East of England
Children's Cancer and Leukaemia

EAST OF ENGLAND SUPPORTIVE CARE GUIDELINES

PAEDIATRIC HAEMATOLOGY AND ONCOLOGY SHARED CARE

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1 Contents

2 Background & Scope

This document has been developed in order to clarify the supportive care management of children with cancer. This guidance applies to all children whose PTC is CUHFT / Addenbrooke's. In this context **children and young people (CYP) are those patients aged 0 until their 16th birthday. The chapters within the guideline mirror the corresponding Addenbrooke's guidelines to ensure alignment between documents from within the PTC and around the region. They have been amended where needed for clarification between roles in POSCU and PTC.**

This guidance is intended for use by the following groups across the region:

- Clinicians within the East of England Paediatric Oncology Shared Care Units (POSCUs)
- Clinicians within the East of England Principal Treatment Centre (PTC) for Paediatric Haematology/Oncology (Addenbrooke's Hospital).

3 Referral guidance

This referral guidance is intended to summarise the pathway between POSCU and PTC (Addenbrooke's Hospital). Referral guidance for GP will follow NICE and CCLG guidance: https://www.cclg.org.uk/Referral-guidance

3.1 New patients presenting in primary care, Emergency Departments or outside of paediatrics

Children or young people who present with symptoms and signs suggestive of cancer to Primary care in the CUFT (Addenbrooke's) geographical area should be referred to the Addenbrooke's Acute Paediatric Consultant (Consultant of the week).

Those who present from primary care in a POSCU geographical area should be referred to a local paediatrician at their local hospital. The Paediatric Haematology Oncology consultant on call at Addenbrooke's is available for advice if needed.

Once a child has been reviewed in a POSCU if the clinical suspicion is high and the child needs further investigation the Paediatric Oncology team on call should be contacted; either the Oncology registrar phone (09:00-17:00) **07523 943717** or the Paediatric Oncology or Paediatric Haematology consultant on call (via Addenbrooke's switchboard). This should be done by calling the main hospital switchboard and asking for the on-call paediatric Oncologist/Haematologist.

(Please see Appendix 1 for the East of England agreed pathway for paediatric cancer patients. ***Please note*** as highlighted in the pathway, Primary Care Practitioners may use the 2 Week Wait (2WW) route to refer paediatric patients to their local hospital; however, it is preferable for the GP to **phone** their local hospital or Addenbrooke's as stated above).

If malignancy is suspected or considered, a request made by telephone or email for urgent paediatric assessment within 24 hours would be expected.

When making a referral, inform the parents and child or young person about the reason for referral and which service they are going to attend so that they know what to do and what will happen next. Establish good communication in order to develop the supportive relationship that will be needed if cancer is found.

3.2 New patients presenting in their local paediatric department

For **all** suspected paediatric malignancies the local paediatrician should contact the Paediatric Oncology registrar on **07523 943717** or the on-call Paediatric Oncology or Haematology Consultant at Addenbrooke's Hospital (via the hospital switchboard). When the referral is made, the following points should be noted:

- Children who are acutely unwell, particularly those with suspected leukaemia or brain tumours may need urgent intervention and should be admitted as an emergency.
- Children who are not acutely ill but have a suspicious 'lump' may be seen in the next appropriate clinic.
- For children with brain tumours or suspected spinal cord compression – please contact the Addenbrooke's neurosurgeons in the first instance; it is helpful for the paediatric oncology team to be made aware too (although they will hear

from the neurosurgeons in due course). If POSCU teams are having trouble contacting the neurosurgical team, then the paediatric oncology team can help make contact with the Paediatric Neurosurgeons. Please note **if** Dexamethasone is started for raised intracranial pressure before transfer the dose is 125mcg/kg/dose qds rounded up to the nearest dose – **MAX dose 4mg qds.**

- For any child who may need an intensive care (PICU) bed, e.g. with a mediastinal mass or pleural effusion – please contact the Addenbrooke's Paediatric Haematology/Oncology team first and **they** will liaise with PICU in the first instance. Local team also need to contact PANDR.
- Non-malignant haematology referrals (e.g. coagulation or blood transfusion enquiries) should in the first instance go to the Paediatric Haematology registrar via switchboard during normal working hours or the Adult Haematology registrar on call via switchboard out of hours (alternatively the Paediatric Haematology or Oncology consultant on call).
- Children with suspected malignancy should not have biopsies performed in POSCU setting.

The Oncology registrar can be reached on the mobile phone on 07523 943717 09:00-17:00 (or via secure chat via switchboard out of hours). The out-of-hours registrar may not be from a Haem/Onc background so, if possible, non-urgent cases should be discussed within hours. Any difficulty reaching the Oncology Registrar should be escalated to the Haem/Onc Consultant on call via switchboard.

4 Initial Assessment

Full initial assessment of new patients will all take place at Addenbrooke's Hospital. This will include full history, examination and investigations. In patients with suspected acute leukaemia, it may be appropriate for some of the steps below to be taken in the POSCU. This will **always be in discussion with the On-Call Consultant from Addenbrooke's**. This may include chest x-ray, transfusion (with appropriate blood samples taken first as listed), commencement of hyperhydration (0.45% NaCl 2.5% dextrose at 2.5 or 3l/m²/day, no added potassium) and management of infection and pain.

4.1 Recording a patient's history

This should include:

- A detailed history of the presenting complaint
- Birth history & PMH
- Immunisation
- History of previous chickenpox or measles infections or recent contact
- Family tree with names and ages of parents and siblings
- Family history of malignancy: ask specifically about grandparents – remember that statistically, 1 in 4 grandparents will have some kind of cancer

4.2 Initial examination

- Record height and weight in growth chart
- Measure any palpable masses or enlarged organs (liver, spleen etc.) and record size in notes
- Check all lymph node stations (neck, axillae, inguinal regions)
- Don't forget to look at the buttocks if there is a history of hip or pelvic pain or any leg oedema
- Remember to examine testes in boys with suspected leukaemia

4.3 Investigations

- FBC and film, Coagulation screen, Group and Save
- U+E, Bone profile, LFT, Uric acid, CRP, Immunoglobulins, LDH.
- AFP and HCG if primary liver tumour or germ cell tumour are possible diagnosis (liver, pelvic, testicular, buttock/sacral, mediastinal, midline intracranial)
- Blood culture if febrile
- Before transfusion: Measles, VZV, HSV, CMV ('Paediatric Oncology screen')
- Urine catecholamines in abdominal tumours.

Suspected ALL: Thiopurine methyl transferase assay and genotype. The Genotype is now used for the primary decision point, although TPMT levels will still be performed on the same sample. Therefore the need to take a pre-transfusion sample has now gone.

Chest X-Ray: Should be arranged prior to anaesthetic in patients with suspected leukaemia (to rule out mediastinal mass)

4.4 Initial Emergency Treatment

4.4.1 Analgesia

- If the child is in pain, give adequate analgesia

4.4.2 Infection

- If the child is febrile, assume this is infection rather than disease
- If the child is neutropenic, **or if there is bone marrow involvement** (suggested by pancytopenia or blasts in the peripheral blood), treat as neutropenic fever even if the child is not neutropenic

4.4.3 Blood products

- Transfuse with blood if Hb<7 or platelets<10 if well, <20 if febrile or unwell **(see caution bullet point below)**
- **Do not give steroids** for platelet reactions etc. to children with ALL or NHL before starting treatment, as this may precipitate tumour lysis

- For platelet reactions give Chlorphenamine (Piriton) + Paracetamol; do not give hydrocortisone

- **Caution: in high count ALL, transfusion with packed cells may precipitate hyperviscosity – discuss with PTC consultant before transfusing**
- For type of blood product required and further advice around transfusion please see transfusion guideline

4.4.4 Tumour lysis prevention

- In ALL and NHL, institute tumour lysis prevention measures (see tumour lysis guideline) – transfuse first if necessary
- In very high count disease, tumour lysis may occur before treatment starts. Start monitoring as per guideline.

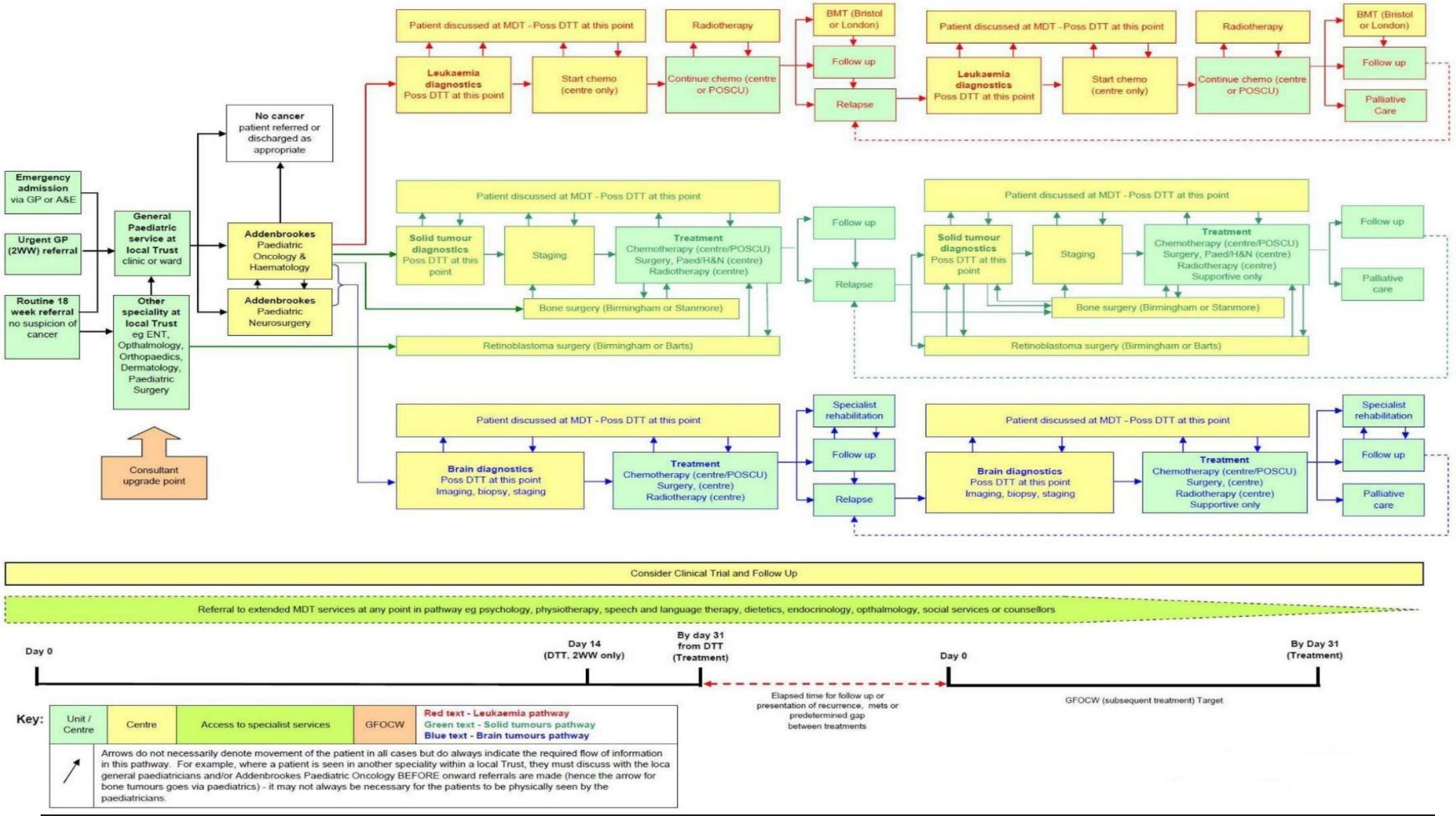
4.5 Staging

All staging investigations, which will vary according to primary tumour type and site, take place at the Addenbrooke's PTC. Any exceptions to this will be arranged between the responsible consultants at the PTC and POSCU. This may include scans that have been performed for other reasons at the POSCU, before the diagnosis of malignancy was suspected and these scans will therefore be reported by the paediatric radiologists at Addenbrooke's and discussed at one of the diagnostic MDT meetings.

The PTC is responsible for communicating the investigation results and treatment plan to the POSCU as agreed in the Paediatric Oncology Shared Care Agreement.

Appendix 1:

Guidelines for the Referral, Initial Assessment and Staging of Children and Young People with Suspected Cancer



5 Management of Fever in Immunocompromised children

Infections in immunocompromised patients can be life-threatening; if in doubt or if dealing with a sick child, contact the consultant on call.

Please let the Addenbrooke's team know within 24 hours when any Oncology or Haematology patient is admitted.

This guideline delineates the management of paediatric patients currently, or recently undergoing systemic anti-cancer treatment or are immunocompromised who have a fever or sepsis, irrespective of neutrophil count. It is based on CCLG guidance. CUHFT guidance reference CSO/N010.

The flow sheet in Appendix 1 will assist in guiding initial management. Other appendices contains additional documents to aid use of the guideline such as patient information leaflet and suggested documentation templates.

5.1 Immunocompromised paediatric patient:

- Any paediatric haematology/oncology patient on active Systemic Anti-Cancer Therapy (SACT), immunosuppressive therapy or who has ceased treatment within the last 3 months.
- Recipients of Haematopoietic Stem Cell Transplant (HSCT) in the last 12 months or on active immunosuppressive therapy post HSCT.
- Paediatric patients with aplastic anaemia or chronic neutropenia.
- Paediatric patients with suspected leukaemia.

Neutropenia is defined as absolute neutrophil count (ANC) <0.5 x 10^9/L

Fever is defined as a single temperature ≥38˚C

5.2 Definitions

ALL	Acute Lymphoblastic Leukaemia
AML	Acute Myeloid Leukaemia
ANC	Absolute Neutrophil Count
AUS	Australia-UK-Swiss rule / scoring system
BMA	Bone marrow aspirate
CCLG	Children's Cancer and Leukaemia Group
CCN	East of England Children's Cancer Network
CMV	Cytomegalovirus
CRP	C-reactive protein blood test
CT	Computerised Tomography
CUH	Cambridge University Hospitals NHS Foundation Trust
CVAD	Central Venous Access Device
CXR	Chest x-ray
CYP	Child and Young Person / Children and Young People

ESBL	Extended spectrum beta lactamase
HSCT	Haematopoietic stem cell transplant. Includes allogeneic (bone marrow, cord blood or peripheral blood) transplant and autologous transplant / stem cell rescue
HSV	Herpes Simplex Virus
IV	Intravenous
LCH	Langerhans Cell Histiocytosis
LFTs	Liver function tests
NG	Nasogastric
NICE	National Institute for Health and Clinical Excellence
PDU	Paediatric Day Unit
PEG	Percutaneous Enteral Gastrostomy
Ph+ ALL	Philadelphia Positive Acute Lymphoblastic Leukaemia
PHE	Public Health England
POSCU	Paediatric Oncology Shared Care Units
SACT	Systemic Anti-Cancer Therapy
US	Ultrasound
VRE	Vancomycin resistant enterococcus
VZV	Varicella Zoster Virus
VZIG	Varicella Zoster Immunoglobulin

5.3 Introduction

Sepsis is the leading cause of non-cancer related death in children currently or recently undergoing cancer treatment. Therefore, a fever and/or sepsis in these patients is considered to be a medical emergency which needs to be managed with assessment in hospital with the prompt administration of empiric broad spectrum IV antibiotics **within one hour of presentation**.

Treatment of febrile neutropenic children until recently has been uniform with IV antibiotics and hospital admission for a minimum of 48 hours. Extensive research into the use of risk stratification tools in this specific clinical context has shown that some children with neutropenic fever are at very low risk of severe sepsis and can therefore be managed as outpatients, i.e. treated with oral antibiotics whilst being closely monitored remotely. The use of such a tool has been adopted by the CCLG (CCLG Managing Febrile Neutropenia 2020 – proposed new management pathway v.1.01 April 2020, available on their COVID-19 resources page). This document details the application of this guideline to practise at CUH whilst taking into consideration the 2012 NICE guidelines for neutropenic sepsis.

Please discuss the admission and management of any child admitted to your POSCU with fever within 24 hours of admission (sooner if concerns arise). The Oncology registrar can be reached on the mobile phone on 07523 943717 09:00-17:00 (or via epic chat via switchboard out of hours). The out of hours registrar may not be from a Haem/Onc background so if possible non-urgent cases should be discussed within hours. Any difficulty reaching the Oncology Registrar should be escalated to the Haem/Onc Consultant on call via switchboard.

5.4 Initial management of all immunocompromised CYP patients

- Fever/sepsis is a medical emergency in the group of CYP as defined above.
- **Empiric IV antibiotics should be administered within 1 hour of presentation to hospital or development of fever whilst an inpatient, ideally immediately after blood cultures are obtained.**
- A full blood count should be taken but treatment with IV antibiotics should not be delayed whilst awaiting results
- Immunocompromised CYP who appear unwell should be treated with empiric IV antibiotics irrespective of body temperature or neutrophil count
- Where appropriate, paediatric sepsis guidelines and early warning scores and escalation should be utilised to support care delivery.

5.4.1 Initial investigations

Commence empiric IV antibiotics immediately after collection of blood cultures.

Do not wait for collection of other samples prior to commencing empiric antibiotics.

Blood cultures:

- CVAD in situ: 1 sample from each lumen (~5ml) into separate bottles and label bottles appropriately.
- No CVAD in situ: single peripheral blood culture only, not from existing IV cannula
- Do not routinely perform peripheral blood cultures in children who have CVAD in situ

Full blood count:
Do not wait for result before giving first dose of IV antibiotics.

Other blood tests:
If accessing line and not unduly delaying administration of IV antibiotics, consider taking electrolytes, liver function tests (LFTs), blood gas, etc. as clinically indicated.

Other investigations:
Check CRP as per local guidelines but this does not have impact on risk stratification

- **Consider additional investigations** to look for a possible source of infection (e.g., wound swab, urine culture, nasopharyngeal aspirate, throat swab, CXR, abdominal x-ray, stool culture, etc.)
- **Swab CVAD exit site** if any signs of exit site infection
- **COVID-19 swab if indicated** – any respiratory symptoms, vomiting/diarrhoea or other clinical suspicion
- **Consider opportunistic infections:** viral (CMV, HSV etc.), fungal, parasitic, bacterial (Pneumocystis)

- **Consider typhilitis** (neutropenic colitis) if severe diarrhoea/abdominal pain and/or right iliac fossa tenderness. Diagnosis by clinical and radiological correlation. Send blood cultures and stool culture for enteric pathogens including Clostridium difficile. Surgical review may be warranted.

Neutropenic CYP may not produce pus at sites of infection.

5.4.2 Initial treatment

IV antibiotics
The first dose of IV antibiotics should be administered **within 1 hour of presentation**.

