

*Available Services*

There are 13 treating centres in major hospitals (the largest is in the Paediatric Department of Cairo University Hospital caring for 2,597 cases). The Ministry of Public Health has another 44 centres and the Red Crescent another 6 centres providing services.

Patient support is provided by the Egyptian Thalassaemia Association which was founded in 1990 with the support of TIF. Standard treatment protocols are followed, but only 48% of the total patients are on regular chelation because of poor compliance.

L-Carnitine is provided as an adjuvant to treatment. Hydroxyurea is given to cases of thalassaemia Intermedia and sickle cell disease. Stem cell transplantation has been carried out in 75 cases. Of these, type I & II cases had an 80% success rate, while category III cases had a 60% success rate (8 year follow-up). All treatment is provided free.

There is no national prevention programme, although the high frequency of carriers and the high number of affected newborn every year along with the burden to the health services and the families is well recognized – The average estimated financial burden for thalassaemia management is ~ 10 million USD per year. Without a prevention programme, the number of patients presenting for treatment is increasing.

Prenatal and pre-implantation genetic diagnosis is acceptable to 'at-risk' mothers.

Patient life expectancy is improving (peak 15½ years). Hepatitis C is still prevalent with 70% of patients being positive for HCV –RNA.

**What needs to prevent thalassaemia in Egypt:**

- Improving public awareness to the disease through mass media;
- Obligatory premarital screening;
- Well-equipped centres for prenatal diagnosis;
- Active centres for pre-implantation genetic diagnosis of thalassaemia for high risk families;

- Increase the SCT centres for cure of thalassaemia – lowest cost;
- Adoption of the high authority in the government to the problem of thalassaemia.

**LEBANON: - Ali Taher**

*Introduction*

Thalassaemia is a rather common disease in Lebanon. Most of the patients are from the suburbs of Beirut and are Muslims, and 53% of the parents are first degree relatives. Around 71% of the families have one affected child and around 2% have more than 3 affected children.

*Epidemiology*

Frequency (carrier rate): 2-3% in the population

Prevalence (number of existing patients) - see below in table 1:

**Table 1: Number of registered haemoglobinopathies' patients in Lebanon**

| | |
|---|---|
| **B-Thalassaemia Major** | **318** |
| **B-Thalassaemia Intermedia** | **175** |
| **α-Thalassaemia** | **7** |
| **Sickle Cell/ Thalassaemia** | **50** |
| **Sickle Cell Disease (HbSS)** | **35** |
| **HbC** | **6** |
| **Rare Anemia (BD, CDA, Sideroblastic)** | **13** |

*Available Services*

All thalassaemia patients are registered and followed up regularly at the Chronic Care Centre (CCC), Hazmieh, Lebanon. The CCC was established in 1994 to follow up patients with childhood chronic diseases, mainly juvenile diabetes and thalassaemia. 604 patients with haemoglobin disorders are registered and regularly monitored at the Centre.

Almost all patients followed up are Lebanese, except for 33, of which 19 are Palestinians. More than 50% of the patients have no health care coverage and depend on CCC to provide them with almost free treatment.

The patients are followed up at CCC through a multidisciplinary team composed of physicians, other health care providers and social workers.

Patients are treated with desferrioxamine (51% of patients), deferiprone (20%), and most recently with deferasirox (29%). More patients will be switched to deferasirox as it is starting to be supplied by the NSSF and Ministry of Health. Thirty two thalassaemia patients have received Bone Marrow Transplantation, of which 30 were successful.

CCC, as a private NGO, has launched a National Prevention Program in 1994 in collaboration with the Lebanese Ministry of Social Affairs. The first phase focused on information to the public, training of health care professionals and development of training material. The second phase concentrated on the development of a new vision and future strategic plans which aim to increase awareness and spread knowledge, the conduct of research and statistical studies and undertaking national screening and other community-based awareness initiatives and campaigns.

The implementation of the premarital screening law in 1994 (despite its several drawbacks) and all the collaborative awareness and prevention campaigns of the CCC with the Lebanese Ministries, has decreased the number of new cases of thalassaemia by about 75% reaching a total of three new cases in 2006. Prenatal diagnosis is also performed to pregnant mothers when both parents are known to be carriers of the disease. An average of 13 amniocenteses are being performed per year since 2000 and have resulted in around 50% carriers, 25% thalassaemia patients and 25% disease-free neonates.

Many initiatives and collaborations are being undertaken in the region to keep up-to-date with the disease. The Middle East Thalassaemia and Thought Leaders annual meeting aims at sharing experiences and ongoing research in the region as well as highlighting new advances and updates on the management and care of Thalassaemia.

**Middle East Region: Saudi Arabia, Iran and Gulf**

The Middle East is characterized by a high prevalence rate with more than 20,000 patients scattered all over the region. In addition, there are a large number of Sickle Cell Disease communities in countries such as Saudi Arabia, Bahrain, Oman and Lebanon.

**Table 2: Thalassaemia major and Intermedia patients diagnosed and receiving iron chelation in the Middle East region**

| | **Levant (Lebanon, Syria, Jordan and Palestine)** | | **KSA** | | **Iran** | **Gulf** | |
|---|---|---|---|---|---|---|---|
| | **Thal Major** | **Thal Inter** | **Thal Major** | **Thal Inter** | **Thal** | **Thal Major** | **Thal Inter** |
| **Patient Diagnosed** | 6323 | 1255 | 1173 | 63 | 18,000 | 800 | 20 |
| **Patient Treated With Iron Chelator** | **4443** | 471 | **872** | 39 | **13,497** | 745 | 6 |

**Available Treatment Centres in the Middle East Region (see Table 2):**

- Lebanon: The Chronic Care Center regroups all Lebanese Thalassaemic Patients;
- Jordan: Several Centers available, However, Al Bashir (MOH) is the main Center that treats the majority of patients
- Syria: several centers affiliated to the MOH, scattered all over the country. The 2 major ones are in Damascus and Aleppo
- Saudi Arabia

  Saudi Arabia is divided into 3 different regions:

  - Riyadh: 6 centers are available treating Thalassaemic Patients
  - Jeddah: 7 centers are available, of which mainly 4 of them treat Thalassaemic Patients
  - Eastern Zone: 5 centers treat Thalassaemic Patients. This region is characterized by a high SCD prevalence
- Gulf
  - There are more than 12 centers in the Gulf, Mainly in the UAE and in Kuwait
  - Oman, Bahrain and Kuwait are mainly characterized by a high SCD prevalence
- Iran
  - There are more than 160 centers in Iran scattered all over the country.

**SUMMARY :**

This is a high frequency area, both for thalassaemia and sickle cell disease. Many problems remain unsolved in this region:

1) Lack of epidemiological information; although many surveys have been conducted, regional data are often lacking;
2) Patient care is confined to limited expert or university centres. In most countries treatment centres have been developed in peripheral areas, but many areas remain with poor services, and high early mortality is evident from the discrepancy, between the expected birth of patients and the actual numbers attending the centres. Of these attending the centres, 25-30% patients with thalassaemia major do not receive iron chelation (Table 2);
3) National prevention programmes are still not universal in the region, although services are available in most countries to a variable extent; examples of progress are represented by Iran and the Kingdom of Saudi Arabia in which consultations on aspects of prevention which involved the religious authorities as well as the health authorities, has led to the

development of effective programmes which are now in varying stages of implementation; another prominent example is the Kingdom of Bahrain in which premarital screening has significantly contributed to reducing the prevalence of births of SCD and has shown that prevention should become a major objective for public health programmes especially in countries with limited resources;

4) Public awareness needs improving in most countries, especially concerning primary prevention.

## WHO European Region

### CYPRUS: - MICHAEL ANGASTINIOTIS

*Introduction*

Cyprus is a country with a high prevalence of thalassaemia.

