Thalassaemia major and other rare transfusion dependant anaemias

–*Acute presentation*

Subject:	Acute presentation thalassaemia and rare anaemias
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Designation of Author:	Consultant Haematologist, Dr Farrukh Shah
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Version Control Sheet

Version	Date	Author	Status	Comment
1.0	Feb 2012	Dr F Shah (Consultant Haematologist)	Off line	New guideline approved at CGC
1.1	April 2012	Dr F Shah (Consultant Haematologist)	Off line	Reviewed with minor change
1.2	October 2015	Dr F Shah (Consultant Haematologist)	Live	Reviewed with change to contact details only

➢ Criteria for use

These guidelines are to be used as a guide for acute management and who to contact if a patient with thalassaemia present acutely unwell. This guideline covers requirements from Quality Requirements for Health Services Caring for Adults with Haemoglobinopathies version 1.5 dated 08.04.2011 QR no:3 (i), and 26 for thalassaemia patients (a and b).

➢ Background/ introduction

It is very rare for young children to present with complications of iron overload but adolescents and adults can present with serious complications and the **consultant haematologist on call should always be called** as soon as it is known that the patient has thalassaemia major.

All patients are under regular review and it is unlikely that a patient will present with acute complications without warning.

➢ Inclusion/ exclusion criteria

Inclusion criteria:

All patients with Thalassaemia Major and transfused Thalassaemia Intermedia.

Patients with rare transfusion dependant anaemias: Diamond Blackfen Anaemia and Congenital Sideroblastic anaemia, Transfusion dependant Glucose 6 Phosphate Dehydrogenase Deficiency (G6PD) and Pyruvate Kinase (PK) deficiency .

Patients with sickle cell anaemia who have developed iron overload.

Exclusion criteria:

Myelodysplastic anaemia

➢ Clinical management

Acutely unwell patient

It is very important that as soon as the patient with thalassaemia major is reviewed that haematology consultants are contacted with a summary of the clinical findings and blood tests. This should happen regardless of the time of day. If the patient is a child or adolescent then the paediatric consultants should be involved in the care from the outset with advice and

support from the consultant haematologists. All adult patients should be admitted to the haematology Ward unless they need to be managed in an ITU/HDU setting as the nursing team are more experienced in thalassaemia and know most of the patients.

Complications

Patients with thalassaemia are more prone to infection for various reasons; the chelation therapy a patient is taking, the degree and severity of iron overload, the presence of a Port-a-cath or Hickman line, splenectomy and diabetes will increase the risk of severe infection.

The most common complications are:

1. Acute Sepsis cause unknown/multi-organ damage
2. Febrile neutropenia due to deferiprone
3. Yersinia Enterocolitica infection with desferrioxamine or in the presence of severe iron overload.
4. Infected port-a-cath or Hickman line
5. Cardiac dysrrhythmia or cardiac failure
6. Diabetes associated complication hypoglycaemia/ Diabetic Ketoacidosis (DKA) / Hyperglycaemic Hyperosmolar State (HHS)
7. Cholecystitis

Iron overload is associated with an increased risk of infection with Gram Negative organisms such as **Yersinia, Klebsiella and Pseudomonas.**

Please refer to trust Antibiotic guidelines for specific regimes and dosage instructions.

	Please see Whittington Health Guideline: **Antimicrobials in Bacterial Infections in Adults** **-Guidelines for Management** http://whittnet/document.ashx?id=613
	Please see Whittington Health Guideline: **Antibiotic protocols for children seen in general Pediatrics** **-Guidelines for Management** http://whittnet/document.ashx?id=602 **Supportive care protocols for paediatric haematology and oncology** http://whittnet/document.ashx?id=4588

Please refer to trust Antibiotic guidelines for specific regimes and dosage instructions

Febrile patient:

Early recognition is critically important as many of these patients have underlying cardiac and liver damage and can decompensate rapidly if the sepsis is left unchecked.

It is important to clinically assess for signs of circulatory collapse and sepsis. Patients with iron overload who are septic do not necessarily develop a fever and the presentation may simply be an unwell patient with a high White cell count (WBC) and a high CRP.