- **First line single agent: Piperacillin-tazobactam (Tazocin)**
  - Dose: 90mg/kg 6 hourly (max dose 4.5g 6 hourly)
  - In cases of penicillin allergy or administration of high dose IV methotrexate 48 hours before, during or 48 hours post, or known/suspected colonisation with extended spectrum beta lactamase (ESBL) producers: use meropenem
  - Meropenem dose: 20mg/kg (max 2g) 8 hourly. Can be doubled to 40mg/kg (max 2g)
  - In case of penicillin anaphylaxis: use IV ciprofloxacin (dose as per BNFC for children is 10mg/kg)
- Unwell/clinically unstable children may require additional treatment with IV gentamicin as per paediatric antibiotic protocol
- Additional Staphylococcal antibiotic cover may be required (e.g. vancomycin or teicoplanin) if suspected skin/CVAD exit site infection. If administering vancomycin, monitor drug levels and renal function as per paediatric antibiotic protocol.
  - Teicoplanin dose for children >2months: 10mg/kg BD for 3 doses then 10mg/kg daily
- Vancomycin is still indicated as first line treatment in children with previous Vancomycin resistant enterococcus (VRE) colonisation

Other aspects

- CVAD removal may be indicated if CYP has an infected line or is shocked / septicaemic without another source of infection. This is performed by paediatric surgeons in consultation with haematology/oncology consultants.
- If there are mouth ulcers/lesions consistent with HSV or VZV infections, obtain viral swabs and start treatment with intravenous aciclovir (doses as per BNFC for treatment in immunosuppressed patients) following discussion with consultant haematologist/oncologist.
- Continue co-trimoxazole prophylaxis (this does not affect choice of IV antibiotics).
- Prophylactic oral ciprofloxacin should be paused whilst on IV antibiotics and resumed on completion of the febrile neutropenic episode.

- Antifungal prophylaxis should continue alongside IV antibiotics.
- For neutropenic or unwell CYP: stop maintenance therapy, e.g. 6-mercaptopurine and methotrexate, in consultation with senior doctor (and discussion with Addenbrooke's Haem/Onc if needed).

5.4.3 Known non-neutropenic CYP patients: ANC >1.0 x 10^9/L

- If clinically unwell, treat as per above guidelines.
- If clinically well, assess and treat possible source of infection (urinary, respiratory, otitis media, bronchiolitis, pneumonia, etc.).
- These children therefore may not need iv antibiotics or may have a shortened course. However in some cases, such as leukaemia patients in induction and new diagnoses of leukaemia the children should be treated as neutropenic even if their counts are above 1.0,
- Continue maintenance chemotherapy as per treatment protocol, based on ANC, in consultation with senior haematology/oncology doctor.

5.5 Subsequent management

Subsequent management will depend on the specific clinical context (see flow chart appendix 1). Clinically unwell CYP will require aggressive resuscitation with involvement of senior staff, notification of attending consultant paediatrician, and in some cases involvement of the paediatric intensive care team. These CYP will require admission, are considered high risk, and are not eligible for risk stratification upon recovery.

POSCU teams should discuss patients as needed (ideally daily) with the CUH team to provide updates and agree management and whether children need transfer to CUH.

CYP who are clinically well at presentation will be risk stratified using the AUS scoring system.

5.6 Risk stratification following initial management

This risk stratification is to be used for all CYP with ANC <1.0 x 10^9/L.

Risk stratification of febrile neutropenic children is based on 3 main factors:

1. Intensity of SACT / immunosuppressive treatment
2. White cell count (WCC)
3. Platelet count

5.6.1 Step 1: Allocate CYP a score based on AUS-rule criteria as outlined below

Variable	Yes	No
Preceding chemotherapy regimen more intensive than ALL maintenance*	1	0
Total white cell count <0.3 x 10^9/L	1	0
Platelet <50 x 10^9/L**	1	0
TOTAL AUS-RULE SCORE		

* includes ALL maintenance, LCH maintenance or weekly vinblastine alone (low grade glioma)

**This remains valid even for recently transfused CYP

5.6.2 Step 2: Determine risk of bacterial infection based on AUS-rule score

Score 0 = very low risk – Require minimum 4-8 hours observation in hospital
Score 1 = low risk – Require more than 4 but within 24 hour admission for observation (4-24 hours)
Score 2 = moderate risk – Require minimum 24 hours inpatient observation
Score 3 = higher risk – Require minimum 48 hours inpatient care
If CYP is clinically stable and fulfils all the safety-net criteria, then discharge home under parental care

5.6.3 Step 3: Determine eligibility for discharge at the stipulated time as per AUS-rule score ("Safety-net criteria")

When considering discharge for a CYP in any risk category as above, CYP must fulfil the following criteria (Appendix 2):

1. CYP reviewed by Paediatric or POSCU consultant to ensure they are safe for discharge.
2. Demonstrated ability to tolerate oral antibiotics (including via NG/PEG route) – tolerated one dose of oral antibiotics in hospital
    a. No vomiting/diarrhoea significant enough to reduce absorption
    b. No mucositis
3. Received appropriate education, home tympanic temperature chart and information leaflet about outpatient based management including contact details for the hospital/ward.
4. CYP socially safe to be at home:
    a. No known social services involvement,
    b. Parent/guardian able to take responsibility of child (check temperature, call hospital for advice and administer antibiotics).

5. Meet **all** of the following eligibility criteria for discharge home/parent-led care (see also appendix 2).

Criteria	**Eligible**	**Not eligible**
Clinical status: Review by consultant paediatrician - Clinically stable: normal observations (BP, HR, O_2 sats). - Fever is not a contraindication for discharge - Blood cultures negative or pending		
Disease status: responding to current therapy		
Low risk disease group: **NOT** any of – - ALL in induction - Infant ALL - AML - Ph+ ALL - Relapse protocol treatment - 'Rapid COJEC' treatment protocol - Post HSCT within 6 months or still on immunosuppression - Congenital immunodeficiency - Aplastic anaemia - Down syndrome - Early discharge not supported by clinical trial if enrolled *Alert to be placed in patient's POSCU folder*		
NO confirmed focus of infection requiring inpatient care e.g. - CVAD site infection (possible or confirmed) - Cellulitis - Perianal cellulitis/pain - Significant pneumonia (confirmed on CXR) - Multi-drug resistant organism previously isolated		
NO medical complication requiring inpatient care e.g. - Pain requiring IV analgesia - Requiring IV hydration *or* poor oral/enteral intake - Requiring oxygen *or* respiratory distress		
NO signs or symptoms of severe sepsis at presentation: - Altered conscious state - Inotrope requirement - Any fluid bolus requirement - Respiratory support requirement (high flow oxygen, non-invasive ventilation or intubation)		
Tolerated at least 1 dose of oral antibiotics in hospital (orally or via NG/PEG)		

Parent or caregiver available 24 hours a day		
CYP and carer adequately informed and educated on reportable symptoms and given temperature diary		
Availability of a telephone and tympanic thermometer		
Within 1 hour drive/travel of hospital		
NO previous history of non-compliance with medical care or current social care involvement		

Pending or positive COVID-19 swabs should not be a contraindication for early discharge if CYP meets all the above criteria.

5.7 Antibiotics for outpatient based management

5.7.1 Oral antibiotic regimen

- Ciprofloxacin: 20mg/kg twice daily; max dose 750mg (even for patients on prophylactic ciprofloxacin), ***and***
- Co-amoxiclav: if tablets: age appropriate dose as per BNF for Children
    - Neonate: 125/31 suspension - 0.25ml/kg 8 hourly
    - Child 1-11months: 125/31 suspension - 0.5ml/kg 8 hourly
    - Child 1-5 years: 125/31 suspension - 0.5ml/kg 8 hourly or 10ml 8 hourly
    - Child 6-11 years: 250/62 suspension - 0.3ml/kg 8 hourly or 10ml 8 hourly
    - Child 12-17 years: 500/125 tablet – 1 tablet 8 hourly
- If allergic to penicillin, use clarithromycin as per BNF for Children.

If above regimen is not suitable for CYP due to allergy or antimicrobial resistance, consider keeping CYP in hospital for IV therapy and/or discuss with local microbiologists for further advice.

If CYP was previously on prophylactic ciprofloxacin (10mg/kg twice daily) prior to this febrile neutropenic episode, this should be recommenced once the entire course of oral antibiotics has been completed.

5.7.2 Duration of antibiotic therapy

Home antibiotics should be provided for up to 5 days and daily phone assessment performed.

Oral antibiotics can be ceased when CYP is:

- Clinically well
- Has negative blood cultures

- Apyrexial >24 hours

If CYP does not meet all the above criteria after 5 days, the CYP should be clinically reviewed on day 5.

5.8 Follow up and outpatient care

- CYP require daily phone review by a senior paediatric haematology/oncology POSCU clinician or delegate until antibiotics have been ceased
- Parents/carers to check CYP's tympanic temperature every 4-6 hours during waking hours and record in diary sheet provided prior to discharge
- Check blood culture results: empiric antibiotics may need to be changed based on these results
- All reviews and readmissions to be discussed with the Paediatric POSCU Consultant on call and to be discussed with PTC if needed or if readmission occurs (discussions may occur the next day).

5.9 Paracetamol use

If temperature:

- <37˚C: can give paracetamol if required for pain
- 37-37.9˚C: withhold paracetamol and recheck temperature in an hour
- >38˚C: record temperature as a documented fever and then proceed with paracetamol dose if required

Ibuprofen should not be used.

5.10 Daily review checklist:

- Temperature diary: any temperatures ≥38˚C or <36˚C?
- New symptoms?
- Chills/rigors/shaking?
- Oral/enteral intake?
- Diarrhoea/vomiting?
- Pain?
- Check blood cultures

If any of the following criteria is met, **CYP should be reviewed in hospital:**

- Ongoing fever >72h from presentation or new fever after being afebrile for 24h
- Feeling unwell/onset of new symptoms
- Parental concern

- Significant decrease in oral/enteral intake or significant increase in output (vomiting and diarrhoea)
- Positive blood culture or new infection identified after discharge home
- Severe or persistent pain
- Chills/rigors/shaking
- Not afebrile by day 5 of outpatient care

If any of the following criteria met, **CYP should be readmitted to hospital:**

- Fever ≥38˚C beyond 5 days from the start of the febrile episode
- Clinically unwell/unstable
- Infection requiring inpatient care

On readmission to hospital:

- Restart broad spectrum IV antibiotics
- Stop oral co-amoxiclav and ciprofloxacin
- Consider fungal screen, as below, and addition of antifungal therapy
- Tailor antimicrobials as per blood cultures/source of infection if one is isolated

5.11 Inpatient management of ongoing febrile neutropenia

If CYP does not meet criteria for outpatient management of febrile neutropenia, continue inpatient care. CYP should have at least daily review by medical team during admission. The management of these children depends on the specific clinical situation and may include change or escalation of antibiotic treatment, further investigations to identify fungal infection, extended viral studies, administration of G-CSF and in extreme cases, buffy coat.

5.12 Blood cultures negative and apyrexial for 48 hours

Stop IV antibiotics if clinically well and no signs of sepsis. Restart prophylactic ciprofloxacin if child was on this prior to febrile neutropenic episode until ANC >0.5 x 10^9/L.

5.13 Blood cultures positive

Continue broad spectrum IV antibiotics until afebrile for 48 hours then rationalise as per microbiology. If ongoing fever, repeat blood cultures daily and consider need for additional anaerobic or antifungal cover.

5.14 Ongoing fever at 72h

- Continue discussions and may need transfer to CUH
- Repeat blood cultures daily at the time of fever

- Reassess for potential source of infection: clinically or radiologically as indicated and after discussion with consultant
- Consider changing to **2nd line antibiotics (meropenem)** after discussion with consultant haematologists/oncologists and microbiologists
- **Fungal screen:** CT chest, US abdomen (spleen, liver, kidneys), galactomannan and beta-D Glucan
- Add **antifungals (3mg/kg ambisome)** if persistent fever beyond 72h; should not be done 'after hours', always discuss with Addenbrooke's first. If on azole prophylaxis consider switching to ambisome
- If already on ambisome prophylaxis (2.5mg/kg twice weekly), increase to high dose ambisome (3mg/kg daily. Consider rounding to nearest 50mg or using alternate daily dosing where appropriate to save vials)
- Monitor renal function and electrolytes daily (especially potassium and magnesium) if also on vancomycin and check vancomycin levels as per general paediatric antibiotic policy
- Aggressive potassium replacement is warranted, consider IV route. Consider need for amiloride
- Stop prophylactic itraconazole
- Continue until afebrile and no microbiological or radiological evidence of fungal infection. There is no need to wait for ANC recovery
- Recommence prophylactic itraconazole/posaconazole/ambisome if previously on this

5.15 Presence of mucositis or peri-anal disease:

- Add IV metronidazole if not already on piperacillin-tazobactam or meropenem
- Consider adding aciclovir
- If abscess/fasciitis present, seek urgent surgical review

5.16 Presence of respiratory symptoms:

- Chest imaging with CXR initially, consider CT chest if ongoing fevers beyond 72h and suspicion of fungal/pneumocystis pneumonia
- Consider repeating COVID-19 swab if previously negative

5.17 References

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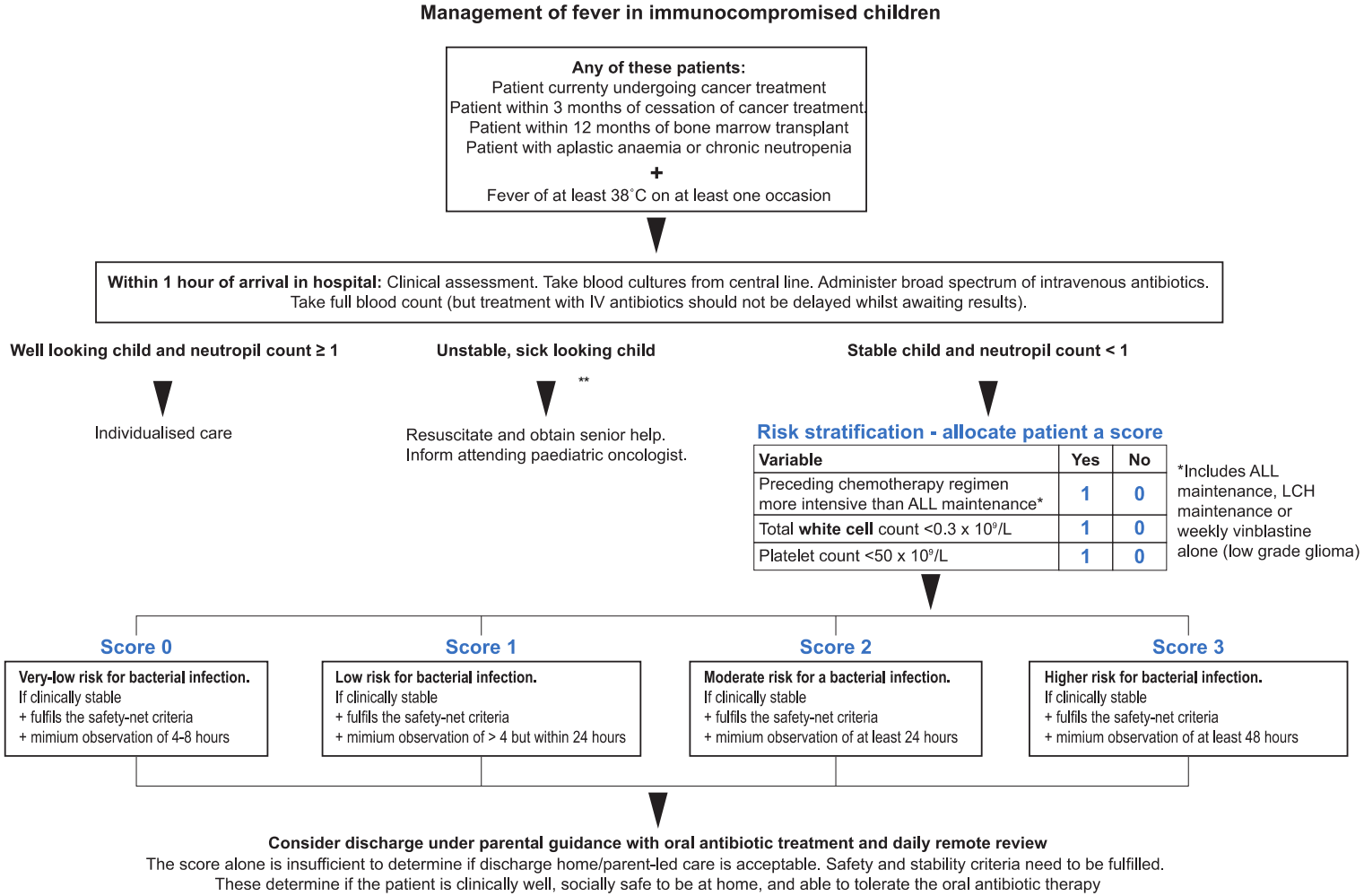
5.18 Appendices:

5.18.1 Appendix 1: Febrile neutropenia flow chart:



** For POSCU team inform attending Paediatric Consultant

5.18.2 Appendix 2: Discharge criteria table

Patients must meet **all** of the following criteria prior to discharge to ambulatory care:

Criteria	**Eligible**	**Not eligible**
Clinical status: Review by consultant paediatrician - Clinically stable: normal observations (HR, BP, pO2 sats) - Blood cultures negative or pending		
Disease status: responding to current therapy		
Low risk disease group: **NOT** any of – - ALL in induction - Infant ALL - AML - Ph+ ALL - Relapse protocol treatment - 'Rapid COJEC' treatment protocol - Post HSCT within 6 months or still on immunosuppression - Congenital immunodeficiency - Aplastic anaemia - Down syndrome - Early discharge not supported by clinical trial if enrolled		
NO confirmed focus of infection requiring inpatient care e.g. - CVAD site infection (possible or confirmed) - Cellulitis - Perianal cellulitis/pain - Significant pneumonia (confirmed on CXR) - Multi-drug resistant organism previously isolated		
NO medical complication requiring inpatient care e.g. - Pain requiring IV analgesia - Requiring IV hydration *or* poor oral/enteral intake - Requiring oxygen *or* respiratory distress		
NO signs or symptoms of severe sepsis at presentation: - Altered conscious state - Inotrope requirement - Any fluid bolus requirement - Respiratory support requirement (high flow oxygen, non-invasive ventilation or intubation)		
Tolerated at least 1 dose of oral antibiotics in hospital (orally or via NG/PEG)		
Parent or caregiver available 24 hours a day		
CYP and carer adequately informed and educated on reportable symptoms and given temperature diary		
Availability of a telephone and tympanic thermometer		
Within 1 hour drive/travel of hospital		
NO previous history of non-compliance with medical care or current social care involvement		

Pending or positive COVID-19 swabs should not be a contraindication for early discharge if CYP meets all the above criteria.

