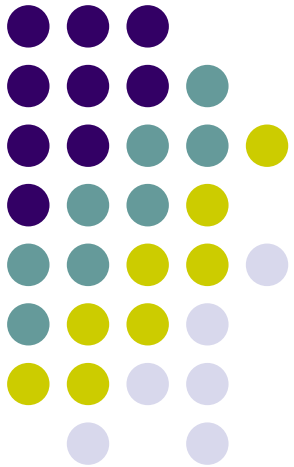
Thalassemia

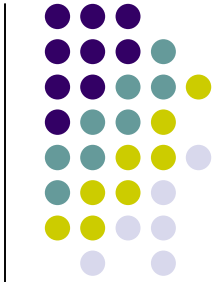
Maria Luz Uy del Rosario, M.D.

Philippine Society of Hematology and Blood Transfusion

Philippine Society of Pediatric Oncology

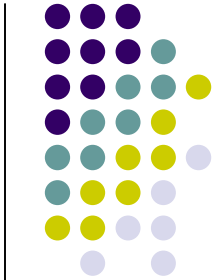


What is Thalassemia



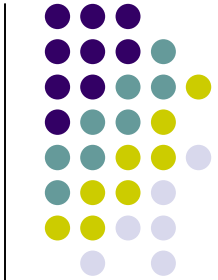
- Hereditary
- Hemoglobin disorder
- Hemolytic anemia

Thalassemia: Who is affected?



- Most single widespread genetic disease worldwide
- About 270 M people affected worldwide (WHO 2001)
- More cases of β thalassemia in the middle east, more α thalassemia in Asia
- α Thalassemia accounts for 60-90% hydrops fetalis in Asia
- Filipinos also affected

Thalassemia in the Philippines



- Still largely under diagnosed and under reported
- Data from the Thalassemia Center of the Philippines as of 2006

Total	457
β-Thal	49.8%
α- Thal	26.4%
β-Thal with HbE	23.8%

Luzon	81%
Visayas	3.5%
Mindanao	15.3%

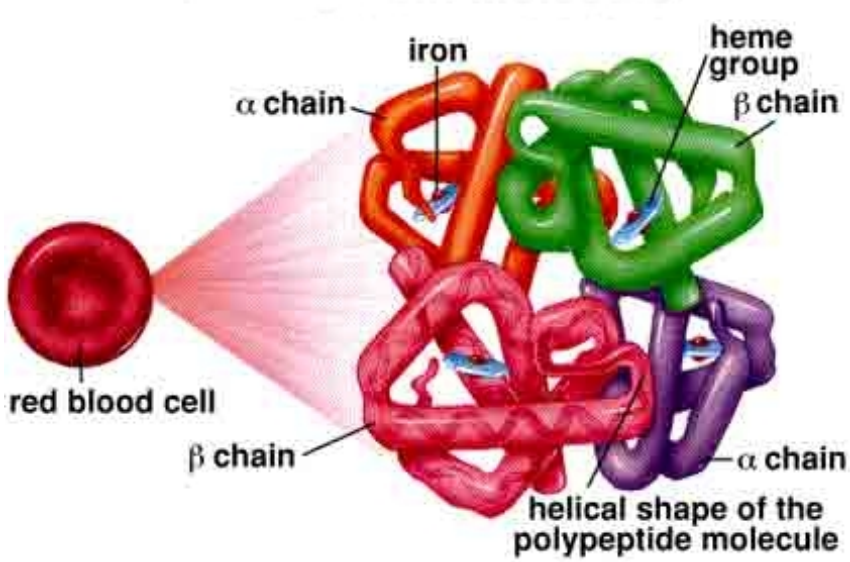
Hemoglobin

Types of Hemoglobin

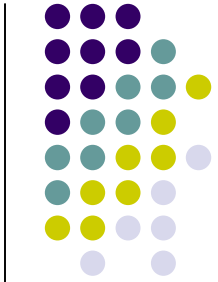
Embryonic hemoglobin
Hemoglobin F
Hemoglobin A
Hemoglobin A2

Normal adult red cells:

98%HbA 2% HbA2
trace Hb F



Hemoglobin Defect and Heredity in Thalassemia



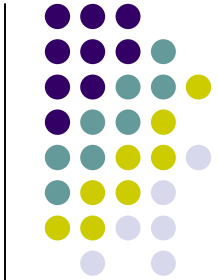
- β-chain

  β Thalassemia
  2 β gene clusters
  chromosome 11

- α-chain

  α Thalassemia
  4 α gene clusters
  chromosome 16

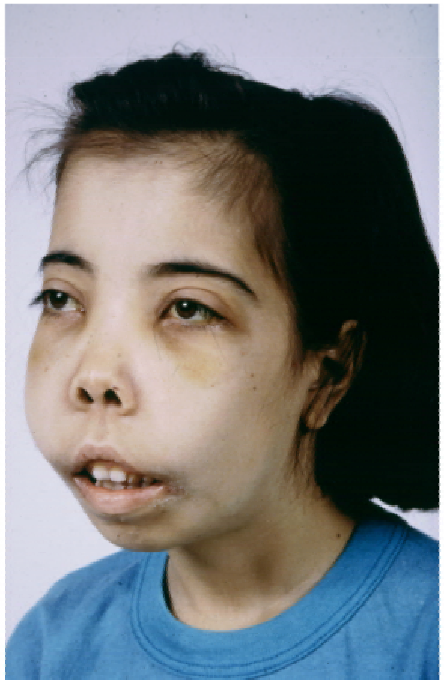
β-Thalassemia



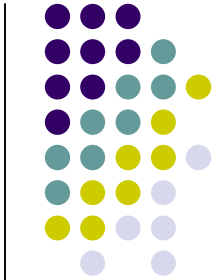
- Major
- Minor
- Intermedia

β-Thalassemia Major

- Anemia onset first few months of life
- Transfusion dependent
- Ineffective erythropoiesis – facial bossing, short stature, splenomegaly
- Hemolysis – jaundice, reticulocytosis
- Iron overload

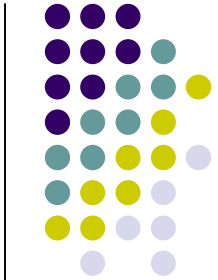


β-Thalassemia Intermedia



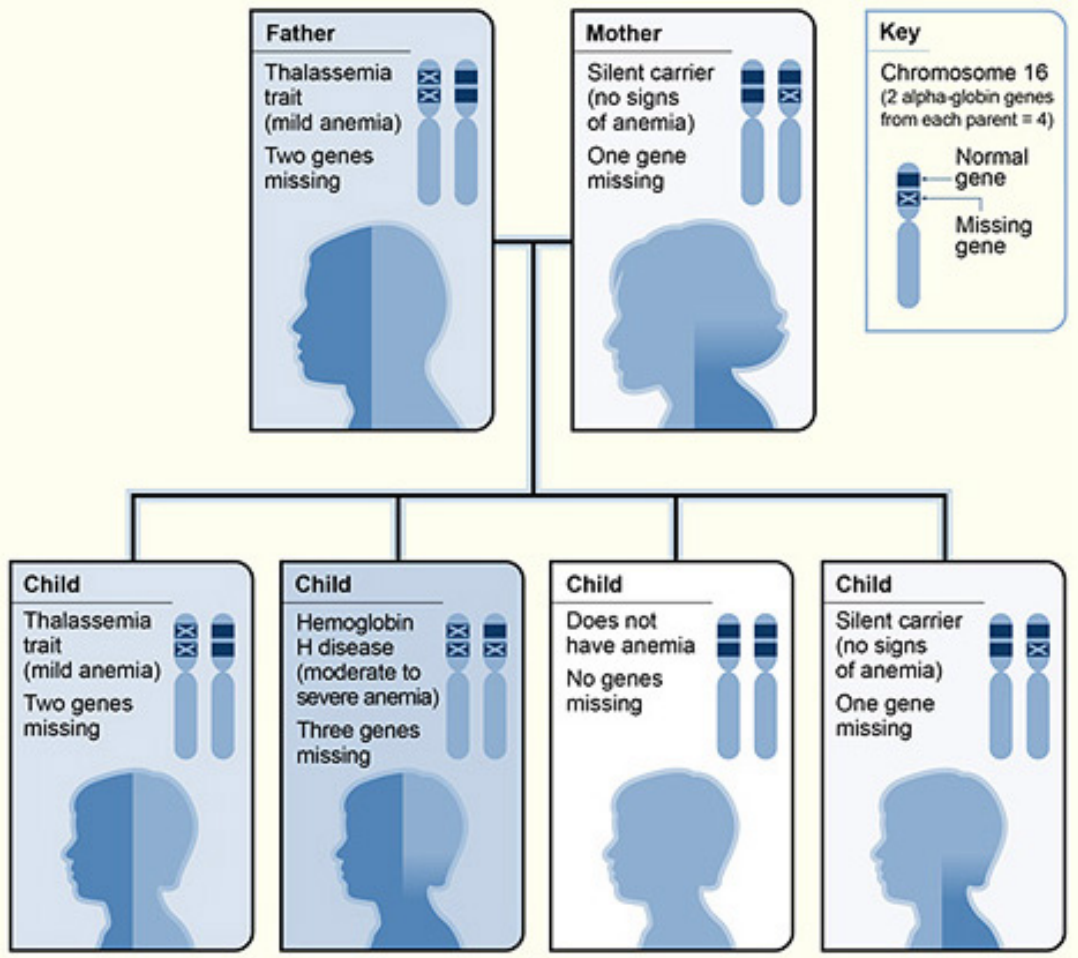
- Due to inheritance of one mild and one severe thalassemia gene
- Clinically variable, may have moderate anemia (Hb 8-9) and/or splenomegaly
- Symptom onset later (usu. > age 2)
- Usually leads a normal life
- May occasionally need transfusions/chelation