1. If the site of infection is obvious, for example pneumonia, then appropriate first line antibiotics can be started for this as per trust policy.
2. Otherwise patients should be started on antibiotics with broad-spectrum coverage as per the neutropenic sepsis clinical guidelines.
3. If the patient has signs and symptoms suggestive of Yersinia infection, (abdominal pain, vomiting and or diarrhoea), then Ciprofloxacillin (500mg BID orally or 400mg IV BID) is the drug of choice. If Yersinia infection is suspected then desferrioxamine infusion should not be used whist the patient is septic.

Febrile Neutropenia:

Patients on deferiprone are at risk of febrile neutropenia. All patients are advised to have a weekly full blood count but compliance to this is relatively poor. It is critical that if a patient stated that they are taking deferiprone that a full blood count is undertaken as a matter of urgency and the patient started on first line antibiotics as per the trust clinical guidelines. Deferiprone should be stopped immediately. The neutropenia takes 2 to 3 weeks to resolve and GCSF can be used to help recovery. Antibiotics should be initiated as per the trust guidelines.

	Please see Whittington Health Guideline: **'Neutropenic sepsis in adults'** http://whittnet/document.ashx?id=3311

Cold Sepsis:

Careful monitoring of the WBC and CRP is needed in unwell thalassaemia major patients. Patients with severe iron overload can present with cold sepsis and fail to mount a febrile response. First line antibiotics should be administered as per the neutropenic sepsis clinical guidelines. A careful

search needs to be made for the source of the sepsis in case there is an abscess. All clinical management should be as per the Early management of sepsis guidelines.

	Please see Whittington Health Guideline: **'Early Management of Severe Sepsis'** http://whittnet/document.ashx?id=4359

Infected Central venous catheters

Patients with severe iron overload or compliance problems with chelation therapy may be treated with Intravenous desferrioxamine. This is administered at home 24hr/day via a permanent indwelling catheter such as a Hickman line or a Port-a-cath. These patients are most at risk of cardiac decompensation as they often have severe myocardial iron loading. Fluids should be used with very careful monitoring to avoid pushing patients into heart failure.

1. Cultures need to be taken ASAP of both the line and peripherally
2. Do not flush the line as hypotensive shock can follow very rapidly.
3. Start immediately as per Trust Guidelines for neutropenic sepsis central venous cannula in situ protocol. If the patient is allergic to penicillin refer to the Trust guidelines and discuss with microbiology. For children please see link below.
4. Haematology review should happen ASAP and the removal of the line considered.

	Please see Whittington Health Guideline: **Supportive care protocols for paediatric haematology and oncology** http://whittnet/document.ashx?id=4588 page 25

Abdominal pain with or without jaundice

A good history and abdominal examination is essential and treatment should be based on clinical findings and likely causation. Patients presenting with abdominal pain should be jointly managed with general surgical teams as well as clinical haematology. Common causes in thalassaemia patients are as follows:

Cholelithiasis:

Is common and biliary colic or obstruction, with or without infection, should also be considered. If there is concern about infection then start antibiotics (Augmentin 1.2g 8 hourly and gentamicin 7mg/kg once daily IV) and ensure referral to surgical team.

Renal Colic/ sepsis/ obstruction:

Thalassaemia patients presenting with severe renal colic as a result of stones can become acutely unwell. Patients should be managed supportively with optimisation of fluids, appropriate antibiotics if there is suggestion of infection and careful monitoring for signs of obstruction. Multi-disciplinary support from urology and interventional radiology is often required. Once the acute episode subsides a referral should be made to: Professor Unwin or Dr Shabbir Moochhala at the renal stones Unit at Royal Free Hospital.

Cardiac Complications:

Most patients with cardiac iron loading are already on aggressive management regimes but due to poor compliance may still present with acute decompensation. Sometimes an intercurrent infection can precipitate a myocarditis associated with decompensation.

Common symptoms are

- ankle oedema, abdominal distension and shortness of breath and palpitations.