5.18.3 Appendix 3: Examples of clerking and documentation templates from PTC electronic system

5.18.3.1 Appendix 3a:

INITIAL CLERKING FOR FEBRILE PAEDIATRIC ONCOLOGY PATIENT

ALL patients require FBC, blood cultures and broad spectrum IV antibiotics within 1 hour of presentation. Do not await results prior to giving antibiotics

Oncological diagnosis

Treatment protocol and cycle

Date of illness onset:

Admitted on

First symptoms noticed

Background:

Active Problems:

Current Symptoms (please expand on details if clinically relevant)
Fever? Yes No
Duration of fever: days
Height of fever (Tmax):
Shortness of breath? Yes No
Cough? Yes No
Wet with mucous? Yes/No
Dry? Yes/No
Myalgia? Yes/No
Fatigue? Yes/No

Other symptoms? Yes / No
(Mucositis, diarrhoea, vomiting, abdominal pain, pain, constipation, pain or redness to perianal region, nappy rash)

Past Medical History

Social History
Members of household:
Do parents have access to a car?
Are parents known to social services?

Exposure History
Travel in 14 days prior to presentation? Yes/No
Other significant travel? Yes/No
Hx of close person conatct with COVID (confirmed or probable case with person who was symptomatic)? Yes/ No

Drug History

Allergies

Examination

Vitals:

Resp

CVS

Neuro:

GI (+perianal area if indicated):

Line site:

Investigations (please request)
FBC (+/- U&E, LFT, gas)
Blood culture
Urine culture
As indicated Wound swab, throat culture, NPA, Covid swab, CXR, AXR

Impression:

Plan:

Risk stratify once counts available

Oncology specific considerations
Empiric antibiotics:

- *Tazocin 90mg/kg QDS (Meropenem 20mg/kg TDS if allergic to penicillin, within 48 hours of high dose methotrexate, or known/suspected ESBL)*
- *Consider Gentamicin if clinically unwell/unstable*
- *Consider vancomycin/teicoplanin if concerns re line infection*
- *Hold prophylactic ciprofloxacin while on IV antibiotics, continue PJP prophylaxis, continue antifungal prophylaxis if relevant*

Risk stratify once counts available

5.18.3.2 Appendix 3b: Discharge Check List:

Diagnosis:

Risk stratification on presentation

Variable	**Yes**	**No**
Preceding chemotherapy regimen more intensive than ALL maintenance*	1	0
Total white cell count <0.3 x 10^9/L	1	0
Platelet <50 x 10^9/L	1	0
TOTAL SCORE	***	

Duration of stay in hospital: ***

Has minimum period of observation been met? Yes/no***

Score	Minimum period of observation (hours)
0	4-8
1	4-24
2	24
3	48

Does patient meet discharge criteria? Yes/no***

Criteria	**Eligible**	**Not eligible**
Review by consultant paediatric haematologist/oncologist Clinically stable: normal observations Blood cultures negative or pending		
Disease status: responding to current therapy		
Low risk disease group: NOTany of – ALL in induction Infant ALL AML Ph+ ALL Relapse protocol treatment Rapid COJEC treatment protocol Post HSCT within 6 months or still on immunosuppression Congenital immunodeficiency Aplastic anaemia Down syndrome Early discharge not supported by clinical trial if enrolled		
NO confirmed focus of infection requiring inpatient care CVAD site infection (possible or confirmed) Cellulitis Perianal cellulitis/pain Significant pneumonia (confirmed on CXR) Multi-drug resistant organism previously isolated		
NO medical complication requiring inpatient care Pain requiring IV analgesia Requiring IV hydration *or* poor oral/enteral intake Requiring oxygen *or* respiratory distress		
NO signs or symptoms of severe **sepsis at presentation**: Altered conscious state Inotrope requirement Any fluid bolus requirement Respiratory support requirement (high flow oxygen, non-invasive ventilation or intubation)		
Tolerated at least 1 dose of oral antibiotics in hospital (orally or via NG/PEG)		
Parent or caregiver available 24 hours a day		

Patient/carer adequately educated on reportable symptoms and given temperature diary + information leaflet (on Oncolnet)		
Availability of a telephone and tympanic thermometer		
Within 1 hour drive/travel of hospital		
Treating team approves discharge		
No previous history of non-compliance with medical care or current social care involvement		

Does patient have any positive blood cultures? Yes/no***

Is patient eligible for early discharge on oral antibiotics? Yes/no***

If eligible for discharge please prescribe 5 days of oral antibiotics:
(Co-amoxiclav (Clarithromycin if penicillin allergic) AND Ciprofloxacin)

Patient meets eligibility criteria but not discharged. Reason ***

Information and observation diary given to parents: Yes/No***

Patient added to list/notified team for daily phone call reviews: Yes/No***

5.18.3.3 Appendix 3c: Risk Stratification of Immunocompromised child

Treatment protocol and cycle (go to summary - Springboard chemo - treatment plan)***

Total white cell count ***
Platelet count ***

Based on initial clinical picture and full blood count results child fits into the following category (delete as appropriate ***)

1) Clinically unwell – continue IV antibiotics and admit to ward until minimum 48 hours afebrile with negative blood culture
2) Clinically well and neutrophil count >1.0 x 10^9/l – assess and treat underlying cause. Consider discharge +/- PO antibiotics depending on focus
3) Clinically well and neutrophil count <1.0 x 10^9/l - risk stratify

	Yes	**No**
Preceding chemotherapy regimen more intensive than ALL maintenance*	1	0
Total white cell count <0.3 x 10^9/L	1	0
Platelet <50 x 10^9/L**	1	0
TOTAL SCORE	***	

* includes ALL maintenance, LCH maintenance or weekly vinblastine alone (low grade glioma)
**This remains valid even for recently transfused

Score	Minimum period of observation (hours)
0	4-8
1	4-24
2	24
3	48

At stipulated discharge timepoint, please complete discharge review document **(.paedoncfeverdc)** to assess eligibility for early discharge

5.18.3.4 Appendix 3d : Phone review template

Diagnosis

Day of febrile illness:

Initial risk stratification score:

Clinical review:

Assessment

	Yes	No
Is patient alert and orientated?		
Any temperatures ≥38c or <36c in last 24 hours		
Any overnight chills or shakes?		
Tolerating normal diet without vomiting?		
Any reported concerns over dehydration?		
Is child passing normal amounts of urine in the last 24 hours?		
Normal bowel pattern with no diarrhoea over the previous 24 hours?		
Patient and carer understand reasons to trigger contact with hospital personnel		
Any pain?		
Any new symptoms?		
Check blood cultures		
Is patient on outlier list		
Does patient need to come for review? Ongoing fever ≥72h from presentation or new fever after being afebrile for 24h Feeling unwell/onset of new symptoms Parental concern Significant decrease in oral/enteral intake or significant increase in output (vomiting and diarrhoea) Positive blood culture or new infection identified after discharge home Severe or persistent pain Chills/rigors/shaking Not afebrile by day 5 of outpatient care		
Does patient need readmission? Fever ≥38˚C beyond 5 days from the start of the febrile episode Clinically unwell/unstable Infection requiring inpatient care		

Advice given to parents***

Does patient need to come for review/readmission?***

5.18.4 Appendix 4: Patient information sheet

Date:……

Home based care for febrile neutropenia
Parent Information Sheet
For Children with Addenbrooke's Hospital as their Primary Oncology Treatment Centre

Shortening the amount of time people need to stay in hospital is particularly important at the moment because of the coronavirus outbreak.

Your child is being treated for **febrile neutropenia (FN).** This means your child has a fever ≥38°C and low neutrophils, which is a type of white blood cell important for fighting infections. Because of this your child is less able to fight infections.

Over recent years, teams from around the world have studied the safest approach to managing this problem in different health care settings. The results from these studies and the experience gained has now been shared to help with the effort to manage patients safely whilst minimising time spent in hospital. The approach taken, means that children experiencing an episode of fever with neutropenia are put into different 'risk' groups, depending on their risk of serious infection (during a particular episode).

With this in mind, the local paediatric team have assessed your child as having a low-risk fever and neutropenia episode. In common with other UK paediatric oncology centres, Addenbrooke's Hospital now has a way to treat low-risk febrile neutropenia safely at home with support from the local hospital. This means your child can complete their antibiotics at home. Your local hospital's paediatric team will work closely with you and your child to monitor your child's progress.

Eligibility for home treatment

- Your child has been assessed by the local paediatric team and deemed to be safe to be discharged home on oral antibiotics
- You live, or have accommodation, within 1 hour drive of ****ins local hospital***
- You must have immediate transport available (either car or taxi) if you have to return to ***ins local hospital***
- You must have a working home phone or mobile phone
- You must agree to the instructions of the local paediatric team.

When you are at home

When your child goes home, a member of the local paediatric team will call you daily until your child is well and has completed their antibiotics. You may be asked to stop giving the antibiotics even though you have some left.

While you are at home, you will need to take your child's temperature every 4 hours when they are awake until you are told by the local paediatric team you can stop.

Your child will be receiving antibiotics as a medicine by mouth or via their Naso-gastric tube. Please follow the instructions for giving these that are given by your local hospital.

When to call the hospital

We expect your child to carry on having temperatures for a while; it might take three or four days for it to settle completely. We will ask about it when we call you, but do not want you to worry just because you child gets hot.

You should contact the ****insert local contact point*** on ******* (24 hours per day/7 days per week) at any time if you are worried about your child or if they have any of the following symptoms:

- Does not feel well or look right to you
- Chills or shaking
- Persistent vomiting or new diarrhoea
- Infection: redness, tenderness or pain anywhere on the body
- Tiredness, paleness or shortness of breath
- Dehydration – decreased urine, dry mouth
- Your child has a low temperature (less than 36°C)
- Pain: severe or persistent
- Refusing to drink

Remember, you know your child best. If you are concerned or worried, or if something doesn't feel quite right, speak to your child's treating team.

In an emergency, call 999

Write patient details or affix patient label

Surname
……

Given names
……..

5.18.5 Appendix 5: Patient held temperature diary

Low-risk febrile neutropenia

Home observation and assessment chart: to be completed by patient					
Intervention /assessment	**Day 1** **Date** ……..……	**Day 2** **Date** ……..……	**Day 3** **Date** ……..……	**Day 4** **Date** ……..……	**Day 5** **Date** ……..……
Patient/carer to complete					
Temperature: Recorded 4-6 hourly during waking hours	1. Time…….. Temp……. 2. Time…….. Temp……. 3. Time…….. Temp……. 4. Time…….. Temp……. 5. Time…….. Temp……. 6. Time…….. Temp…….	1. Time…….. Temp……. 2. Time…….. Temp……. 3. Time…….. Temp……. 4. Time…….. Temp……. 5. Time…….. Temp……. 6. Time…….. Temp…….	1.Time…….. Temp……. 2.Time…….. Temp……. 3.Time…….. Temp……. 4.Time…….. Temp……. 5.Time…….. Temp……. 6. Time…….. Temp…….	1.Time…….. Temp……. 2.Time…….. Temp……. 3.Time…….. Temp……. 4.Time…….. Temp……. 5.Time…….. Temp…… 6. Time…….. Temp…….	1. Time…….. Temp……. 2. Time…….. Temp……. 3. Time…….. Temp……. 4. Time…….. Temp……. 5. Time…….. Temp……. 6. Time…….. Temp…….

Assessment form

Clinician to complete

	Day 1		Day 2		Day 3		Day 4		Day 5	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Is Patient alert and orientated?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Any overnight chills or shakes?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Tolerating normal diet without vomiting?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Any reported concerns over dehydration?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Is child passing normal amounts of urine in the last 24 hours?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Normal bowel patterns with no diarrhoea over previous 24 hours?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Patient & carer understand reasons to trigger contact with hospital personnel	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Any pain?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Any new symptoms?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Check blood cultures										
Clinician signature	……		……		……		……		……	

Document any issues identified (these must be discussed with CNS nurse co-ordinator and/or treating team)

6 Prophylactic antibiotics

6.1 General antibiotic & antifungal prophylaxis

A number of children will be discharged from Addenbrooke's on oral antibiotic & antifungal prophylaxis to cover their period of neutropenia, where this is expected to be prolonged and profound: for example, children receiving treatment for AML or B-ALL/NHL.

Doses:

Ambisome	2.5mg/kg twice weekly
Ciprofloxacin	10mg/kg/dose bd PO
Itraconazole	2.5mg/kg bd daily PO (discuss with Addenbrooke's)
Corsadyl mouthwash	5ml qds diluted if unable to brush teeth

This prophylactic combination is continued until the child's neutrophils are >0.5 x 10^9/L. If the child develops an episode of neutropenic fever, start iv antibiotics (see above), stop oral ciprofloxacin, but continue itraconazole and mouth care. Restart oral ciprofloxacin and itraconazole (if stopped) when iv antibiotics are discontinued and continue until neutrophil count >0.5 x 10^9/L.

6.2 Pneumocystis prophylaxis

All children on immunosuppressive regimens should receive prophylaxis against *Pneumocystis jirovecii* pneumonia during treatment - usually with oral co-trimoxazole (this is taken twice daily for 2 days a week – usually Saturday & Sunday). This should be **continued** during episodes of neutropenic fever.

Co-trimoxazole prophylaxis should stop 3 months after completion of chemotherapy. In rare cases with additional risk factors (e.g. recurrent significant respiratory infections, previous PJP infection), this may be extended beyond this time. POSCUs will be notified of such cases by Addenbrooke's.

Patients who are unable to tolerate co-trimoxazole prophylaxis should be discussed with the PTC and an alternative will be given (Dapsone, Atovaquone, or Pentamidine).

Following HSCT, co-trimoxazole should be continued until at least 6 months, so long as lymphocyte count has recovered.

6.3 Herpes Simplex prophylaxis

Children with positive Herpes simplex titres at diagnosis AND a history of recurrent herpetic mouth ulcers should receive prophylactic Aciclovir at least during intensive phases of chemotherapy.

7 Viral infections in paediatric haematology / oncology patients

Measles and chicken pox (Varicella zoster Virus) may be life-threatening in the immunosuppressed child and may present with atypical or minimal rashes. Duration of immunosuppression:

- Conventional chemotherapy: on treatment and for first 6 months off treatment
- HSCT (sibling donor) and autologous graft):12 months (maybe longer if prolonged GvHD present)
- HSCT (unrelated donor or haplotype): 18 months

7.1 Chicken Pox (VZV) Contact & Prophylaxis

Significant contact is defined as play or direct contact for more than 15 minutes with an individual with chicken pox (VZV) or shingles if in an exposed area during the infectious period (from 2 days before the onset of the rash until all vesicles are crusted). The day of exposure is defined as the date of the rash if the index is a household contact and date of first or only contact if the exposure is on multiple or single occasion(s) respectively.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/812526/PHE_PEP_VZIG_guidance_for_health_professionals.pdf

VZV-seropositive children, receiving conventional chemotherapy, do not require prophylaxis.

Regardless of prior VZV history or antibody status, children undergoing HSCT should receive prophylaxis if exposed.

VZV prophylaxis: Oral aciclovir given from day +7 following direct contact to day +14 from contact.

Infection control: Exposed individuals receiving prophylaxis in hospital should be isolated from day 8 to day 21 post exposure.

Dose of aciclovir:

- 10mg/kg (max 800mg) qds po for 7 days, to be started 1 week after exposure

A very limited supply of VZIG (Varicellar zoster immunoglobulin) may be available from PHE & can be given as a single intramuscular dose in those children in the very rare situations where compliance with oral aciclovir is likely to be a problem and the individual is VZV seronegative. Please discuss with Addenbrooke's Haem/Onc consultant if this is considered.

7.2 Treatment of chicken pox & shingles

If the child is systemically well, a trial of oral aciclovir may be undertaken. If a child on oral treatment becomes unwell or new lesions continue to appear at 48 hours, then iv aciclovir is needed.

See Children BNF for the most up-to-date doses of aciclovir.

- Aciclovir PO (for 5 days at least, continued till 2 days after crusting of lesions):
  - 200 mg qds (age 1 - 23 months)
  - 400 mg qds (age 2 - 5 years)
  - 800 mg qds (age 6 -11 years)
  - 800 mg 5x daily for 7 days instead of 5 days (age12-17 years)
- Aciclovir IV:
  - 3 months – 11 years: 500mg/m^2 tds usually for 5 days
  - 12 – 17 years: 10mg/kg tds usually for 5 days

The child should be nursed separately in a cubicle.

Oral aciclovir may be substituted when the child has had no new lesions for 24-48 hours

7.3 Measles Contact & Passive Immunisation

Passive Immunisation is required following direct contact with Measles during the period of immunosuppression regardless of immune status or immunisation history. Every attempt should be made to confirm the diagnosis in the index case, but if virology is unavailable and the diagnosis is clinically plausible, the child should receive passive immunisation with Normal Human Immunoglobulin (NIG) within 72 hrs of contact (if given after 72 hours but before 6 days, NIG may still attenuate the infection). See most up to date DoH guidance for dosing.

Please contact consultant virologist at PHLS (Addenbrooke's, Norwich, Ipswich, Chelmsford, Peterborough/Hinchingbrooke or Papworth) for approval, as required by DOH guidelines, May 2009. IV Immunoglobulin 0.4g/kg may be used if the patient is thrombocytopenic. (See also Health Protection Agency Post Exposure Prophylaxis for Measles: Revised Guidance May 2009).

8 Immunisations

Addenbrooke's immunisation letters:


PTL011_re-immunisations_after_conventi


PTL012_re-immunisations_after_high_do

Addenbrooke's siblings immunisation letter:


PTL019_immunisations_during_chemoth

This guideline is adapted from the CCLG guidance: Vaccinations for Paediatric Patients Treated with Standard-Dose Chemotherapy and Haemopoietic Stem Cell Transplantation (HSCT) Recipients
Authors: Dr Soonie R.Patel, Professor Rod Skinner and Professor Paul T.Heath
Date: Updated guideline 2023.

8.1 General principles

In view of the secondary immunodeficiency of children treated for cancer, particularly HSCT recipients, and their improved long-term survival after completion of treatment, it is important to ensure that they are protected against vaccine-preventable diseases. This can be achieved by optimising the vaccination strategy in children during chemotherapy and by re-vaccination of children after completion of chemotherapy. In view of the diversity of malignant diseases and their treatment protocols, it would be difficult to propose different vaccination schedules for each disease. Rather it is sensible to divide into children treated with standard-dose chemotherapy and children treated with high-dose chemotherapy (+/- radiation) followed by allogeneic or autologous haematopoietic stem cell transplant (HSCT).

8.2 Precautions during immunosuppression

Avoid administration of all live vaccines to patients on chemotherapy and within 6 months following completion of chemotherapy.

- VZV vaccine should be offered to healthy susceptible siblings and other family members of patients receiving chemotherapy.
- Avoid administration of live vaccines, **except** Measles/Mumps/Rubella (MMR), Varicella Zoster Virus (VZV), Live attenuated Influenza vaccine (LAIV) and Rotavirus vaccines, to siblings of patients on chemotherapy (or within 6 months following completion of chemotherapy).
- Inactivated Influenza vaccine should be offered to all patients receiving chemotherapy or are within 6 months of completion of chemotherapy.

