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1.
INTRODUCTION
1. Introduction

**Quick Search Function**
Similar to last edition, the electronic version of this document has a built-in quick search function.

For your assistance, in order to find your page or section, go to Contents (pages 2-6), and click the link to jump to correct page, this will facilitate your search.

At the top of every page, there is a “Home button”. Clicking on this will take you back to the Contents pages.

All “Text in Blue” can also be clicked to jump to the referred section.

Within the London area the three principal treatment centres (PTCs), the paediatric shared care centres (POSCUs) and community nursing teams, provide a high quality, comprehensive treatment for children with cancer. While the PTCs are responsible for the cancer treatment, the POSCU and community teams deliver much of the supportive care that many children receive. The supportive care guidelines were written to ensure the POSCU and community teams follow the same (as far as possible) practice to facilitate consistent, optimal treatment of children with cancer and blood diseases.

These supportive care guidelines have been produced collaboratively between the three London PTCs (Royal Marsden, GOSH, UCLH) and representatives from POSCU. This is the fourth edition of the protocol (previous editions were produced in 2003, 2007 and 2011).

The current supportive care protocol 4th edition v1.0 (2014) was produced following extensive revision incorporating up to date evidence, national and/or local guidelines for management. No new chapters have been added. However, the chapters have been reshuffled with the “Oncological Emergencies” chapter being moved to a more prominent position (Chapter 6 instead of Chapter 12 previously). All the guidelines have been revised, sometimes after a lot of debate.

Wherever possible the PTCs have agreed uniform guidelines, although some differences remain between centres. These differences have been clearly highlighted in the document. For some issues where there are both lack of concrete evidence and strong bias in different doctor’s personal practice, it was just not possible to come to a complete consensus between the 3 PTCs. For POSCU and community teams who share care with more than one PTC, these differences may cause confusion, I can only apologise on behalf of all 3 PTCs.

Please see below for significant changes that have been made in the new edition.

I hope that everyone involved in the shared management of children will find the protocol useful. We will continue to produce regular updates and any suggestions or comments will be very welcome. Please email: danny.cheng@gosh.nhs.uk.

Lastly, I want to thank all the lead authors and contributors who have put in a huge amount of effort to make this revision possible. A special thanks to Sonja Tattermusch who edited and formatted the protocol.

**Dr Danny Cheng**

**Associate Specialist in Haematology & Oncology, Great Ormond Street Hospital**

**Lead Editor & Chair of Pan-Thames Supportive Care Protocol Update Group**

27th May 2014 (Date of final approval)
Summary of Significant change between SCP 4th edition and previous 3rd edition (Supportive Care Protocol version 5.0 August 2011)

Chapter 2: Use of Blood Components and haemopoietic cytokines

CMV negative components
Regrettably, the 3 PTC’s have different approaches in adopting the guidelines from Department of Health Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO). Refer to this section for details.

Chapter 3: Treatment of Infections in the neutropenic or immunosuppressed patient

Neutropenic sepsis/Febrile neutropenia protocol
Please read this chapter carefully. Extensive changes have been made based on evidence reported in “Neutropenic sepsis: prevention and management of neutropenic sepsis in cancer patients” National Institute for Health and Clinical Excellence Clinical Guideline (NICE clinical guideline 151 - published in Sept 2012. http://guidance.nice.org.uk/cg151 - last read on 14/4/14)

<table>
<thead>
<tr>
<th>Description of change</th>
<th>Previous guidance (SCP 5.0 Aug 2011)</th>
<th>New guidance SCP 4th edition v1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition of neutropenia</td>
<td>&lt; 0.75 x 10^9/l</td>
<td>0.5x10^9/l or lower</td>
</tr>
<tr>
<td>Definition of fever</td>
<td>Fever &gt; 38°C:</td>
<td>38°C or higher</td>
</tr>
<tr>
<td></td>
<td>• for &gt; 4 hours or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• twice at least 4 hours apart</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fever &gt; 38.5°C once</td>
<td></td>
</tr>
</tbody>
</table>

Initial monotherapy is not recommended for any patients even for those with neutrophils above 0.5 x 10^9/l in view of the frequency of pиптазобактам resistant organisms among PTC patients in London.

Febrile non-neutropenia Protocol
Treatment of fever in immunosuppressed patients without neutropenia
Expanded with new guidance.

In response to comments from POSCUs after the publication of Supportive Care Protocol Version 5.1 (updated 9th May 2014 Protocol Amendment Replacing pages 16 to 29 of Supportive Care Protocol V5.0 August 2011) – some minor changes have been made to the neutropenic sepsis section. (Comparing with v5.1)

Chapter 6: Oncological emergencies

Tumour lysis syndrome
In patients at low risk of TLS, avoid hyperhydration till 12 to 24 hours prior to start of treatment. Risk of iatrogenic problems outweighs the small risk of TLS in low risk category.

Leukostasis and Hyperleukocytosis
For patients with high count leukaemia and at high risk of leukostasis (determined by PTC consultant), then the POSCU consultant will need to arrange immediate intensive care (CATS/STRS) transfer. The patient should arrive at PICU within 2 hours of referral to PTC. Refer to this section for details of other changes.
Chapter 11: Drug treatment of hypertension

The chapter has been reviewed and edited. The main changes are that the table of drug doses is now in keeping with BNF-C.

Chapter 12: Basic Principles of symptom management

Pain and codeine

Management of acute (procedure-related) and persisting pain
ON chemotherapy, targeted therapy or radiotherapy treatment
Off treatment (ie with sustained count recovery)

Significant change in practice is introduced in the usage of paracetamol and second line analgesia for the management of pain in neutropenic patients. Please read this section carefully. The rationales for change are:

In July 2013, the MHRA published a Drug Safety Update restricting the use of codeine in children under 12 years because of concerns over morphine toxicity. It also restricted the use of codeine in patients aged 12-18 years with obstructive sleep apnoea. The WHO guidelines (2012) no longer recommend the use of codeine as a weak opioid for the management of persisting pain in children due to similar concerns over its metabolism. Subsequently a joint statement relating to the use of codeine issued by RCPCH and other associated professional bodies were published in Nov 2013.

Chapter 15: Social and financial support available to families

There are major changes between the versions. Please treat as a completely new document.
2. USE OF BLOOD COMPONENTS AND HAEMATOPOIETIC CYTOKINES
2. Use of blood components and haematopoietic cytokines

Introduction

Transfusion practice has advanced over the last 2 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.

The following guideline deals with common scenarios in paediatric haematology/oncology when blood components (red cells, platelets, granulocytes and plasma) need to be administered. The detailed use of manufactured blood products (such as immunoglobulin, albumin and specific clotting factor concentrates) will not be discussed.