Investigations at time of admission should include:

- ECG,
- CXR,
- ECHO within 24 hours (on weekdays)

Management should be:

- **All these patients with cardiac complications should be nursed on CCU/ HDU/ ITU** with regular monitoring under the supervision of consultant cardiologists with haematology support.
- Careful daily assessment of electrolytes and correction of Ca^{2+}, Mg^{2+}, K^{+} and Na^{+} is important in reducing the risk of dysrrhythmias
- Initial management is with general supportive care with diuretics, ACE inhibitors, and anti arrhythmic drugs and Inotropes as needed.
- **All patients should be on desferrioxamine IV infusion at 50mg/kg/day, 24 hours a day 7 days** a week as this provides a cardioprotective effect.

If a cardiac T2* MRI assessment has not been done in the last 6 months then it should be arranged as matter of urgency during working hours at UCLH once the patient is stable in order to assess the severity of the cardiac iron loading and Ejection Fraction. When the patient is clinically better a review with Dr Malcolm Walker at UCLH must be organised.

Once the patient is stable, chelation therapy and mode of administration should be reviewed to optimise compliance.

Endocrine complications:

These will invariably be recognised by routine clinic screening and treated before the patient becomes symptomatic.

Diabetic patients may present with hypo or hyperglycaemias and should be treated for this under the combined care of haematology and the diabetes team. Please follow Trust specific guidance for diabetes emergencies.

Please see Whittington Health Guidelines:

‘ hypoglycaemia management for adult inpatients with Diabetes’

http://whittnet/document.ashx?id=2451

‘Hyperglycaemic Hyperosmolar State-HHS’

http://whittnet/document.ashx?id=2445

‘Diabetic Ketoacidosis in adults’

http://whittnet/document.ashx?id=1524

Rarely patients may present with acute onset hypocalcaemia due to hypoparathyroidism. Symptoms are a sensation of tingling or numbness peripherally and peri-orally, or tetany. Management is correction of the calcium initially IV followed by oral therapy under the supervision of the Endocrinology team.

Liver complications:

It is rare for patients to present with acute liver decompensation, but some hepatitis C positive patients have significant cirrhosis and this is a possibility. In addition variceal bleeds are a potentially life threatening complication and all patients with cirrhosis are under review with the Liver unit at the Royal Free Hospital. Should a patient present with symptoms of decompensation then they should be managed by Gastroenterology colleagues and close liaison with haematology.

Early consideration should be given to transfer and support by the liver unit at the royal free hospital if patients present with liver failure and the cause is not clear.

	Please see Whittington Health Guideline: **'Decompensated liver disease'** http://whittnet/document.ashx?id=1409

➢ References (evidence upon which the guideline is based)

1. Guidelines for the clinical management of thalassaemia –2nd revised edition 2008
2. Standards for the clinical care of children and adults with thalassaemia in the Uk 2nd edition 2008
3. Quality Requirements for Health Services Caring for Adults with Haemoglobinopathies version 1.5 dated 08.04.2011
4. The National Haemoglobinopathies Project-a guide to effectively commissioning high quality sickle cell and thalassaemia services July 2011: ISBN 978-0-9565846-5-6

➢ Contacts (inside and outside the Trust including out-of-hours contacts)

1. Consultant paediatrician on call if child
2. Haematology specialist registrars bleep 3060 or 3037
3. Dr Shah, consultant haematologist
4. Dr Davis, consultant haematologist
5. Haematology Nurse specialist ext 5225
6. Local specialist consultants via switch board

Specialist clinical referrals and tests:

Dr. James Moon **for CMR (cardiac T2*) assessment**

Senior Lecturer & Honorary Consultant Cardiologist

The Heart Hospital

16-18 Westmoreland Street

UCLH & UCL

London W1G 8PH

Tel No. 0203 456 3081 Fax 0203 456 3086

Dr. J. Malcolm Walker for cardiology review

Consultant Cardiologist

Department of Cardiology

The Hatter Institute

51-67 Chenies Mews

London WCIE 6DB

Tel No: 0203 447 9951 Fax No: 0203 447 9039

Professor Unwin **for renal stones**

Renal Consultant

Royal Free Hospital

Pond Street

London NW3 2QG

Tel: 0207 794 0500

Sec Maureen ext 35681 Fax: No 0207 472 6476

- **Compliance with this guideline (how and when the guideline will be monitored e.g. audit and which committee the results will be reported to) Please use the tool provided at the end of this template**

Compliance will be monitored annually by Audit.
All patients with a diagnosis of thalassaemia major or rare transfusion dependant anaemia who have had an acute admission will be reviewed to assess compliance with guidelines.
Results of audit will be presented at the haemoglobinopathy MDT at the whittington hospital and discussed at the local Network haemoglobinopathy group where they will be reported under morbidity and mortality outcomes.

