Management of
TRANSFUSION DEPENDENT THALASSAEMIA

QUICK REFERENCE FOR HEALTH CARE PROVIDERS

MINISTRY OF HEALTH MALAYSIA

MALAYSIAN SOCIETY OF PAEDIATRIC HAEMATOLOGY & ONCOLOGY

MALAYSIAN PAEDIATRIC ASSOCIATION

ACADEMY OF MEDICINE MALAYSIA

KEY MESSAGES

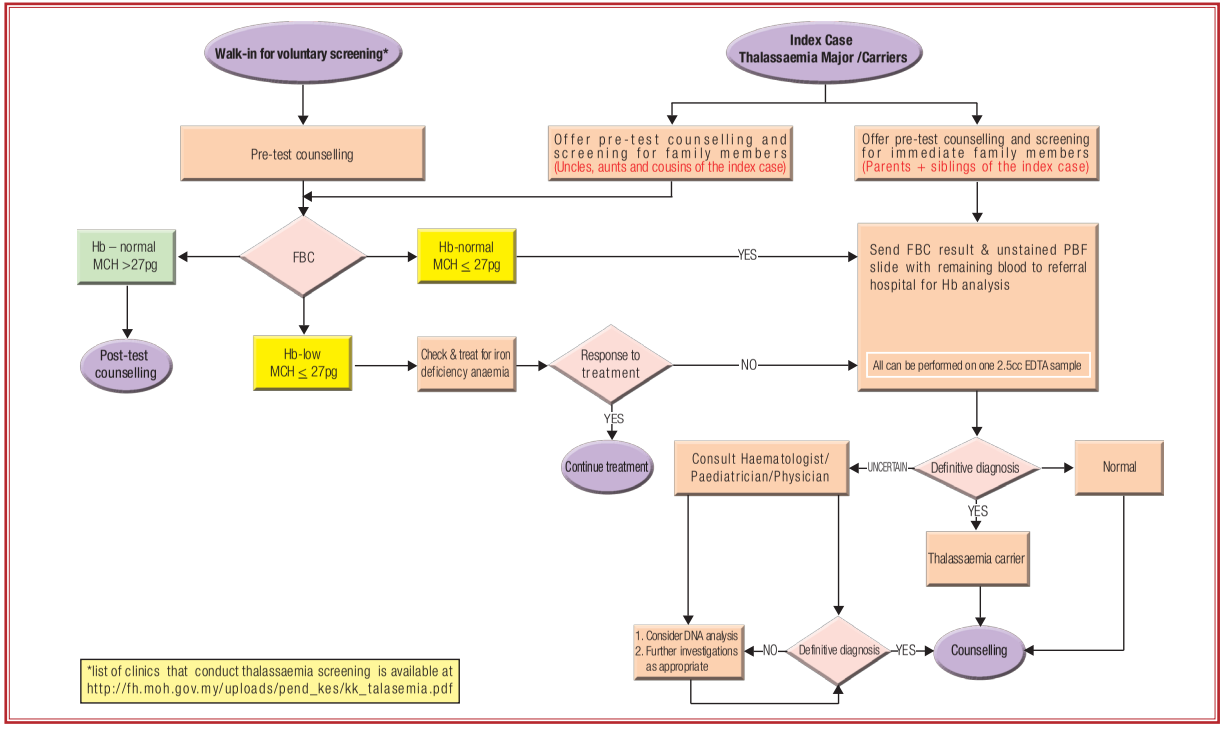
- Thalassaemia is an inherited blood disorder affecting all major ethnicities in Malaysia.
- All patients with MCH < 27 pg should be screened for thalassaemia.
- Cascade screening and appropriate genetic counselling should be provided to the immediate and extended family members of an index patient.
- All thalassaemia major patients should receive safe and optimal blood transfusions.
- Monitoring and treatment of iron overload must be optimised to improve survival.
- Monitoring and treatment of cardiac, infective and endocrine complications will ensure better quality of life and survival.
- Effective patient management requires good collaboration between transfusion medicine, laboratory and clinical services.
- Bone marrow transplantation from a matched sibling donor is an established curative treatment option.

This Quick Reference provides key messages and a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Transfusion Dependent Thalassaemia (November 2009).

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following websites:

Ministry of Health Malaysia : http://www.moh.gov.my
Academy of Medicine Malaysia : http://www.acadmed.org.my

ALGORITHM FOR VOLUNTARY AND CASCADE SCREENING



DIAGNOSTIC CRITERIA

	CLINICAL FEATURES	LABORATORY FEATURES
Thalassaemia Major (presentation usually at 4-6 months or child younger than 2 years old)	Anaemia Hepatosplenomegaly Growth failure / retardation	Hb : < 7 g/dL HbF : > 90% HbA2 : normal or high HbA : usually absent
Thalassaemia Intermedia (presentation at later age)	Milder anaemia Thalassaemia facies Hepatosplenomegaly	Hb : 8-10 g/dL HbF : > 10% HbA2 : 4-9%, if > 10% - suggests HbE HbA : 5-90% HbH disease : presence of H band
β Thalassaemia Trait	Normal to mild anaemia No organomegaly	Hb : > 10 g/dL MCH : < 27 pg HbF : 2.5 - 5% HbA2 : 4-9%, if > 20% suggests HbE trait HbA : > 90%
α Thalassaemia Trait	Normal to mild anaemia No organomegaly	Hb : > 10 g/dL MCH : < 27 pg Hb analysis : normal H inclusion may be present DNA studies may be necessary