General Information

Medical and nursing staff become very familiar with administering blood components to children with malignant diseases. However, it should always be remembered that families with no previous experience of blood transfusion can be very concerned about its safety and may require much explanation and reassurance. Information leaflets should be offered to the family and informed consent should be obtained before a child receives their first transfusion, just as would be done prior to administration of chemotherapy. Leaflets are available to order or download from the NHS Blood & Transplant (NHSBT) service and include:

- **A parent’s guide for children needing a blood transfusion**
  
  This leaflet pack contains a parent guide, a comic for older children entitled Voyages on the Microsub Discovery’ and a sticker book for younger children entitled ‘Amazing You – Let’s Learn About Blood’

- **Information for patients needing a platelet transfusion**

- **Information for parents of children needing fresh frozen plasma**

- **Information for patients needing irradiated blood**
  
  This leaflet contains a sticker for the front of the child’s notes and a card that should be completed and handed to the parents

The link for download of these leaflets is:

http://hospital.blood.co.uk/library/patient_information_leaflets/leaflets/index.asp
Special Requirements

Patients with certain conditions will require special components. Each PTC and POSCU should have robust systems in place to ensure that their blood transfusion laboratory and all staff treating these patients are aware of their special requirements prior to the first transfusion being administered and at the point in treatment where the requirements may change. The London Regional Transfusion Committee has produced shared care documents which may be used to facilitate communication of these requirements (click to follow link):
http://www.transfusionguidelines.org.uk/Index.aspx?pageid=7694&section=28&publication=RTC

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.

The following groups of patients must always receive irradiated red cells and platelets:

- All patients with Hodgkin lymphoma
  - continue indefinitely
- All patients treated with regimens containing purine analogue drugs
  - fludarabine, cladribine (2-cda), deoxycoformycin, clofarabine, nelarabine & bendamustine
  - continue indefinitely
- All patients treated with anti-thymocyte globulin (ATG)
  - continue indefinitely
- All patients treated with alemtuzumab (Campath)
  - continue indefinitely
- 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 or until lymphocytes >1x10^9/l
  - continue indefinitely if chronic GvHD present or on-going immunosuppression is required
- 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 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 total body irradiation (TBI) was used in conditioning
- All cases where there may be a shared haplotype between the donor and the recipient
  - donations from first or second-degree relatives
  - HLA-matched platelets
- Neonates who have previously received blood components in utero (IUT)
  - Continue until 6 months after the expected date of delivery
- Children with severe T lymphocyte immunodeficiency syndromes, such as
  - Combined Immunodeficiency (CID)
  - Severe Combined Immunodeficiency (SCID)
  - 22q11 Deletion Syndrome (DiGeorge Syndrome / Velo-Cardio-Facial Syndrome)
  - Wiskott-Aldrich Syndrome

In addition, granulocyte transfusions should always be irradiated.

It is not necessary to irradiate fresh frozen plasma or cryoprecipitate.
CMV negative 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. (www.dh.gov.uk/health/2012/03/sabto/)

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.

Regrettably, therefore, there are currently different guidelines for patients being managed by each of the 3 different PTC, as follows:

<table>
<thead>
<tr>
<th>Marsden patients</th>
<th>GOSH patients</th>
<th>UCLH patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow the SaBTO recommendations from diagnosis throughout therapy</td>
<td>Follow the SaBTO recommendations up to the point of conditioning for allogeneic BMT / PBSCT</td>
<td>Not currently following the new SaBTO recommendations</td>
</tr>
<tr>
<td>Give standard leucodepleted components regardless of CMV status</td>
<td>Only require CMV negative components if they have a BMT / PBSCT protocol stating this</td>
<td>All patients who are CMV negative or CMV status unknown should receive CMV negative components if there is any possibility that they may in future require a BMT/PBSCT</td>
</tr>
<tr>
<td>No need to give CMV negative components at any stage</td>
<td>See below for details*</td>
<td></td>
</tr>
</tbody>
</table>

*GOSH patients only:

- For GOSH patients who are undergoing/have undergone BMT/PBSCT and have a protocol stating that they require CMV negative blood components during and post-transplant (RMH & UCLH patients see above):
  - adhere to this protocol
- For all other GOSH haematology / oncology patients (RMH & UCLH patients see above):
  - give standard leucodepleted components regardless of CMV status. *ie majority of haem/onc (non-BMT) patients DO NOT require CMV negative blood products.*
  - note that this includes patients who may in the future require BMT / PBSCT (as it is accepted by the GOSH team that their risk of acquiring CMV from leucodepleted components is very small prior to conditioning)

Importantly, even if CMV negative components are said to be required, do not delay emergency platelet / blood transfusion for clinically significant bleeding if CMV negative components are not immediately available.

For completeness, it should be noted that SaBTO also concluded that CMV negative blood components should continue to be provided for the following:
- Intra-uterine transfusions
- Neonates
- Planned transfusions during pregnancy (eg for haemoglobinopathies)
Granulocyte transfusions (as these can obviously never be leucodepleted) to patients who are CMV IgG negative and are receiving, or may in the future receive an allogeneic transplant from a CMV IgG negative donor, unless the risks of delay / unavailability outweigh the benefits.

Individual Blood Components

Red blood cells

Indications:

- Top up transfusions due to disease / treatment
  - usual threshold is 7g/dl
  - always check patient protocol, as some will have a higher threshold (eg children with thalassemia major) whilst some may have a lower threshold
  - in children undergoing radical radiotherapy, aim for haemoglobin around 12g/dl
  - if symptomatic from anaemia at a level above their usual threshold, usually appropriate to transfuse on clinical grounds
  - beware newly presenting patients with high count leukaemia (see below)

- Anaemia due to bleeding
  - if significant on-going bleeding, transfuse on clinical grounds
  - refer to local major haemorrhage protocol

Dose:

- Calculate the desired rise in haemoglobin (Hb):
  - 3 ml/kg will raise the Hb by 1g/dl (or 10g/l)
  - Therefore, dose in mls = 3 x weight (in kg) x desired rise in Hb (in g/dl)
  - But note that many laboratories have changed their units for measuring Hb to g/l; in which case: dose in mls = 0.3 x weight (in kg) x desired rise in Hb (in g/l)

- If the volume calculated is <200mls:
  - order and prescribe the red cells in millilitres at a maximum rate of 5ml/kg/hr
  - paedipacks (6 packs divided from one adult unit) are available for small volume transfusions; these reduce wastage and limit donor exposure

- Volumes >200mls:
  - can be rounded to the nearest adult unit (same rate)

Precautions:

- Newly presenting patients with high count leukaemia (>50x10^9/l)
  - discuss urgently with PTC consultant
  - risk of worsening leukostasis with red cell transfusion
  - if required, do not give more than 5ml/kg over 4 hours
  - rarely needed to raise Hb to >6g/dl
  - for more details, see chapter 6 on emergencies

- Transfusion reactions
  - see local guidelines for management (NB: may require reporting to SHOT and MHRA)

Shelf-life and storage:

- 35 days (or 14 days post-irradiation)
- Stored at 4°C (+/- 2°C), transfusion must be started within 30 minutes of removal from fridge
Platelets

Indications:

