

THALASSEMIA AND COMPREHENSIVE CARE

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Objectives

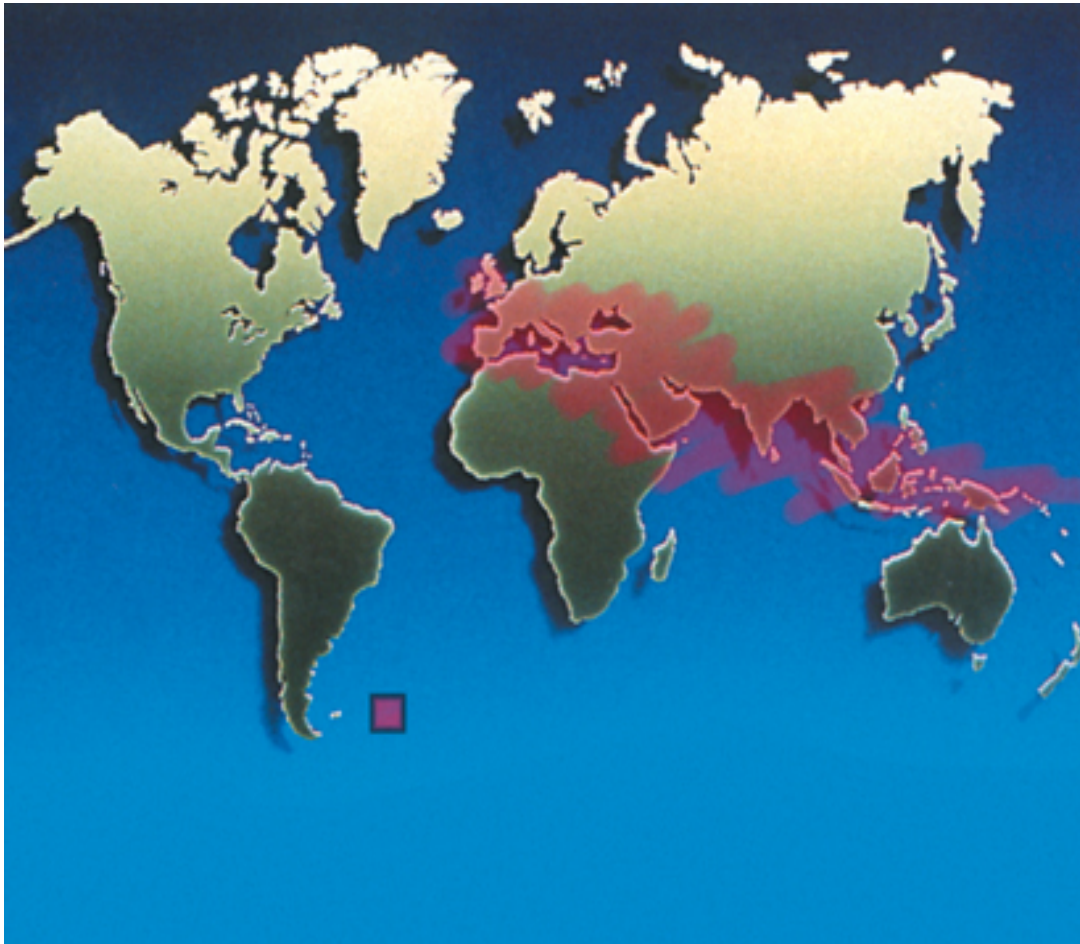
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By the end of this presentation, participants should have:

1. an understanding of the world distribution of Thalassemia
2. An appreciation for the differences and similarities of the α and β – thalassemias and the pathophysiology of these disorders
3. A familiarity of what constitutes comprehensive care for themselves in a Thalassemia care program and this should serve as a brief introduction to the upcoming talks.

