South Thames Sickle Cell & Thalassaemia Network

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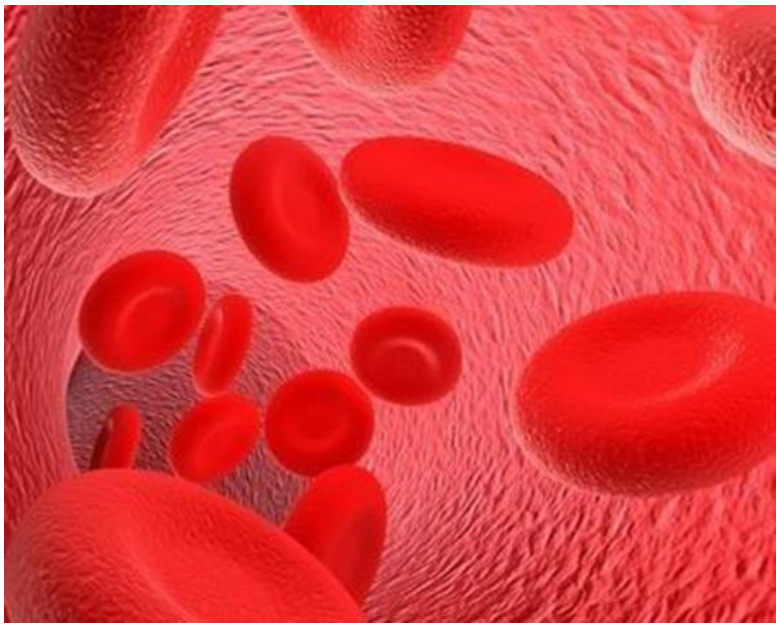
Adult Haemoglobinopathy Workbook



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AKNOWLEDGEMENTS
This Adult Haemoglobinopathy Workbook has been produced collaboratively with input from both Paediatric and Adult Haemoglobinopathy teams. It is intended for the training of nurses and allied healthcare professionals involved in the care of Haemoglobinopathy patients, and is based on published documents including the National Standards of Care and the Royal College of nursing (RCN) competencies 'Caring for people with Sickle Cell Disease and Thalassaemia syndromes', as well as relevant published guidelines and research.

We are grateful to all members of the Kings College Hospital Haemoglobinopathy teams, South Thames Sickle and Thalassaemia Network (STSTN) and members of the multi-disciplinary teams and the wider specialist teams including nephrologists, orthopaedic surgeons, cardiologists, hepatologists and obstetricians with whom we collaborate.

We also thank our training day sponsors ROALD DAHL and NOVARTIS.

We thank attendees for raising awareness, improving knowledge and skills and being part of working towards offering haemogloboinopathy patients the optimal care.

INTRODUCTION TO WORKBOOK
The Haemoglobinopathy Workbook is intended to illustrate key clinical issues and management strategies in the care of haemoglobinopathy patients. It is hoped that this will enable the widespread use of effective preventative and therapeutic interventions for adult haemoglobinopathy patients. Completion of the workbook and attendance at the study day is required for the successful completion of this haemoglobinopathy training event. You can contact your area Practice Development Educator to notify them of your successful completion so that they can update your training record

AIMS and OBJECTIVES
This workbook is designed for registered nurses, junior doctors and allied health professionals (AHP) who have some basic experience in caring for haemoglobinopathy patients (including Sickle Cell disease and Thalassaemia). We aim to promote high consistent standards of nursing and medical care. This workbook should be studied in combination with attendance at the training day.

The training day aims to update and build on your specialist knowledge of haemoglobinopathies. There will be an opportunity to discuss specific issues and queries with specialist haemoglobinopathy consultants, nursing staff and psychologists.