- Influenza vaccine should be advised for close contacts
- Update primary health care records if vaccination has taken place in hospital

8.3 Vaccinations for patients receiving standard-dose chemotherapy (or within 6 months of completion)

Consider following the timing and content of the routine childhood vaccination programme, using only non-live vaccines provided the child's general condition is stable and is expected to stay so for 3 weeks from vaccination.

Avoid vaccination during the period that the patient is receiving steroids (the immune response will be suboptimal) or the patient is neutropenic (neutrophil count <0.5).

Inactivated influenza vaccine is recommended annually in the autumn for all patients on chemotherapy or within 6 months of its completion. The live attenuated intranasal vaccine should not be given to this group of patients, but it could be given to family members during treatment and within six months of completion of treatment. Those who have not received influenza vaccine previously should be offered a second dose of vaccine, at least four weeks later.

8.4 Conventional/Standard dose chemotherapy: Re-immunisation 6 months after completion of treatment

Six months after completion of standard dose chemotherapy a booster dose of vaccinations should be given. This is detailed in the table below.

If the child did not complete the course of childhood vaccinations prior to starting treatment then this should be completed.

Time after EOT	Age under 10 years Vaccine	Age 10 years and over Vaccine
6 Months	DTaP/IPV/Hib/HepB[1] Men ACWY-conjugate PCV13 Men B[2] MMR[3]	dTaP / IPV Hib/Men C Men ACWY-conjugate PCV13 Men B[2] MMR[3] HPV[4]

[Vaccines: DTaP = Diphtheria/ Tetanus/ acellular Pertussis, dTaP = Low dose Diphtheria/ Tetanus/ acellular Pertussis, Hib = *H.influenzae b* conjugate, HepB =Hepatitis B, HPV = Human papillomavirus, IPV = Inactivated polio virus vaccine, Men B = Meningococcal B conjugate, Men C = Meningococcal C conjugate, Men ACWY = Menincococcal ACWY conjugate, MMR = Measles/Mumps/Rubella, PCV13 = 13 valent Pneumococcal conjugate, PnPS 23 = 23 valent pneum ococcal polysaccharide]

[1] Give DTaP/IPV/Hib/HepB (Infanrix hexa) to children (including those born before 1/07/17).
[2] Give Men B vaccine to children born after 1/09/15
[3] If patient did not receive MMR prior to starting chemotherapy give 2 doses MMR, if patient only received 1 dose of MMR prior to starting chemotherapy then should receive 2 doses of MMR after completion of chemotherapy. The 2nd dose should be given 6 months after the 1st dose. The 2nd dose can be given 3 months after the 1st dose or can be considered even earlier (1 month after 1st dose) in measles outbreak.
[4] HPV vaccine should be offered to girls and boys ≥12 years old: 2 doses of HPV vaccine should be given at 0 and 6 months from starting vaccination. If patient is aged 15 years and over, 3 doses recommended at 0, 1, 6 months from starting vaccination. For girls and boys that did complete the course, a booster dose should be given.

(Table from CCLG guidelines 2019)

Subsequent routine booster doses will not be necessary if scheduled to be given within one year of the above booster doses.

If patient has not received full vaccination schedule prior to diagnosis and treatment then complete the schedule.

BCG Vaccine: If patient has previously had BCG and is considered to be at high risk of tuberculosis, perform Mantoux test and, if negative, re-vaccinate. If patient has not previously had BCG then vaccinate according to local policy.

For children receiving HSCT see section on high dose therapy/SCT

8.5 Immunisation of siblings

Vaccination of close contacts of patients receiving standard-dose chemotherapy (or within 6 months of completion)

The following live vaccines can be administered to siblings / close family contacts of patients on chemotherapy or within 6 months following completion of chemotherapy.

- MMR Vaccine should be given to contacts as per the national vaccination schedule.

- VZV vaccine should be offered to healthy susceptible siblings (and adult family members who are VZV seronegative) of VZV seronegative patients. There is theoretical risk of transmitting the attenuated vaccine virus to a susceptible individual; as a precautionary measure, any person who develops a vesicular rash after receiving VZV vaccine should avoid direct contact with the patient until the rash is dry and crusted.
- Shingles vaccine: Is offered to adults aged 70-79 years old, so the patient's grandparents may be offered this vaccine. Rarely the transmission of vaccine virus may occur between those vaccinated who develop a varicella-like rash and susceptible contacts. As a precautionary measure, any person who develops a vesicular rash after receiving the vaccine should avoid direct contact with the patient until the rash is dry and crusted.
- Rotavirus vaccine: Is given to infants aged 6-24 weeks. Rotarix should not be given to the patient but can be given to siblings. There is potential for transmission from the infant to immunocompromised contacts through the faecal-oral route for at least 14 days postvaccination. However, vaccination of the infant will offer protection to household contacts from wild-type rotavirus disease and outweigh any risk from transmission of vaccine virus to any immunocompromised close contacts. Good personal hygiene should be observed following administration.
- Live attenuated influenza vaccine (LAIV): Consideration should also be given to giving LAIV to household contacts that are eligible for LAIV. Other household contacts who are not considered suitable to receive LAIV should be given the inactivated Influenza vaccine. Siblings that are due should be given this; there is a theoretical potential for transmission of live attenuated influenza virus from LAIV to immunocompromised contacts for one to two weeks following vaccination so assess each individual case.

8.6 Travel Abroad

Live vaccines such as BCG, VZV, MMR, oral typhoid and yellow fever should be avoided during chemotherapy and for 6 months after completion of chemotherapy.

8.7 Immunisations following High Dose Therapy/HSCT

Passive Immunisation following Chickenpox or Measles Contact.

See CUH guideline for viral infections in oncology/haematology patients: CSO/V002

8.8 Re-immunisation programme following High Dose Therapy (12 months after completion of therapy)

HSCT recipients are profoundly immunosuppressed for several months, even years after transplantation. Immune reconstitution after HSCT occurs in a well-defined manner. The various components of the new immune system develop and mature at different rates and this dictates the timing and type of specific infections as well as the response to different antigens.

- The aim in HSCT recipients is to commence re-vaccination as soon as it is safe and as soon as a protective immune response can be achieved. Potentially this would be once the patient is off immunosuppressive therapy. In most published studies, however, vaccination schedules have been started ≥12 months after HSCT.
- All children should be considered for re-vaccination after allogeneic or autologous HSCT.
- In comparison to recipients of allogeneic HSCT, autologous HSCT recipients are less immune suppressed. However, both transplant types follow the same vaccination schedule content.
- The use of live vaccines is potentially dangerous until the child has been off all immunosuppressive treatment for at least 12 months and has no evidence of active chronic GvHD.
- Chronic GvHD and its treatment cause immune suppression, therefore these patients are at high risk of infectious complications.
- In view of the difficulty in predicting the extent of immune suppression and immune recovery, a pragmatic approach is to recommend re-vaccination of all recipients of allogeneic and autologous HSCT:

Re-Vaccination should commence:

- 12 months after any HSCT (transplant team can review this on case-by-case basis
- Normal serum immunoglobulins, CD4 count >15% and / or >300 x 10^6/L)

Providing that:

- No evidence of active chronic GvHD
- Off all immunosuppressive treatment for at least 6 months, and for at least 12 months for live vaccines
- Off IVIg for at least 3 months
- NB. In infants who have undergone allogeneic HSCT for primary immunodeficiency it may be appropriate to start vaccination earlier than specified above.

See next page for immunisation schedule.

3.3 Re-vaccination Schedule for HSCT Recipients

Time after HSCT	Age under 10 years Vaccine	Age 10 years and over Vaccine
Every autumn (start 6 months after transplant)	Inactivated influenza vaccine[1]	Inactivated influenza vaccine[1]
12 Months	DTaP/IPV/Hib/HepB PCV13 Men B	DTaP/IPV/Hib/HepB PCV13 Men B HPV[2]
13 Months	DTaP/IPV/Hib/HepB[2]	DTaP/IPV/Hib/HepB HPV[2]
14 Months	DTaP/IPV/Hib/HepB PCV13 Men B	DTaP/IPV/Hib/HepB PCV13 Men B
18 Months	MMR[3]	MMR[3] HPV[2]
24 Months	MMR[4] Men ACWY Men B PCV13 or PnPS23	MMR[4] Men ACWY Men B PCV13 or PnPS23
48 Months	DTaP / IPV or dTaP / IPV Hib / Men C	dTaP / IPV Hib / Men C
School leaver booster	dT / IPV Men ACWY (once reach 14 years of age)	dT / IPV Men ACWY

[Vaccines: DTaP = Diphtheria/ Tetanus/ acellular Pertussis, dTaP = Low dose Diphtheria/ Tetanus/ acellular Pertussis, Hib = *H.influenzae b* conjugate, HepB =Hepatitis B, HPV = Human papillomavirus, IPV = Inactivated polio virus vaccine, Men B = Meningococcal B conjugate, Men C = Meningococcal C conjugate, Men ACWY = Menincococcal ACWY conjugate, MMR = Measles/Mumps/Rubella, PCV13 = 13 valent Pneumococcal conjugate, PnPS 23 = 23 valent pneumococcal polysaccharide]

[1]The intranasal live-attenuated influenza vaccine should not be given to HSCT recipients. Note that the immune response to influenza vaccine is not optimal during the first 6 months after HSCT, which is the period of greatest risk; therefore vaccination should be offered to family members and hospital staff.

[2] HPV vaccine should be offered to girls and boys ≥12 years old: 2 doses of HPV vaccine (Gardasil) should be given at 0 and 6 months from starting re-vaccination. If patient is aged 15 years and over, 3 doses recommended at 0,1, 6 months from starting re-vaccination.

[3] 1st dose of MMR should be given at 18 months provided patient is at least 12 months off all immunosuppressive treatment and fulfils criteria

[4] The 2nd dose of MMR is usually given 6 months after the 1st dose, but can be given 3 months after the 1st or even earlier (1 month after 1st dose) in outbreak situations.

Table from CCLG guideline: Vaccinations For Paediatric Patients Treated With Standard-Dose Chemotherapy And Haemopoietic StemCell Transplantation (HSCT) Recipients

Authors: Dr Soonie R.Patel, Professor Rod Skinner and Professor Paul T.Heath

Date: Dec 2019

Other Vaccines

Hepatitis B vaccine, travel vaccines and BCG vaccine may be considered for individual cases (after discussion with the transplant team).

There is little data about the safety and effectiveness of the BCG vaccine in HSCT recipients. Its use is not recommended unless there is a clear case of need such as travel to or residence in an area with a high incidence of tuberculosis (greater than 40/100,000 per year), and provided the patient has no active chronic GvHD and there is evidence of immune function recovery (such as normal serum immunoglobulin concentrations, recovery of lymphocyte function and CD4-lymphocyte numbers). Prior to administering BCG, particularly in patients that have previously had BCG, a tuberculin skin test should be done.

Vaccines contraindicated for HSCT Recipients

- BCG (except in specific circumstances and only after discussion with transplant or immunology team)
- Rotavirus
- Intranasal live attenuated Influenza vaccine
- VZV vaccine
- Yellow fever
- Live attenuated Typhoid vaccine

Vaccination of close contacts of HSCT Recipients

The following live vaccines can be administered to siblings / close family contacts of HSCT recipients: MMR, VZV, Shingles and Rotavirus vaccines.

- MMR Vaccine should be given to contacts as per the national vaccination schedule.
- VZV vaccine should be offered to healthy susceptible siblings (and adult family members who are VZV seronegative) of VZV seronegative patients. There is theoretical risk of transmitting the attenuated vaccine virus to a susceptible individual; as a precautionary measure, any person who develops a vesicular rash after receiving VZV vaccine should avoid direct contact with the patient until the rash is dry and crusted.
- Shingles vaccine is offered to adults aged 70-79 years old, so the patient's grandparents may be offered this vaccine. Rarely the transmission of vaccine virus may occur between those vaccinated who develop a varicella-like rash and susceptible contacts. As a precautionary measure, any person who develops a vesicular rash after receiving ZostavaxR should avoid direct contact with the patient until the rash is dry and crusted.
- Rotavirus vaccine is given to infants aged 6-24 weeks. Rotarix should not be given to the patient but can be given to siblings. There is potential for transmission from the infant to immunocompromised contacts through the faecal-oral route for at least 14 days postvaccination. However, vaccination will offer protection to household contacts from wild-type rotavirus disease and outweigh any risk from transmission of vaccine virus to any

immunocompromised close contacts. Good personal hygiene should be observed following administration of Rotarix.

9 Tumour Lysis syndrome

Ref: CUHFT tumour lysis guideline v2.0 April 2020.

9.1 Background

- Tumour Lysis Syndrome (TLS) occurs in haematological malignancies and lymphoproliferative disorders. It is caused by the rapid lysis of malignant cells following the start of chemotherapy (may also occur following a single dose of corticosteroid and occasionally spontaneously or following anaesthesia).
- Rapid cell breakdown leads to hyperuricaemia, hyperphosphataemia, hyperkalaemia and hypocalcaemia, caused by the spillage of intracellular contents into the circulation exceeding physiological buffers and renal excretory mechanisms. These electrolyte disturbances then precipitate urate nephropathy and acute renal failure.
- Hyperuricaemia: caused by massive, rapid nucleic acid catabolism. Uric acid pKa is 5.4; soluble in plasma (pH 7.4) but less soluble in the renal tubules and collecting ducts (pH 5). There is a risk therefore of uric acid crystallisation in the tubules causing acute renal failure.
- Hyperkalaemia: caused by spillage of intracellular potassium and potentiated by acute renal injury. Risk of lethal cardiac arrhythmias.
- Hyperphosphataemia and reciprocal hypocalcaemia: caused by spillage of intracellular phosphate, can exceed the calcium phosphate solubility product (4.6mmol/L) in spite of hypocalcaemia, leading to metastatic tissue calcification and nephrocalcinosis, further precipitating acute renal failure.
- Acute Renal Failure: Secondary to uric acid nephropathy, calcium phosphate precipitation and dehydration. Oliguria secondary to renal damage will also worsen hyperkalaemia and hyperphosphataemia causing further kidney injury.

9.2 Risk assessment

Risk	Example	Prophylaxis	Frequency of blood monitoring	
High Risk of TLS – Discuss all patients with Consultant On Call			**Pre-Treatment**	**Post-Treatment**
Bulky, highly chemotherapy sensitive malignancies	• Leukaemia with WCC >100x10^9/L • Non-Hodgkin's Lymphoma (NHL) – B or T Cell (e.g. Large Mediastinal Mass) • Large Tumour Bulk (e.g. Large Organomegaly) • Bulky lymphoproliferative disease (LPD) or post-transplant lymphoproliferative disease (PTLD) • Evidence of renal impairment or renal infiltration (on scan)	Rasburicase (Urate Oxidase) 0.2mg/kg/dose Single Dose (Consider further doses at discretion of Consultant)	8 hourly	6 hourly
Intermediate Risk of TLS				
Widespread, chemotherapy sensitive malignancies	• Leukaemia with total WCC 20-100x10^9/L with absence of large tumour bulk or renal impairment	Consider either: Rasburicase (if G6PD normal) or Allopurinol 100mg/m^2/dose TDS	12-24 hourly	6-8 hourly
Low Risk of TLS				
Widespread chemotherapy sensitive malignancies	• Leukaemia with total WCC <20x10^9/L with absence of tumour bulk or renal impairment • Non bulky NHL, LPD or PTLD with normal renal function	Allopurinol 100mg/m^2/dose TDS (maximum 400mg per day)	24 hourly	8-12 hourly
Rare to Develop TLS				
Most other malignancies	• Solid malignancies and HLH	None	None	None

9.3 Prevention – Management in POSCU

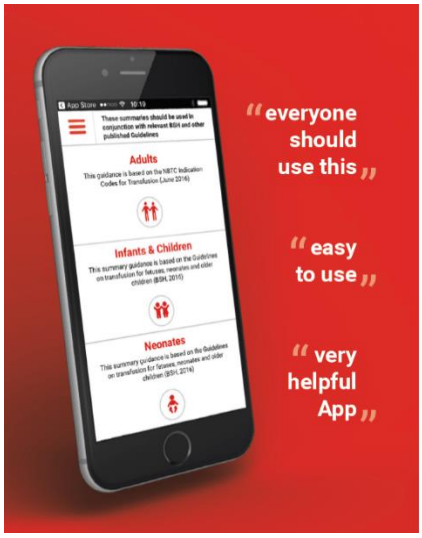
- All children with leukaemia and non-Hodgkin's lymphoma should receive **hydration** (as below) **and anti-urate therapy** as per table above
- However **consider risk of haemodilution** in anaemic patients, if a transfusion is required transfuse first prior to starting hydration therapy
- In cases of high count leukaemia requiring transfusion **always discuss with PTC Consultant prior to transfusing** due to risk of leucostasis
- **Hydration:** 0.45% NaCl + 2.5% Dextrose at 3L/m^2/day, start 24 hours prior to chemotherapy and continue until there are no further signs of tumour lysis. Other preparations may be used according to local practice (e.g. 0.9% NaCl + 2.5% Dextrose). Regardless of preparation, do **NOT** add potassium even if serum potassium is low).
- **POSCU:** In high and intermediate risk cases consider starting hyperhydration in the POSCU prior to transfer – discuss with Consultant. Low risk cases can usually be managed with full maintenance IV fluids and allopurinol before transfer to the PTC.

Any queries or concerns about metabolic disturbances should be discussed with the PTC.

10 Transfusion in children and neonates

Summarised from CUH guideline Transfusion in Children and Neonates V1.0 Oct 2020.

The app below can be downloaded from the app store and is a useful resource for blood product prescribing.



NHS Blood and Transplant

BLOOD COMPONENTS

"Bringing key transfusion guidelines to your fingertips"

Developed by Hospital doctors, the National Blood Transfusion Committee and the NHS Blood and Transplant Patient Blood Management Team.

10.1 Definitions

The term 'blood/blood components' used within this document include:

- Leucocyte depleted red cells
- Platelets
- Fresh frozen plasma (FFP)
- Cryoprecipitate
- Granulocytes
- IUT (Intra uterine transfusion)

10.2 Introduction

Transfusion practice has advanced over the last two decades, particularly with respect to improved safety measures introduced to reduce the risk of transfusion transmitted infections including variant Creutzfeldt Jacob disease (vCJD). Additional safety enhancements have been put in place specifically for neonatal & paediatric blood components. Nevertheless, care should always be taken to ensure that blood components are only transfused when necessary and that the most appropriate component is used for each individual patient in any given situation.

Occasionally some patients may experience a reaction whilst having a transfusion. The early recognition and safe management of these adverse effects of transfusion is essential in order to optimise treatment and therefore reduce patient morbidity and mortality.

It is essential for the transfusion laboratory and transfusion practitioners to be informed of a transfusion reaction in order for the Trust to report to the relevant bodies such as Serious

Hazards Of Transfusion (SHOT) and the National Health Service Blood and Transport (NHSBT).