Background

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- Thalassemia diagnosed in Cyprus in 1944.
- Most common single gene disorder
- 94 million carriers
- 127,000 births /yr

Epidemiology

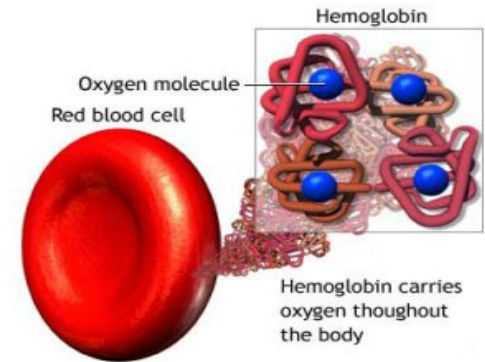


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- Thalassaemia is a blood disorder passed down through families in which the body makes an abnormal form of hemoglobin - the protein in red blood cells that carries oxygen. The disorder results in excessive destruction of red blood cells, which leads to anemia.
- Regions of origin are India, Asia, the Mediterranean and the Middle East
- In Canada the numbers of patients with Thalassaemia has grown and continues to increase with changing migration patterns.
- Toronto, Montreal and Vancouver have higher numbers with other cities having fewer patients.

The Thalassemias

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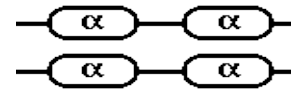


- Hemoglobin is made of two protein chains : 2 Alpha globin and 2 beta globin.
- Thalassemia occurs when there is a defect in a gene that helps control production of one of these proteins.
- There are two main types of thalassemia:
 - Alpha thalassemia occurs when a gene or genes related to the alpha globin protein are missing or changed (mutated).
 - Beta thalassemia occurs when similar gene defects affect production of the beta globin protein

The α -Thalassemias

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- α -Thalassemia is caused by reduced or absent production of α – globin chains.
- Each person normally has 4 α - genes



- Hb Barts hydrops fetalis



- Hb H disease



- α -thalassemia trait



- Silent carrier



The β -thalassemias

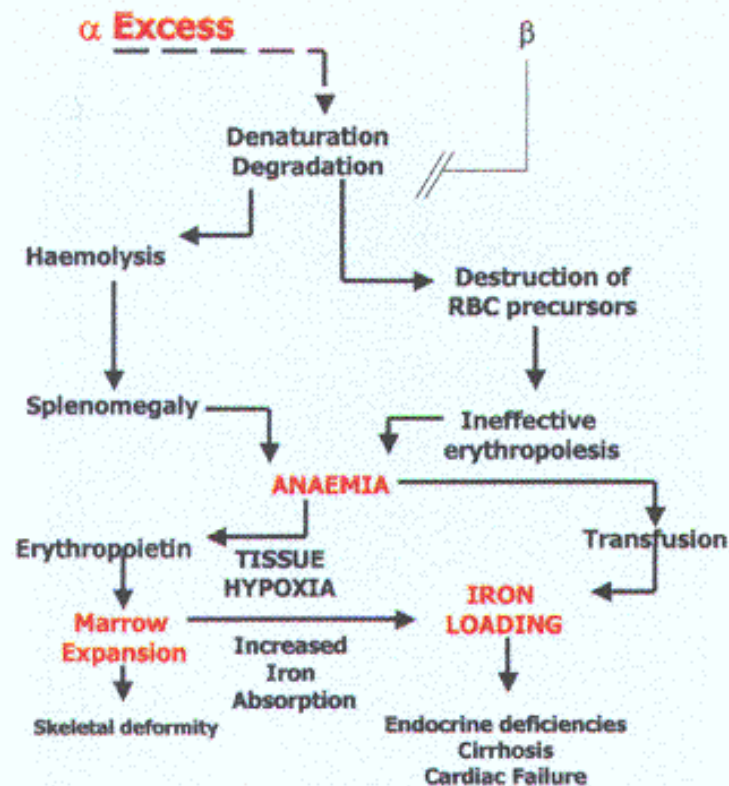
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β -thalassemia is caused by a decreased or absent β -globin chain production.

Each person normally has two β -globin genes.