ACCREDITATION

This programme has been accredited by the RCN Centre for Professional Accreditation until September 4th 2018

Accreditation applies only to the educational content of the programme and does not apply to any product

RESOURCES, REFERENCES AND FURTHER READING

1. Identification and management of stroke risk in children with sickle cell disease 2004. http://www.nhlbi.nih.gov/health/prof/bloods/sickle/sc-mngt.pdf in the UK 2008 (Sickle Cell Society)
2. Local central venous access device policy.
3. NHS Sickle Cell and Thalassaemia Screening Programme Standard for the linked Antenatal and Newborn Screening Programme 2nd edition. 2011.
4. Piel FB, Steinberg MH, Rees DC. Sickle Cell Disease. New England Journal of Medicine 2017 April 20;375 (16):1561-1573.
5. RCN Competencies: Caring for People with Sickle Cell Disease and Thalassaemia Syndromes. A Framework for Nursing. NHS Screening programmes. 2011.
6. Russell E Ware, Mariane de Montalembert, Léon Tshilolo, Miguel R Abboud. Sickle Cell Disease. Lancet 2017 S0140-6736(17)30193-9.
7. Sickle Cell Disease in Childhood 'Standards and Guidelines for Clinical Care'. 2nd edition. October 2010 (NHS Screening Programmes).
8. Sickle cell disease: acute painful episode overview. Nice Guidelines (2016/2017).
9. Standards for the Clinical Care of Adults with Sickle Cell Disease. 2008.
10. Standards for the Clinical Care of Children and Adults with Thalassaemia in the UK 3rd Edition, 2016. UK Thalassaemia Society.
11. STSTN South Thames Sickle and Thalassaemia network. Guidelines, policies, and leaflets created by Network. website http://www.ststn.co.uk/
12. The NHS Sickle Cell and Thalassaemia Screening Programme. https://www.gov.uk/topic/populatoipn-screening-programmes/sickle-cell-thalassaemia
13. Thalassaemia International Federation (TIF) Guidelines http://www.thalassaemia.org.cy
14. Transcranial Doppler Scanning for Children with Sickle Cell Disease - Standards and Guidance, second edition. September 2016.
15. Guidelines on red cell transfusion in sickle cell disease. Part I: principles and laboratory aspects. Bernard A. Davis, Shubha Allard, Kate Ryan et al on behalf of the British Committee for Standards in Haematology. 7 November 2016.
16. Guidelines on red cell transfusion in sickle cell disease Part II: indications for transfusion. Bernard A. Davis, Kate Ryan et al, on behalf of the British Society for Haematology. 18 November 2016
17. Vichinsky E. Consensus document for transfusion-related iron overload. Semin Hematol 2001;38:2-4

    http://www.b-s-h.org.uk/media/2640/transfusion_scd_01178_part_ii-1.pdf.
18. Learning Outcomes and Competencies in conjunction with the RCN Competencies, NHS Screening Programmes for Sickle Cell and Thalassaemia. Streetly, Tangayi and Anionwu. 2011

Adult Haemoglobinopathy workbook

1. Where can you find Sickle Cell and Thalassaemia policies?

2. Where is a patient's individual care plan?

Admission

3. What blood tests should be taken on acute admission?

4. What complications should be considered when a patient presents with oxygen saturations of less than 94%?

5. What should you consider when admitting a patient with a painful veno-occlusive episode (painful sickle cell crisis)?

Discharging a patient

6. What should you ensure is in place when a patient is discharged (from day care or inpatient ward)?

Vital Signs and observations

On admission:

7. How often should vital signs been taken on admission?

8. When can the time between recording vital signs be extended?

9. What should you do if a patient appears to have opiate overdose?

10. When monitoring oxygen saturations, ideally this should be....

Pain scoring:

11) How often should you score a patient's pain?

12) What should you do if a pain score of 5 or above is reported by the patient?

13) Patient controlled analgesia (if available):

What are the current trust guidelines for the monitoring of patients using PCA?

14) What is the current recommendation on administering parental opiates alongside a PCA?

Recognising the deteriorating patient:

15) Which of the following would prompt you to escalate a deteriorating patient, including urgently contacting the red cell team?

Blood Transfusion

16) If an unknown patient attends hospital with severe anaemia, and a transfusion planned, what additional information should be obtained regarding transfusion history?

17) If an individual is known to have antibodies you should.....

18) What actions should you take if you suspect a red cell transfusion reaction?