10.3 Responsibilities

The decision to transfuse must be based on the clinical assessment of the patient and their individual needs. Unnecessary transfusions expose patients to an increased risk of morbidity or mortality, as well as being expensive and wasteful. The decision to transfuse a patient is a serious one. Specialist advice is always available via the Paediatric Haematology/Oncology team at the PTC.

Formal consent for transfusion should be taken.

10.4 General principles

The most serious complication of blood transfusion is ABO mismatch, which is potentially fatal.

Samples for cross-match must be clearly identifiable.

Note that it is now a legal requirement for all transfusions to be documented in the medical notes, to include indication, details of administration and response (clinical or laboratory confirmation).

10.5 Transfusion to neonates

One of the major causes of anaemia in neonates is iatrogenic due to blood sampling, and so efforts to minimise this (including appropriate sampling of cord blood and minimising blood volumes taken) should be utilised.

To avoid exposure to multiple donors and minimise waste, blood will be supplied in "Octa-pack/Paedipack" unless specified otherwise. This blood will be issued as packed red-cells with a packed cell volume (PCV) of about 60% and hence is suitable for top-up transfusions without further manipulation. Order the number of mL required and the lab will supply/allocate a Paedipack to the baby.

Blood should be CMV negative.

Neonatal specification blood products are appropriate for all children less than 1 year of age.

It is vital to communicate the need for irradiated blood components for neonates and infants <6 months old who received an intrauterine transfusion (IUT).

Further details regarding neonatal transfusions can be found in the Neonatal Handbook.

10.6 Transfusion to infants and children

10.6.1 Transfusion of Red cells

10.6.1.1 General principles

Prescription of blood components for paediatric red cell transfusion should be in millilitres. The maximum volume transfused should not be greater than one adult unit (300-350mL or >20mL/kg), except for circumstances like resuscitation. If you are considering more than this, discussion with the local haematologist or PTC Paediatric Haematology will be appropriate.

Give furosemide 0.5mg/kg with transfusion in the presence of hypertension, tachycardia or fluid overload. Routine administration of frusemide is NOT required.

Transfusion rate: 5 mL/kg/hr (usual max rate 150 mL/hr).

10.6.1.2 Volume calculation

Calculation: desired rise in Hb (g/l) x weight (kg) x 0.4.

In paediatric haem/onc for top-up transfusions a target Hb of 100 can be used.

If long-standing anaemia or signs of heart failure, transfuse in stages, aiming to increase Hb by no more than 20-30 g/l at a time.

10.6.1.3 Transfusion thresholds

Give packed red cells if Hb falls below 70g/l in stable non-cyanotic patients or if there are symptoms due to anaemia (teenagers in particular may be symptomatic at higher Hb levels).

Patients with chronic anaemia due to red cell aplasia may require a Hb threshold of 80 g/l.

Infants and children undergoing radiotherapy should be transfused if Hb falls below 100 g/l.

Patients with haemoglobinopathies on a regular transfusion programme are hyper-transfused to suppress endogenous haemoglobin production – the threshold is generally 100 g/l and the post-transfusion target is 120-130 g/l.

Neonatal red cell transfusion thresholds are described in the Neonatal Unit Handbook.

Discuss patients with leukaemia with a white cell count >50 with the Paediatric Haematology/Oncology consultant on call before transfusion, as they are at risk of hyper-viscosity and smaller volume transfusions may be advised and a lower Hb level may be accepted.

10.6.1.4 Surgery

The preoperative Hb should be optimised by treating iron deficiency anaemia.

A perioperative Hb transfusion threshold of 70 g/l should be used in stable patients without major co-morbidity or bleeding.

Tranexamic acid should be considered in all children undergoing surgery where there is a risk of significant bleeding.

Red cell salvage should be considered in all children at risk of significant bleeding undergoing surgery and where transfusion may be required.

10.6.2 Platelet transfusion

10.6.2.1 General principles

Prescription of platelet components for paediatric transfusion should generally be in millilitres for all children and the maximum volume should not be greater than one adult unit (approx. 300mL) or 20mL/kg. Neonatal specification platelets should be used for neonates and for children up to the age of 1 year.

Give furosemide 0.5mg/kg with transfusion in the presence of hypertension, tachycardia or fluid overload. Routine administration of frusemide is NOT required.

Transfusion rate 10-20 mL/kg/hr.

If bleeding occurs with a platelet count >20 x 10^9/L, perform a coagulation screen.

For children > 1year of age either standard apheresis or pooled platelet components can be used.

10.6.2.2 Volume calculation

Typical transfusion volume 10-20 mL/kg (generally 1 adult unit for children ≥ 15kg).

10.6.2.3 Transfusion thresholds

For most stable children, transfuse prophylactic platelets when platelet count <10 x 10^9/L (excluding immune thrombocytopenia, thrombotic thrombocytopenic purpura/haemolytic uremic syndrome and heparin-induced thrombocytopenia, where platelets are only transfused for life-threatening bleeding).

For infants and children undergoing systemic anti-cancer therapy, transfuse when platelets are <10 x 10^9/L if well and <20 x 10^9/L if febrile.

For children on anticoagulant therapy, transfuse when platelets are <20 x 10^9/L.

Further information on neonatal transfusion can be found in the Neonatal Handbook. However updated guidance on platelet thresholds for neonates suggests that for preterm neonates with very severe thrombocytopenia (platelet count <25x10^9/L platelet transfusions should be administered in addition to treating the underlying cause of the thrombocytopenia. For non-bleeding neonates platelet transfusions should not be routinely administered if platelet count >25 x10^9/L.

10.6.2.4 Surgery and procedures

Transfuse to keep platelets >20 x 10^9/L for lumbar puncture or nasogastric tube insertion.

Per local paediatric surgical guidelines, transfuse to keep platelets >100 x 10^9/L before any surgery, and aim to keep >100 x 10^9/L for at least 48 hours following a neurosurgical operation.

10.6.3 FFP and cryoprecipitate

10.6.3.1 General principles

Prophylactic FFP should not be administered to non-bleeding children with minor prolongation of the prothrombin time (PT)/activated partial thromboplastin time (APTT) including prior to surgery, although it may be considered for surgery to critical sites. Appropriate age and gestation specific reference ranges should be used for infants under 6 months of age.

Prophylactic cryoprecipitate should not be routinely administered to non-bleeding children with decreased fibrinogen including prior to surgery. It may be considered for fibrinogen <1g/L for surgery at risk of significant bleeding or to critical sites.

Make sure that patients are vitamin K replete; this may mean giving it routinely to sick children.

Neonatal and infant specification FFP components should be used for neonates and infants up to the age of 1 year.

10.6.3.2 Volume calculation

Transfuse FFP volumes of 15–20 ml/kg, using the higher volumes particularly in bleeding patients, and ensure monitoring of clinical outcome. Care should be taken to avoid volume overload, particularly in vulnerable patients, therefore infusion rate should be 10-20mL/kg/hr.

Transfuse cryoprecipitate volumes of 5–10 ml/kg, using the higher volumes particularly in bleeding patients, and ensure monitoring of clinical outcome and fibrinogen levels. Infusion rate should be 10-20mL/kg/hr.

Fibrinogen levels should be kept >1g/L and in a bleeding patient sometimes a higher target is used. Cryoprecipitate is used as a source of fibrinogen.

10.6.3.3 Transfusion indications

- **Disseminated intravascular coagulation (DIC)**

  FFP may be beneficial in children with DIC who have a significant coagulopathy (PT/APTT >1.5 times midpoint of normal range or fibrinogen <1 g/l) associated with clinically significant bleeding or prior to invasive procedures.

  Cryoprecipitate may be given if the fibrinogen is <1 g/l despite FFP, or in conjunction with FFP for very low or rapidly falling fibrinogen.

- **Liver disease**

  Standard coagulation tests do not reflect bleeding risk and should NOT be used alone to trigger transfusion with FFP/cryoprecipitate.

- **Warfarin reversal**

  FFP should NOT be used for urgent warfarin reversal unless four factor prothrombin complex concentrate is unavailable. Discuss any need for urgent warfarin reversal with the POSCU/PTC Haematology on call.

- **Inherited bleeding disorders**

  FFP should NOT be used in the management of inherited factor deficiencies unless specific factor concentrates are not available.

  Cryoprecipitate should NOT be used for congenital hypofibrinogenaemia unless fibrinogen concentrate is unavailable.

10.6.4 Granulocytes

Granulocyte transfusions may be considered for treatment of refractory infections in children with severe neutropenia, but should only be undertaken with specialist advice.

10.7 Major haemorrhage

Where immediate blood component support is required please discuss early with your hospital transfusion laboratory and refer to local policy on major haemorrhage. It is imperative that when discussing emergency blood requirements with the lab that the correct patient identification is provided; FULL name, DOB and MRN CHECK. Where the patient's details are not known, emergency blood components will be issued on an 'unidentified patient' basis.

Local policies for major haemorrhage should be followed.

10.8 Transfusion Reactions

A transfusion reaction may be defined as an adverse event occurring whilst administering a blood component to a patient. These can range from minor events such as itching, urticaria and/or mild fever to severe, life-threatening reactions such as anaphylaxis, ABO

incompatibility, bacterial contamination of products, transfusion associated lung injury (TRALI) and transfusion associated circulatory overload (TACO) that must be managed quickly and appropriately.

Refer to local policies for management of transfusion reactions.

See also: http://www.transfusionguidelines.org.uk/transfusion-handbook/5-adverse-effects-oftransfusion/5-2-non-infectious-hazards-of-transfusion

NB DO NOT give hydrocortisone to ALL or NHL patients before the start of therapy as this could precipitate tumour lysis.

Any significant reaction should be investigated and discussed with your transfusion lab.

10.9 Special Requirements

10.9.1 Irradiated blood components:

All cellular blood components have been leucocyte depleted in the UK since 1999. However, residual lymphocytes can cause fatal transfusion-associated graft versus host disease (TA-GvHD) in patients who are severely immunocompromised. Irradiation of blood components at 25Gy effectively inactivates these lymphocytes, thus preventing this complication from occurring.

It is imperative that patients are clinically assessed to determine if any special requirements are necessary. Where this process is inadequate patients are put at risk of harm or even death. Where it has been identified that a patient has a special requirement related to transfusion this should be clearly documented. If this is the first time these requirements have been identified, the specialist product request form should also be completed and faxed or delivered by hand to the laboratory immediately.

10.9.1.1 Indications for irradiated products

- All blood or platelets for in-utero transfusion (IUT)
- Neonates/infants who have previously received blood components in utero (IUT): continue until 6 months after the expected date of delivery.
- All neonates receiving red cell exchange transfusion.
- All patients with Hodgkin's lymphoma: continue indefinitely
- All patients with chemotherapy regimens containing purine analogue drugs such as fludarabine: continue indefinitely
- All patients treated with anti-thymocyte globulin (ATG) (or other T cell depleting serotherapy): continue indefinitely
- All patients treated with alemtuzumab (Campath): continue indefinitely** (see note regarding multiple sclerosis and solid organ transplants)
- All recipients of allogeneic bone marrow (BMT) or peripheral blood stem cell transplant (PBSCT)

  - start from the initiation of conditioning chemo/radiotherapy
  - continue for the duration of GvHD prophylaxis/immunosuppression
  - lymphocytes >1 x 10^9/L
  - continue indefinitely if chronic GvHD present or ongoing immunosuppression is required
  - Continue indefinitely if other factors such as conditioning (for example purine analogue) or diagnosis (Hodgkin's) are present.
- All donors of bone marrow (BM) or peripheral blood stem cells (PBSC) from 7 days prior to/during the harvest
- All patients undergoing BM or PBSC harvesting for future autologous re-infusion from at least 7 days prior to/during the harvest
- All patients undergoing autologous BMT or PBSCT
  - start from the initiation of conditioning chemo/radiotherapy: continue until 3 months post-transplant or 6 months post-transplant if TBI was used in the conditioning
- All cases where there may be a shared haplotype between the donor and the recipient (ie donations from first or second-degree relatives, HLA-matched platelets; also including fresh plasma)
- All severe congenital T-lymphocyte immunodeficiency syndromes with significant qualitative or quantitative T-lymphocyte deficiency should be considered as indications for irradiation of cellular blood components (1/B).

Once a diagnosis of severe T-lymphocyte immunodeficiency has been suspected, irradiated components should be given while further diagnostic tests are being undertaken. A clinical immunologist should be consulted for advice in cases where there is uncertainty.

- Neonates and infants with suspected immunodeficiency syndromes should undergo T-lymphocyte enumeration prior to cardiac surgery wherever possible. If the T-lymphocyte count is >400 cells/µl, of which 30% are naive T lymphocytes, there is no need to irradiate red cells or platelets. If it is not possible to undertake T-cell investigations prior to surgery, irradiated cellular blood components should be given until immunological investigations have been undertaken.

  Adults, and children aged > 2 years without a significant history of infection, referred for elective cardiac surgery for problems associated with DiGeorge syndrome, such as aortic arch anomalies and pulmonary artery stenosis, or in whom DiGeorge anomaly is suspected, do not need to receive irradiated cellular blood components, unless there is a significant history consistent with severe T-lymphocyte-associated immunodeficiency, as the risk of TA-GvHD is extremely low
- Granulocytes should ALWAYS be irradiated.
- Patients (adult and paediatric) undergoing peripheral blood lymphocyte collections for future CAR-T cell re-infusion should receive irradiated cellular blood components for 7 days prior to and during the harvest, to prevent the collection of viable allogeneic T lymphocytes. Irradiated blood components should continue to be used until 3 months following CAR-T cell infusion unless

conditioning, disease or previous treatment determine indefinite duration, e.g. previous diagnosis of HL or previous purine analogue treatment

- **Use of irradiated cellular blood components is not indicated following treatment with alemtuzumab using the schedule currently recommended for MS or vasculitis.
- **Use of irradiated cellular blood components is not indicated for patients undergoing solid organ transplantation who have received alemtuzumab or ATG as induction therapy or for treatment of graft rejection
- Treatment of patients with rituximab is not an indication for use of irradiated cellular blood components unless this is indicated for a different reason (underlying diagnosis, type of component or previous treatment)
- It is NOT necessary to irradiate fresh frozen plasma or cryoprecipitate.

10.9.2 CMV negative blood components:

In March 2012, the Department of Health Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) released a new position statement on Cytomegalovirus (CMV) testing of blood components. This concluded that leucodepletion of blood components (routine since 1999) offers sufficient protection against the risk of CMV transmission in most patient groups and that CMV negative components should no longer be considered necessary for CMV negative patients undergoing chemo/radiotherapy or requiring BMT/PBSCT.

In accordance with this, the recommendation from CUH is that CMV negative products should not be routinely requested for paediatric haematology/oncology patients, even those who may require allogeneic bone marrow transplants in future.

However, some BMT teams do not fully agree with this statement and feel that there is still a significant risk of CMV transmission when transfusing blood components from CMV positive donors to CMV negative BMT / PBSCT recipients. Patients who have received an allograft BMT / PBSCT should have a discharge letter from their transplant centre which will clarify the components/special requirements needed. Great Ormond Street do still routinely request CMV negative components for their post-transplant patients.

However, if a CMV negative child who has previously been given CMV negative products needs platelets in an emergency, and the only products available are CMV unscreened, these should be used, regardless of previous products given.

10.9.2.1 Indications

- Pregnant women
- IUT
- Neonates up to six months from birth
- Granulocyte transfusions to patients who are CMV IgG negative

10.9.3 HLA-matched platelets

Fever and certain medications can cause refractoriness to platelet transfusion. Additionally, repeatedly transfused patients may develop antibodies to platelet antigens and become refractory to platelet transfusions.

If you suspect platelet refractoriness, take a blood count 1 hour & 4 hours after a platelet transfusion to confirm poor increment.

HLA matched platelets can be arranged by the transfusion lab for refractory patients. Please note these platelets need to be ordered several days in advance and cannot be provided in an emergency.

NB HLA-matched platelets must be irradiated.

10.9.4 Hepatitis E negative

There is now universal hepatitis E screening for all blood components in the UK, so there is no longer a requirement to request specific Hepatitis E negative components for immunosuppressed patients and/or neonates.

10.9.5 Extended phenotyped red cells

Children who are on a regular transfusion program (e.g. thalassemia) will require extended phenotyped red cells. The child's full Rh phenotype will have to have been established (which may be via genotype if they have been transfused) and the fully Rh matched red cell component will need to be requested specially via the transfusion laboratory. These patients include patients with sickle cell anaemia, thalassaemia and other rare anaemias.

10.10 References

- Foukaneli T, Kerr P, Bolton-Maggs PHB, Cardigan R, Coles A, Gennery A, Jane D, Kumararatne D, Manson A, New HV, Torpey N; BCSH Committee. Guidelines on the use of irradiated blood components. Br J Haematol. 2020 Dec;191(5):704-724. doi: 10.1111/bjh.17015. Epub 2020 Aug 18. PMID: 32808674.
- New HV, Stanworth SJ, Gottstein R, Cantwell C, Berryman J, Chalmers EA, Bolton-Maggs PHB; BSH Guidelines Transfusion Task Force. British Society for Haematology Guidelines on transfusion for fetuses, neonates and older children (Br J Haematol. 2016;175:784-828). Addendum August 2020. Br J Haematol. 2020 Dec;191(5):725-727. doi: 10.1111/bjh.17109. Epub 2020 Nov 18. PMID: 33207000.
- New HV, Berryman J, Bolton-Maggs PH, Cantwell C, Chalmers EA, Davies T, Gottstein R, Kelleher A, Kumar S, Morley SL, Stanworth SJ; British Committee for Standards in Haematology. Guidelines on transfusion for fetuses, neonates and older children. Br J Haematol. 2016 Dec;175(5):784-828. doi: 10.1111/bjh.14233. Epub 2016 Nov 11. PMID: 27861734.

11 Management of Hickman Lines and Indwelling Ports

In many haematology/oncology patients, indwelling, tunnelled central lines are inserted to ensure venous access and to minimise the need for venepuncture and cannulation. Specific management is required to minimise complications.

Prior to the insertion of any tunnelled central line, all babies/children must bath/shower in Octenisan wash which is supplied by the PTC. This must take place within 24 hours of this procedure. NB: Octenisan wash is licensed for use in babies from birth.

Do not use syringes smaller than a 10ml except for drug accuracy e.g. chemotherapy. In these circumstances Hickman lines & accessed indwelling ports must be flushed initially and have the position of the line checked by obtaining blood flash back with a 10ml or larger syringe.

A needleless bung should be used at all times and all interventions must be carried out using aseptic non touch technique (ANTT).

Hickman lines and accessed indwelling ports must be kept secured at all times (role of 'wiggly bags', adapted vests/bra tops, etc.) to reduce risk of line or indwelling port needle being dislodged.

Care should be taken when bathing/showering. Line tips should not be allowed to sit in bath water or a child's nappy.

11.1 Accessing Indwelling Ports

- Skin preparation with 2% chlorhexidine in alcohol is paramount prior to inserting needle.
- Always use a non-coring needle to access, and position of the needle must be checked prior to all drug / fluid administration.
- The needle must be changed every 7 days when in use.