Without prevention around 50 new cases of homozygous β-thalassaemia would be born every year and this is expected to lead to an accumulation of case if treatment is provided to all with no prevention measures to limit new affected births. This accumulation of cases would lead to a strain on resources such as the supply of adequate amounts of blood and inevitably lead to sub-optimal treatment regimes in the future. This realization led to the development of a comprehensive control programme to include both treatment and prevention. After a WHO consultation in 1971, governmental policy for thalassaemia control evolved from 1972-1978. A parent/patient support association founded in 1968 played a significant role in promoting these policies and achieved a free-of-charge implementation for both treatment and prevention programmes by 1978.

*Epidemiology*

Frequency (carrier rate): 1 in 7 or ~15% in the population for β-thalassaemia; 20-25% carry the α-thalassaemia gene, and 1:500 carry the sickle cell gene.

Incidence (new cases per year): Currently 0-5 new cases per year because of the prevention programme.

Prevalence (number of existing patients): 684 β-thalassaemia, 158 patients with HbH-Disease are currently followed up at the centres. In addition, there are 35 cases of registered patients with SCD (β-thal/sickle cell).

*Available Services*

The prevention programme included health education with information directed to the public as well as health professionals. A programme of screening for carriers was implemented, targeting school leavers and premarital couples. Genetic counselling, prenatal diagnosis and pre-implantation genetic diagnosis were added, and successfully reduced the number of new births from 70 in the 1980's to 0-2 per year.

These patients receive treatment and follow-up in 4 specialized clinics, where international treatment protocols are followed and because of the mainly adult population and evidence of iron

deposition in the heart, many patients are on more intensive chelation using a combination of Desferrioxamine and Deferiprone.

As a result ferritin levels are significantly lower since 2001, and cardiac deaths are reduced, even though they are still the commonest cause of death. Stem cell transplantation has been offered to only 12 cases, especially since the patient population is older and most do not have sibling donors.

The Cyprus Thalassaemia Centre is a WHO Collaborating Centre, since 1985, for community awareness, and with a mandate to disseminate policies, train clinical and laboratory personnel from other countries and conduct educational activities for health professionals, patients, families and the community.

**GREECE: - MARINA BOUSSIOU**

*Introduction*

Haemoglobin disorders, which include β-thalassaemia, α-thalassaemia and sickle cell anaemia, are the most common genetic disorders in Greece causing a major social and health problem. The increasing number of affected persons as well as the high incidence of heterozygotes urged the authorities to develop and apply a National Program of Prevention (1973 onwards) with the aim of limiting the number of affected births, coupled with treatment of the major thalassaemia syndromes. Application of this program in Greece for over 30 years has dramatically reduced the number of new thalassaemia major cases and (as a consequence) has insured the appropriate funds for optimum management. Services are all free of charge for everybody. During the last decade, the settlement of immigrants mainly from the Balkans, but not only, as well as new thalassaemia births that belong to this group or other minorities (Roman populations - gypsies) has directed a new approach.

*Epidemiology*

Frequency (carrier rate): β-thalassaemia (8%), α-thalassaemia (8%) and sickle cell anemia (1%)

Incidence (new cases per year): ~ 7 cases per year – mostly from immigrants

| **New thalassaemia major births 1998-2003 (37 births)** |
|---|
| 19 Immigrants (11 Albanians), (4 Africans), (4 Romanies), |
| 7 The laboratory diagnosis in the private sector was wrong |
| 6 cases from In Vitro Fertilization (IVF)-for the donor was not examined |
| 3 personal decisions of the couple concerned |
| 2 The examination was not suggested by the doctor |

Prevalence (number of existing patients): ~ 2,500-3000 registered patients with β-thalassaemia.

*Available Services*

- Phase I: The program started as a research project undertaken by the academic community. Upon development of the National program, it was provided as part of the National Health care system. It included sensitization of the public, mass screening for the identification of

carriers, genetic counseling and prenatal diagnosis (PND), mainly by chain biosynthesis at the 2nd trimester of pregnancy (Central unit in Athens). In this phase population education mainly involved the obstetricians: they steadily advised pregnant women to undergo carrier identification.

- Phase II: Screening was provided by dedicated prevention units of thalassaemia situated in public hospitals- central and peripheral units. Patients were treated in specialized one- day clinics in public hospitals. The Central unit in Athens includes screening, genetic counseling, prenatal diagnosis and management. It also serves as a Reference unit.

  In this phase, population education was more systematic and involved, mainly the units of prevention but also the obstetricians and many other sectors of society, including the media, public health workers, local authorities and the medical community. Screening for thalassaemia should ideally be offered prior to pregnancy, so that individuals and couples can choose from the fullest range of available options. Several local programs indicated that the most effective target group is the students at the termination of schooling.

  Study of the prevalence and distribution of the common mutations in the Greek population allowed the switch to DNA based 1st trimester PND. The high incidence of both alpha and beta thalassaemia along with the marked molecular heterogeneity and the presence of $\delta\beta$, HPFH and $\delta$-thalassaemia complicated the screening procedures and genetic counseling and demanded redesigning the Program.

- Phase III: This phase is characterized by:

  - A 'fine tuning': genetic counseling personalized for each single case (genotype-phenotype correlation);
  - The application of EMQN Best Practices, of external quality control and a quality management system, and;
  - The considerable changes in the level of community screening, information and genetic counseling needs because of the influx of 1,000, 000 immigrants (10% of the total population; most immigrants are employed, speak the language and have access to the health services.

- New challenges: IVF and pre-implantation PND; New multi-screening DNA technology. Dissemination of the information: molecular genetic diagnosis in several laboratories of the private and public sector all over Greece. Identification of new problems should lead to reconsideration of policies.

  Further actions necessitated:

  - National registers of patients, new thalassaemia major births and of prenatal diagnosis
  - A centralized control of all relevant laboratories, common guidelines
  - Application of external and internal quality control
  - The existence of expert centers in the country.

Taking into account the current data, the Programme has to be adapted to the future needs under the cooperation of the Health authorities, the units of Prevention as well as the Parents and Patient support groups.

Patient care: In Greece all expenses for treatment and prevention are covered by the Ministry of Health.

## ITALY: - RENZO GALANELLO – ANTONIO PIGA – DOMENICA CAPPELLINI

*Introduction*

In Italy there is no universal National Programme for the control of Haemoglobin disorders, but it is rather dealt with on a regional basis. Few regions have specific legislation for global management of haemoglobinopathies. Prevention on a National basis does not exist, although several regions have well established programmes.

Where prevention is an ongoing programme, such as in Sardinia since the 1970's, the birth rate of homozygous β-thalassaemia has fallen by over 90%.

*Epidemiology*

Frequency (carrier rate): 1 – 12 % (with high prevalence in islands and costal regions). In the big cities of Northern Italy such as Milan and Torino the incidence is high due to recent immigration.

Incidence (new cases per year): < 100 (raising trends for immigration as well as informed decision to have homozygous neonates)

Prevalence (number of existing patients): About 6.000

*Available Services*:

PREVENTION:

In Italy there are more than 100 screening centres spread in the country and 8 centres for prenatal diagnosis. Knowledge about the disease is diffused and usually there are no problems of referral for pregnancy. Preimplantation diagnosis is not allowed by recent legislation.

In Sardinia a formal preventive program based on population screening, genetic counselling and prenatal diagnosis, on a regional basis is active since more than 30 years. In the last 10 years this program has been extended to 14-year-old students (Cao A et al 2007). As a result of preventive program the birth rate of neonates with homozygous beta-thalassaemia decreased by about 90%. Other regions including Piemonte, Lombardia, Sicilia and Lazio have services for screening and prenatal diagnosis. Knowledge of the disease is extensive and there are no problems of referral for pregnancy.