Blood transfusion in Sickle Cell Disease:
Consideration of sickle cell patients for transfusion, particularly long-term regimens, should weigh up the potential benefits against potential risks.

Cerebrovascular disease
Regular transfusion to maintain HbS <30% should be offered as initial treatment to children with SS or S/β^o thalassaemia aged 2–16 years judged to be at high risk for a first stroke on the basis of Transcranial Doppler ultrasonography (TCD).

Hydroxycarbamide treatment should be considered for the primary prevention of stroke in children with sickle cell anaemia and high TCD velocities but not severe Magnetic Resonance Angiography (MRA)-defined cerebral vasculopathy after an initial period of transfusions. The duration of the initial period of transfusion should be tailored to the individual patient but should be for a minimum of 1year; the transition to hydroxycarbamide should be done gradually and transfusion should be withdrawn after the hydroxycarbamide has been escalated to the maximum tolerated dose.

Regular transfusion to maintain HbS <30% effectively reduces the incidence of recurrence of cerebral infarction (defined as a stroke or a new or enlarged silent cerebral infarct) in children with sickle cell anaemia and S/β^o thalassaemia aged 5–15years. Treatment options including transfusion should be discussed with families of children who are found to have silent cerebral infarcts. Transfusion should be offered to children who are identified to be at greatest risk for recurrence of infarction after discussion of its benefits and risks.

Long-term transfusion to maintain HbS <30% is recommended for the prevention of recurrent ischaemic stroke due to sickle cell disease in both children and adults.
Adults or children who present with signs or symptoms suggestive of acute ischaemic stroke should be transfused without any delay to maintain HbS <30% pending further investigation. Those with confirmed stroke due to sickle cell disease should continue regular transfusions long-term.

Surgery
Preoperative transfusion is recommended for sickle cell disease (HbSS and HbSC) patients undergoing medium-risk surgery (e.g. abdominal, tonsillectomy, orthopaedic).
Transfusion is recommended for sickle cell patients of all genotypes requiring high-risk surgery (e.g. cardiovascular, brain).
All sickle cell patients with other genotypes undergoing surgery should be individually assessed, taking into account previous history and complexity of surgery, and a management plan should be formulated to include the need for transfusion.
Particular care should be taken to ensure that all aspects of perioperative care, including oxygenation, hydration, warmth and anaesthetic and surgical technique, are optimised in all sickle cell patients undergoing surgery.
For patients requiring emergency surgery, the urgency and complexity of the procedure should be taken into account in the timing of perioperative transfusion. Simple transfusion should be given preoperatively if Hb <90g/l provided this will not result in undue delay to surgery. If transfusion is likely to cause an unacceptable delay to surgery, it is reasonable to proceed to surgery while arranging to transfuse the patient intra- or post-operatively if necessary.

Acutely ill patients
Transfusion is recommended and may be life-saving in acute sickle complications such as splenic sequestration, hepatic sequestration, aplastic crisis and severe acute chest syndrome.
Transfusion should be considered in the unwell patient with acute multi-organ failure, mesenteric syndrome and patients with severe sepsis. Such cases should be discussed with the specialist haemoglobinopathy team (SHT).

Transfusion for other causes of acute anaemia requires individual assessment and should be discussed with the SHT. Transfusion may be given by simple transfusion (top up) or exchange depending on clinical severity under the guidance of the SHT.

Pregnancy

Prophylactic transfusion is not routinely required for sickle pregnancy, but should be considered for women with:

- previous or current medical, obstetric or fetal problems related to SCD
- women previously on hydroxycarbamide because of severe disease
- multiple pregnancy.

Women on long-term transfusions for stroke prevention or for amelioration of severe sickle complications should continue with regular transfusions throughout pregnancy.
Transfusion should be considered in women with worsening anaemia or those with acute SCD complications (acute chest syndrome, stroke etc.).

Amelioration of severe disease

In selected patients with severe disease, blood transfusion can be effective in ameliorating disease, resulting in reduction in hospital bed days. Hydroxycarbamide is recommended as first line treatment for prevention of recurrent acute chest syndrome or repeated painful episodes associated with chest syndrome. Regular transfusion should be considered for patients failing this treatment or for whom hydroxycarbamide is contraindicated or not acceptable.