11.2 Flushing

- Hickman lines should be flushed with 3-5ml Heparinised saline **10 units per ml** after use and once a week if not in use. If the line is being accessed more frequently than 24 hours it only requires flushing with saline after each intervention.
- Indwelling ports, when not in use, should be flushed when the needle is removed and every 4 weeks with 5-6ml Heparinised saline **100 units per ml**. If the line is being accessed daily (e.g. for daily cytarabine), flush with Heparinised saline **10 units per ml.** If accessed more frequently than 24 hours it only requires flushing with saline after each intervention.
- Always flush lines off under 'positive pressure' using a pulsating method.

11.3 Dressings

- Either Opsite IV 3000 or IV Tegaderm dressing should be used to cover the Hickman line exit site and to secure an indwelling port needle in position. The dressing must be dated when applied and changed every **seven days** or sooner if peeling off.
- Alternative dressing to use for babies/children who react to both Opsite and Tegaderm dressings is Mepore dressing. The use of Cavilon sponges as a skin barrier is recommended before applying Mepore dressings, which must be changed daily.
- The Hickman line exit site should be cleaned with 2% chlorhexidine in alcohol **weekly**. **NB 2% chlorhexidine in alcohol is not** licensed for use in babies under 2 months. In such cases, sterile 0.9% normal saline should be used instead.
- A biopatch (1 inch) 360° protective disk (chlorhexidine impregnated) is applied to the Hickman line site at the time of insertion. This is changed every 7 days (or earlier if swollen) for the first 4 weeks only.

11.4 Trouble-shooting

- If CYP reports any pain/discomfort when the line is being accessed, ensure the line is patent by obtaining a flashback and flushing.
- **Blockage:** If line becomes stiff or blocks, instill Urokinase 5000 -10,000units, leave for a minimum of an hour (ideally longer), then remove. Label line ends. For indwelling ports consider replacing needle prior to instilling Urokinase.

  If Urokinase is unavailable consider alteplase.
- **Dislodgement – Hickman lines: If there is a history of the line being accidentally "pulled" or the cuff is visible or** if line moves outwards, check position with chest x-ray. If line falls out apply pressure over neck point where line inserted
- **Perforation – Hickman lines:** If develops a perforation, clamp above level of hole. Line may be repairable. Always discuss with Addenbrooke's.

12 Prescribing and administration of Systemic Anti-Cancer Therapy (SACT) for Children and Young People (CYP)

The decision to treat with a course of chemotherapy and the choice of a particular regimen will only be taken by a consultant paediatric oncologist or haematologist at the PTC.

The first course or cycle of chemotherapy of the chosen regimen will be prescribed by a consultant or SAS (including associate specialist) in paediatric haematology or oncology or a specialist trainee (ST4 or above) at Addenbrooke's. If prescribed by a training grade doctor the prescription will be countersigned by a consultant.

The following is reproduced from the Addenbrooke's guidelines CSO/C007

Definitions

ANC	Absolute neutrophil count
CVAD	Central Venous Access Device
CYP	Children and Young People
FBC	Full Blood Count
GFR	Glomerular Filtration Rate
IM	Intramuscular
IT	Intrathecal
IV	Intravenous
LFTs	Liver Function Tests
MAR	Medication Administration Record
NaCL	Sodium Chloride
NG	Naso-gastric
PEG	Percutaneous Enteral Gastrostomy
PO	Per oral
PPE	Personal Protective Equipment
SACT	Systemic Anti-Cancer Therapy
SC	Subcutaneous

12.1 Training

All new medical staff, ST4 and above, will receive training and education in the prescription and administration of SACT. Once deemed competent, their training certificate will be signed & their name will be entered on the respective register of persons trained and approved to prescribe and administer PO/PEG, IV, IM, SC and IT SACT.

All nursing staff undergo a stipulated programme of SACT training and education.

Prior to commencing the SACT Administration Package, nurses must fulfil the following criteria:

- be qualified nurses who are working within paediatric oncology/haematology
- be competent in medication administration via all relevant routes
- be competent in the care of CVADs
- have a minimum of 6 months experience in children's oncology (3 months minimum on ward C2/paediatric day unit if had prior oncology experience)
- work within The Code (NMC 2018)

SACT training must cover:

- legal and professional responsibilities
- principles of SACT
- health and safety issues
- supervised practice and complete competency document

Once assessed as competent, nurses will be entered onto the respective oral, IV and IT parts of the SACT register.

12.2 SACT: principles of prescribing

12.2.1 Pre-treatment blood counts

A common side effect of SACT is myelosuppression. The nadir (lowest point) of the FBC occurs at approximately 10 days from the start of SACT. Bone marrow recovery should occur before the next course of SACT can start in most protocols. This usually occurs about 3 weeks after the start of the previous course.

As FBC requirements are protocol dependant, please check carefully and consider the following points:

- Ensure the ANC (absolute neuropils count) is within protocol limits
- Ensure GCSF, if prescribed, has been stopped at least 24 hours before SACT. Check if protocol requires ANC to be unsupported by GCSF for a specified period of time
- Ensure the platelet count is within protocol limits. Check protocol to consider if platelet count needs to be unsupported by transfusion
- Further FBCs are usually unnecessary during SACT as the count is not expected to fall until the following week

12.2.2 Further tests and considerations

Ifosfamide, Cisplatin and Carboplatin may cause renal tubular electrolyte loss.

- Check electrolytes including Ca^{2+} & Mg^{2+} are normal as a baseline. Bicarbonate levels may also need to be tested.

- As a minimum, repeat electrolytes on alternate days whilst receiving SACT and daily if on Intravenous hydration.

Anthracyclines such as Doxorubicin, Daunorubicin and Mitoxantrone may cause cardiotoxicity. Ensure that an up to date ECHO result is available.

- Dexrazoxane should be prescribed (following MDT approval) if the cumulative dose is ≥300mg/m^2. Discuss with consultant responsible for the child's care.

Dactinomycin and Methotrexate may cause liver impairment.

- Confirm LFTs are within normal range pre commencing SACT

Confirm if other results e.g. audiology, GFR, echocardiogram are required before a course of SACT.

Confirm tumour markers e.g. AFP, hCG or VMA have been measured where appropriate, and that other tumour reassessment scans have been performed at the appropriate time.

Ensure that the appropriate tests are satisfactory **before** signing go ahead. Results from other hospitals may be displayed under the EPIC MEDIA tab.

12.3 Giving go ahead for treatment

This is the responsibility of competent clinicians on the SACT register.

Newly diagnosed / protocol change

- For newly diagnosed CYP, or when there has been a change in protocol, go ahead should be given by a consultant on the SACT register. This confirms verification of the SACT prescription. This should be documented in the Onc Haem tab under "Clinician go ahead to treat" as "Second signature for C1 prescribed by SpR".
- The CYP may be clinically reviewed by a SACT competent registrar to determine that they are "fit" to proceed with SACT, providing a consultant has verified the SACT prescription as above. This must be documented in the Onc Haem tab under "Clinician go ahead to treat" or notes.

Subsequent courses

- Go ahead for subsequent courses can be given by a SACT competent Registrar.

12.4 Checking SACT

- Administration of IV, IM, SC and PO SACT is generally the responsibility of nurses.
- In times of SACT competent nursing staff shortages, it is appropriate for an administering SACT competent nurse to check SACT with a SACT competent doctor on the register.

- All SACT administered by a SACT competent doctor should be checked by a SACT competent nurse
- IV peripheral SACT is **generally** administered by SACT competent medical staff, however if approved by a consultant, peripheral IV non-vesicant SACT **may** be administered by two SACT competent nurses as an exception. This should be documented in the CYP's notes.
- IT SACT is **always** administered by medical staff.

12.5 SACT administered PO or via an NG tube/PEG

Two people are necessary to check SACT given PO or via an NG/PEG, following NG guidelines as appropriate:

- Two oral SACT competent nurses, or
- A SACT competent doctor and an oral SACT competent nurse

12.6 SACT administered via SC/IM injection

Two people are necessary to check SACT given as a SC or IM injection:

- Two SACT competent nurses, or
- A SACT competent doctor and a SACT competent nurse

12.7 SACT via a peripheral cannula

Two people are necessary to check IV peripheral SACT:

- An IV SACT competent doctor administering and the IV SACT competent nurse checking (with the possible exception of IV peripheral non-vesicant SACT as above, see 9.4).

12.8 SACT via a CVAD

Two people are necessary to check SACT via a CVAD:

- Two IV SACT competent nurses, or
- An IV SACT competent doctor with an IV SACT competent nurse

12.9 SACT via IT route

Two people are necessary to check IT SACT, the IT SACT competent doctor administering and the IT SACT competent nurse checking.

13 Administration of SACT procedure

IT SACT has its own checking and administration guidelines.

Administration should comply with Trust medication administration policies, adhering to ANTT principles.

Administration of SACT should always be given via a separate lumen to blood products or parental nutrition.

- Review child's allergy status
- Ensure consent has been signed by the appropriate parent/carer
- Ensure all go ahead criteria, under "nursing communications" in the onc haem tab, have been met including investigations and blood result criteria
- Ensure the prescription matches the flow sheet in the protocol (see reference links associated with the prescription, paed oncolnet or the blue sheet)
- Check child's weight and surface area. If changed, ensure resultant drug dosage is not </> 10% of original dosage
- Ensure the drug has been prescribed by a SACT competent doctor
- Ensure the prescription has been checked by a SACT competent pharmacist
- Ensure the 'go ahead' has been signed by a SACT competent doctor (a SACT competent consultant if this is the first course of SACT, can be an SpR if it is a subsequent course of SACT, as per 11.3)
- Release and prepare the SACT and any supporting fluid and / or medication to the MAR
- Retrieve drug from fridge / cupboard and sign SACT log sheet. Check storage has been appropriate as per label
- Check the dose of the drug and diluent fluid, and volume of fluid on the syringe/infusion bag against the prescription.
- Check the expiry date of the drug, name and hospital number of the CYP (and date of birth if it is IT SACT)
- Ensure the syringe/bag has a pharmacy check signature
- Add the SACT batch number into comments within the MAR

13.1 Bedside check

- proceed as per section 12.2, depending on SACT to be administered
- administration should take place in designated SACT administration locations
- administration should take place ideally at the child's bedside, always in a non-carpeted area
- discuss SACT with parent /carer, and CYP as appropriate, and reaffirm consent to proceed
- check CYP's name band against the MAR

- confirm CYP's allergy status
- ensure IV access is patent
- review and confirm any concurrent hydration is administered at the correct rate
- review and confirm supportive, additional medication is administered e.g. mesna
- ensure CYP has received anti-emetic as prescribed
- discuss additional nursing considerations with parent/carer and CYP's nurse
- ensure all SACT is signed for on the MAR including the drug batch number

13.2 Safety

NB: detailed policies for safe handling of SACT can be found on oncolnet.

The following is a summary:

13.2.1 Safety re SACT administration timing

- Courses of SACT should normally start on Monday to Friday
- SACT should be administered, or infusions commenced, during normal working hours
- SACT should only be administered outside normal working hours in exceptional circumstances, agreed and documented in CYP's notes, by the consultant

13.2.2 PPE safety

- Wash hands before & after handling SACT
- Gloves and apron to be worn,
- Goggles to be worn when administering cytotoxic IV SACT
- SACT to be connected/disconnected to a giving set at the waist height of the administrator
- Ensure you are familiar with the 'Cytotoxic solution spillage procedure':

p_oh_c018_cytotoxi
c_solution_spillage_v

13.3 Administration of Vesicant chemotherapy: Vinca Alkaloids & Dactinomycin

NB: VINCRISTINE SHOULD NOT BE GIVEN ON THE SAME DAY AS INTRATHECAL DRUGS

These drugs are vesicant if extravasated into soft tissues. Caution is required to minimise the possibility of extravasation.

Always:

- Use diluted preparations of vinca alkaloids
- Flush with 5-10mls of 0.9% sodium chloride after administration

13.3.1 Peripheral administration of vesicant SACT

- Must be given by a doctor
- **Do not use EMLA** (masks pain from extravasation)
- Ethyl chloride spray may be useful
- Use hand veins **NOT** antecubital fossa veins for peripheral administration as extravasation of vesicant material over a joint may result in contractures
- **Draw back blood** and flush with 0.9% sodium chloride first
- **ONLY** give if blood flows back freely and 0.9% sodium chloride flushes in easily with no swelling or blanching
- Ensure blood flashback and check site throughout administration – if any swelling or acute discomfort arises, treat as an extravasation. Liaise with consultant re any remaining SACT to be administered

Vesicant chemotherapy may be given via a cannula already in situ ONLY if:

- It has been in situ for <48hours and there is no redness
- Blood flows back freely on aspiration
- 0.9% sodium chloride flushes in easily with no swelling or blanching

13.3.2 CVAD administration of vesicant SACT

- Ensure blood flashback prior to administration to ensure patency
- Ensure there is no swelling over the track of the line before giving the drug
- Flush CVAD with 5-10mls 0.9% sodium chloride
- Flush with 5-10mls of 0.9% sodium chloride after administration
- If infusional SACT is administered the nurse should be competent to use the infusional pump and nursing care delivered as per Trust guidance
- Infusion rates should be checked by the 2 SACT competent nurses or the SACT competent nurse and the SACT doctor involved in the administration process
- If infusional vesicant SACT is administered monitor CYP for any change in sensation/discomfort around the CVAD. If concerned, immediately stop the infusion, confirm line patency and liaise with medical team as required

13.3.3 Peripheral administration of non-vesicant SACT

- Must be given by a doctor unless if approved by a consultant, peripheral IV non vesicant SACT may be administered by two SACT competent nurses as **an exception**. This should be documented in the CYP notes
- Emla or ethyl chloride spray may be used
- Draw back blood and flush with 0.9% sodium chloride first
- **ONLY** give if blood flows back freely and 0.9% sodium chloride flushes in easily with no swelling or blanching
- Ensure blood flashback and check site throughout administration – if any swelling or acute discomfort arises, treat as an extravasation. Liaise with consultant re any remaining SACT to be administered

13.3.4 CVAD administration of non-vesicant SACT

- Ensure blood flashback prior to administration to ensure patency
- Ensure there is no swelling over the track of the line before giving the drug
- Flush CVAD with 5-10mls 0.9% sodium chloride
- Flush with 5-10mls of 0.9% sodium chloride after administration
- If infusional SACT is administered the nurse should be competent to use the infusional pump and nursing care delivered as per Trust guidance
- Infusion rates should be checked by the 2 SACT competent nurses or the SACT competent nurse and the SACT doctor involved in the administration process
- If infusional SACT is administered monitor CYP for any change in sensation/ discomfort around the CVAD. If concerned, immediately stop the infusion, confirm line patency and liaise with medical team as required

14 Anti-emetics

This information is reproduced from the CUHFT trust Paediatric Oncology guideline CSO/E005 v1 and based on CCLG guidance.

14.1 Key messages

- Children and young people about to undertake chemotherapy should have their chemotherapy assessed for emetogenicity.
- Children and young people about to undertake chemotherapy should have their emetogenicity-assessed anti-emetic treatment prescribed prior to chemotherapy, adapted to their own personal experience.
- Prophylaxis: For children and young people receiving very highly emetogenic chemotherapy, a combination of 5HT3 antagonist (ondansetron), dexamethasone and aprepitant should be prescribed unless there is a contraindication.
- If breakthrough or refractory nausea or vomiting occurs, move up to the next permitted level for this and subsequent courses.
- Anti-emetics should be administered on each day of chemotherapy and for 3 days afterwards.
- For children and young people who develop anticipatory nausea and/or vomiting, psychological interventions are appropriate first-line therapy. Low dose lorazepam may be prescribed the day before, and from the first day of chemotherapy if required.

14.2 Introduction

Chemotherapy-induced nausea and vomiting (CINV) are said to be the most frequently documented distressing side-effect of childhood cancer treatment, potentially influencing compliance with future treatments if not managed appropriately (Wood et al. 2015). Managed incorrectly, they can lead to physical problems such as anorexia, malnutrition and dehydration, plus psychological complications that in turn may lead to anticipatory nausea and vomiting (Rodgers et al. 2012; Dewan, Singhal and Harit, 2010).

Nausea and vomiting are reflexes initiated by the body to expel toxic substances from the stomach and intestine (Navari, 2013). Emesis is co-ordinated by the vomiting centre situated in the medulla which receives input from the chemoreceptor trigger zone (CTZ) found in the area postrema and is outside of the blood-brain barrier. It is stimulated by circulating toxins or drugs such as chemotherapy. The CTZ possesses many $5HT_3$ receptors, NK1 receptors and dopamine receptors (D2). The vomiting centre is stimulated by drugs, smells, sights, emotions etc. as well as G.I input. CINV may result from chemo or CSF fluid acting directly on the CTZ in the vomiting centre but chemotherapy may also induce the release of serotonin and substance P from cells within the gastric mucosa.

The different stages of CINV are acute (0-24hrs after 1st dose); delayed (24hrs-5 days post chemotherapy) and anticipatory (prior to the start of chemotherapy). Physiological differences exist in acute and delayed CINV. Acute CINV is mediated by the neurotransmitter serotonin, whereas delayed CINV is mediated by substance P. Therefore, optimal management of CINV may require targeting the peripheral pathways with a $5HT_3$ receptor antagonist **and** the central pathway with an NK1 receptor.

Risk factors for emesis include:

- High levels of anxiety
- First course of chemotherapy
- Emetic history
- Age: adolescents/young adults are more susceptible than young children
- Female sex
- History of motion sickness

Caution: symptoms of the patients' disease may cause emesis. These symptoms may need evaluation e.g.:

- Raised intracranial pressure
- Concomitant medication
- Side effects of other treatment (e.g. constipation)
- Enteral feeding
- Hypercalcemia

14.3 Prescribing anti-emetics

Identify the most emetogenic drug and prescribe the appropriate level of anti-emetics. Always start anti-emetics at the level reached from the previous course.

If breakthrough or refractory nausea or vomiting occurs, move up to the next permitted level for this **and subsequent** courses. For all levels, failure to control nausea and/or vomiting is defined as two hours of nausea or 1-2 vomits in 24 hours.

Anti-emetics should be administered on each day of chemotherapy and for 3 days afterwards (NB dexamethasone at 50% dosage and aprepitant may only be administered together on the days of most emetogenic chemotherapy).

For children and young people who develop anticipatory nausea and/or vomiting, psychological interventions are appropriate first-line therapy. Low dose lorazepam may be prescribed the day before, and from the first day of chemotherapy if required.