Pre-implantation genetic diagnosis is not allowed by recent legislation.

MANAGEMENT:

Standard treatment in accordance with the international guidelines is given to all patients. Provision of treatment is uniform in the country. There are several reference expert centres and many (about 100) dedicated units at primary care hospitals.

Blood for transfusion is safe and available in adequate amount. Three chelators (Desferal, Ferriprox and Exjade) are available for clinical use. Advanced technologies for organ iron overload assessment (SQUID and MRI) are accessible to the patients. A dedicated computerized record (WebThal) is being used in 37 centres for patient clinical care and clinical research. It allows care continuity for patients moving across the country.

Prevention and treatment costs are fully provided by National Health Care system. The improvement and wide availability of treatment resulted in a better survival and quality of life (Borgna-Pignatti C et al 2004).

Further actions needed:

- Realization of an Italian Registry of patients
- Implementation of clinical and basic multicentre research programs
- Specific actions for prevention and treatment of haemoglobinopathies in immigrants.

## UNITED KINGDOM: -JOHN B. PORTER

*Introduction*

In the United Kingdom there are patients with sickle cell disorders who are mostly immigrants from the Caribbean and Africa, and those with thalassaemia are immigrants from Cyprus, Pakistan, India, Bangladesh and other countries of the South East Asian region.

*Epidemiology*

100,160 out of the total births per year come from within ethnic minorities and represent 16.2% of the total births in the UK. The “at-risk couples” are estimated to be 1,390.

Incidence (new cases per year): 348 births per year – 280 SCD and 68 thalassaemia (if no prevention)

Prevalence (number of existing patients): SCD ~ 10,000; thalassaemia 900.

*Available Services*

The newborn screening programme utilizes the dried blood spot system which is sent to three centralized screening laboratories. The estimated cost per case detected through the National Screening Programme is £20,000.

The rationale for this includes early diagnosis of affected neonates, timely treatment with prophylactic penicillin, observation of complications and reduction in morbidity and mortality, allowing vigilance before severe clinical features appear.

Antenatal screening in low prevalence areas is selective, based on ethnic perceived background, but in high prevalence areas, this is now universal. Detection of a pregnant carrier is followed by offering testing of partners and making use of a network of counselors. Chorionic Villous Sampling (CVS) is offered at 10 weeks and DNA diagnosis is conducted in 3 laboratories.

Often, timely referrals are a problem (David et al, 2001). The uptake for prenatal diagnosis varies according to the ethnic origin: it is almost universal among Cypriot and much less in Pakistani minorities.

Provision of treatment in the United Kingdom is also not uniform. Decisions about which chelation to provide is determined by each of more than 100 primary care trusts. Because of the geographical distribution of the immigrant groups, many patients are treated by clinicians who see very few patients. 71 physicians see only one patient each and 72 see less than 9 patients while only 4 see more than 50 patients.

The need for reference centres is demonstrated by the different survival rates in patients followed in an expert centre, such as the University College London Hospital (UCLH), where 78% have survived to 40 years, while for the whole of the country 50% die before the age of 35 years (Modell, 2000) (see Table 3). The same uneven care provision applies to sickle cell disease, with no official centres and payment is on 'tariff' system.

**Table 3: Crude mortality rates in thalassaemia major**

| **BIRTH COHORT** | **UK AS A WHOLE** | **University College London Hospital (UCLH)** |
|---|---|---|
| 1955-1964 | 56% | 29% |
| 1964-1974 | 34% | 15% |
| 1975-1984 | 14% | 0% |
| 1985-1994 | 3% | 0% |
| 1995-2000 | 2% | 0% |
| **OVERALL** | **24%** | **11.7%** |

## FRANCE, GERMANY, SPAIN, PORTUGAL & BELGIUM: - PATRICIA AGUILAR-MARTINEZ – Data from the ENERCA programme of the EU.

*Introduction*

The prevalence of Hemoglobin Disorders was relatively low in European countries such as France, Germany, Spain or Belgium, except in some specific areas (mainly the South east of France and Corsica).

*Epidemiology*

a) France:
Frequency (carrier rate): SCD: high in the Paris area ~5% and 3.2% in the whole country. Thalassaemia: studied only in South France 0.8-0.9% and in Corsica 3.1% Probably ~0.7% overall.

Incidence (new cases per year): 285 new cases per year for SCD; thalassaemia UNKNOWN

Prevalence (number of existing patients): SCD ~7,000 (5,000-10,000); thalassaemia 362 – 249 thalassaemia major, 81 thalassaemia Intermedia and 32 HbE/β-thal- French thalassaemia registry.

The areas of higher prevalence are big cities, especially Paris, Lyon, Marseille and Lille.

*Available Services*

There is no French national registry for SCD and the total number of patients with SCD in the total French population in not precisely known. The national neonatal screening was officially implemented in France since 1994. This screening is, however, unfortunately not universal. It is targeted to the so called "at risk population" in the maternities.

Both, thalassaemia and SCD have a national reference center officially labeled by the Health Authorities. In addition, a national network of expert centers is currently being organized in France.

b) Germany:

*Epidemiology*

Prevalence (number of existing patients): 1,500 SCD; 450 thalassaemia

*Available Services*

There is no ongoing registry on hemoglobin disorders in Germany.
Non-officially labeled Expert centers do exist in a number of big German cities (SCD: Bonn-St Augustin, Berlin, Heidelberg; Thalassaemia: Heidelberg, Ulm, Göettingen).

c) Spain:

*Epidemiology*

Frequency (carrier rate): SCD in Madrid 0.4% (from universal neonatal screening) and 2.5% in Barcelona from targeted screening. For thalassaemia 0% - 5% (overall 0.4%); But higher in some areas e.g. Menorca 2.7%

Incidence (new cases per year): SCD 1: 5,500; thalassaemia not estimated.

Prevalence (number of existing patients): SCD 138 registered cases in 2004; Thalassaemia -

*Available Services*

Expert centers for SCD and Thalassaemia exist in the two main Spanish cities, Barcelona (2 centers) and Madrid (2 centers).

d) Belgium:

*Epidemiology*

Frequency (carrier rate): SCD 1.8% in the Brussels area. thalassaemia not known.

Incidence (new cases per year): SCD 1: 2,000 new births; thalassaemia 1 in 20,000 new births

Prevalence (number of existing patients): SCD 346; Thalassaemia 71

*Available Services*

These patients are concentrated in big cities (Brussels, Liege, Antwerpen) where the number of immigrants (mainly from Sub-Saharan Africa, Mediterranean Basin, Asia) is expected to be the highest.

A universal neonatal screening in the Brussels area has been implemented. This screening is now officially supported by the Health Authorities.

Non-officially labeled reference expert centres are located Brussels.

Synthesis for Continental Europe:

*Total prevalence of thalassaemia in some European countries (France, Germany, Spain, and Belgium).*

Table 4 summarizes the total prevalence of thalassaemia for all 4 countries plus Portugal. The total number of patients affected with thalassaemia in these 5 countries is around 920, which is not negligible, even though the calculated prevalence is relatively low (around 1/228 000).

**Table 4:** Synthesis: Prevalence of thalassaemia

| Country | Total pop | Total nb patients | Prevalence |
|---|---|---|---|
| Germany | 82,500,000 | 450 | 1/ 183,333 |
| France | 62,900,000 | 362 | 1/ 173,757 |
| Spain | 44,700,000 | NA | NA |
| Belgium | 10,326,000 | 71 | 1/ 145,437 |
| Portugal | 10,536,000 | 40 | 1/ 263,400 |
| Total | 210,962,000 | 923 | 1/ 228,561 |

*Total prevalence of SCD in some European countries (France, Germany, Spain, and Belgium).*

As shown in Table 5, the total number of patients suffering from SCD in these countries is roughly ten times higher than for thalassaemia. The prevalence by country ranges from 1 out of 6846, for the worst estimation in France, to 1/82 500 for the lightest estimation in Germany.