- **β -thalassemia major**: refers to a clinically severe phenotype due to absence of β -globin chain production as a result of inheriting genes for the same severe mutation of the β -globin gene or 2 different β -thalassemia mutations.
- **β -thalassemia intermedia**: clinically moderate phenotype due to inheritance of milder mutations and other genetic modifiers.
- **β -thalassemia trait/carrier**: refers to a clinically mild phenotype with only one mutated β -globin gene

The Pathophysiology of Thalassemia



Excess α Globin Chains

- Major cause of anemia
- Precipitate in early nucleated erythroid progenitors in marrow
- Lead to ineffective erythropoiesis
- Precipitate in mature red cells
- Lead to hemolysis
- Undergo proteolysis

Thalassemia Clinical Severity Spectrum

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Mild

Generally asymptomatic

Non Transfusion dependent

Intermediate severity

Moderate anaemia

Diagnosed usually in late childhood

Transfusion dependant

Severe anaemia

Diagnosed in early childhood

α -thalassemia silent carrier/
trait

β -thalassemia minor/trait

Hemoglobin Constant Spring

α -thalassemia intermedia-HbH

β -thalassemia intermedia

Hemoglobin E β -thalassemia

α -thalassemia major/Hb Barts

β -thalassemia major

Severe Hb E β -thalassemia

Evolution of therapy



<u>Year</u>	<u>Therapy</u>	<u>Clinical outcome</u>
1945-1965	Irregular transfusion	Death in infancy or childhood
1965-1980 adolescence	Regular transfusion	Growth failure & death in
1980	Regular transfusion Parenteral Deferioxamine	Prolonged survival with effective chelation
1985	Bone marrow transplantation	Cure
1995	*Deferiprone	Effective oral chelator
2005	Deferasirox	Effective oral chelator

* Not licensed in Canada

Comprehensive care

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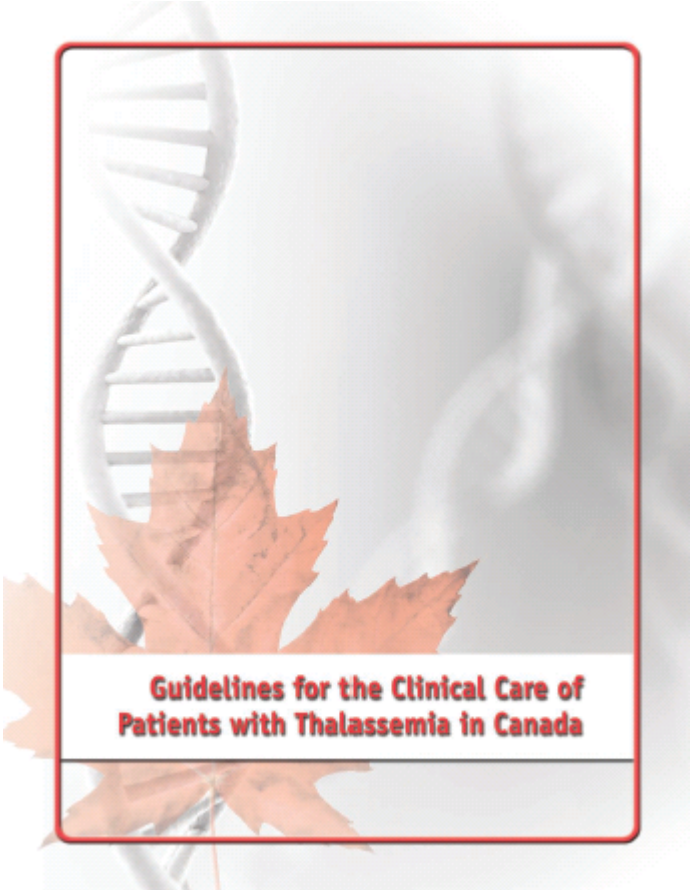
Mainstay of treatment is transfusion support to maintain an hemoglobin level which allows for adequate growth and development. This will also reduce bone marrow expansion and its sequelae

Optimising total body iron stores and prevention of complications related to iron overload and medications used to treat it.

Management of complications related to excessive iron burden when they do occur

Ensuring patients have care which is least disruptive to their lives , assessing and supporting psychosocial needs of patients and their families to enable them to lead normal self-fulfilling lives and contribute to society.