• For more difficult cases, molecular studies may be employed

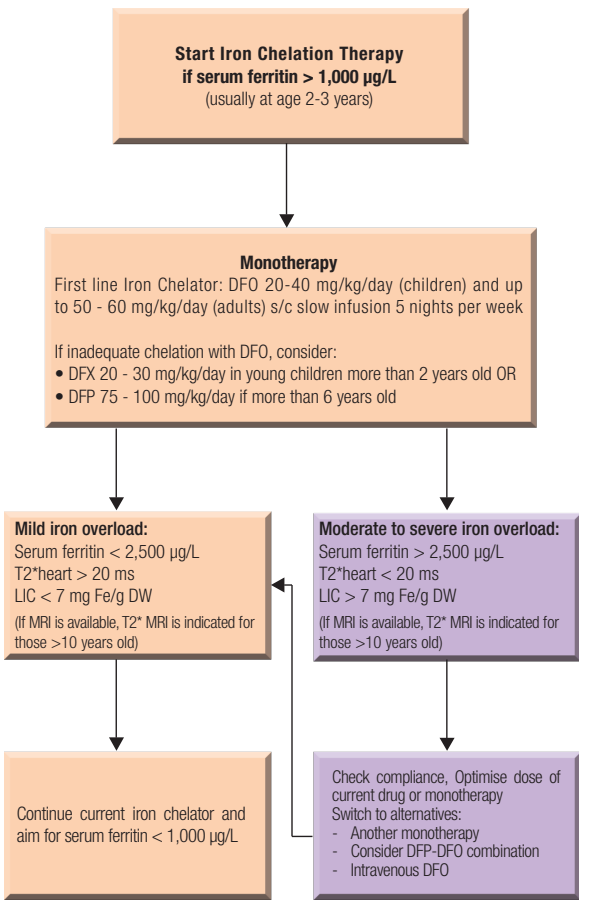
BLOOD TRANSFUSION THERAPY

Transfusion should be initiated when the patient is confirmed to have thalassaemia major and Hb < 7 g/dL more than 2 weeks apart.
In thalassaemia intermedia, consider transfusion when patient has failure to thrive or bony deformities or extramedullary masses.
All patients should have full red cell phenotyping consisting of ABO, Rh, Kell, Kidd, Duffy and MNSs prior to first transfusion.
Pre-transfusion Hb should be kept between 9 – 10 g/dL.
Post transfusion Hb should be between 13.5 - 15.5 g/dL.
Fresh blood < 14 days and leucodepleted blood are advisable.
Volume of transfusion: 15 – 20 ml/kg, 2 – 4 weeks apart.
In the presence of hypersplenism, consider splenectomy.

DEGREE OF IRON OVERLOAD

	MILD	MODERATE	SEVERE
Serum ferritin (µg/L)	< 2500	2500 - 5000	> 5000
LIC (mg Fe/g DW)	< 7	7 - 15	> 15
Cardiac T2* MRI (ms)	> 20	10 - 20	< 10

ALGORITHM FOR IRON CHELATION THERAPY



Abbreviations: DFO – Desferrioxamine DFP – Deferiprone DFX – Deferasirox LIC – Liver Iron Concentration