- Top up transfusions
  - see flow diagram on next page

- Prior to surgical procedures
  - see flow diagram on next page

- Active bleeding
  - aim to keep platelet count >50x10⁹/l
  - or >100x10⁹/l if bleeding at critical site (eg lungs / CNS)

Dose:

- If child weighs <20kg
  - 10ml/kg over 30 minutes

- If child weighs >20kg
  - 1 adult unit over 30 minutes

- Double doses may be required in the following circumstances:
  - Active bleeding
  - Sepsis / DIC
  - Splenomegaly

- In these patients, platelet counts may need to be checked every few hours to identify when to administer next transfusion and to decide if a double dose is required

Precautions:

- It is extremely rare for platelet transfusions to be contraindicated and they should never be withheld if a patient has life-threatening bleeding with a low platelet count

- They may, however, become relatively ineffective due to poor increments:
  - in practice, defined as:
    - failure to rise >20-30x10⁹/l at 1 hour or 10-20x10⁹/l at 24 hours post-transfusion

- If clinical / numerical concern about poor response to platelet transfusions:
  - document 1 hour / 24 hour increments
  - check for potential non-immune causes (see above) and treat appropriately
  - if no cause identified, send samples to NHSBT to test for HLA antibodies
  - if HLA antibodies identified, request HLA matched platelets (this requires the NHSBT to call up specific donors, so needs forward planning and regular communication)
  - monitor increments as before and inform NHSBT of results
  - if good response, continue with effective donors
  - if poor response, take advice from Consultant in NHSBT

Shelf-life and storage:

- 5 days at 22°C (+/- 2°C) with continuous gentle agitation
Platelet Transfusion Guidelines

Haematology/Oncology patients at presentation / on treatment
(Children with chronic non-malignant thrombocytopenia excluded)

Platelet count < 10 x 10⁹/l

→ Yes → Transfuse

↓

No

↓

Platelet count < 20 x 10⁹/l and either: febrile/septic or platelet count likely to fall to below 10 x 10⁹/l before next check

→ Yes → Transfuse

↓

No

↓

Platelet count < 30 x 10⁹/l and either: Child has brain tumour or requires a bone marrow trephine biopsy*

→ Yes → Transfuse

↓

No

↓

Platelet count < 50 x 10⁹/l and either: bleeding, coagulopathy / on heparin or due lumbar puncture or surgery (eg line insertion / removal, not neuro/eyes)

→ Yes → Transfuse

↓

No

↓

Platelet count < 100 x 10⁹/l and either: life-threatening bleeding, bleeding at critical site (lungs/CNS) or due surgery to brain/spine/eyes

→ Yes → Transfuse

*Discuss with operator in advance – some may be comfortable to proceed with a lower platelet count

Try to predict when the platelet count is likely to fall below the threshold for a particular patient and monitor accordingly, so that transfusions can be given to keep the count above that threshold

Always assess that the platelet transfusion given has had the desired effect, either clinically (eg cessation of bleeding) or by a rise in the platelet count above the threshold

In some circumstances it is appropriate to give a platelet transfusion immediately prior to a surgical procedure without checking the count in between – always discuss with the surgeon / operator
**Fresh Frozen Plasma**

**Indications:**

- Correction of coagulopathy due to:
  - DIC / severe sepsis
  - severe liver disease
  - major haemorrhage
  - severe vitamin K deficiency (give vitamin K as well)
  - reversal of warfarin (if prothrombin complex concentrate not available / not advised)
  - clotting factor deficiencies if specific concentrate not available (eg Factor V deficiency)

- Usually FFP is given to correct a coagulopathy if a child is bleeding or requires a surgical procedure

- Occasionally warranted to correct a very severe (or rapidly worsening) coagulopathy in the absence of bleeding/surgery, eg new presentation of leukaemia (especially AML)

- Correction of coagulopathy with FFP in other situations is rarely needed

- FFP should **not** be given as a volume expander

**Discussion with a consultant haematologist is advised in the following situations:**

- Rapidly worsening coagulopathy
- Major haemorrhage
- Reversal of warfarin
- Specific clotting factor deficiencies

**Dose:**

- 10-15ml/kg over 30 minutes

- If child weighs over 20kg, can round to nearest unit (approx. 250ml)

**Source, shelf-life and storage:**

- Sourced from untransfused, male, non-UK donors (to reduce risk of vCJD)
  - treated with methylene blue (as viral inactivation step)
  - final methylene blue concentration <0.15µM
- Can be stored for 3 years at -25°C or below
- Once thawed, can be stored in the fridge (4°C) for up to 24 hours before transfusion

**Octaplas**

- Alternative source of plasma
  - pharmaceutically produced pooled human plasma
  - sourced from countries with low vCJD risk
  - solvent detergent treated (viral inactivation)

- Each unit is exactly 200ml
- Can be stored for 4 years at -18°C or below
- Once thawed, can be stored in the fridge for up to 24 hours
- But once removed from the fridge, must be transfused within 4 hours
Cryoprecipitate

Indications:

- Correction of a low fibrinogen level due to:
  - DIC / severe sepsis
  - severe liver disease
  - major haemorrhage
  - congenital hypofibrinogenemia / afibrinogenemia (if fibrinogen concentrate unavailable)

- Usually given to correct a low fibrinogen if a child is bleeding or requires a surgical procedure

- Occasionally warranted to correct a very low (or rapidly falling) fibrinogen in the absence of bleeding/surgery, eg new presentation of leukaemia (especially AML)

- Correction of fibrinogen with cryoprecipitate in other situations is rarely needed

- Occasionally used as a rich source of factor VIII and von Willebrand factor (if specific factor concentrates not available)

Dose:

- Initially 5ml/kg over 30 minutes

- Young children may require 10ml/kg

Source, shelf-life and storage:

- Sourced from non-UK donors (to reduce risk of vCJD)
  - methylene blue treated
  - each unit is 10-40ml in volume
  - older children may therefore need large number of units (see below)

- Can be stored for 3 years at -25°C or below

- Once thawed, must be kept at room temperature and used within 4 hours

Alternative source:

- Pooled cryo from 5 UK donors
  - Used routinely for adults and children >16 years (due to shortage of non-UK cryo)
  - Should not be used for young children
  - Can be considered for older children (where large volumes are required) after discussion with consultant haematologist

NB: Pooled non-UK, methylene blue treated cryoprecipitate may become available in near future

Fibrinogen concentrate

- A blood product, pharmaceutically manufactured from human plasma
- Can be used to correct low fibrinogen levels in the same situations as cryoprecipitate
- Requires discussion with consultant haematologist
- NB: Does not contain other clotting factors!
**Major haemorrhage**

- As well as requiring large volumes of red cells, patients will become severely thrombocytopenic and coagulopathic

- Patients need very frequent monitoring of blood counts and clotting screens

- At all times, as a minimum, aim to maintain:
  - platelet count > 75x10⁹/l
  - APTT ratio <1.5
  - INR <1.5
  - Fibrinogen >1.5 g/l

- Some patients will benefit from having a much higher fibrinogen level (eg >3g/dl)