Other indications

- Transfusion is not recommended to treat steady state anaemia provided that Hb has not fallen over a period of time to symptomatic levels (e.g. with developing chronic kidney disease).
- There is no evidence that transfusion shortens the duration of a painful crisis.
- Transfusion is not recommended in uncomplicated painful crises but should be considered if there is a substantial drop in Hb from baseline (e.g. >20 g/l or to Hb <50 g/l), haemodynamic compromise or concern about impending critical organ complications.
- The benefit of transfusion to relieve established acute priapism has not been shown in randomised controlled trials. Many patients require a shunt or drainage procedure under general anaesthesia, which may require a transfusion. Such cases should be discussed with the SHT.
- Transfusion has been shown to reduce the incidence of symptomatic avascular necrosis in children receiving regular transfusions to maintain HbS <30% for prevention of recurrence of cerebral infarction. However, there is no consensus on the use of transfusion for the sole purpose of preventing this complication in routine practice.
- Where transfusion is considered for indications where there is insufficient evidence for its benefit (e.g. leg ulcers, pulmonary hypertension, end stage renal or liver disease, progressive sickle cell retinopathy), a full risk-benefit assessment should be carried out in liaison with the SHT and each case should be considered on its own merits.

Investigation of a haemolytic transfusion reaction:

1) Document evidence of haemolysis.
Check haemoglobin concentration and review blood film

Check bilirubin, lactate dehydrogenase and reticulocyte count

Check urine for haemoglobinuria and if positive and hyperhaemolysis suspected, consider serial high performance liquid chromatography analysis of the urine

(2) Serological testing on pre-transfusion and post-transfusion blood samples.
Repeat ABO/Rh D typing

Check antibody screen on both samples

Red cell units transfused within 12–24 h should be crossmatched against both the pre- and post-reaction samples

Check the direct antiglobulin test (DAT). A positive DAT may be encountered as part of an investigation

(3) If antibody screen positive
Determine the specificity of the antibody (ies) – (antibody investigations may demonstrate a new alloantibody or antibodies in a patient with a delayed haemolytic transfusion reaction)

If the specificity of the red cell antibody is not clearly determined the sample should be sent to a red cell reference laboratory

(4) If DAT positive
Prepare an eluate to test for the presence of specific alloantibodies

Even if no new red cell alloantibody is detected in post-transfusion sample as above, but DAT is positive, red cell eluate studies should be undertaken

(5) Selection of red cell units for further transfusion
Carefully consider the need for further transfusion with consultant input and discussion with the National Blood Service if complex transfusion requirements

Select ABO extended Rh and K matched units negative for the relevant antigen(s) to which there are current or historical antibodies

Undertake serological crossmatch to check compatibility; **electronic issue should not be used**
If the identity of the new alloantibody is in doubt despite further specialist testing, consider providing extended antigen matched blood (if serological phenotyping cannot be used because of the presence of transfused donor red blood cells, the sample should be sent to an appropriate reference laboratory for molecular red cell genotyping)

Any adverse events or reactions related to transfusion should be appropriately investigated and reported to local risk management systems and to National Haemovigilance Schemes (e.g. Serious Hazards Of Transfusion – SHOT).

19) What are the current national and trust requirements regarding monitoring of vital signs when receiving blood products?

20) Give at least two reasons why you would give a blood transfusion to a patient with sickle cell disease.

Red Cell Exchange:

21) What blood tests are needed prior to red cell exchange transfusion?

Chronically transfused SCD patients should be regularly monitored for iron overload with serum **ferritin at least every 3 months**; liver iron measurements (Liver MRI or Ferriscan) should be performed every 1–2 years for those with suspected or proven iron overload. Intermittently transfused patients should also be monitored for iron overload as part of their routine care.

Virology testing [hepatitis B, hepatitis C and human immunodeficiency virus (HIV)] should be undertaken at presentation and hepatitis B vaccination should be given to all patients with SCD irrespective of previous or prospective planned transfusions. SCD patients on regular transfusions should be screened annually for hepatitis B, hepatitis C and HIV.