β-Thalassemia Minor

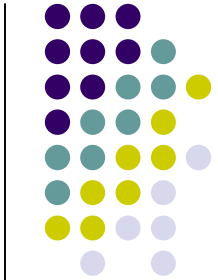


- Only one β globin gene affected
- Mild anemia
- Usually mistaken for iron deficiency anemia
- Iron not needed/harmful

α-Thalassemia: Types

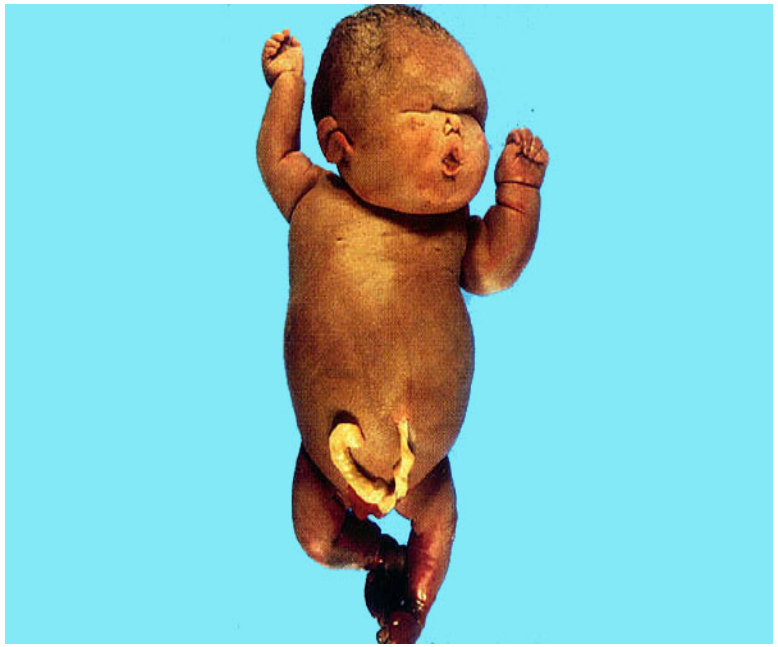


Hemoglobin H disease



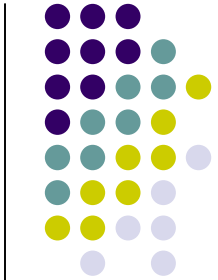
- 3 gene deletion
- Excess β chains form Hb H
- HbH precipitates forming inclusion bodies, causing red cell destruction/hemolysis
- Often symptomatic at birth – neonatal jaundice/hemolytic anemia
- Hemolysis with oxidant stressors such as infections

Hydrops Fetalis



- 4 gene deletion
- Due to absence of globin genes, no fetal hemoglobin produced in utero
- High output failure
- Anasarca
- hepatomegaly

Signs and Symptoms



Hemolysis	splenomegaly, anemia, jaundice
Ineffective erythropoiesis	anemia, marrow expansion and bone deformity, increased metabolic rate, poor growth, folic acid deficiency
Iron overloading	endocrine deficiencies cirrhosis cardiac failure death