**Table 5: Synthesis: Prevalence of Sickle Cell Disease**

| Country | Total pop | Total nb patients | global prevalence |
|---|---|---|---|
| Germany | 82,500,000 | 1,000 | 1/ 82,500 |
| | | 1,500 | 1/ 55,000 |
| France | 62,900,000 | 5,000 | 1/ 12,580 |
| | | 10,000 | 1/ 6,290 |
| Spain | 44,700,000 | NA | NA |
| Belgium | 10,326,000 | 346 | 1/ 29,844 |
| Portugal | 10,536,000 | *500* | *1/ 21,072* |
| Total | 210,962,000 | 6,846 | 1/ 30,815 |
| | | 12,346 | 1/ 17,087 |

*Specific aspects*

From the data reported here, we can assume that there are an increasing number of patients affected with Hb disorders in France, Germany, Spain and Belgium, where these diseases were

not endogenous except in rare areas. This is mainly due to immigration of people from at risk countries. In all these countries the highest prevalence is found in big cities and industrial areas.

National registries exist only in France for thalassaemia.

Neonatal screening is implemented in the whole country in France, but it is targeted It also exists in specific geographical areas in Spain and Belgium (where it is universal).

Reference care centers exist in all the studied countries, but are not officially labeled by the health authorities, except in France.

*Conclusion and perspectives*

In order to improve the prevention of Hb disorders we may use a number of tools which are summarized in the following table.

| Current situation : | Means to improve the current situation : |
|---|---|
| **•Registries :**<br>–Existence (France, thalassaemia),<br>–Problems of maintenance (Germany)<br>**•Neonatal screening :**<br>–France all the country (but targeted)<br>–In specific areas : Belgium (universal), Spain<br>**•Reference centers:**<br>–Non officially labeled (except in France )<br>**•Patients' support groups** | To be developed (and supported) in all the countries. Interesting to estimation of the exact number of affected people.<br>Improve patients' care. Mandatory to adapt the provision of Health Services and …<br>Should be officially labeled (to improve the quality of care)<br>Should be encouraged |

**SUMMARY:**

In general the European region is divided into two main groupings – those countries with high prevalence of haemoglobin disorders (in this meeting represented by Cyprus, Greece and Italy) and those countries where there is very low prevalence in the indigenous population, but an increasing influx of immigrants has introduced the conditions, creating a need for both curative and preventive services.

In the high frequency countries, services have been developed over three decades with a resultant increase in patient survival, a reduction in morbidity (complication rates) and a reduction in new affected births through organized prevention programmes. In these countries research must be supported to further improve clinical outcomes and to introduce new methods of prevention.

More complex problems are faced in the low frequency areas:

1. Epidemiological data are difficult to collect as the immigrant groups are scattered across Europe, although urban areas and capital cities have the highest concentrations. It is in

these areas that services are mostly available. National registries are required to locate services where they are most needed.

2. Patient access to services must be improved.
3. Neonatal screening for SCD is limited to few countries (UK, France & Belgium mainly) and in addition there are few localized programmes.
4. Primary prevention is lacking, although programmes of ante-natal clinic screening based on ethnic origin are offered in some areas.
5. Treatment centres exist in many localities but expert centres with high throughput are limited and access is difficult for many patients. Networking between expert centres and between expert and secondary centres requires enhancement.
6. Patient support groups are strong in high prevalence areas and in the UK, but need strengthening in all other countries of Europe.

## WHO South-East Asia Region

### INDIA: - ROSHAN COLAH – THALASSAEMIA

*Introduction*

The population of India is 1.027 billion according to the last census held in 2001. The urban group comprises of <30% of the population living in 200 towns and cities while the majority of people (>70%) live in rural areas in more than 550,000 villages. There is considerable ethnic, linguistic, religious, cultural and genetic diversity. 8% of the total population comprises of 572 tribal groups. Although nutritional anaemia and communicable diseases are major health priorities, thalassaemia and other haemoglobinopathies also pose a significant public health problem in India.

*Epidemiology*

Frequency (carrier rate): 1-17%, with high frequencies of 5-17% in various groups - β-thalassaemia; α-thalassaemia varies from 1 to 97% in different communities. The overall carrier rate for the whole of India is 3-4% (β-thalassaemia), amounting to 30-40 million carriers. HbE is seen primarily in the eastern part of the country (4-5%) and in the north eastern region (3-50%).

Incidence (new cases per year): Estimated > 10,000 new cases per year.

Prevalence (number of existing patients): Estimated 100, 000 thalassaemia major cases.

*Available Services*

There are 15-20 centres where molecular analysis for β- and α-thalassaemia are being done in India. There are around 10 centres in major cities in the country where first trimester prenatal diagnosis of thalassaemia syndromes is done. Many couples at risk are referred late in the second

trimester for prenatal diagnosis and they are given the option of fetal blood sampling. During the last 5 years, about 30% of all couples were referred to our centre in the second trimester. Our experience with around 2000 fetal diagnosis done during the last 20 years has shown that prenatal diagnosis and termination of pregnancies when the fetus is found to be affected is acceptable by all communities. However, majority of the couples still come retrospectively after having one or more affected children and only around 10% come prospectively for diagnosis.

Only 10-15% of patients receive optimum therapy with blood transfusion and adequate iron chelation mainly in urban areas. The major constraints are the high cost of management (Rs.1, 00,000 to Rs.1, 50,000 annually), compliance and the availability of safe blood).

Facilities for bone marrow transplantation for thalassaemia are available at 5 to 6 centres in the country.
There are around 50 thalassaemia welfare societies formed mainly by parents of children with thalassaemia, doctors and well-wishers in different cities. They provide psychological support to patients and their families and also some financial assistance for management. Several NGO groups are actively involved in conducting awareness and screening programmes particularly among college students.

*The future needs for India*

A major programme for education and creation of awareness is required throughout the country. This must target medical professionals, health care workers and the general public. Mass media could help to reach out to the remotest of areas.

There is a need for micro-mapping reaching out to the district and village level to get accurate figures on prevalence of thalassaemia. More centers for genetic counseling and prenatal diagnosis must be established to make these facilities available within reach to all couples who require them.

All this would require infrastructure and manpower development at all levels – technical workers, counselors and obstetricians/sonologists for fetal tissue and fetal blood sampling.

A registry of thalassaemia major patients and carriers needs to be prepared and maintained. Better care for children already born must be made available to all sections of society. At least 5 regional reference centers in Western, Eastern, Southern, Central and Northern India would be needed for giving training, undertaking quality control programmes and solving diagnostic problems. Each of these centers could have 3 or 4 sub centers under them which could reach out to the district level in every State.

Commitment from politicians and both the Central and State Governments would be required to initiate a National Thalassaemia Control Programme along with adequate financial support from National and International agencies. The Indian Council of Medical Research and Department of Biotechnology are planning pilot studies to explore the feasibility of a National Control Programme.

Collaboration with other countries in South Asia would be mutually beneficial and the Asian Thalassaemia Network has been working towards this goal.

## INDIA: - ISHWAR C. VERMA – SICKLE CELL DISEASE

*Introduction*

The sickle cell gene in India is regarded as "mild" and similar to the East Saudi Asian variant sharing the same genotype. However, the severity of clinical symptoms, seen in some studied populations and the low survival rates do not support the description of a mild disorder.

*Epidemiology*

Frequency (carrier rate): 0-44%, estimated 5 million carriers.