22) What blood tests are needed after a red blood cell exchange transfusion?

23) What blood is required during an exchange?

Blood provided for SCD patients should be:
HbS negative and, where possible, should be <7 days old for exchange transfusion (<10 days old for simple transfusion), but older blood may be given if the presence of red cell antibodies makes the provision of blood difficult

Blood should also be ABO-compatible, extended Rh- and Kell-matched units. If there are clinically significant red cell antibodies (current or historical) then the red cells selected should be negative for the corresponding antigens.

Transfusion to HbS <30% will prevent or reverse most acute sickle complications and significantly reduce long-term complications in chronically transfused patients. Baseline Hb and % HbS should be taken into consideration in setting target post-transfusion Hb in order to avoid **hyperviscosity**. In SCD patients with baseline Hb <90 g/l and not on regular transfusions, the **post-transfusion Hb should not exceed 100 g/l, particularly if %HbS is greater than 30%**. The post-transfusion Hb can be set at a higher target in chronically transfused patients or if %HbS is low, but should be individualised to each patient. Patients with high baseline Hb (>100 g/l) should not be transfused above their steady state Hb

24) Where can the proforma for manual red cell exchange be found?

All hospitals that are likely to admit SCD patients should have staff trained in manual exchange procedures and clearly identified manual exchange protocols, as this can be lifesaving in emergency situations.

Automated exchange transfusion should be available at all specialist centres and all patients with SCD should have access to it.

25) What additional information is needed prior to an automated exchange?

All patients with SCD should carry a transfusion card indicating they have ‘special requirement’ and, in particular, information as to whether they have formed a red cell antibody.

Central Venous Access

26) Which type of port may some sickle cell patients have in situ for apheresis purposes?

27) Who can access these ports?

28) How long should a vascath stay in after insertion?

Iron Overload

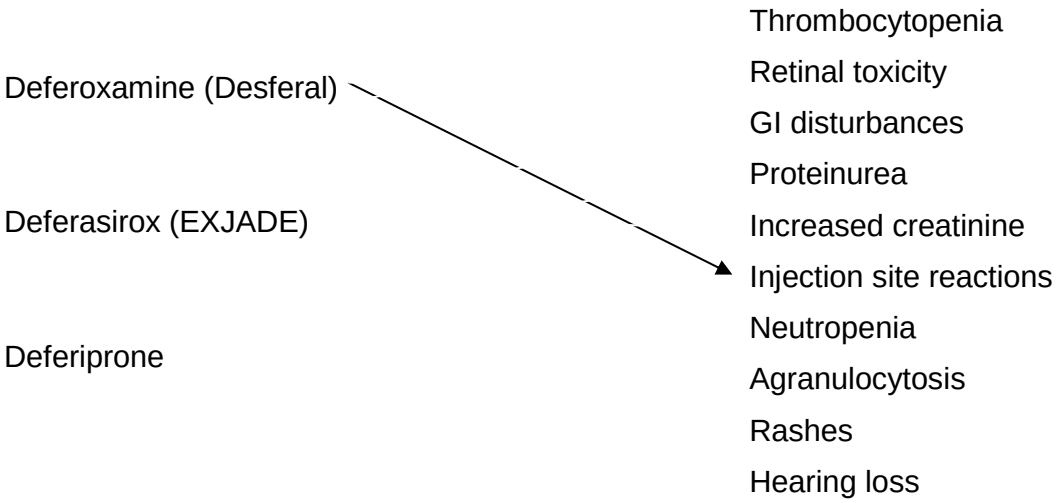
29) Untreated iron overload can lead to (name 3):-

a)

b)

c)

30) The following chelating agents relate to which side effects?



Long term management of sickle cell disease

31) Which of the following may alleviate long term complications of sickle cell?

a) Hydroxycarbamide
b) Red cell exchange transfusions
c) Allogeneic bone marrow transplantation
d) Erythropoietin

Pain Management

32) How quickly should a person with sickle cell be provided with analgesia once booking in to the hospital (including Emergency Department, Day Care and inpatient wards)?