Guidelines for the Clinical Care of Patients with Thalassemia in Canada 2009



Guidelines for the Clinical Care of Patients with Thalassemia in Canada 2009

A. Components of Comprehensive Thalassemia Care

A1. A Network of Care

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Principles

- To provide a high standard of care that is delivered by a multidisciplinary network of specialist centres and satellite clinics.
- To ensure patients can receive regular treatment that is convenient and easily accessible with minimal disturbance to normal, everyday activities.
- To focus on excellent routine care by following high standards of clinical practice, including prevention of, and appropriate management of complications in order to decrease morbidity and mortality, and improve quality of life.

Components of Comprehensive Thalassemia Care

A2. Lifelong Education and Communication Between Patient and Health Care Team

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Principles

- Thalassemia patients and families should be educated, supported, and treated in age appropriate ways so that they can take an active role in optimizing their health and quality of life.
- Patients and their families should work together with professionals in a multidisciplinary team to optimize their care.
- Accurate and effective communication within a family, between the patient and health care team and between health professionals, should be maintained to ensure the successful management of this life-long condition.

Management of Thalassemia

B1. Initial Management of the Newly Diagnosed Infant

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Principles

- To promptly establish the correct diagnosis for the infant with thalassemia.
- To promptly start an appropriate treatment program for the infant with thalassemia.
- To provide education and psychosocial support tailored to the education level, culture and language of the family

B. Management of Thalassemia

B2. Transfusion Support in Thalassemia

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Principles

- To use clinical and genetic information to help identify thalassemia major patients who will depend on transfusions to maintain acceptable development, health and quality of life, and prolonged life.

- To use clinical and genetic information to help identify thalassemia intermedia patients who do not need routine transfusions to maintain acceptable development, health and quality of life.

Initiation of Transfusion therapy

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- confirmed diagnosis
- Hb < 70g/L - 2 consecutive occasions > 2 weeks apart
- +/- facial changes
- poor growth and limited weight gain
- bone fractures
- extramedullary hematopoiesis
- occasionally Hb 6-7 g/L

Initiation of chelating therapy-Deferoxamine.

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- Start after 12 to 15 transfusions
- Direct liver iron assessment preferred.
- Dose is based on the weight (per kg) and LIC.
- Serum ferritin > 1000ug/l
- For very young children dose should not exceed 35mg/kg/day SC.
- Older children > 5years do not exceed 50mg/kg/day SC.