- Recombinant factor VIIa (NovoSeven) is no longer considered safe or effective in this situation and **should not be used**

- Please consult your local major haemorrhage protocol for more details specific to your hospital and always involve your consultant haematologist in any major haemorrhage

**Granulocytes**

- Clear evidence for their benefit is lacking, but they are sometimes used for patients with severe neutropenic sepsis, unresponsive to antibiotics / GCSF

- Will always be administered at the PTC (following decision made by the patient’s PTC Consultant)

- Quickest option is to request **pooled granulocytes** from the NHSBT:
  - Discuss case with NHSBT Consultant
  - If agreed, requests must be made by 3pm for granulocytes to be delivered the following day (usually will arrive by 2pm)
  - PTC transfusion laboratory can liaise directly with NHSBT laboratory for subsequent requests on the same patient
  - They will **not** be available on Sundays, Mondays or the day following a Bank Holiday

- Other option is directed single donor granulocytes:
  - These are collected by apheresis from volunteers (usually family members / close friends)
  - Potential donors need to have appropriate blood group to donate and may need to be CMV negative (see earlier)
  - Once suitable donors are identified, they then need to go to King’s College Hospital for further blood tests and a medical consultation to ensure that they are safe to donate
  - They are then stimulated with GCSF and dexamethasone prior to undergoing apheresis the following day
  - Whole process can take several days before the first granulocyte transfusion is ready
  - Therefore, early liaison with the team at King’s College Hospital is advised
  - Contact details as follows:

**Dr. Aleksandar Mijovic**  
Consultant (Apheresis)  
Telephone: 020 3299 2034  
a.mijovic@nhs.net

**Denovan Hess / Elizabeth Tatam**  
Clinical Nurse Specialists (Apheresis)  
Telephone: 020 3299 2051 or ext. 8850  
d.hess@nhs.net or elizabeth.tatam@nhs.net
Administration of granulocytes:
- Plan to transfuse as soon as possible after collection
- If there is an unavoidable delay, granulocytes can be stored at room temperature (must not be agitated or refrigerated) until midnight on the day of collection (pooled granulocytes) or for a maximum of 24 hours (apheresis granulocytes)
- Ensure that the granulocytes have been irradiated
- Pre-medicate patient with paracetamol and chlorphenamine
- If previous reactions, also use hydrocortisone
- Dose is max 10-20ml/kg (pooled) or 10-15ml/kg (apheresis)
- Infuse over 1-2 hours through a standard red cell giving set

Haematopoietic Cytokines

Granulocyte Colony Stimulating Factor (GCSF)

GCSF is commonly used following allogeneic bone marrow transplant and high dose therapy with autologous stem cell rescue, as well as prior to stem cell harvest. It is also used routinely in some protocols to support dose intensive therapy. In addition, its use should be considered in the following situations and every case should be discussed with the responsible consultant:

- Febrile neutropenic episodes not responding to antibiotics and antifungals within an expected timeframe
- Neutropenic patients with extensive cellulitis, necrotising fasciitis, peri-anal infections or severe fungal infections
- Clinically deteriorating patients with neutropenic sepsis
- Patients who have had severe delays in previous chemotherapy courses due to neutropenia

GCSF may be administered intravenously over 30 minutes, or by subcutaneous injection.

Thrombopoietin Receptor Agonists (TPO-RA)

Two TPO-RA (romiplostim and eltrombopag) are licensed for use in adult patients with chronic refractory immune thrombocytopenia (ITP). There is also good evidence for their effectiveness in children with chronic ITP and they are being increasingly used for this indication. Their use in children with marrow suppression due to malignant disease and its treatment has not been studied and at present cannot be recommended.

Erythropoietin

Erythropoietin is used particularly for patients with anaemia due to chronic renal failure. However, there is insufficient evidence to support its use in children with anaemia due to malignant disease or its treatment.
3.
TREATMENT OF INFECTIONS IN THE NEUTROPENIC OR IMMUNOSUPPRESSED PATIENT

Including Neutropenic sepsis/febrile neutropenia

and

Treatment of fever in immunosuppressed patients without neutropenia
3. Treatment of infections in the neutropenic or immunosuppressed patient

Neutropenic Sepsis / Febrile Neutropenia

Introduction
Children with cancer are at increased risk of infection as a result of their disease and/or its treatment. Fever with neutropenia is the commonest manifestation of infection in children with cancer; such infection is potentially fatal. Febrile neutropenia is a medical emergency requiring urgent investigation and the administration of intravenous empirical antibiotic therapy within 1 hour. Aggressive use of inpatient intravenous antibiotic therapy has reduced morbidity and mortality rates and reduced the need for intensive care management.

This chapter is written taking into account of local microbiological sensitivities/resistance and incorporating recommendations based on “Neutropenic sepsis: prevention and management of neutropenic sepsis in cancer patients” (NICE clinical guideline 151 - published in Sept 2012. http://guidance.nice.org.uk/cg151 - last read on 14/4/14)

Definition of neutropenia and fever

- Diagnose neutropenic sepsis in patients having anticancer treatments whose neutrophil count is 0.5 x 10^9 per litre or lower and who have either:
  - a temperature higher or equal to 38°C (by any measurement) or
  - other signs or symptoms consistent with clinically significant sepsis

'Any patient with a low neutrophil count who appears unwell with or without fever should be treated with intravenous antibiotics, even if they do not quite fit the definition of febrile neutropenia'

Neutropenia in children and young people with cancer

- A fever documented at home by parents requires the same urgent treatment as a fever recorded in hospital.
- Any patient who is febrile and could be neutropenic should be seen and assessed immediately by a doctor, nurse practitioner or nurse consultant trained in the management of children and young people with cancer.
- If a child is febrile and the neutrophil count is not known at presentation, the patient must be assessed immediately while awaiting the results of the urgent full blood count and other investigations initiated as indicated in Table 2.
- If a child is febrile and the neutrophil count is higher than 0.5 x 10^9/L but expected to fall in the next 24 - 48 hours, consider starting empirical antibiotics.
- If a child is febrile and the neutrophil count is higher than 0.5 x 10^9/L and there are other concerning clinical risk factors such as significant mucositis, patients with Down syndrome or an HSCT patient, consider starting empirical antibiotics.
- Classic signs of sepsis may be masked by steroids, e.g. during ALL induction and delayed intensification. If in doubt and a neutropenic child on steroids seems unwell, start empirical antibiotics.
- Fever should be unrelated to the transfusion of blood products.
Summary of the emergency management of neutropenic sepsis

0hr

Regardless of neutrophil count or temperature, if unwell, ask for senior review and start antibiotics

- Neutrophils ≤ 0.5 x 10^9/L
- Fever ≥ 38°C

History and examination (and see Table 2)
- Blood cultures (peripheral if no central line)
- Urgent full blood count, renal & liver function tests, CRP and lactate
- Urinalysis for < 5 years
- No routine chest x-ray (unless symptomatic or chest signs)

Use scoring system (Table 1) on admission to assess child’s risk of septic complications

Review patient’s previous Gram negative isolates - if none are resistant to antibiotics below

- Start empirical intravenous antibiotics within 1-2 hours
  - Piperacillin/tazobactam 90mg/kg iv (max 4.5g) 6 hourly
  - Gentamicin 7mg/kg once a day

Aminoglycosides should not be used in the following 3 different group of patients.