Incidence (new cases per year): Estimated 6,000 new cases per year.

Prevalence (number of existing patients): Estimated 100,000 homozygotes

*Available Services*

Both carrier screening and prenatal diagnosis are available. A programme of community and individual counseling should be integrated into primary healthcare. Authorities still need to be convinced that SCD is an important health problem, so that special facilities for SCD testing and management can be created, especially newborn screening with proper case management.

## SRI LANKA: - ANUJA PREMAWARDHENA

*Introduction*

Sri Lanka has a population of 20 million with three ethnic groups (Sinhalese 74%, Tamil 12% and Muslim 7%). 23% of the population are below the poverty line, but the literacy rate is high (95.6%) and is higher in females. The infant mortality rate is 11/1,000 live births. Thalassaemia was first described in 1951, the first national survey was conducted in 2000.

*Epidemiology*

Frequency (carrier rate): 1-5% - Overall 2.2% -β-thalassaemia. 0-2% HbE – Overall 0.5%. $\alpha^{+}$-thalassaemia – 13.6%

Incidence (new cases per year): 2250 with beta thalassaemia and 1000 with HbE b thalassaemia

Prevalence (number of existing patients): 2,000 thalassaemia major cases and HbE/β-thal 1,000 cases.

*Available Services*

There is no centrally coordinated programme for patients. Blood is freely provided for thalassaemia patients and regulated by the central transfusion service.

There are a few specialized centres:

1 The Kurunegala centre which caters for 284 thalassaemia major cases, 127 HbE/β-thalassaemia patients and 17 others – established in 2005

2 The Ragama Adolescent and Adult Thalassaemia care Unit – established in 2006, with 60 patients

3 Thalassaemia units in Chilaw, Anuradhapura, Pollonaruwa and Badulla.

Desferrioxamine is the most widely used chelating agent with a few patients, using Deferiprone. Both drugs are provided by government and shortages are common. There is a central diagnostic reference laboratory in Ragama which offers free screening and is supported by government. Molecular diagnostics are under development.

No prevention programme exists and government has yet to give a support to one.

## SOUTH -EAST ASIA: - SUTHAT FUCHAROEN

*Introduction*

Thalassaemia is very prevalent in South-East Asia (S.E. Asia) causing public health and socioeconomic problems to many countries. The types and frequencies of thalassaemias are heterogeneous in this vast region even within a country. Alpha-thalassaemia, beta-thalassaemia, haemoglobin (Hb E), commonly noted as the hallmark of S.E. Asia, Sri Lanka, Bangladesh, Maldives and the eastern region of India. Haemoglobin Constant Spring (Hb CS) is also prevalent in the S.E. Asia region. Furthermore, the most serious form of alpha - thalassaemia, Haemoglobin *Bart's hydrops fetalis*, is almost exclusively found in S.E. Asians and south China. In Japan and Korea very large population examinations reveal very few thalassaemia cases. Both alpha and beta-thalassaemia are prevalent among Southern Chinese, most cases traced to the Guangxi and Guangdong provinces.

These abnormal genes in different combinations lead to over 60 thalassaemia syndromes. Different thalassaemia genotypes have greatly variable severity even patients with apparently identical genotypes can have remarkably different severity. The two major alpha thalassaemic diseases are Hb *Bart's hydrops fetalis* or homozygous alpha-thalassaemia 1 (homozygous $alpha^0$ thalassaemia) and Hb H disease that occur from the interaction between alpha thalassaemia 1 ($alpha^0$ thalassaemia) and alpha thalassaemia 2 ($alpha^+$ thalassaemia) or between alpha thalassaemia 1 and Hb CS. Interaction between beta thalassaemia genes or beta thalassaemia and

Hb E genes leads to homozygous beta thalassaemia and beta thalassaemia/Hb E that are major beta thalassaemic syndromes in this region. In beta thalassaemia/Hb E disease, although the patients have identical genotype, the degree of anaemia varies greatly with hemoglobin levels ranging from 3-13 g/dl.

Due to the large number of patients with thalassaemia in Asia and limited medical service resources it is not possible to give optimal blood transfusions and iron chelating agents to the majority of patients. Estimated direct cost for the management of ONE thalassaemia major patient, who lives until 10-30 years old is about 1.3 to 6.6 million Baht (US$ 32,500-185, 1660). Thus many patients receive no or minimal blood transfusions and no iron chelators which is too expensive. These masses of untreated patients with thalassaemia develop multitude of complications such as congestive heart failure, infection, cirrhosis, osteoporosis etc. Although we are prepared to use all available cure, they are either not yet available or available to the very few. Moreover, we need to develop human resource and infrastructure to cope with the sheer number of the patients. We are thus left to face with taking care of a large mass of patients with complications not now seen in the West. The best approaches to cope up with thalassaemia in developing countries, including many countries in Asia, is to prevent birth of a new cases with major thalassaemic disease. Thalassaemia is now recognized as one of the public health problems in many Asian countries.

*Prevention and Control Program for Thalassaemia in South-East Asia*

The thalassaemia carriers are detected mainly through the expanded family study of cases with thalassaemic diseases. Accurate frequencies are still not available in many S.E. Asian countries due to inherent difficulty in the diagnosis of thalassaemia traits. However, laboratory progress during these last few years has enable us to do mass screening for beta thalassaemia and Hb E carriers with accurate diagnosis by using the automatic high performance liquid chromatography (HPLC) system. In recent years, a nationwide program has commenced to prevent and control homozygous beta thalassaemia, beta thalassaemia/Hb E, and Hb *Bart's hydrops fetalis*, with encouraging results in many countries.

But in some S.E. Asians countries the actual number of thalassaemia genes is not available at present. Diagnoses of the diseases and management of the patients in the majority of these Asian countries are still far from satisfaction. The patients and families suffer miserably from ignorance of the diseases, misunderstanding, malpractices, etc. These require proper education of health personnel, not only the physicians but downstream to the auxiliaries working in the communities.

Genetic counseling, at least for families already afflicted by the diseases or in those who demand it, is not avoidable. This requires accurate diagnoses and good understanding of the conditions. While conventional therapy involving blood transfusions and iron chelation are intolerably expensive, prenatal diagnosis and selective abortion are more economical. However, these should not be carried out indiscriminately. Some thalassaemic diseases of identical genotypes may greatly vary in their severity because of environmental factors or modifying genes.

This points out the need of accurate diagnoses and good understanding of the diseases. It is time for international health organizations such as the World Health Organization to consider

thalassaemias as international public health problems also in need of good health planning, if Health for All is to be achieved.