33) What opiate should NOT be given to individuals with sickle cell disease?

34) What medications should be prescribed/ offered to patients receiving opiates?

35) Briefly define acute and chronic pain.

36) What non-pharmalogical treatments could be offered to an individual during a sickle cell crisis?

Management of sickle cell crisis:

37) What can prevent/ treat the following sickle cell crises?

Give as many answers as possible.

a) Acute Chest Syndrome

Prevention	Treatment

b) Priapism

Prevention	Treatment

c) Sickle cell painful vaso-occlusive

Prevention	Treatment

c) Leg Ulceration

Prevention	Treatment

d) Renal Disease

Prevention	Treatment

e) Sickle stroke

Prevention	Treatment

<u>Perioperative</u>

38) Before any planned surgical procedure, an individual with sickle cell should:

Pre-operative outpatient review with a haematology consultant with a specialist interest in haemoglobinopathies for peri-operative planning will include documented decisions about:

- Red cell transfusion (Exchange transfusion or top up to Hb of 10g/l) with blood fully matched for ABO, full-Rhesus phenotype (Cc/D/Ee), and K1 antigen, plus any other red cell allo-antigens present.
- Pain relief
- Hydration/fluid balance
- Oxygenation (including hyperoxygenation at induction of anaesthesia and careful monitoring of peri-operative oxygenation by pulse oximetry), incentive spirometry, chest physiotherapy, and consideration of prophylactic CPAP for 24 hours particularly post major abdominal and thoracic surgery
- Prophylactic antibiotics and infection screening and early management of any post-operative infections (hyposplenism)
- Thromboprophylaxis
- Temperature regulation (including consideration of warm air blankets, warmed IV fluids and adjustment of temperature in theatre)
- Avoidance of tourniquets and red cell salvage (neither suitable in sickle patients)
- Discharge planning and follow up.

39) What is the current national recommendation on prophylactic antibiotics in individuals with sickle cell and those without a functioning spleen?

National guidelines recommend the following:

- All routine vaccines, including live vaccines such as measles, mumps and rubella (MMR) can be given safely to children or adults with an absent or dysfunctional spleen.
- Asplenia or hyposplenism is not a contra-indication for live vaccinations prior to travel (eg, yellow fever and live oral typhoid vaccine).
- Re-immunisation with Pneumovax of hyposplenic/asplenic patients is currently recommended every five years. Re-immunisation in these patients may be made on the basis of antibody levels.
- Influenza vaccination - annual influenza vaccination is recommended after 6 months of age.

Lifelong prophylactic antibiotics

These are recommended in patients at high risk of pneumococcal infections and the antibiotics of choice are oral phenoxymethylpenicillin or macrolides. Patients developing infection, despite measures, must be given systemic antibiotics and admitted urgently to hospital.

- Risk factors for high risk in hyposplenism include:
    - Age <16 years or >50 years.
    - Poor response to pneumococcal vaccination.
    - Previous invasive pneumococcal illness.
- Use phenoxymethylpenicillin (adult 250-500 mg bd - although 500 mg od may be more realistic if compliance is a particular problem), amoxicillin (adult 250-500 mg daily), erythromycin (adult 250-500 mg daily) orally.
- Consider recommending that the patient take a full therapeutic dose of antibiotics if they develop infective symptoms such as pyrexia, malaise, shivering, etc and that they seek medical advice immediately.
- Allowing patients to have a reserve supply of antibiotics at home or on holiday may also seem appropriate.
- If not deemed to be high-risk then the pros and cons of taking lifelong antibiotic prophylaxis need to be discussed with each individual patient.

The British Committee for Standards in Haematology recommends the following:

- Patients should be given written information and carry a card to alert health professionals to the risk of overwhelming infection. Patients should wear an alert bracelet or pendant.
- Patients should be aware of the potential risks of overseas travel, particularly with regard to malaria and unusual infections - e.g., those resulting from animal bites.
- Patient records should be clearly labelled to indicate the underlying risk of infection. Vaccination and re-vaccination status should be clearly and adequately documented.