14.4 Emetogenic Potential of Chemotherapy and Anti-emetics

Emetogenicity of Chemotherapy	Drugs	Suggested Anti-emetics
Very high	Cisplatin Cyclophosphamide >2g/m^2 Ifosfamide Melphalan Thiotepa *Combination chemotherapies:* Cyclophosphamide + anthracycline Etoposide + ifosfamide Doxorubicin + ifosfamide Cytarabine 300mg/m^2 + etoposide Doxorubicin + methotrexate 5g/m^2	**Step 1: Cisplatin based regimen, ifosfamide or melphalan:** Ondansetron IV pre-chemotherapy then IV/oral regularly *and* Dexamethasone IV/oral (if appropriate) *and* >6mths: aprepitant oral ONCE daily for 3 days. <6mths: levomepromazine instead of aprepitant **Step 1: For non-cisplatin based regimen: ondansetron and dexamethasone as above +/- levomepromazine (for <1yr to 17yrs)** **Step 2:** *Ensure all doses in step 1 have been optimised before moving onto step 2 and add* aprepitant oral if not used in step 1 for subsequent cycles -> 6 months old. Add levomepromazine for breakthrough if not given up front. **Delayed:** give levomepromazine. Care with aprepitant and ifosfamide. **Metoclopramide can be used instead of levomepromazine for >1 year olds.**
High	Dactinomycin Carboplatin Carmustine >250mg/m^2 Cyclophosphamide 1g/m^2 – 2g/m^2 Cytarabine 3g/m^2/dose Dacarbazine Methotrexate ≥12g/m^2	**Step 1:** **Ondansetron** IV pre-chemotherapy then IV/oral regularly *and* **Dexamethasone** IV/oral (if appropriate) **Step 2:** *(Ensure all doses in step 1 have been optimised before moving on to step 2)* *Add* levomepromazine IV/oral if not used in step 1 [add **Aprepitant** oral if not used in step 1 ***for subsequent cycles -> 6months old]***. **Step 3:** Consider levomepromazine infusion. [Add **Aprepitant** oral if not used in step 1 ***for subsequent cycles for >6months old].*** Metoclopramide can be used instead of levomepromazine for >1 year olds. **Delayed:** Dexamethasone (if appropriate) IV/oral and metoclopramide (up to 5 days after chemotherapy completed).

Moderate	Aldesleukin Arsenic trioxide Azacitidine Cladribine Clofarabine Cyclophosphamide <1g/m^2 Cytarabine >200mg/m^2 to <3g/m^2 Daunorubicin Daunorubicin liposomal Docetaxel Doxorubicin Etoposide Epirubicin Idarubicin Imatinib Inotuzumab Irinotecan Lomustine Methotrexate >1g/m^2 to <12g/m^2 Mitoxantrone Oxaliplatin >75mg/m^2 Procarbazine Temozolomide Treosulfan	**Step 1:** **Ondansetron** IV pre-chemo then IV/oral regularly +/- dexamethasone. If contraindication to steroids, prescribe levomepromazine/metoclopramide instead. **Step 2:** *Add* dexamethasone (if appropriate). Then add levomepromazine or metoclopramide if not already added. [Consider **dexamethasone IV/oral** for subsequent courses if appropriate]. **Delayed:** Dexamethasone (if appropriate) and metoclopramide.
Low	Amsacrine ATG Bortezomib Busulfan Capecitabine CH14.18 antibodies Cyclophosphamide <300mg/m^2 Cytarabine <200mg/m^2 Fludarabine 5-fluorouracil Gemcitabine Gemtuzumab Hydroxyurea Intrathecals Nilotinib Paclitaxel Topotecan Vinblastine/Vincristine Vindesine Vinorelbine	**Step 1:** Use PRN **ondansetron** **Step 2:** **Ondansetron** oral/IV regularly.

Minimal	Alemtuzumab Asparaginase Bevacizumab Bleomycin Chlorambucil Dasatinib Lenalidomide Mercaptopurine Methotrexate <1g/m^2 Nelarabine Rituximab Sorafenib Sunitinib Temsirolimus Thalidomide Thioguanine	**Step 1:** No antiemetics required unless previous history of emesis. If previous history, use **ondansetron**.
Anticipatory	Refers to significant nausea or vomiting prior to the delivery of chemotherapy.	**Lorazepam oral:** give one dose evening before and one dose 1 hour before starting chemotherapy.

14.5 Anti-emetics: Recommended Dosages and Usage Instructions (including contraindications)

<table>
<tr><th>Drug</th><th>Drug dose and route</th><th>Side effects</th><th>Comments</th></tr>
<tr>
<td>Aprepitant

Drug class:
NK1 receptor antagonist

Formulations:

125mg, 80mg capsule
125mg powder for suspension

Indication:

Treat and prevent acute and delayed CINV for cisplatin-based regimens.</td>
<td>Administered orally 1 hour prior to chemotherapy on Days 1, 2 and 3. If no chemotherapy is given on Days 2 and 3, administer in the morning.
<table>
<tr><th>Weight</th><th>Day 1</th><th>Day 2</th><th>Day 3</th></tr>
<tr><td><6kg</td><td colspan="3">Not recommended for <6 months old</td></tr>
<tr><td>6kg-7.9kg</td><td>25mg</td><td>15mg</td><td>15mg</td></tr>
<tr><td>8kg-9.9kg</td><td>30mg</td><td>20mg</td><td>20mg</td></tr>
<tr><td>10kg-11.9kg</td><td>35mg</td><td>25mg</td><td>25mg</td></tr>
<tr><td>12kg-14.9kg</td><td>45mg</td><td>30mg</td><td>30mg</td></tr>
<tr><td>15kg-19.9kg</td><td>60mg</td><td>40mg</td><td>40mg</td></tr>
<tr><td>20kg-24.9kg</td><td>75mg</td><td>50mg</td><td>50mg</td></tr>
<tr><td>25kg-29.9kg</td><td>90mg</td><td>60mg</td><td>60mg</td></tr>
<tr><td>30kg and above</td><td>125mg</td><td>80mg</td><td>80mg</td></tr>
</table>
</td>
<td>Hiccups
Headache
Decreased appetite
Cough
Neutropenia</td>
<td>NB: Can increase ifosfamide mediated neurotoxicity. Monitor closely.

Avoid aprepitant with the following: pimozide, terfenadine and St. John's Wort.

Caution with the following as they may affect aprepitant level and efficacy: ketoconazole, itraconazole, voriconazole, posaconazole, ciclosporin, tacrolimus, sirolimus, everolimus, irinotecan and clarithromycin.

Aprepitant may reduce the efficacy of warfarin. Also reduces the efficacy of hormonal contraception during and for 28 days after its use.

Dose of oral dexamethasone must be reduced by 50%.</td>
</tr>
</table>

<table>
<tr><th>Drug</th><th>Drug dose and route</th><th>Side effects</th><th>Comments</th></tr>
<tr>
<td>Cyclizine

Drug class:
Antihistamine

Formulations:

50mg tablets
IV injection

Indication:

Emesis of raised intracranial pressure, palliative care, irradiation sickness and opiate-induced vomiting.</td>
<td>IV/Oral:

<table>
<tr><td>1mo-5y</td><td>500microgram-1mg/kg up to 3 times daily (Max 25 mg/dose)</td></tr>
<tr><td>6y-11y</td><td>25mg up to 3 times daily</td></tr>
<tr><td>12y+</td><td>50mg up to 3 times daily</td></tr>
</table>

Continuous IV or SC infusion:

<table>
<tr><td>1mo-23mo</td><td>3mg/kg over 24 hours</td></tr>
<tr><td>2y-5y</td><td>50mg over 24 hours</td></tr>
<tr><td>6y-11y</td><td>75mg over 24 hours</td></tr>
<tr><td>12y-17y</td><td>150mg over 24 hours</td></tr>
</table>
</td>
<td>Drowsiness
Dry mouth
Blurred vision
Urinary retention
Restlessness
Insomnia
Tachycardia
Drug-induced rash
Extrapyramidal side effects (rare)</td>
<td>Avoid using with hyoscine and levomepromazine

For continuous IV or SC infusion – dilute with glucose 5% or water for injection.

Crush the tablets and disperse in water prior to administration.</td>
</tr>
<tr>
<td>Dexamethasone

Drug Class:

Corticosteroid

Formulations:

2mg tablets
0.5mg tablets
2mg/5ml liquid
IV injection

Indication:

Effective for delayed emesis and acute CINV.</td>
<td>IV/Oral:

Loading dose 8mg/m2 (max single dose 12mg).
Then:

<table>
<tr><th>SA m^2</th><th>IV/Oral Dose</th></tr>
<tr><td>≤ 0.6m^2</td><td>2mg TWICE a day</td></tr>
<tr><td>> 0.6m^2</td><td>4mg TWICE a day</td></tr>
<tr><td>> 1.2m^2</td><td>8mg TWICE a day</td></tr>
</table>

Or prescribe 2.5mg-5mg/m2 up to three times a day.

Prescribe TWICE daily doses early morning and afternoon to reduce insomnia (e.g. 6am and 4pm). Frequency can be increased to TDS.</td>
<td>Adrenal suppression
Gastric irritation
Osteoporosis
Weight gain
Insomnia
Mood and behavioural problems</td>
<td>Give 1st dose with ondansetron, before chemotherapy.

For maximum of 5 days.

IV dose should be infused.

Dose of dexamethasone must be halved when used in combination with aprepitant.

Contraindications:
Brain tumour patients and those already on steroids (allogenic BMT, SCT and ALL) & those on mifamurtide. Caution in osteosarcoma patients.</td>
</tr>
</table>

<table>
<tr><th>Drug</th><th>Drug dose and route</th><th>Side effects</th><th>Comments</th></tr>
<tr>
<td>Granisetron patch

Formulations:

3.1mg/24 hour patch

Indication:

Treat and prevent acute and delayed CINV.</td>
<td>12 years – 18 years

Apply 1 patch 24-48hrs before chemotherapy due.</td>
<td>Constipation
Headache
Rash

Transient increase in liver enzymes</td>
<td>Patch can be kept on for 7 days.

Remove at least 24 hours after chemotherapy has been completed.

Not licensed in children. Only consider for nausea and vomiting induced by cytotoxic chemotherapy for planned duration of 3-5 days where oral antiemetics cannot be used.</td>
</tr>
<tr>
<td>Hyoscine Hydrobromide

Drug Class:

Anticholinergic/ Antimuscarinic

Formulations:

1mg/72hr patch

Indication:

Refractory CINV</td>
<td>Topically:

Will take up to 6 hours to work.

<table><tr><td>1mo-2y</td><td>¼ of a patch every 72 hours</td></tr><tr><td>3y-9y</td><td>½ of a patch every 72 hours</td></tr><tr><td>10y+</td><td>1 patch every 72 hours</td></tr></table></td>
<td>Drowsiness
Dry mouth
Dizziness
Blurred vision
Difficulty with micturition</td>
<td>Avoid using with metoclopramide and levomepromazine

Apply to a clean, dry, hairless area of skin behind the ear, avoiding any cuts or irritation. Wash hands after applying and the skin area after removal.

Scopaderm patches can be cut.</td>
</tr>
</table>

<table>
<tr><th>Drug</th><th>Drug dose and route</th><th>Side effects</th><th>Comments</th></tr>
<tr>
<td>Levomepromazine

Drug Class:

Phenothiazine

Formulations:

25mg tablet
(tablets may be halved/quartered and dispersed)
IV injection

Indication:

Delayed emesis, refractory and breakthrough CINV.

Useful in vomiting due to raised intracranial pressure.</td>
<td>Oral:

<table>
<tr><td>1mo-11y</td><td>50-200microgram/kg once or twice a day.

Dose may be increased as necessary and as tolerated.

Max 1mg/kg/dose once or twice a day (max 25mg/dose)</td></tr>
<tr><td>12y-17y</td><td>3mg-6.25mg once or twice a day.

Dose may be increased as necessary and as tolerated.

Max 25mg twice daily.</td></tr>
<tr><td>Dose rounding

Important as no liquid formulation available</td><td>Doses less than 3mg – prescribe to the nearest 0.5mg.

Doses greater than 3mg – routed to nearest 3mg or 12.5mg. Liquid can be manufactured in some centres.</td></tr>
</table>
Slow IV infusion over 30 minutes:

25-100mcg/kg TWICE daily or daily

Continuous IV or SC infusion:

<table>
<tr><td>1mo-11y</td><td>Continuous infusion 100-400microgram/kg in 24 hours. Maximum 25mg/24 hours.</td></tr>
<tr><td>12y-17y</td><td>5mg to 25mg over 24 hours increasing as necessary to a max of 25mg/24 hours.</td></tr>
</table>
</td>
<td>Somnolence
Asthenia
Dry mouth
Hypotension
Sedation
Site reaction
Constipation</td>
<td>Avoid using with cyclizine, hyoscine and metoclopramide.

Avoid use in hepatic impairment.

Reduce dose in renal impairment.

Care in patients receiving ifosfamide since sedation may mask signs of encephalopathy.</td>
</tr>
</table>

<table>
<tr><th>Drug</th><th>Drug dose and route</th><th>Side effects</th><th>Comments</th></tr>
<tr>
<td>Lorazepam

Drug Class:

Benzodiazepine

Formulations:

1mg tablet
2mg tablet
(tablets may be halved)
IV injection

Indication:

Anticipatory nausea and vomiting. Breakthrough and refractory CINV.</td>
<td>Slow IV bolus/Oral:

50-100mcg/kg (max 4mg) every 8-12 hours

For anticipatory nausea and vomiting, give one dose evening before and one dose 1 hour before starting chemotherapy.</td>
<td>Drowsiness
Amnesia
Confusion
Ataxia
Pain with IV injection</td>
<td>Care in patients receiving ifosfamide since sedation may mask signs of encephalopathy.</td>
</tr>
<tr>
<td>Metoclopramide

Drug Class:

Dopamine antagonist

Formulations:

10mg tablet
5mg/5mL liquid
10mg/2mL injection

Indication:
Prevent delayed nausea and vomiting. Effective for severe intractable vomiting due to radiotherapy.</td>
<td>IV/Oral:

150mcg/kg TDS – dose banded as below

Prescribe for as short a duration as possible and review regularly.

Contraindicated in children <1 year.
Maximum 10mg per dose TDS.

<table>
<tr><th>Weight</th><th>Oral Dose</th><th>IV dose</th></tr>
<tr><td>10-14.9kg</td><td>1mg</td><td>1mg</td></tr>
<tr><td>15-19.9kg</td><td>2mg</td><td>2mg</td></tr>
<tr><td>20-29.9kg</td><td>2.5mg</td><td>2.5mg</td></tr>
<tr><td>30-60kg</td><td>5mg</td><td>5mg</td></tr>
<tr><td>>60kg</td><td>10mg</td><td>10mg</td></tr>
</table>
</td>
<td>Extrapyramidal side effects
Hyperprolactinemia
Drowsiness
Restlessness</td>
<td>Should be used after levomepromazine failed for maximum 5 days.

Reduce dose in renal and hepatic impairment.

Use with caution with cyclizine and hyoscine – will reduce prokinetic effects.

Treat dystonic reactions with IV bolus of procyclidine:

<table>
<tr><td><2y</td><td>0.5mg-2mg as a single dose</td></tr>
<tr><td>2y-10y</td><td>2mg-5mg as a single dose</td></tr>
<tr><td>>10y</td><td>5mg-10mg as a single dose</td></tr>
</table>

Usually effective in 5-10 mins but may take up to 30 min.</td>
</tr>
</table>

Drug	Drug dose and route	Side effects	Comments
Nabilone **Formulations:** 1mg capsule **Indication:** For delayed and refractory CINV in adolescents. Used for highly & very highly emetogenic chemotherapy regimes when 1st, 2nd & 3rd line anti-emetics failed for subsequent cycles.	**Oral:** 1mg TDS for children weighing >30kg	Dizziness Drowsiness Behavioural alterations Dry mouth Ataxia Postural hypotension Hallucinations Euphoria Psychotic reactions	A cannabinoid drug with central action. Used in adolescents when refractory to dexamethasone and ondansetron. Start the night before, duration of chemo and until 48 hours after chemo. Do not use with levomepromazine and lorazepam. Not routinely stocked by pharmacy, but is possible to obtain for individual patients with notice.
Ondansetron **Drug Class:** *5HT3 antagonist* **Formulations:** 4mg tablet 8mg tablet 4mg/5mL liquid IV 2mg/mL Sublingual melts: 4mg and 8mg **Indication:** Prevent delayed nausea and vomiting	**IV/Oral:** 5mg/m2 two to three times a day (max 8mg per dose). BSA used should be from the chemotherapy treatment plan (CCLG) rather than the BSA calculated by Epic (DuBois calculation).	Constipation Headache Occasional diarrhoea	Reduce dose in moderate or severe hepatic impairment Do not use with drugs that prolong QT interval

Drug	Drug dose and route	Side effects	Comments
Procyclidine **Drug Class:** *Anticholinergic* **Formulations:** 5mg/mL injection 5mg/5mL liquid 2.5mg/5mL liquid 5mg tablet	**Dystonias:** 7-12 years 1.25mg 8 hourly >12-18 years 2.5mg 8 hourly **Acute dystonia doses: single doses** <2 years 500mcg to 2mg 2-10 years 2-5mg >10 years 5-10mg	Anti-cholinergic	Effective in 5-10 mins but may take up to 30 mins Contra-indicated in GI obstruction, myasthenia gravis. Caution in liver impairment.

14.6 References:

- CCLG Guideline on the Management of Chemotherapy Induced Nausea and Vomiting, Version 1.0 March 2018 https://www.cclg.org.uk/write/MediaUploads/Member%20area/Treatment%20guidelines/CCLG_CINV_Guideline_March_2018.pdf
- Baxter, A., Watcha, M., Baxter, W., Leong, T. and Wyatt, M. (2011) Development and Validation of a Pictorial Nausea Rating Scale for Children. *Pediatrics*, 127(6), pp.1542–1549.
- Dupuis, L.L., Taddio, A., Kerr, E., Kelly, A. and MacKeigan, L. (2006) Development and Validation of the Pediatric Nausea Assessment Tool for Use in Children Receiving Antineoplastic Agents. *Pharmacotherapy*, 26(9), pp.1221-1231.
- Rhodes, V. and McDaniel, R. (1999) The Index of Nausea, Vomiting, and Retching: A New Format of the Index of Nausea and Vomiting. *Oncology Nursing Forum*, 26(5), pp.889-894.
- Wood, J.M., Chapman, K. and Eilers, J.(2011) Tools for Assessing Nausea, Vomiting, and Retching. *Cancer Nursing*, 34(1), E14-E24.
- Dewan, P., Singhal, S. and Harit, D. (2010) Management of Chemotherapy-Induced Nausea and Vomiting. *Indian Pediatrics,* 47, pp. 149-155.
- Kraukauer , E.L., Zhu, A.X., Bounds, B.C., Sahani, D., McDonald, K.R., and Brachfel, E. (2005) Case 6-2005: A 58- Year Old Man with Esophageal Cancer and Nausea and Vomiting and Intractable Hiccups. *New England Journal of Medicine,* 352(8), pp.817-825.
- Navari, R. (2013) Management of Chemotherapy-Induced Nausea and Vomiting: Focus on Newer Agents and New Uses for Older Agents. *Drugs,* 73, pp.249-262.
- Rodgers, C., Norville, R., Taylor, O., Poon, C., Hesselgrave, J., Gregurich, M. and Hockenberry, M. (2012) Children's Coping Strategies for Chemotherapy-Induced Nausea and Vomiting. *Oncology Nursing Forum,* 39(2), pp.202-209.