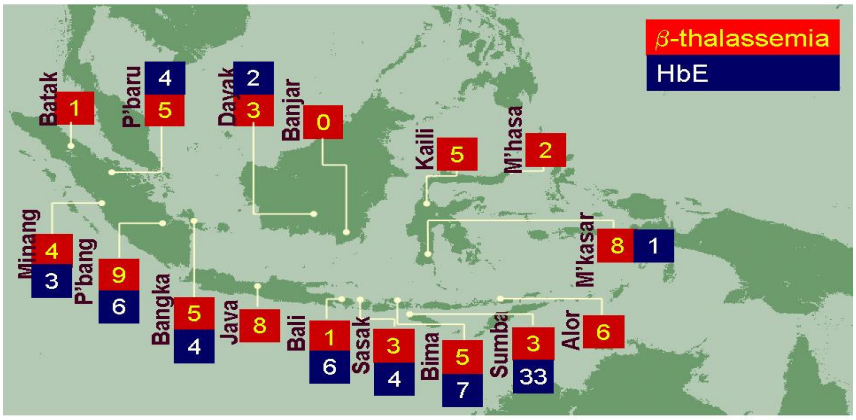
## THALASSEMIA IN THAILAND

| | | |
|---|---|---|
| α- Thalassemia | 20 - 30 % | α - Thal 1<br>α - Thal 2 |
| Hb Constant Spring (α- thalassemia 2 like effect ) | 1 - 8 % | |
| β- Thalassemia | 3 - 9 % | |
| Hemoglobin E | 10 - 53 % | |

Total number of thalassemic patients and the number of births per year (total births ~ 1 million/year)

| Disease | Couple at Risk per year | Birth per year | Living patient |
|---|---|---|---|
| Homozygous β-Thal | 2,500 | 625 | 6,250 |
| β-Thalassemia/Hb E | 13,000 | 3,250 | 97,500 |
| Hb Bart's Hydrops Fetalis | 5,000 | 1,250 | 0 |
| Hb H Disease | 28,000 | 7,000 | 420,000 |
| TOTAL | 48,500 | 12,125 | 523,750 |

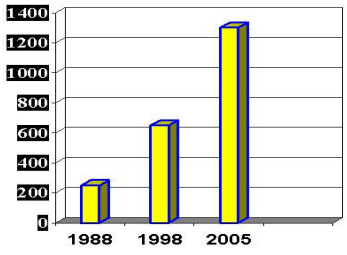
## The distribution and the frequency (%) of thalassaemia beta carriers in Indonesia




## Thalassaemia situation in Indonesia

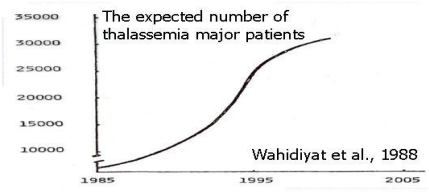
Severe thalassaemia patients in Jakarta

Type of thalassaemias:
- 52% Beta thalassaemia
- 46% Beta/HbE
- 2% HbH + others




## INDONESIA
## Estimation of new β-thalassemia patients

- Population 224 million
- Annual birth rate: 2.3%
- Carrier frequency 5% - 3,000 new patients/year
- Only 3,000 patients registered



## The Thalassemia Situation in Cambodia

*60 – 90% of children are anemic*

## Diagnosis of Hemoglobinopathies

**No diagnosis done in government labs**
- Only CBC result and morphology

**The Pasteur Institute in Phnom Penh**
– Hb electrophoresis

**The Angkor Hospital for Children in Siem Reap**
– DCIP screening test for Hb E
- Brilliant cresyl blue stain for Hb H bodies

## The Thalassaemia Situation in Cambodia

- **Prevalence of Hemoglobinopathies (?)**

~ 60 - 90% of children are anemic
(Hb < 105 g/L)

~ 40% related to iron deficiency (IDA)

**Thalassaemia in Viet Nam (12,928 survey)**

| Ethnic Group | Hb E | β Thal | Hb E/β Thal | $\alpha^{3.7}$ | $\alpha^{-SEA}$ | $\alpha^{-SEA}$ | $\alpha^{PAKSE}$ |
|---|---|---|---|---|---|---|---|
| Kinh | 4.0 | 1.1 | 0 | 2.6 | 0 | 3.6 | 0 |
| Dao | 0 | 9.3 | 0 | - | - | - | - |
| Tay | 3.5 | 6.9 | 0 | - | - | - | - |
| Nung | 1.7 | 8.2 | 0 | - | - | - | - |
| S'Tieng | 44.7 | 0.9 | 0.2 | 23.6 | 3.4 | 5.4 | 0.2 |
| M'Nong | 35.7 | 0.2 | 0.5 | - | - | - | - |
| Rac Lay | 25.9 | 0.0 | 0.2 | - | - | - | - |
| E De | 40.2 | 1.5 | 0 | - | - | - | - |

**Incidence of Thalassaemia in Hong Kong SAR**

| | | |
|---|---|---|
| $\alpha^{o}$ thal | = | 2.2% |
| $\alpha^{+}$ thal | = | 2.3% |
| β thal | = | 3.5% |

## Number of NTR Registrants: Singapore

| | |
|---|---|
| β-thal minor | 8947 |
| β-thal major | 80 |
| HbE thal | 74 |
| Thal intermedia | 7 |
| α-thal carrier | 7772 |
| αβ-thal carrier | 145 |
| HbH disease | 335 |
| HbE trait | 2129 |
| Other | 159 |
| Normal | 7074 |
| Total | 26,722 |

**Total number of family registered : 12,500**

## Incidence of Thalassaemia Traits in Singapore

**1635 unrelated individuals:**

| | |
|---|---|
| α Thalassaemia | 2.92 % |
| β Thalassaemia | 0.93 % |
| HbE | 0.64 % |
| Total | 3.85 % |

**Comparison of the cost of treatment and prevention of 1000 severe thalassaemia cases in Thailand**

| | Prevention | Expected No. Birth | Treatment (av. life= 30 yrs) |
|---|---|---|---|
| Hb Bart's hydrops fetus | 48,280 B (US$ 1379) | 2 | 21,250 B (US$ 607) |
| Beta thalassemic Disease* | 48,280 B (US$ 1379) | 4# | 6,660,000 B (US$ 190,457) |

**(* include both homozygous beta thalassaemia and beta thal/HbE, #1 homozygous beta thalassaemia and 3 beta thal/HbE )**

**Thalassaemia in Southeast Asia and South China**

| Country | % Carriers | | | |
|---|---|---|---|---|
| | α | β | Hb E | Hb S |
| Cambodia | (+) | (+) | (+) | - |
| China: Guangxi | 15 | 5 | (+) | - |
| China: Hong Kong SAR | 2.2 | 3.6 | - | - |
| China: Province of Taiwan | 4 | 1-3 | (+) | - |
| Indonesia | 6-16 | 3-10 | 1-25 | - |
| Laos | (+) | (+) | (+) | - |
| Malaysia | 16 | 4.5 | 0.8-3.4 | - |
| Myanmar | | 0.5-3.4 | 6-48 | - |
| Philippines | (+) | (+) | (+) | - |
| Singapore | 2.92 | 0.93 | 0.64 | - |
| Thailand | 20-30 | 3-9 | 10-50 | - |
| Viet Nam | 2.5 | 1.5 | (+) | - |

| Thalassaemia treatment available in different South-East Asian countries | | | | | | | |
|---|---|---|---|---|---|---|---|
| Country | Blood Transfusion | Iron Chelation | | | BM Transplant | PND | National Programme |
| | | DFO | L1 | Exjade | | | |
| Cambodia | (+) | (+) | - | - | - | - | - |
| China: Guangxi | + | (+) | (+) | - | (+) | + | - |
| China: Hong Kong SAR | + | + | + | (+) | + | + | + |
| China: Province of Taiwan | + | + | + | (+) | + | + | + |
| Indonesia | (+) | (+) | (+) | - | - | (+) | - |
| Laos | (+) | (+) | - | - | - | - | - |
| Malaysia | + | + | + | (+) | + | + | + |
| Myanmar | (+) | (+) | + | - | - | - | - |
| Philippines | + | (+) | - | (+) | - | - | - |
| Singapore | + | + | + | (+) | + | + | + |
| Thailand | + | + | + | (+) | + | + | + |
| Viet Nam | (+) | (+) | (+) | - | (+) | (+) | - |

## SUMMARY: WHO South-East Asia Region & WHO Western Pacific Region:

These are areas with huge populations and high frequencies, of mainly thalassaemia genes. Largely composed of low resourced countries, the problem of providing high cost treatment is paramount and prevention programmes are limited:

1) Epidemiological data, especially on carrier frequencies, are being gathered, including regional and tribal frequencies. This effort requires support to cover all areas;
2) Scattered treatment centres exist, but few patients have access, compared to the large numbers that are being born and under 5 year mortality, due to haemoglobin disorders remains high as derived from the numbers attending centres compared to the expected numbers born;
3) Supplies of necessary aspects of treatment are very limited. This includes safe blood in adequate amounts and chelating agents to control iron overload. Patient access to optimal treatment is very poor.
4) Public information is limited and counselling services are few;
5) Prevention programmes are mostly lacking and where they exist they are utilized by only a minority of at risk couples.