MONITORING OF PATIENT

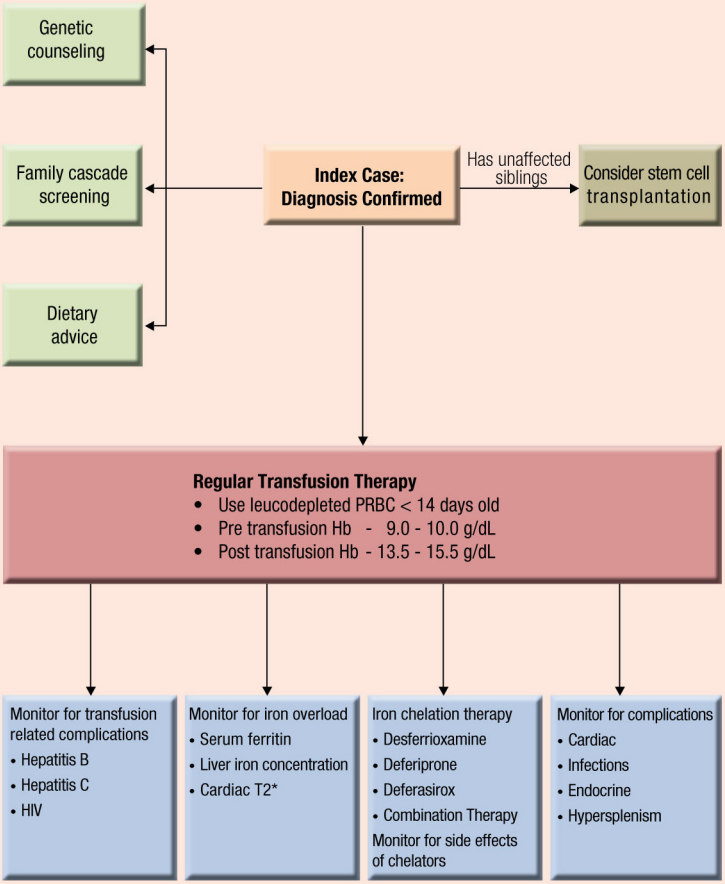
NO.	MONITORING	ASSESSMENT AND INVESTIGATIONS
1.	Blood transfusion	HBsAg, Anti HCV and Anti HIV 6 monthly
2.	Growth	Weight, height and physical examination 3 - 6 monthly
3.	Iron overload	Serum ferritin 3 monthly
	Patient > 10 years old	ECG and cardiac echocardiography annually LIC by MRI 1 – 2 yearly Cardiac MRI T2* 1 – 2 yearly
4.	Drug toxicity	
	Desferrioxamine	Auditory/ophthalmology annually
	Deferiprone	Full blood count weekly ALT 3 monthly
	Deferasirox	Renal profile and urine protein monthly ALT monthly Auditory/ophthalmology annually
5	Complications*	Especially in older patients > 10 years old
5.1	Growth failure	Test for diabetes mellitus, hypothyroidism, delayed puberty, zinc deficiency, bone disorders, DFO toxicity Bone age assessment GH stimulation tests (in referral centre)
5.2	Delayed puberty and hypogonadism	Tanner staging 6 monthly LH, FSH, oestradiol or testosterone Pelvic ultrasound for girls Gonadotropin releasing hormone (GnRH) stimulation test if necessary
5.3	Hypothyroidism	Free T4 and TSH
5.4	Diabetes mellitus	Fasting plasma glucose or OGTT
5.5	Osteoporosis/Osteopaenia	Serum calcium, phosphate, alkaline phosphatase 25-OH Vitamin D Serum zinc Spinal radiograph (AP and lateral views) DEXA scan
5.6	Hypoparathyroidism	Serum calcium, phosphate, alkaline phosphatase Serum magnesium Parathyroid hormone
5.7	Hypoadrenalism	Baseline cortisol at 8.00 – 9.00 am ACTH stimulation test

*Monitor annually and refer to appropriate specialist for management

MANAGEMENT OF COMPLICATIONS

TREATMENT CRITERIA	TREATMENT
HEPATITIS B	
1. HBsAg positivity > 6 months AND 2. Serum HBV DNA > 20,000 IU/ml (10^5 copies/ml) in HBeAg positive cases, serum HBV DNA > 2,000 IU/ml (10^4 copies/ml) in HBeAg negative cases AND 3. Persistent or intermittent elevation in ALT/AST levels, > 2 X upper limit of normal or significant liver disease on liver biopsy	Interferon α (IFN α) for 4-6 months for HBeAg positive patients and at least a year for HBeAg negative patients or Peg-IFN for at least six months for HBeAg positive patients and 12 months for HBeAg negative patients or Lamivudine
HEPATITIS C	
1. Persistent anti-HCV positivity > six months AND 2. Serum HCV RNA positivity (regardless of viral titre) AND 3. Significant liver disease on liver biopsy	Combination therapy (either conventional or PEG-IFN) with ribavirin Treatment duration depends on HCV genotype
BACTERIAL INFECTIONS	
Significant fever especially post-splenectomy	Stop iron chelation therapy Broad spectrum anti-Klebsiella and anti-Pseudomonal agents (3rd generation cephalosporin ± aminoglycoside)
CARDIAC SIDEROSIS	
Asymptomatic, mild to moderate cardiac siderosis (T2* 10 -20 ms) and normal cardiac function	Intensify iron chelation monotherapy or switch to combination therapy
Symptomatic or severe cardiac iron overload	Appropriate cardiac therapy, continuous iv DFO or combination therapy
DELAYED PUBERTY	
Absence of pubertal changes at 13 years old (girls) and 14 years old (boys)	Girls : Oral ethinyl oestradiol or conjugated oestrogen preparation Boys : Depot testosterone
SHORT STATURE	Treat other causes of short stature Growth hormone injection may be considered if confirmed growth hormone deficiency
DIABETES MELLITUS	Subcutaneous insulin injection
HYPOTHYROIDISM (primary or central)	Oral L-thyroxine
OSTEOPOROSIS/OSTEOPAENIA	Oral calcium and Vitamin D supplements Bisphosphonates may be considered in osteoporosis
HYPOPARATHYROIDISM	Oral calcitriol and calcium
HYPOADRENALISM	Oral hydrocortisone

ALGORITHM FOR MANAGEMENT OF TRANSFUSION DEPENDENT THALASSAEMIA



CLINICAL PRACTICE GUIDELINES SECRETARIAT
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