In these 3 groups of patients, oral ciprofloxacin can be used to replace aminoglycosides (if clinician is concerned with acutely unwell patient, possible CVC infection or if patient is unable to tolerate oral ciprofloxacin, then IV ciprofloxacin should be used instead of oral. Also note: if concerns with Gram positive organism infection, then teicoplanin or vancomycin may be needed to add to piperacillin/ciprofloxacin combination. Piptazobactam/Ciprofloxacin has poor Gram Positive cover.):

- Bone tumour patients (page 33) – empirical treatment is Ciprofloxacin with Piperacillin/tazobactam – if endoprostheses in situ, add teicoplanin also
- Patients with established or potential renal impairment (see page 34)
- GOSH patients only (NOT UCLH or RMH) with A1555G mitochondrial mutation or where result not known

Continue 48 hours of intravenous treatment

Has the patient remain afebrile for 48 hours since start of neutropenic sepsis episode AND blood cultures negative?

- No exclusion criteria
- In these 3 groups of patients, oral ciprofloxacin can be used to replace aminoglycosides (if clinician is concerned with acutely unwell patient, possible CVC infection or if patient is unable to tolerate oral ciprofloxacin, then IV ciprofloxacin should be used instead of oral. Also note: if concerns with Gram positive organism infection, then teicoplanin or vancomycin may be needed to add to piperacillin/ciprofloxacin combination. Piptazobactam/Ciprofloxacin has poor Gram Positive cover.):
- Bone tumour patients (page 33) – empirical treatment is Ciprofloxacin with Piperacillin/tazobactam – if endoprostheses in situ, add teicoplanin also
- Patients with established or potential renal impairment (see page 34)
- GOSH patients only (NOT UCLH or RMH) with A1555G mitochondrial mutation or where result not known

- Consider starting antibiotics if neutrophil count higher than 0.5 x 10^9/L but concern about dropping counts or if other risk factors such as mucositis, patients with Down Syndrome or stem cell transplant. See page 42

- For patients with penicillin allergy, use IV ciprofloxacin 10mg/kg (max 400mg) every 8 hours instead of piperacillin/tazobactam

- If blood cultures positive
  - Has exclusion criteria from Table 1
  - Continue IV antibiotics beyond 48 hours and follow Standard Risk Protocol

- If patient afebrile (<37.5°C) for 48 hours, clinically well and blood cultures negative, consider stopping all antibiotics at 48 hrs (See page 36 and page 39)

Has the patient remain afebrile for 48 hours since start of neutropenic sepsis episode AND blood cultures negative?

No exclusion criteria

Low risk protocol (page 36)

(If negative blood cultures, child well, and no low risk exclusion criteria present from Table 1 on admission or at 48 hours)

- Consider step down to oral antibiotics at 48 hours
- For flowchart go to page 38

Yes

If patient afebrile (<37.5°C) for 48 hours, clinically well and blood cultures negative, consider stopping all antibiotics at 48 hrs (See page 36 and page 39)

Use scoring system (Table 1) at 48 hours to assess child’s suitability for low risk protocol

Any exclusion criteria according to Table 1? Fever at 48 hrs does not exclude from low risk protocol

Low risk protocol (page 36)

(If negative blood cultures, child well, and no low risk exclusion criteria present from Table 1 on admission or at 48 hours)

- Consider step down to oral antibiotics at 48 hours
- For flowchart go to page 38

No exclusion criteria

Standard risk protocol (page 39)

Continue IV antibiotics beyond 48 hours and follow Standard Risk Protocol

For flowchart go to page 41
### Table 1. Criteria excluding patients from Low Risk Protocol (Modified Alexander Rule)

Use this table at presentation and at 48 hours to decide whether a patient can follow the low risk protocol at 48h. The presence of one or more of the following exclusion criterion on admission or at 48h means that the patient must follow the standard risk protocol. All other cancer patients are considered low risk and therefore eligible for oral antibiotics at 48 hours. Fever at 48h does not exclude from low risk protocol if no exclusion criteria present during admission.

<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
<th>Admission</th>
<th>48h</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>&lt;1 year</td>
<td></td>
</tr>
<tr>
<td><strong>History</strong></td>
<td>Inpatient at onset of FN</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Down Syndrome</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PICU during last febrile neutropenia episode</td>
<td></td>
</tr>
<tr>
<td><strong>Diagnosis/treatment protocol</strong></td>
<td>Aplastic anaemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Infant ALL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Induction for Acute Lymphoblastic Leukaemia (ALL) &amp; T-non Hodgkin's Lymphoma (TNHL)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Relapsed ALL up to week 12 of R3 protocol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acute Myeloid Leukaemia (AML)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Myelodyplasia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>B-Non Hodgkin’s Lymphoma (BNHL/Burkitt’s)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anaplastic Large Cell Lymphoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Relapsed solid tumour with bone marrow involvement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>High risk neuroblastoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Any haematopoietic stem cell transplant (HSCT)</td>
<td></td>
</tr>
<tr>
<td><strong>Clinical features</strong></td>
<td>Hypotension/shock</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rigors</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Altered mental status</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mucositis (unable to tolerate oral fluids or requiring IV analgesia)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Respiratory distress / compromise</td>
<td></td>
</tr>
<tr>
<td></td>
<td>New changes on chest radiography</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Significant focus of soft tissue infection (e.g. tunnel infection, perirectal abscess, cellulitis)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other comorbidity requiring inpatient admission (e.g. organ failure, haemorrhage, significant dehydration, severe vomiting or abdominal pain; severe bony pain, particularly back pain)</td>
<td></td>
</tr>
<tr>
<td><strong>Compliance with outpatient therapy</strong></td>
<td>Inability to tolerate oral antibiotics</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patient compliance</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Social/family concerns</td>
<td></td>
</tr>
<tr>
<td><strong>48h assessment</strong></td>
<td>Neutrophils &lt; 0.1 x 10⁹/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive blood cultures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not clinically “well”</td>
<td></td>
</tr>
</tbody>
</table>

One or more exclusion criteria on admission or at 48h exclude patients from the low risk protocol.
### Table 2. Assessment of patients with febrile neutropenia

The initial clinical assessment of all patients with febrile neutropenia should include the following:

<table>
<thead>
<tr>
<th>Assessments for all patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detailed history and examination</td>
</tr>
<tr>
<td>Scoring system to assess patient’s risk of septic complications</td>
</tr>
<tr>
<td>Blood cultures</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Full blood count and differential</td>
</tr>
<tr>
<td>Other blood tests</td>
</tr>
<tr>
<td>Urinalysis</td>
</tr>
</tbody>
</table>

#### Assessments to consider

| Other blood tests                                                                 | Lactate if patient significantly unwell                                               |
| Chest x-ray                                                                   | Only if symptomatic or chest signs                                                   |
| Stool                                                                         | For culture and virology if acute diarrhoea                                          |
|                                                                                             | Consider C. diff toxin and cryptosporidium antigen                                  |
| Sputum/nasopharyngeal aspirate                                                  | If signs of respiratory tract infection                                              |
| Swabs for culture                                                              | From sites of clinical infection only                                               |
Empirical antibiotic treatment of febrile neutropenia in all patients (except patients with bone tumours)

**Piperacillin / tazobactam**\(^*\) 90mg/kg four times a day (max 4.5g)

AND

**Gentamicin** 7mg/kg once daily\(^*\) (check level prior to second dose)

(For inpatients within GOSH only, amikacin is empirical aminoglycoside due to gentamicin-resistant organisms.)