## APPENDIX D: INTERNATIONAL GROUPS AND INSTITUTIONS

In recent years, international groups have been formed which are contributing to networking and closer ties between health professionals dealing with haemoglobin disorders, at various levels. The networks are both national and international and constitute important media for dissemination of information, sharing of problems, gathering data and promoting multi-centre research. Some of the projects were presented at this meeting:

### EUROPEAN NETWORK FOR RARE CONGENITAL ANAEMIAS (ENERCA): - PATRICIA AGUILAR-MARTINEZ

This is a project funded by the European Commission's Health and Consumer Protection Directorate – General (SANCO). This reflects the interests of the Commission in international collaborations within the EU and in rare diseases. The project was launched in 2002 to deal with congenital anaemias whose prevalence is less than 5 per 1,000 inhabitants in a given community.

Haemoglobin disorders fall into this category as far as the indigenous population is concerned, with the exception of the thalassaemias in countries of the Mediterranean basin. However, immigration is increasing the numbers of patients in Europe especially Sickle Cell Disease.

The main objectives of ENERCA are:

a) Cooperation between member states in education, training and diagnosis and management of rare anaemias;

b) The creation of registries of rare anaemias which will contribute to epidemiological surveillance and improve health information;

c) Contribute to the standardization of procedures by creating internationally agreed guidelines for diagnosis and clinical management and developing quality and accreditation systems;

d) The identification of European Experts and Centres of Expertise in rare anaemias. So far 60 such centres have been identified across the EU.

The common goals with the WHO 2006 resolution include the public health role of ENERCA, its education and training programme, the dissemination of appropriate technologies, guidelines, expert groups and the promotion of research.

### SICKLE CELL DISEASE INTERNATIONAL ORGANISATION (SCDIO): - LÉON TSHILOLO ON BEHALF EDWIGE BADASSOU

SCDIO is an NGO whose priority is currently international lobbying for the recognition of SCD as a health priority. This was recognized by the UNESCO 34$^{TH}$ session General Conference (34C/INF.5). "The SCDIO is one of the leading civil society entities in raising awareness on issues related to the disease…"

The WHO resolution on Sickle Cell Anaemia (see Appendix I) was largely subsequent to actions taken by SCDIO, including an international plea launched in November 2004, the promotion of an African Union decision (Assembly/All/Dec.81.V) dated 4-5$^{TH}$ July 2005 (Syrte, Libya) and a UNESCO resolution (33C/COM.II/DR.7) of the 33$^{RD}$ General Conference in Paris 2005.

The SCDIO has branches in Africa, Europe and the Caribbean. It has organized or contributed to many international conferences, and implemented awareness campaigns in many countries, such as Congo DR, Congo and Togo. It has also implemented screening in 5 African countries and organized Pneumo23 vaccinations in Brazzaville and Pointe Noire, Congo in 2006.

SCDIO is accredited to the World Summit on the Information Society (WSIS), Geneva (PrepCom 3, 2003) and Tunisia (2005). The programmes that SCDIO is promoting include screening, vaccination and prevention of infectious disease healthcare staff training, the creation of SCD dedicated centres, a special web-site ("Drepanet"-presented during the WSIS process in Geneva and Tunis), and SCD control plus (for youth education, women and children's information and preventive education).

## ITHANET – ELECTRONIC INFRASTRUCTURE FOR THALASSAEMIA RESEARCH NETWORK: - MICHAEL ANGASTINIOTIS

The objectives of the network are:

a) To strengthen research in the field of haemoglobinopathies, including thalassaemia and sickle cell disease, using existing and emerging infrastructures and tools of European research networks;

b) To effectively use these e-infrastructures and tools for the coordination of existing research activities and future collaborative projects;

c) To introduce a common approach to these infrastructures for the promotion of networking, research and the dissemination of information to health professionals and the public;

d) To establish networks of clinical researchers and scientists specialized in diagnostic/research services for thalassaemia and other haemoglobinopathies who will develop and utilize a disease specific infrastructure based on electronic tools, and;

e) To introduce media broadcasting and streaming technologies into conferences and teaching courses on haemoglobin disorders.

To achieve these objectives a portal has been set up targeting researchers, clinicians and the public. The portal will soon be able to utilize Grid-enabled resources for efficient exchange of information/data and dissemination of research results. This is a preliminary developmental phase for a permanent communications centre which is being developed in the EU, funded by the FP6 Information Society and Media (ICT) Programme.

The development of ITHANET is by a consortium of 26 partners from the fields of informatics, clinical research and scientific research, from 16 countries of the EU, the

North Africa and the Middle East. The portal (www.portal.ithanet.eu), as well as researchers, targets all health professionals, providing services for haemoglobin disorders, patient support groups (including patients and families), students and the general public.

Research data are protected but databases, guidelines and protocols are freely available including interactive services, such as "Ask an expert", discussion for a for difficult cases and video conferencing. There are under development, repositories of internet learning courses, laboratory methods, clinical guidelines etc.

## LONDON FOCUS GROUP ON SICKLE CELL IN AFRICA – SICKLE CELL UK: - ASA'AH NKOHKWO

The focus group aims at a community-focused health promotion campaign on Sickle Cell Disorders in Africa. The group has prepared an action plan which is a business case to translate the recent WHO resolutions on Sickle Cell Disease, into an effective, grass-root, community based campaign aimed at addressing the challenges and burden of sickle cell disorder on the patient, the family and the community.

While recognizing the urgent need for medical services, the need for adopting the social model, so hat the community as a whole is involved in taking care and responsibility for the Sickle cell problem, since community action can make things happen, and participate in the delivery of the WHO objectives, such as advocacy, prevention, counseling, early detection, data collection, surveillance and research, community education and partnerships.

There is currently lack of community support services in Africa where 400,000 new sickle cell babies are born every year with a high infant mortality and morbidity.

This is due to a dearth of information, community education, advocacy and solidarity. Without community involvement, a holistic model of care cannot be achieved, so that a major objective is to sensitize and prime the population and prepare for a sustainable platform for policy implementation.

A typical country plan for Africa would include the elements of market research (mapping needs and risks), planning, community sensitization, support structures – advocacy groups, training, capacity building, evaluation and indicative casting.

Implementation of the policies must include health impact assessment (Göthenburg Consensus paper, European Centre for Health Policy and WHO Europe-Regional Office, 1999), risk management which includes government patronage, and involving existing NGO's, financial assurance and accountability. There should be successful association with the governments' social policy and the national SCD programme. Other deliverables of a country programme include:

- Prevention – this includes public awareness of the hereditary causes of SCD;
- Counseling – considering the number of sessions to individuals, couples and families;
- Early detection and management – the need for newborn screening;

- Data collection;
- Surveillance and research, and;
- Community involvement and education through partnerships especially by forming local Sickle Cell clubs.

Initially, such a plan may be implemented by a suitable, charitable health promotion activity which the government will eventually own. The Sickle Cell Society-UK experience serves as a model for this programme, although this may not necessarily fit a prescriptive application in Africa, hence careful planning is required in adaptation to an African model.

For transfer of this programme to Africa, direct communication and meetings have taken place with government representatives in Cameroon, Nigeria, Ghana and Sierra Leone.