40) Where can you find the haemoglobinopathy antibiotic guideline?

<u>Thalassaemia</u>

41) How can you identify a patient's pre-transfusion trough haemoglobin level?

42) Name at least three co-morbidities or conditions associated with thalassaemia.

43) What blood tests should individuals with thalassaemia have prior to every transfusion?

44) Details of special blood transfusion requirements can be found.....

45) In thalassaemia patients who are red cell transfusion dependent and iron overloaded, on chelation, urine should be tested monthly for:

46) What annual tests should Thalassaemia patients receiving blood transfusions have?

47) What is the only medicine currently licenced in the UK and Europe for the prevention of prevention of recurrent painful episodes in SCD patients?

Hydroxycarbamide (HU) BSH Guideline in progress 2017

Who should be offered HU?

- Infants 9-42 months
  - offer Rx regardless of clinical severity
- Children > 42 months, adolescents and adults
  - consider Rx regardless of clinical severity
- Recurrent acute pain
  - >3 moderate to severe pain episodes in 12/12
  - SCD pain that interferes with daily activities and QOL
- Severe =/- recurrent acute chest syndrome
- Children with abnormal TCD
  - Offered after 1 year of blood transfusion
  - Children with conditional risk TCD velocities (MTD)
- Second line Rx for children & adults with ischaemic stroke Hx

Also consider HU in:

- Sickle nephropathy with persisting proteinuria despite ACE1/ARB therapy
- Pulmonary hypertension or chronic hypoxia
- Symptomatic chronic anaemia interfering with daily activities or QOL
- Discuss possible benefits of HU in prevention and treatment of other chronic disease complications

Hydroxycarbamide improves quality and length of life in SCD

- Reduces morbidity and mortality
  - Reduces need for blood transfusion, number and severity of painful episodes, stroke, lung damage and chest syndrome
- Well tolerated
  - No significant short-term toxicities or long-term safety concerns
  - No evidence for leukaemogenesis or MDS
  - Mild GI symptoms, darkening of skin and nails (dose dependent)
- "Disease-modifying therapy for all SCA patients regardless of age or clinical severity" Ware et al 2011

Baseline investigations prior to commencing hydroxycarbamide:
FBC and reticulocytes, HbF%, Renal function, Liver function including ALT

Recommended Dose
Therapeutic dose: 15-35 mg/kg daily
Starting dose: 15-20mg/kg daily, unless increased risk of myelosuppression, or in renal or liver dysfunction, when lower starting doses should be used.

Increase dose by 5mg/kg every 1-3 months until evidence of clinical benefit.
Lowest effective dose as assessed by clinical improvement is often used.
For some indications, e.g. cerebrovascular disease, dose should be increased until limited by myelosuppression (maximum tolerated dose).

Monitoring of Patients
FBC, reticulocytes, renal and liver function should be checked 2 weeks after starting.
FBC, reticulocytes, HbF%, renal and liver function should be checked every 1-3months during maintenance treatment (when no dose change has been made).

If the dose is increased, blood tests should be performed after two weeks on the higher dose, before resuming 1-3 monthly monitoring.

Stop hydroxycarbamide if toxicity occurs – contact patient with instructions to stop treatment and arrange further blood tests at approximately 7 days to monitor recovery.

Markers of toxicity (exact parameter cut off values may alter in the final published version due end 2017):

Neutrophils < 1.25 $x10^9$/l
Platelets < 80 $x10^9$/l
Reticulocytes < 80 $x10^9$/l
> 50% or more increase in serum creatinine
> 100% increase in ALT

Parents should be advised to attend hospital for assessment and urgent blood count if they develop symptoms suggestive of sepsis, or unusual bruising or bleeding, because of the possible risk of bone marrow suppression.

For a copy of the answer book all Practice Development Nurses can email Eleanor Baggley: 0203 299 5102 / Eleanor.baggley@nhs.net / info@ststn.co.uk/ www.ststn.co.uk

Or Giselle Padmore-Payne 0203 299 1424 / Giselle.Padmore-Payne@nhs.net

Thank you

Please note: The RCN **cannot confirm competence of any practitioner**