* Aminoglycosides should not be used in the following 3 different group of patients.
In these 3 groups of patients, oral ciprofloxacin can be used to replace aminoglycosides
(if clinician is concerned with acutely unwell patient, possible CVC infection or if patient is unable to tolerate oral ciprofloxacin, then IV ciprofloxacin should be used instead of oral. Also note: if concerns with Gram positive organism infection, then teicoplanin or vancomycin may need to be added to piptazobactam/ciprofloxacin combination.
Piptazobactam/Ciprofloxacin has poor Gram Positive cover.):
- Bone tumour patients – empirical treatment is Ciprofloxacin with Piperacillin/tazobactam – if endoprosthesis in situ, add teicoplanin also (see below)
- Patients with established or potential renal impairment (see page 34)
- GOSH patients only. (NOT UCLH or RMH) with A1555G mitochondrial mutation or where result not known (unless seriously unwell, septic, hypotensive on PICU, then do use aminoglycosides. See page 35 below)

**Piperacillin / tazobactam is not appropriate if meningitis is suspected.**

Empirical antibiotic treatment of febrile neutropenia in patients with bone tumours

IV **Piperacillin / tazobactam** (Tazocin) 90mg/kg (max 4.5g) four times a day

AND

**Oral Ciprofloxacin** 15mg/kg (max 750mg) twice a day\(^*\)

*Give ciprofloxacin orally unless poor absorption is suspected

*Teicoplanin must be added as empirical treatment of patients with bone tumours if endoprosthesis in situ
Antibiotic choice in febrile neutropenia

- Alternative broad-spectrum antibiotics according to Trust local written policy, agreed with local microbiologists, taking into account local bacterial resistance patterns could be used instead of piperacillin / tazobactam and gentamicin.
- All Trusts should monitor resistance patterns including ESBL-producing bacteria and MRSA.
- Initial monotherapy is not recommended for any patients even for those with neutrophils above 0.5 x 10^9/l in view of the frequency of piperacillin resistant organisms among PTC patients in London.
- It is recommended to stop aminoglycoside treatment early (before or at 48 hours) if blood cultures are negative and if clinically appropriate.
- The empirical regimen is the same irrespective of previous antibiotic courses unless there are known antibiotic resistance guiding recommendations for an individual patient.
- If meningitis is suspected, use meropenem (meningeal doses) as piperacillin / tazobactam is not appropriate and seek specialist advice from microbiology/infectious diseases.
- Continue cotrimoxazole prophylaxis during febrile neutropenic episode.
- If patient has an endoprosthesis, teicoplanin must be added to first line antibiotics of piperacillin-tazobactam and ciprofloxacin on admission.
- Consider adding teicoplanin or vancomycin for penicillin allergic patients receiving ciprofloxacin and gentamicin who have significant mucositis to improve cover for gram positive organisms.
- Consider shunt infection in patients presenting with fever and a VP shunt in situ. These patients must be discussed promptly with the PTC and neurosurgical team.

Patients at risk of renal impairment

- Care must be exercised when using nephrotoxic antibiotics in the following groups of children who are at increased risk of nephrotoxicity:
  - patients receiving cisplatin (e.g. hepatoblastoma, osteosarcoma, medulloblastoma)
  - those with a single kidney (e.g. Wilms post nephrectomy)
- For patients with suspected Gram negative sepsis at risk of renal impairment, the benefits of aminoglycosides may outweigh the risks. This requires individual patient discussion and careful monitoring.
- Consider using regimens for patients with established renal impairment.

Patients with established renal impairment

- Piperacillin / tazobactam with ciprofloxacin are appropriate alternative to the standard empirical antibiotics.

Aminoglycoside monitoring

- Blood for aminoglycoside levels may be taken from the central venous access device and should be taken prior to the second dose and twice weekly thereafter.
- Divided daily dosing requires different monitoring (discuss with local microbiologist).

Aminoglycoside pre-dose trough

- The pre-dose trough for gentamicin should be <1mg/l.
- Dose and/or schedule must be altered if the trough is elevated or the patient has diminished renal function.
- Monitoring of peak levels not normally indicated in patients receiving a single daily dose.
- Amikacin trough monitoring should be discussed with local microbiologist.
- Method of monitoring is accurate whether gentamicin is given as slow bolus or by infusion.
**GOSH patients only (NOT UCLH or RMH patients) with mitochondrial A1555G mutation or where result unknown**

- Patients from RMH or UCLH will not have this test done. Thus RMH/UCLH patients will follow the neutropenic sepsis guidelines without using any sections referencing A1555G mutation.
- For a small group of patients with A1555G mutation, the administration of aminoglycosides can lead to profound sensorineural hearing loss. In one large cohort with mostly Caucasian children, prevalence was 1 in 520 (0.19%). Avon Longitudinal Study of Parents & Children: N Engl J Med. 2009;14(6):640–642. An adult cohort from UK showed prevalence of 1 in 385 (0.26%) BMJ Open 2012;2:e000411.
- Newly diagnosed children from GOSH will have this test done on the first admission to the GOSH. The results of A1555G should be ready 2 weeks after initial diagnosis.
- Ideally, aminoglycosides should be avoided in the first week in newly diagnosed patients or until the result is known.
- Sometimes the benefit of using aminoglycoside outweighs the risk of avoiding aminoglycosides e.g. child seriously unwell, hypotensive, clinical suspicion of Gram negative sepsis, on PICU etc. In these situations, aminoglycosides should be used irrespective of A1555G status. Otherwise in children who are clinically well with fevers within first week of diagnosis, give piperacillin/tazobactam with ciprofloxacin.
- The rationale for above is because it is uncommon for newly diagnosed patients to present with Pseudomonas or Gram negative sepsis in the first week of diagnosis. The fevers of newly diagnosed patients are usually due to malignancy rather than septicaemia. After the “fever due to malignancy” resolves with initiation of chemotherapy, any subsequent fevers will most likely be due to infection and/or septicaemia. In any case, for children who are seriously unwell, hypotensive or clinically suspected to have Gram negative sepsis, the benefit of using aminoglycosides will outweigh the risk of using it in children with unknown A1555G status.
- In children with known A1555G mutation, use regimen for established renal impairment. (p 34)
Low Risk Neutropenic Sepsis: 
Management of low risk patients with febrile neutropenia

The low risk protocol for oral antibiotics after 48 hours of IV antibiotics is applicable only for the following patients:

- no exclusion criteria on admission and at 48 hours
- negative blood cultures at 48 hours
- clinically well
- Neutrophils $\geq 0.1 \times 10^9$/l at 48 hour
- Fever at 48 hours does not exclude from low risk protocol

Management of low risk patients after 48 hours intravenous antibiotic treatment

- Ensure risk assessment complete and appropriate

  - At 48 hour assessment, all intravenous antibiotics may be stopped if:
    - Patient afebrile ($< 37.5^\circ$C) for 48hrs
    - All blood cultures are negative
    - Patient is clinically well

- Patient does NOT need oral antibiotics if already afebrile ($\leq 37.5^\circ$C) for 48h at time of discontinuing iv antibiotics.