- Wood, M., Hall, L., Hockenberry, M. and Borinstein, S. (2015) Improving Adherence to Evidence-Based Guidelines for Chemotherapy-Induced Nausea and Vomiting. *Journal of Pediatric Oncology Nursing,* 32(4), pp.195 –20.

15 Side Effects of Commonly Used Cytotoxic Drugs

Below is a list of the most commonly used cytotoxic drugs and their most frequently seen adverse effects. The list is by no means complete, so if you do see a patient post-chemotherapy with a problem not listed, please do contact us.

Drug	Adverse effect	Comments/Precautions
Asparaginase	Hypersensitivity and anaphylaxis Coagulopathy Hepatopathy Pancreatitis	Observe for 30-60 minutes after injection. Warn family about signs of anaphylaxis
Dactinomycin (Actinomycin D)	Myelosuppression Nausea/vomiting Liver dysfunction Mucositis	Toxicity increases if combined with radiotherapy
Carboplatin	Hypersensitivity and anaphylaxis Myelosuppression Nephrotoxicity Ototoxicity Nausea and vomiting	Less nephrotoxic and ototoxic than Cisplatin More myelosuppressive Prolonged myelosuppression
Cisplatin	Myelosuppression Nephrotoxicity Ototoxicity Nausea and vomiting	Renal function tests and audiograms performed regularly during treatment
Cyclophosphamide	Myelosuppression Nausea and vomiting Mucositis Haemorrhagic cystitis Infertility Hair loss	Patient should be well hydrated before during and after administration. Mesna given to protect the bladder when cyclo used in high dosage (>1g/m^2)
Cytarabine	Myelosuppression Nausea and vomiting Mucositis/abdo pain/ diarrhoea Conjunctivitis Rash & fever Arachnoiditis when given IT	NB. avoid steroids during high dose Cytarabine - increases risk of colitis
Daunorubicin Doxorubicin Epirubicin	Myelosuppression Nausea and vomiting Cardiotoxicity Mucositis Extravasation burns Hair loss Fatigue	Acute toxicity with arrhythmias uncommon Delayed cardiomyopathy increasingly recognised. Regular echocardiograms performed on and off treatment. Urine red for 24hrs after administration
Etoposide	Myelosuppression Nausea and vomiting Secondary malignancy	
Ifosfamide	Myelosuppression Nausea and vomiting Renal dysfunction Haemorrhagic cystitis Encephalopathy-rare Infertility	Patient should be well hydrated before during and after administration. Mesna given to protect the bladder.
Mercaptopurine	Myelosuppression Liver toxicity Rashes Anorexia, nausea-rare	

Drug	Adverse effect	Comments/Precautions
Methotrexate	Myelosuppression Liver toxicity Nausea and vomiting Mucositis/diarrhoea Renal dysfunction Headache and dizziness Arachnoiditis Peripheral neuropathy Encephalopathy	Oral (maintenance ALL) High dose intravenous MTX Intrathecal
Vincristine	Neurotoxicity- loss of ankle jerks constipation muscle weakness jaw ache Extravasation burns	Toxicity is cumulative N.B. use dilute solution 1mg in 10 ml
Vinblastine Vinorelbine	As for vincristine, but less neurotoxic May be myelosuppressive	Will need FBC monitoring, unlike vincristine
Temozolomide	Myelosuppression (especially platelets) Nausea and vomiting	
Topotecan	Myelosuppression Nausea and vomiting Renal dysfunction	

15.1 Hypersensitivity, Allergy and Anaphylaxis following chemotherapy administration

- Symptoms may include rash, itchiness, facial swelling, wheeze or breathlessness and shock in most severe cases.
- Highest risk with asparaginase – observe for at least one hour after administration; also seen with carboplatin.
- Follow local anaphylaxis protocols in the event of severe reactions.
- In the event of mild skin reactions during infusions, such as occasionally seen with carboplatin, slowing of the infusion rate may be sufficient to control symptoms.

Please inform Addenbrooke's team of all such cases and discuss further management

15.2 Mucositis

- Particular problem with anthracyclines, high dose melphalan, radiotherapy.
- Symptoms include painful mouth, oesophageal and epigastric pain, mucosa looks dull and white, tongue may have 'scalloped' appearance.
- Topical preparations may help, including lignocaine and hydrocortisone, difflam, gelclair.
- Analgesia is important, may need IV morphine or other opiate.
- Consider the possibility of infection with Candida, Herpes simplex and treat appropriately. If febrile and on antibiotics, include anaerobic cover.
- May need TPN if unable to eat.

16 Radiotherapy: general principles

All radical courses of radiotherapy for children, and any radiotherapy requiring sedation or general anaesthesia, will be delivered either at the Addenbrooke's PTC under the supervision of one of the consultant clinical oncologists, who are core members of the PTC diagnostic and treatment MDT, or at one of the national proton beam therapy centres for eligible patients.

Palliative courses of radiotherapy will usually be delivered at Addenbrooke's.

17 Side Effects of Radiotherapy

17.1 Skin

17.1.1 Erythema

Reddening of the skin can occur following some types of radiotherapy. It occurs in the area included in the radiation field, but may also occur in the skin creases. It is more likely to occur in fair skinned people.

17.1.2 Moist desquamation

This occurs in a proportion of patients who have involvement of skin with tumour and the skin has to be taken to a high dose to eradicate this. Although the skin may become raw and weep, this does not usually last for longer than a week. Steroid creams may help to soothe the area.

17.1.3 Pigmentation

The skin in the area treated frequently becomes brown like sunburn. This may last several months before fading.

17.1.4 Dry desquamation

There may be some dry flaking of the skin in the area that has been treated.

17.2 Gut and mucous membranes

Radiation in the area of the mouth, throat and abdomen can cause considerable upset. The buccal mucosa becomes inflamed and superficially ulcerated for about 3 weeks but will heal completely. In the same way oesophagitis occurs when the oesophagus is irradiated. Irradiation of the abdomen will usually cause some nausea which will require anti emetics. After a couple weeks of treatment to the abdomen most people will develop diarrhoea.

17.3 Hair loss

Hair loss will occur in the area treated. It may regrow, but in areas treated to high dosage e.g. brain tumours this may be far from complete.

17.4 Myelosuppression

If large areas of marrow-producing bone (e.g. pelvis or spine) are irradiated, there may be a drop in the blood count. This is only transitory and will recover in a few weeks. If radiation is combined with chemotherapy a greater and more prolonged drop in the blood count can be expected. A patient's Hb should be kept >100g/L during radiotherapy.

17.5 Effects on the eye

When treating patients in the region of the head and neck, the radiation fields are arranged to minimise the dose to the eye if possible. If the area does receive a high dose, there may be redness and soreness and the eyebrows and eyelashes may be lost. The lens is very sensitive to radiation and a relatively low dose may produce a cataract at any time from 1-10yrs after treatment. Lachrymal glands tend to dry up leading to dryish eyes, which are prone to ulceration.

17.6 Effects on the ear

Most children will develop serous otitis media following cranial irradiation.

17.7 Gonads

Direct gonadal irradiation in males will produce sterility and failure to go through normal puberty.

In females irradiation of the ovaries may be direct such as in abdominal irradiation or dose dependant due to scatter from spinal irradiation.

17.8 Brain

Children who receive cranial irradiation may experience a short period of sleepiness 4-6 weeks after treatment (somnolence). In the long term (1-2yrs post radiation) many children will develop pituitary problems e.g. growth hormone deficiency. Growth and development must be watched closely. Cranial irradiation is avoided in the very young child <2yrs and preferably <3yrs because of the effects on intellectual development.

All children who received significant cranial irradiation (e.g. TBI) will need to be referred to endocrinologists.

18 Clinical trials and safety monitoring

A large proportion of the children to whom these guidelines apply are treated within a clinical trial.

All shared care clinicians are GCP trained and research collaboration agreements with the PTC at Addenbrooke's Hospital are in place for all POSCUs.

Many of the situations described in these guidelines, when occurring in trial patients, will be 'events' as determined by the EU directive for Clinical Trials or detailed specifically in the protocol on which a given patient is being treated.

In order to comply with the clear reporting requirements for purposes of safety monitoring, any clinical intervention or event occurring in a patient, should be considered in the light of the need for safety reporting and notified to the PTC team, including any areas of doubt, whether or not the clinical situation is likely to lead to clinical input from the PTC.

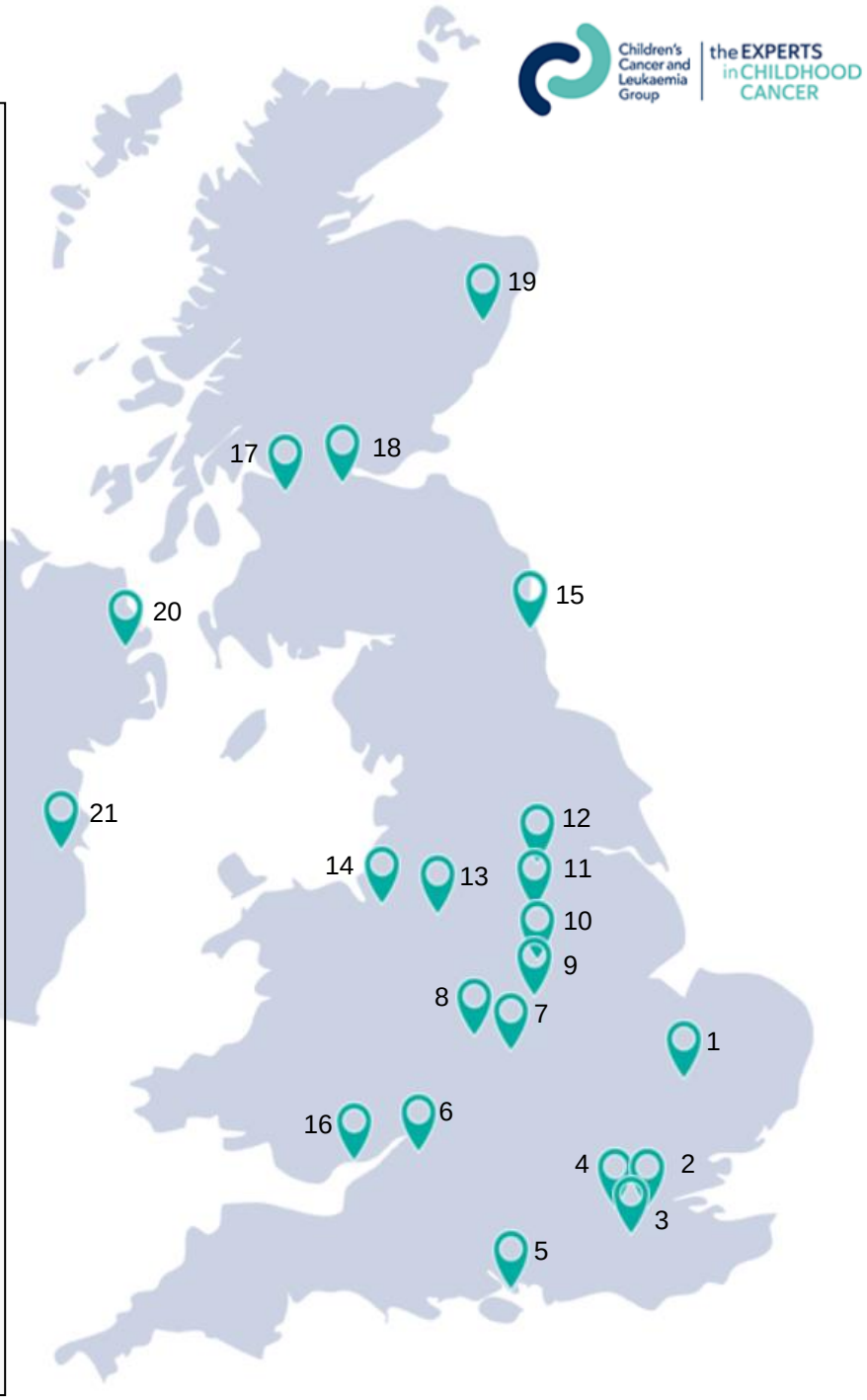
19 Appendices

19.1 Appendix 1: The East of England Children's Cancer Service

Paediatric oncology care in the UK is provided by **21 centres**, affiliated to the Children's Cancer and Leukaemia Group (CCLG). Addenbrooke's Hospital (CUHFT) is the specialist centre which co-ordinates care for the **eastern region**, and was designated by the East of England Specialised Commissioning Group (SCG) as the **East of England Principal Treatment Centre (PTC)** for Paediatric Oncology.

Fig (i): *A map of PTCs in the UK*

1. Cambridge University Hospitals
2. Royal Marsden Hospital
3. University College London Hospital
4. Great Ormond Street Children's Hospital
5. Southampton General Hospital
6. Bristol Royal Hospital for Children
7. John Radcliffe Children's Hospital
8. Birmingham Children's Hospital
9. Leicester Children's Hospital
10. Nottingham Children's Hospital
11. Sheffield Children's Hospital
12. Leeds General Infirmary
13. Royal Manchester Children's Hospital
14. Alder Hay Children's Hospital
15. Great North Children's Hospital
16. The Noah's Ark Children's Hospital for Wales
17. Glasgow Royal Hospital for Sick Children
18. Edinburgh Royal Hospital for Sick Children
19. Royal Aberdeen Children's Hospital
20. Royal Belfast Hospital for Sick Children
21. Our Lady's Children's Hospital



Within the eastern region, a proportion of patient care can be provided closer to their home in one of 10 named hospitals. In this context they are referred to as the **Paediatric Oncology Shared Care Units (POSCUs).**

A list of the East of England POSCUs:

- West Suffolk Hospital, Bury St Edmunds
- Chelmsford & Essex Hospital
- Colchester Hospital
- Princess Alexandra Hospital, Harlow
- Ipswich Hospital
- Queen Elizabeth Hospital, King's Lynn
- Luton & Dunstable Hospital
- Norfolk & Norwich Hospital
- Peterborough City Hospital
- Lister Hospital, Stevenage

Fig (ii): *A map of the approximate area covered by the East of England Children's Cancer Service*

19.2 Appendix 3: Useful Contacts

Paediatric Oncologists	**Dr Gemma Barnard,** Consultant Paediatric Oncologist Tel: 01223 256298 Email: gemma.barnard1@nhs.net
	Dr Sam Behjati, Honorary Consultant Paediatric Oncologist Tel: 01223 256298 Email: sbehjati@nhs.net
	Dr Esther Blanco, Consultant Paediatric Oncologist Tel: 01223 256298 Email: esther.blanco@nhs.net
	Dr Charlie Burns, Consultant Paediatric Oncologist Tel: 01223 256298 Email: charlotte.burns2@nhs.net
	Dr Matthew Murray, University Reader and Honorary Consultant Paediatric Oncologist Tel: 01223 256298 Email: matthew.murray1@nhs.net
	Dr James Nicholson, Consultant Paediatric Oncologist Tel: 01223 256298 Email: james.nicholson4@nhs.net
	Dr Aditi Vedi, Consultant Paediatric Oncologist Tel: 01223 256298 Email: a.vedi@nhs.net
	Dr Anny Wong, Associate Specialist Tel: 01223 256298 Email: anny.wong@nhs.net
Paediatric Haematologists	**Dr Emmy Dickens,** Consultant Paediatric Haematologist Tel: 01223 348151 **Email:** emmy.dickens@nhs.net
	Dr Michael Gattens, Consultant Paediatric Haematologist Tel: 01223 348151 Email: michael.gattens@nhs.net
	Dr Arun Mahendrayogam, Consultant Paediatric Haematologist Tel: 01223 348151 Email: a.mahendrayogam@nhs.net
Paediatric Oncology Speciality Doctors	**Dr Jonathan Tan,** Paediatric Oncology Speciality Doctor Tel: 01223 256298 Email: jonathan.tan4@nhs.net **Dr Lisa Rebello,** Paediatric Oncology Speciality Doctor Tel: 01223 256298 Email: lisa.rebello1@nhs.net
Clinical Nurse Specialists (CNS)	**Clare Clark,** Non-Malignant Haematology CNS Tel: 01223 216692 Email: clare.clark6@nhs.net
	Jo Neville, Non-Malignant Haematology CSN Tel: 01223 216692 Email: joanne.neville2@nhs.net
	Alison Dowsett, Oncology CNS Tel: 01223 216485 Email: alison.dowsett@nhs.net
	Nichola Lightfoot, Late Effects Specialist Nurse Tel: 01223 586695 Email: nichola.lightfoot@nhs.net
	Amanda LeFebvre, Oncology CNS Tel: 01223 216485 Email: amanda.lefebvre@nhs.net
	Hannah Parsons, Oncology CNS Tel: 01223 216485 E-mail: hannah.parsons8@nhs.net
	Lyndsay Salisbury, Neuro-Oncology CNS Tel: 01223 216485 E-mail: lyndsay.salisbury@nhs.net
	Mark Sawrey, Neuro-Oncology CNS Tel: 01223 216485 Email: mark.sawrey1@nhs.net
	add-tr.paedhaemonc@nhs.net **add-tr.paedhaemoncbloods@nhs.net (for results only)**

Department contacts	Oncology SpR:	07523 943717 (M-F 9-5)
	Haematology SpR:	via switchboard (M-F 9-5)
	Ward SpR:	via switchboard (M-F 9-5)
	Paeds SpR:	via switchboard (overnight / weekends)
	PDU:	01223 257157
	C2:	01223 217231

20 Evidence of Agreement

This Guideline was originally developed and agreed for CCN use in 2010.

Version 1 was published on 11 June 2010, and version 2 on 23 June 2011. Version 4 was agreed in September 2016 and January 2017.

Version 5 was agreed in January 2021 by:

The East of England Children and Young People's Cancer Network Co-ordinating Group (CYPCNCG) **Name**: **Position**: Head of Specialised Services (Midlands and East SCG Team) and Chair of the CYPCNCG **Date agreed:**
East of England Strategic Clinical Network **Name**: **Position:** **Date agreed:**
The SSG Members Changes to this document were discussed and agreed to by the East of England Children's Cancer Network SSG at their meeting on 22/01/2021
The CYPCNCG Members This document was agreed to by the East of England Children's Cancer Network Co-ordinating Group at their meeting on in

This version (version 6) has small revisions only, and was overseen by Dr Charlie Burns.

Disclaimer
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Please notify any changes required to Paediatric Haematology and Oncology Quality Assurance team at Addenbrooke's: cuh.paedhaemoncqa@nhs.net

Approval:	Paediatric Haematology and Oncology SDU		
JDTC approval:	n/a		
Owning department:	Paediatric Haematology and Oncology, Addenbrooke's Hospital		
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