B. Management of Thalassemia

B2. Transfusion Support in Thalassemia

Red Cell Transfusion Practices and Monitoring

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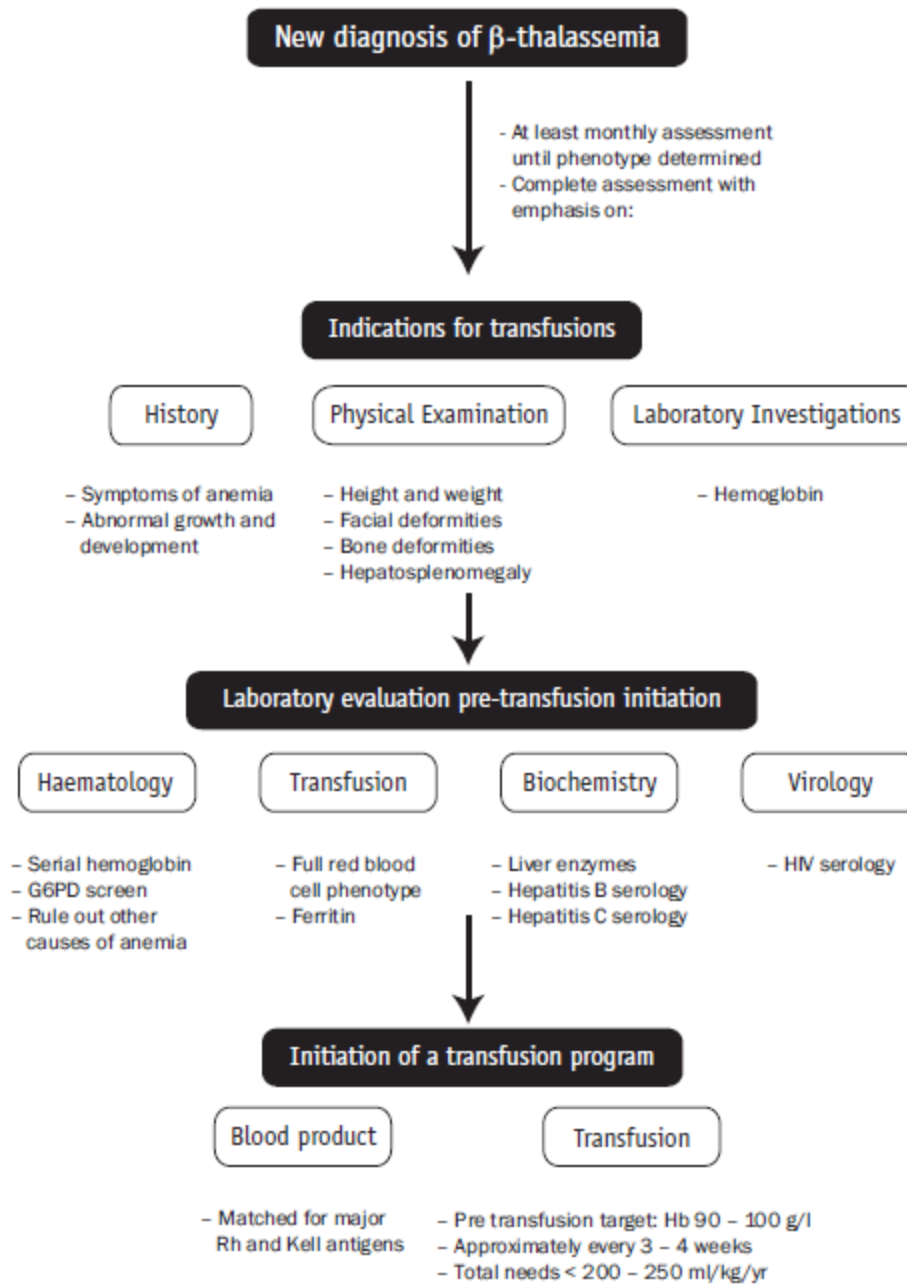
Principles