- Patients who have fever at 48 hours are NOT excluded from low risk protocol.

- If patient remains febrile but blood cultures negative and patient clinically well, discontinue IV antibiotics at 48 hours and commence oral co-amoxiclav. Give first dose in hospital to confirm that child will tolerate it.

- If allergic to penicillin or co-amoxiclav, consider oral clarithromycin for 5 days.

Co-amoxiclav dosing regimen

<table>
<thead>
<tr>
<th>Age</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-6 years</td>
<td>125/31 suspension 0.5ml/kg tds</td>
</tr>
<tr>
<td>6-12 years</td>
<td>250/62 suspension 0.3ml/kg tds</td>
</tr>
<tr>
<td>&gt; 12 years</td>
<td>500/125 tablet 1 tablet 3 x day or 250/62 suspension 0.27ml/kg tds (max 32mls/day in 3 divided doses)</td>
</tr>
</tbody>
</table>

Follow up for patients discharged on oral antibiotics after 48 hours

- Arrange for review at 72 hours (phone call from nurse or doctor as per local policy)

- Arrange for review at 96 hours (phone call from nurse or doctor as per local policy and check outstanding blood culture results)

- Ask family to monitor and record temperature twice daily
• If there is clinical deterioration at any time after discharge, review at POSCU and admit to ward if necessary

• Continued fever up until 96 hours should not by itself be a criterion for readmission if child is well

• Readmit to ward if fever > 38°C beyond 96 hours from the start of the febrile neutropenic episode

• If readmission needed, follow standard febrile neutropenia management protocol at the appropriate time point i.e. restart iv antibiotics as per empirical regimen but adjusted for sensitivities of any known organisms and commence antifungal therapy once patient is febrile >96 hours from the start of the febrile neutropenic episode.

• For patients who remain at home, oral antibiotics can be discontinued once temperature < 38°C for 48 hours
Management of low risk patients with febrile neutropenia after 48 hours

48 hrs
If patient remains febrile but blood cultures negative and patient clinically well, discontinue IV antibiotics at 48 hours and Commence oral Co-amoxiclav. Give first dose in hospital to confirm that child will tolerate it. Confirm 72 and 96 hr Contact/Review

HOME
Monitor temperature twice daily and keep record

Clinically well
Clinical deterioration
Parental concern
Unable to tolerate Co-amoxiclav

Hospital Review
If penicillin allergic- use Clarithromycin

If admission is necessary follow Standard Febrile Neutropenia Management Protocol at relevant time point

PHONE CALL
Child remains well

72 hrs

Temp ≥ 38°C or +ve blood culture requiring inpatient care or Clinical deterioration

Temp < 38°C and Clinically well

Remain at home

Discontinue antibiotics when Temp < 38°C for 48 hrs

If temp ≥ 38°C at any time beyond 96 hrs
Standard risk neutropenic sepsis:
Management of standard risk patients with febrile neutropenia
Management of standard risk patients after 48 hours intravenous antibiotic treatment

- Ensure risk assessment complete and appropriate
- At any stage at or after 48 hour assessment, all antibiotics may be stopped if:
  - Patient afebrile (<37.5°C) for 48hrs
  - All blood cultures are negative
  - Clinical judgement that patient is safe to stop antibiotics
- Repeat daily blood cultures from all lumens if temperature > 38°C
- Review all culture results regularly. If cultures are positive, repeat blood cultures at 48 hours (to ensure clearance of bacteremia) and review antibiotics as soon as sensitivities are available.
- Only consider switching antibiotics if clinical deterioration or microbiological indication
- Even if patient continues to be febrile, consider whether aminoglycoside can be safely discontinued at 24-48 hours if patient clinically stable and blood cultures are negative.
- Close monitoring of full blood count, electrolytes and aminoglycoside levels
- No routine addition of vancomycin or teicoplanin if unresponsive fever (unless microbiological indication or local signs of infection from central venous access device or endoprosthesis).
- For patients with an endoprosthesis, if clinically well at 48 hours and no positive cultures, teicoplanin should be discontinued.
- No routine removal of central venous access device (unless clinically or microbiologically indicated).
Standard risk patients after 96 hours intravenous antibiotic treatment if persistent fever

- All patients who are febrile and neutropenic at 96 hours should be discussed with the PTC.
- Start empirical antifungal treatment for GOSH/RMH patients.
- For UCLH patients, always discuss with UCLH before commencing antifungals.
- Consider early chest CT, abdominal ultrasound scan for hepatosplenic candidiasis and echocardiogram for vegetations, especially for children post haematopoietic stem cell transplant.
- No routine switching of initial empiric antibiotics in patients with unresponsive fever unless clinical deterioration or a microbiological indication
- No routine removal of central venous access devices as part of initial empiric management of suspected neutropenic sepsis unless clinically or microbiologically indicated
- No routine addition of glycopeptides (teicoplanin / vancomycin) unless signs of local infection of central venous access device. Glycopeptides can be considered if there is severe mucositis and fever is unresponsive.
- Even if patient continues to be febrile, consider whether aminoglycoside can be safely discontinued if patient clinically stable and blood cultures negative if not stopped earlier.

Standard risk patients with persistent fever (> 7 days)

- Discuss with Principal Treatment Centre

Standard risk patients - duration of intravenous antibiotic therapy

- If blood cultures are negative and patient is clinically well, discontinue antibiotics once afebrile for 48 hours
- Positive blood cultures or bacteraemia due to catheter related infection: these patients usually need treatment for at least 10 days from first negative blood culture. If needed discuss with local microbiology team and PTC.
- Certain infections such as osteomyelitis, fungal infections and staphylococcus aureus will require longer treatment. Discuss with local microbiology team and PTC.
- If blood cultures are positive for the following organisms, they should never be treated as ‘contamination’: Gram negative organisms including Pseudomonas aeruginosa, Enterobacteriaceae (eg E coli, Klebsiella spp Enterobacter spp), Staphylococcus aureus, fungus (Candida etc)
- If on AmBisome, continue until resolution of fever, lack of evidence of fungal infection on radiology, improving clinical signs and rising neutrophil count, usually 24 hours after stopping antibacterials and patient can then be discharged.