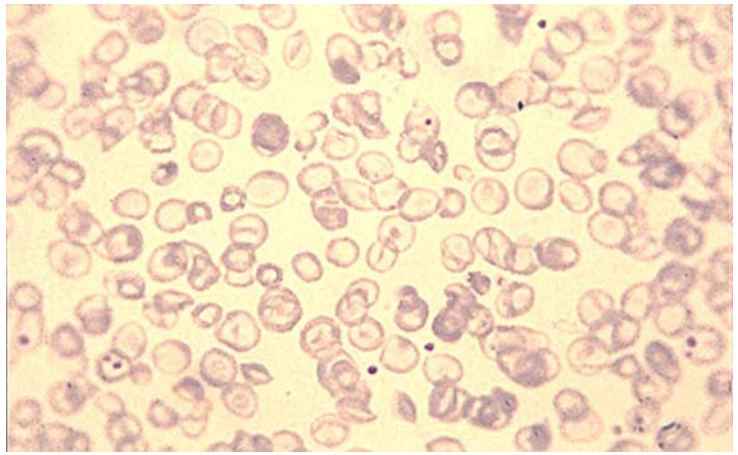
Diagnostic Evaluation

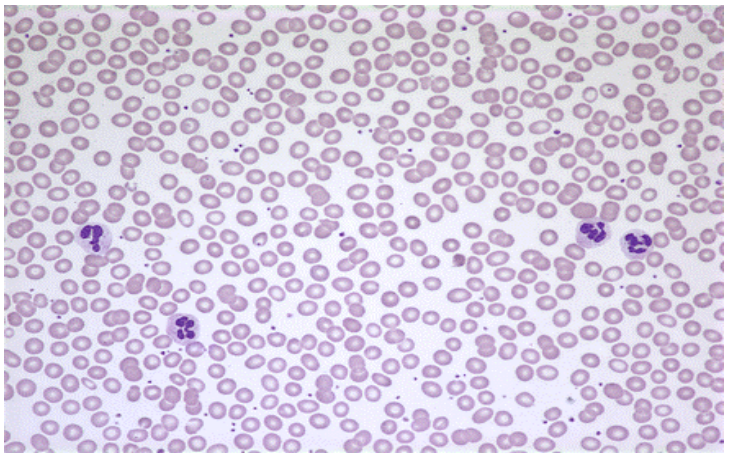
Complete blood count

- anemia
- low MCV < 70 fl
- low MCH
- inc. reticulocytes

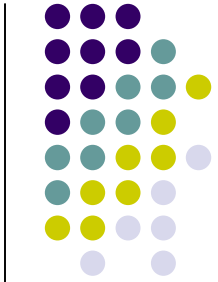
Peripheral blood smear

- hypochromia
- microcytosis
- anisocytosis
- poikilocytosis
- target cells





Diagnostic Evaluation



Supravital staining

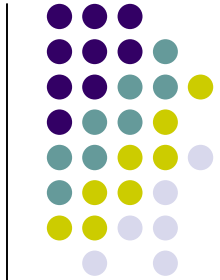
identifies inclusion bodies in pts with HbH disease