Key factors to be assessed will be:

number of patients with acute presentation

what was the diagnosis

did the management plan follow that recommended in guidelines

if there was a deviation from the guideline what was the indication

what was the clinical outcome for patient

What complications occurred and why

Action plan on how to avoid similar problems arising in future

To be completed and attached to any procedural document when submitted to the appropriate committee for consideration and approval

		Yes/No	Comments
1.	**Does the procedural document affect one group less or more favourably than another on the basis of:**		
	• Race	No	
	• Ethnic origins (including gypsies and travellers)	No	
	• Nationality	No	
	• Gender	No	
	• Culture	No	
	• Religion or belief	No	
	• Sexual orientation including lesbian, gay and bisexual people	No	
	• Age	No	
	• Disability - learning disabilities, physical disability, sensory impairment and mental health problems	No	
2.	**Is there any evidence that some groups are affected differently?**	No	
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	No	
4.	**Is the impact of the procedural document likely to be negative?**	No	
5.	**If so can the impact be avoided?**	N/A	
6.	**What alternatives are there to achieving the procedural document without the impact?**	N/A	

		Yes/No	Comments
7.	**Can we reduce the impact by taking different action?**	N/A	

If you have identified a potential discriminatory impact of this procedural document, please refer it to the Director of Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact the Director of Human Resources.

Checklist for the Review and Approval of Procedural Document

To be completed and attached to any procedural document when submitted to the relevant committee for consideration and approval.

	Title of document being reviewed:	Yes/No	Comments
1.	**Title**		
	Is the title clear and unambiguous?	Yes	
	Is it clear whether the document is a guideline, policy, protocol or standard?	Yes	
2.	**Rationale**		
	Are reasons for development of the document stated?	Yes	
3.	**Development Process**		
	Is it clear that the relevant people/groups have been involved in the development of the document?	Yes	
	Are people involved in the development?	Yes	
	Is there evidence of consultation with stakeholders and users?	Yes	
4.	**Content**		
	Is the objective of the document clear?	Yes	
	Is the target population clear and	Yes	

	Title of document being reviewed:	Yes/No	Comments
	unambiguous?		
	Are the intended outcomes described?	Yes	
5.	**Evidence Base**		
	Are key references cited in full?	N/A	
	Are supporting documents referenced?	N/A	
6.	**Approval**		
	Does the document identify which committee/ group will approve it?	Yes	
7.	**Dissemination and Implementation**		
	Is there an outline/plan to identify how this will be done?	Yes	
8.	**Document Control**		
	Does the document identify where it will be held?	Yes	
9.	**Process to Monitor Compliance and Effectiveness**		
	Are there measurable standards or KPIs to support the monitoring of compliance with and effectiveness of the document?	Yes	
	Is there a plan to review or audit compliance with the document?	Yes	
10.	**Review Date**		
	Is the review date identified?	Yes	
	Is the frequency of review identified? If so is it acceptable?	Yes	
11.	**Overall Responsibility for the Document**		
	Is it clear who will be responsible for co-ordinating the dissemination, implementation and review of the document?	Yes	

Executive Sponsor Approval			
If you approve the document, please sign and date it and forward to the author. Procedural documents will not be forwarded for ratification without Executive Sponsor Approval			
Name		Date	
Signature			
Relevant Committee Approval			

The Director of Nursing and Patient Experience's signature below confirms that this procedural document was ratified by the appropriate Governance Committee.			
Name		Date	
Signature			
Responsible Committee Approval – only applies to reviewed procedural documents with minor changes			
The Committee Chair's signature below confirms that this procedural document was ratified by the responsible Committee			
Name		Date	
Name of Committee		Name & role of Committee Chair	
Signature			