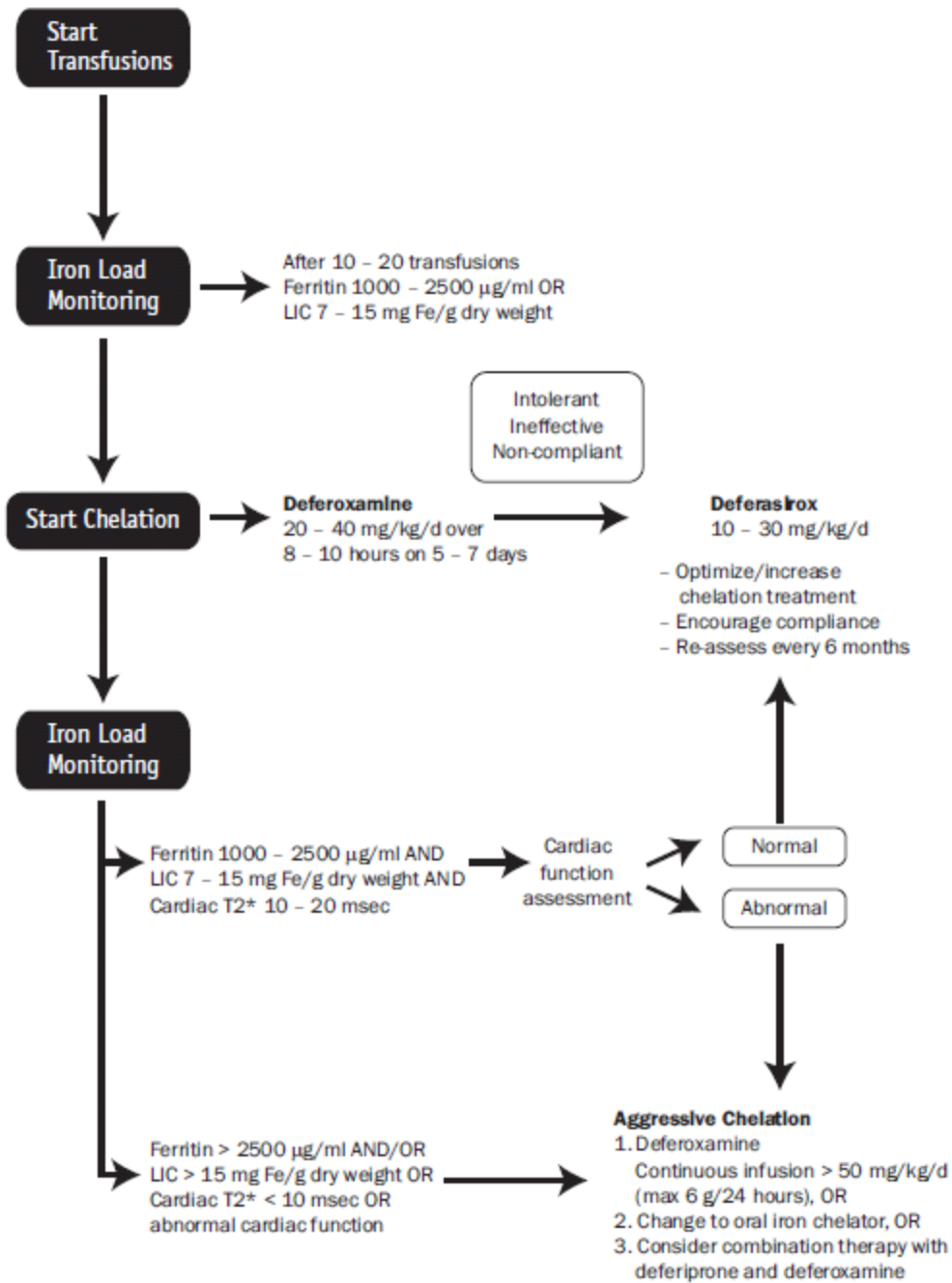
- To ensure that children and adults are transfused to an acceptable hemoglobin level necessary to suppress endogenous erythropoiesis and to promote normal development with good quality of life.

- To prevent complications related to under-transfusion.

- To ensure that safe blood transfusion practices are closely followed.

- To deliver transfusion services in a way that is least disruptive to the patient's routine of daily life





Components of Comprehensive Thalassemia Care

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Principles

- To be aware of complications of iron overload, to monitor routinely and accurately for iron overload and to reduce iron accumulation using chelation therapy, with the goal of preventing organ damage and toxicity.
- To monitor and treat adverse side effects of iron chelators.

Components of Comprehensive Thalassemia Care

Psychosocial aspects of Thalassemia care

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- To help patients and families cope with the changing social and psychological aspects of living and growing up with thalassemia.
- To promote self care and improve well being of patients.

Components of Comprehensive Thalassemia Care

Transition from paediatric to adult care setting

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- To ensure a smooth transition and continuity of care for adolescents/young adults and families as they move from the paediatric to the adult setting.
- provide support to these patients as they face new challenges of adulthood.
- To ensure long term and optimal care throughout adulthood.

Components of Comprehensive Thalassemia Care

Care of iron overload complications

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- Prevention of excess loading of iron is the ideal and achievable, however any complications that arise such as cardiac, endocrine, bone and liver should be treated effectively and with appropriate sub-specialists consultations.

The present and future

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- Cleaner blood
 - Oral chelators
 - Non-invasive ways of monitoring LICs
 - Non-invasive and more reliable cardiac monitoring- T2*
 - BMT more successful
 - Better understanding of iron overload and chelation
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- The future is bright.