Hemoglobin electrophoresis

identifies various hemoglobins

quantitation of hemoglobin A, A2, F

Diagnostic Evaluation



High performance liquid chromatography

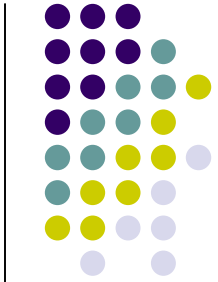
hemoglobin separation

complementary to hemoglobin electrophoresis

DNA analysis

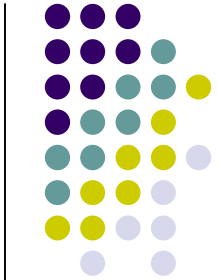
identifies α or β gene mutations

Common Problems Encountered by Patients with Thalassemia



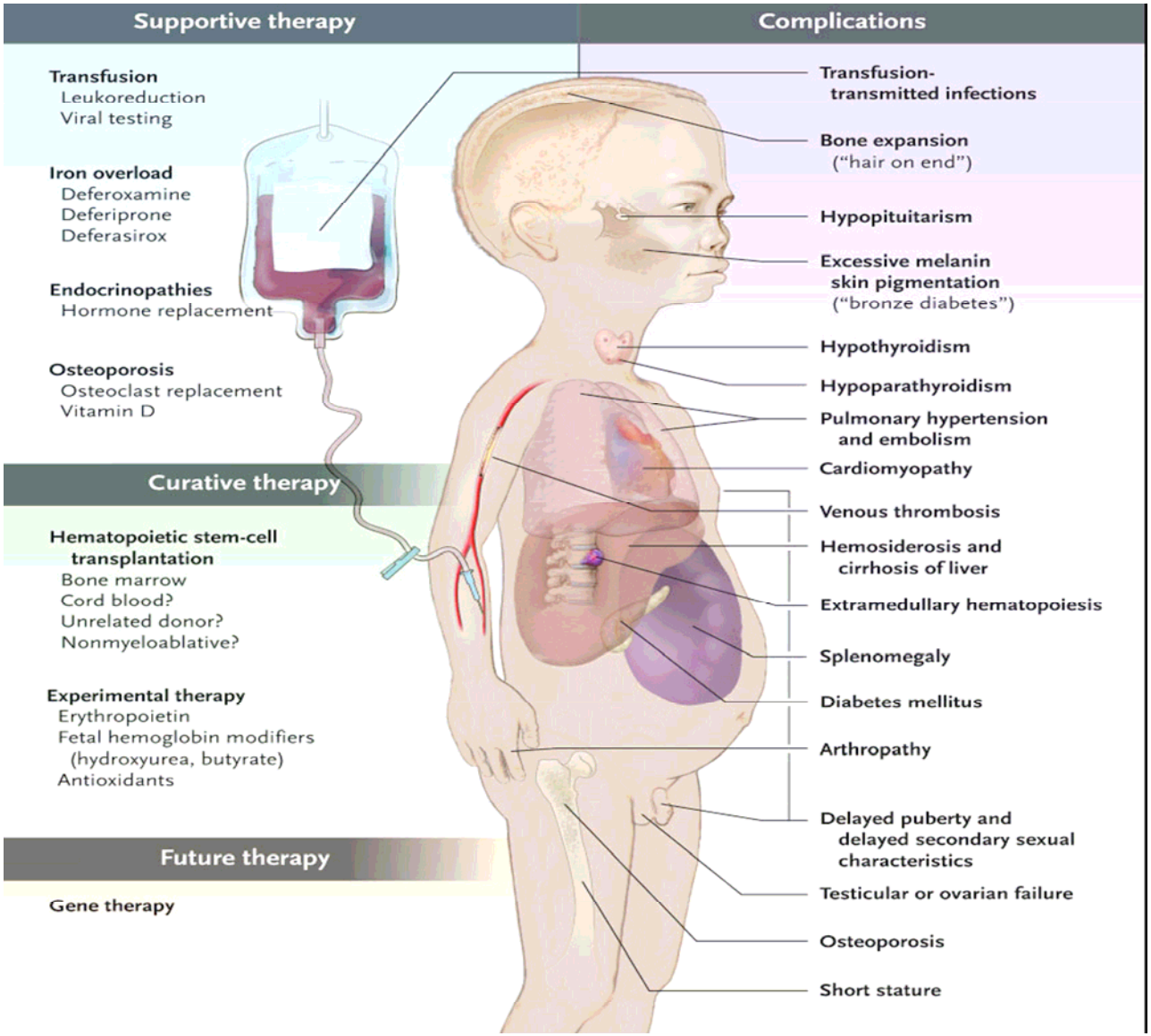
- Chronic anemia
- Hypersplenism
- Iron overload
- Infections
- Venous thrombosis

Iron Overload



- Leading cause of mortality and organ injury
- From transfusion and increased intestinal absorption
- Free iron toxic to tissues
- Measures of iron overload – serum ferritin, liver iron content, SQUID
- Requires iron removal using chelating agents

Treatment of Thalassemia



Supportive Care

TRANSFUSION

maximize growth and development

minimize extramedullary hematopoiesis

decrease iron absorption from gut

decrease splenomegaly

delay onset of complications

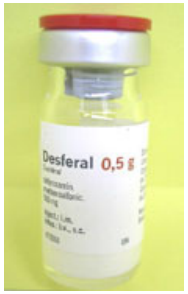
CHELATION

bind free extracellular iron

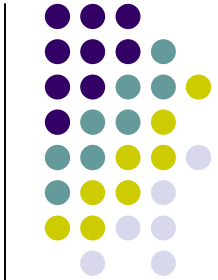
desferrioxamine(IV, SQ)

deferiprone (oral)

deferasirox (oral)