## SICKLE CELL DISEASE ASSOCIATION OF AMERICA: - KWAKU OHENE-FREMPONG ON BEHALF OF WILLARDA EDWARDS

The aim of this organization as expressed by its President Emeritus, Charles F. Whitten, is to achieve a national coordinated approach to addressing the issues related to Sickle Cell Disease, through the united efforts of community sickle cell organizations. The mission statement is:

"To advocate for and enhance our membership's ability to improve the quality of life and services for individuals, families and communities affected by Sickle Cell disease and related conditions, while promoting the search for a cure for all people in the world with Sickle Cell Disease."

There are 56 member community-based organizations represented in 26 states. The services provided include:

Summer camps for patients, health fair displays, research fellowships, convention service recognition, public education (in-print and on-line) and support to affected families. Over 3.5 million were served through these means over the past 12 months. There are also 41 affiliate members in the USA and Canada which include comprehensive sickle cell centres, universities and other institutions.

Other objectives include raising awareness among the public and health professionals, training health professionals in evidence-based treatment, sharing clinical trial opportunities with health professionals and their patients/families and providing research opportunities. The need for early treatment, home treatment, improving access to care and genetic counseling are also promoted. There is also partnership with government promoting legislation, such as the Sickle Cell treatment network, including annual Capitol Hill visits, partnerships with national and state medical organizations (e.g., AMA, ASH), the National Institute of Health (NIH) and other many other groups.

## THE NATIONAL INSTITUTE OF HEALTH (NIH): - GREG EVANS

Across the USA, there are 25 Sickle Cell Centres and 6 Thalassaemia Centres. The US National Sickle Cell Disease Programme started in 1972, when Congress passed the National Sickle Cell Anaemia Control Act. This allowed releasing to the NIH funds for SCD research which started at 5 million USD in 1973, and rose to 25 million USD by 2006. In addition, the Health Resources and Service Administration (HRSA) received funds for community education, screening and genetic counseling activities.

With this positive involvement of government, the major benefits apart from funding were political visibility and positive action. The accomplishments of the US National Sickle Cell Disease Programme from 1972-2007, include many studies such as the Cooperative Study of Sickle Cell Disease (CSSCD 1979-1999), the prophylactic Penicillin study (PROPS, 1983-1986) and partnerships with state governments. Since the National Sickle Cell Act and the implementation of the programmes described, life expectancy of this condition has been rising from around 15 years in the 1970's to 45 years by the year 2000.

Concerning Thalassaemia, the NIH promoted the Thalassaemia clinical research Network (2000-2007). As a result of this, a registry of patients in North America with a natural history follow-up of patients, as well as studies on bone disease, chronic iron chelation, induction of fetal haemoglobin were carried out.

The USA Federal funding for research and management of haemoglobinopathies in 2007 included:

- NIH - ~ 65 million USD (SCD >> Thalassaemia);
- HRSA - ~ 2.5 million USD (SCD >> Thalassaemia), and;
- CDC - ~ 1.5 million (Thalassaemia).

Despite this, barriers still exist to optimum patient care:

- Poor follow-up for both patients and carriers in 32 States. Nationwide only 15% of HbS trait diagnoses are confirmed in secondary testing;
- There is limited patient access to qualified care – all NIH centres combined reach only 23% of SCD patients (18,000/80,000);
- These are inadequate numbers of qualified committed, culturally sensitive medical and public health staff;
- Government agencies which could bridge this gap in training, surveillance and health services, such as HRSA and CDC have little or no funding for these activities, and;
- Differences in mortality between States.

Planning is required to overcome these problems which should include priorities for screening, research and services within the geographical regions of greatest need. There is a need for lobbying to increase funds and for partnerships between government agencies with complementary expertise.

Additional haematologists and other healthcare workers need to be trained.

## HEALTH RESOURCES AND SERVICES ADMINISTRATION (HRSA) – INITIATIVE IN SCD: - BRAD THERRELL

The U.S Department of Health and Human Services is composed of many different agencies including several that have a role in SCD activities. The Health Resources and Services Administration (HRSA) serves to ensure that patients have access to detection, care and other ancillary services for persons with special health care needs. Various other activities are included in the missions of sister agencies including the Centre for Disease Control and Prevention (CDC) for epidemiology and quality assurance, and the National Institute of Health (NIH) for research. Newborn screening for SCD is required for all States and since 1999 HRSA has funded the National Newborn Screening and Genetics Resource Centre (NNSGRC) in Austin Texas to serve as a national focal point for resources and information about newborn screening and public health genetics activities. Some of the activities of the NNSGRC are:

- Point of contact about newborn screening (NBS) accessible to all through telephone, web-site (http://genes-r-us.uthscsa.edu) various list serves etc;
- Provides expert consultative services to state NBS programmes as a means of improving and refining ongoing activities;
- Collects and reports national NBS data concerning cases detected, new births, time diagnosis etc (National Newborn Screening Information System – NNSIS available at http://www2.uthscsa.edu/nnsis);
- Provides input into issues of national and regional importance by sponsoring meeting of experts, the creation of white paper etc.

Newborn screening in the USA is ultimately decided by State legislatures usually with recommendations from the State Health Officer in consultation with Boards of Health and Advisory Committees. NBS for SCD is now mandated by all states, as a result of evidence that early treatment can positively impact health outcomes and cost benefits to the health care system can be realized through early detection and treatment. SCD and thalassaemias account for the highest number of cases diagnosed through NBS of any of the conditions included in NBS (1:2400 across the entire US newborn population of 4 million births annually.

One of the roles of HRSA is to ensure access to comprehensive quality healthcare for those with low income, the uninsured, those isolated and vulnerable and for special needs populations.

The Maternal and Child Health Bureau, Division of Children with Special Health care needs of HRSA, has undertaken two initiatives for SCD, which are legislative mandated:

- The Newborn Screening Programme which includes support for community-based models of delivering SCD and SCD carrier, counseling and follow-up access to newborn screening and inclusion in comprehensive system of care.

- The Sickle Cell Disease Treatment:-Demonstration Programme which aims is to develop and establish mechanisms for enhancing the prevention and treatment of Sickle Cell disease through coordinated of service delivery, genetic counseling and testing, comprehensive technical services, training of health professionals and other related efforts.

HRSA also has two primary areas of focus:

a) Demonstration projects – 17 are running in 14 States;

b) The National SCD newborn screening and evaluation coordination centre: This centre supports the activities of the 17 demonstration projects, such as counseling, education and referrals to medical home and supportive services. The centre also focuses on technical assistance/information exchange, data collection and evaluation, materials development, counselor certification and partnership building. There is also a cooperative agreement with the Sickle Cell Disease Association of America to support the 17 centres.

The Sickle Cell Disease Treatment Demonstration Programme (SCDTDP) was authorized by public law (108-357) in 2004. Its purpose is to increase access to and the capacity and capabilities of primary health care providers, to offer coordinated and comprehensive services to individuals and families with SCD and to carriers. Funds are allocated to support 4 regional SCD treatment demonstration networks (TDN) and a national coordination centre.

There are 7 regional genetic services and newborn screening collaborative funded by HRSA/Maternal and Child Health Bureau, plus one national coordinating centre. Their role is to ensure that individuals with heritable disorders and their families have access to quality care and appropriate genetic expertise and information to strengthen communication and collaboration among public health, patient, families, primary care providers and genetic medicine and other sub-specialty providers.

For guidance to physicians, the American College of Medical Genetics (ACNG) has developed action sheets (ACT Sheets), so that physicians, upon receipt of screening results can take informed action – available at:- www.acmg.net/resources/policies/ACT).

ISBN 978 92 4 159712 8

Cover designed by D.Meissner GOV/GRA - Ref. Doc. WHO-HGN / Printed by GMG/DUP