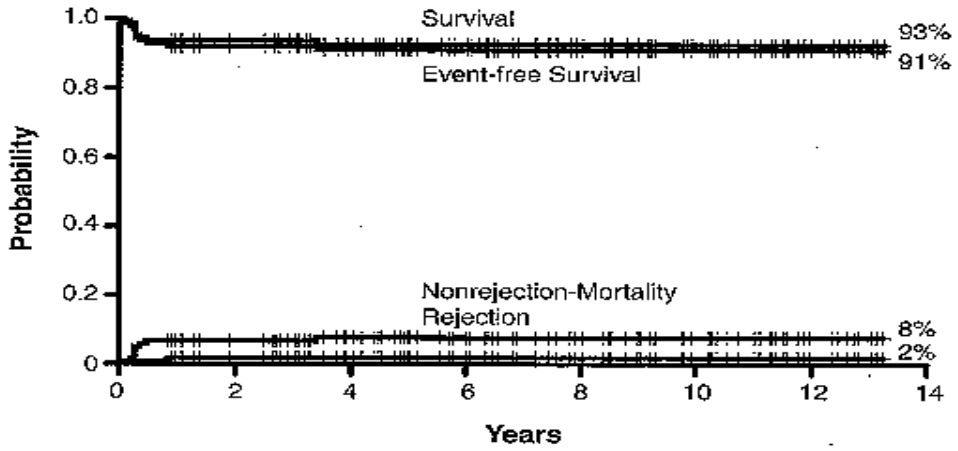
Supportive Care



- Folic acid 1 mg/day
- Hepatitis B vaccination
- Cholecystectomy for gallstones
- HIV monitoring
- Hormone replacement
- Management of osteoporosis
- Genetic counseling
- Splenectomy

Bone Marrow Transplantation

- Rationale – replace defective marrow with normal marrow from a healthy donor
- Only established curative therapy
- Risky, expensive, not always feasible



Other Therapies

- Cellular and Molecular Modifiers

  Hydroxyurea
  Azacytidine
  Erythropoietin

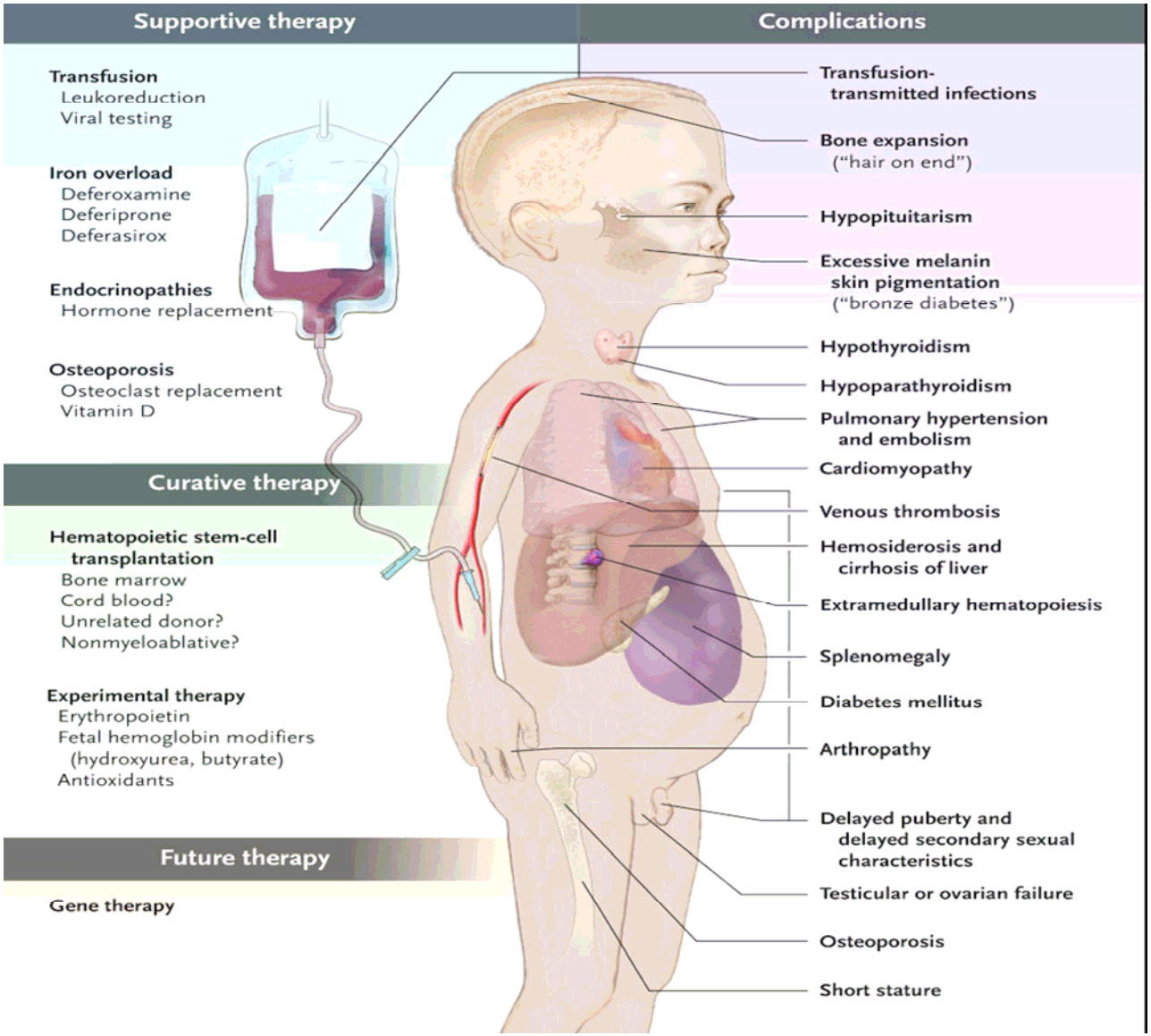
- Gene Therapy

  insertion of normal β or α globin genes into hematopoietic stem cells

  requires a “safe” vector (virus derived)

  still highly experimental

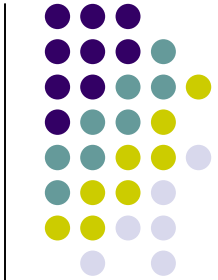
Complications of Thalassemia



Summary of Features of β-Thalassemia

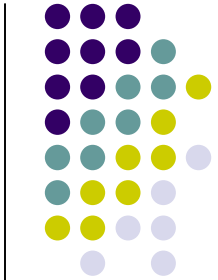
Minor/Trait	**Asymptomatic** **Mild anemia** **Low MCV**	**Normal to elevated Hb A2** **Mildly elevated Hb F**	
Intermedia	**Variable clinical findings**		**Variable transfusion dependency, need for chelation**
Major	**Severe anemia**	**Variable Hb A2** **Marketdly elevated Hb F**	**Transfusion dependent** **Requires chelation**

Summary of Features of α-Thalassemia



Silent carrier	**No anemia** **Normal to slightly dec. MCV**	**Normal Hb A2 and F**	**No Hb H inclusions**
Trait	**Mild anemia** **Low MCV**	**Low to normal Hb A2**	**Occasional Hb H** **inclusions**
Hb H disease	**Moderate to severe anemia** **Low MCV** **Chronic hemolysis**	**Low to normal Hb A2**	**Trace to + Hb H** **inclusions**
Hydrops fetalis	**Generally incompatible with extrauterine life**	**Low Hb A2**	**+++ Hb H inclusion bodies**

Local Resources for Patients with Thalassemia



- **Thalassemia Center of the Philippines**
  located at **Fe del Mundo Medical Center**
  DOH Dept Order 301-IS, 1999
  thalctr_tcp@yahoo.com.ph
  Tel. 712-0845 loc 156
  Fax 743-1818
  Hotline 09915-4440053

- **Balikatang Thalassemia (Ba-Tha)**
  www.ba-tha.org.ph

- **Partners:**
  Philippine Society of Hematology and Blood Transfusion
  National Institutes of Health, UP Manila
  Thalassemia International Federation
  Mindanao Thalassemia Foundation

Summary

- Thalassemia is a hereditary disorder of hemoglobin synthesis resulting in hemolytic anemia
- Found worldwide, Filipinos are also affected by both α- and β-thalassmia
- There is a need to determine the true incidence/prevalence of thalassemia
- Clinical presentation is variable and although there are are potential serious problems, many patients can live productive lives with proper care