Discharge of Standard risk patients

- Patients may usually be discharged immediately after stopping antibiotics
- Inform parents to return should the child become febrile again or unwell
Management of standard risk patients with febrile neutropenia

Risk Assessment
Empirical antibiotic regimen

0 Hours

48 Hours

REASSESS

Persistent Fever
Fever Settling

Negative Blood Cultures
Positive Blood Cultures
Negative Blood Cultures and clinically well

96 Hours

REASSESS
Discuss with PTC

Negative Blood Cultures
Positive Blood Culture

? Stop aminoglycoside
Consider anti-fungal treatment

Review antibiotic sensitivities
Duration of therapy dependent on organism isolated
Stop all antibiotics once afebrile (≤37.5°C) for 48 hrs

Negative Blood Cultures
Positive Blood Cultures

Stop aminoglycoside
? S
Non-neutropenic patients with fever do not all need to receive antibiotics routinely but each should be assessed individually and treated according to clinical findings. In addition to standard paediatric assessment for infection, clinician should examine any central venous catheters, shunts or endoprosthesis in situ. Examine along central venous catheter and exit site to look for tunnel infection or cellulitis. Send micro swabs. If needed discuss with PTC.

If ventriculo-peritoneal shunt or endoprosthesis infection is suspected, ensure discussion with the PTC and the patient’s lead neurosurgeon or orthopaedic surgeon respectively. Do not aspirate without discussion with PTC & the surgeons.

* Discuss with microbiology and/or PTC if blood cultures are positive or previous Gram negative isolates resistant to Piptazobactam or Aminoglycosides. Adjust antibiotics as appropriate.
Although many fevers in non-neutropenic patients do not represent serious infection, in one series 25% of deaths occurred in children who were not neutropenic at presentation. **Unwell,** immunocompromised patients with an in-dwelling line should receive piptazobactam and an aminoglycoside within 1 hour of presentation irrespective of the neutrophil count.

All patients with fever should be clinically assessed. Minimum investigations are full blood count and blood culture from central venous access device.

Non-neutropenic patients with fever do not all need to receive antibiotics routinely but each should be assessed individually and treated according to clinical findings.

Central venous access devices can harbour organisms that on flushing lead to bacteraemia. Coagulase negative staphylococci are the typical responsible organism, but it is vital not to miss streptococcal or gram negative infections. Fever and rigor within hours of flushing are the classical symptoms of line infection, but other more non-specific symptoms such as vomiting and abdominal pain without fever are also described. Thus any patient who is unwell within 8 hours of line flush should receive immediate standard dual therapy as above. Early discussion with the PTC and consideration of line removal is mandatory.

For central venous access device exit site or tunnel infections, treat with glycopeptides (teicoplanin/vancomycin) after taking blood cultures and/or skin swabs.

Well, non neutropenic children with line infections caused by coagulase negative staphylococcus can often be managed at home with intravenous teicoplanin (check sensitivities and repeat blood cultures to ensure clearance of bacteraemia).

If there is doubt about whether an infection is a true bacteraemia or a line infection only, take peripheral blood cultures in addition to cultures from the central venous access device.

Children within first 6 months post HSCT usually require admission for iv antibiotics and further investigation of fever – discuss with PTC team.

Consider PCP in a child with leukaemia or Hodgkin’s disease who has missed co-trimoxazole prophylaxis.

If endoprosthesis infection is suspected, ensure discussion with the PTC and the patient’s lead orthopaedic surgeon at Stanmore. Do not aspirate without discussion with Stanmore surgeon.
References

4.
PREVENTION AND TREATMENT OF SPECIFIC INFECTIONS AND VACCINATIONS IN PATIENTS WHO HAVE RECEIVED CHEMOTHERAPY OR HAEMATOPOIETIC STEM CELL TRANSPLANT (HSCT)
4. Prevention and Treatment of Specific Infections and Vaccinations in Patients who have Received Chemotherapy or Haematopoietic Stem Cell Transplant (HSCT)

Varicella-Zoster

Varicella zoster virus (VZV) is a human alphaherpesvirus, which causes varicella (chicken pox) as the primary infection; VZV then establishes latency and re-activates to cause herpes zoster (shingles).

Varicella can be life threatening in children with cancer, and infection is associated with cancer treatment delays. Ask about a history of clinical varicella in the patient and household contacts at diagnosis and arrange vaccination of household contacts with a negative history of chickenpox (see below). Pre-transfusion VZV antibody status should be checked on all patients at the time of diagnosis and should be recorded in the parent held record.

Special circumstances occur after autologous or allogeneic HSCT where the child should be considered at risk irrespective of VZV antibody status until at least 2 years post HSCT and at least 12 months off all immunosuppressive therapy. This should be guided by the BMT team.

Prevention of VZV

Vaccination of siblings/household contacts

Exposure within the household is the setting most likely to cause varicella in the immunocompromised child. It is recommended that healthy susceptible close household contacts of immunocompromised patients receive the VZV vaccine; household contacts that are over one year of age and without clinical history of chickenpox should be vaccinated. The small risk of vaccine related varicella (usually within 1 month of vaccination) should be discussed with the patient and parents. If vaccine related varicella does occur in the vaccine recipient, give the immunocompromised patient prophylactic VZIG.

Post exposure prophylaxis

Patients receiving standard-dose chemotherapy and up to 6 months after receiving standard-dose chemotherapy and following HSCT are at risk of developing varicella following a significant VZV exposure. For definitions of significant exposure see below.

Management is as per the flow diagram below (Figure 1).

If urgent VZV antibody testing is required for patients presenting late, VZIG can be ordered at the same time that the blood is sent for testing and can be returned if the result is positive. If there is significant exposure and VZV status is unknown, send a blood sample to check VZV serostatus. It is usually necessary to recheck VZV serostatus of VZV antibody negative patients with a significant exposure before VZIG is released. However, VZIG administration should not be delayed past 7 days after initial exposure while an antibody test is done. Under these circumstances VZIG should be given on the basis of a negative history of varicella.

For the group of patients with a positive VZV IgG at diagnosis, there is evidence to show that this group of patients may become VZV negative whilst on chemotherapy. Subsequently, the VZV IgG may return to positive naturally. If the patient’s VZV IgG serostatus changes from positive (at
diagnosis) to negative whilst on chemotherapy, there is currently lack of available evidence to support an increased risk of patients developing clinical VZV infection. Therefore, there is currently insufficient evidence to recommend universal re-testing of VZV status in children who were previously VZV positive.

VZIG is not indicated in immunosuppressed patients with detectable VZV antibody as the amount of antibody provided by VZIG will not significantly increase VZV antibody titres in those who are already antibody positive.

Varicella can occasionally occur in immunosuppressed VZV antibody positive patients, but these are likely to be related to defects in cell-mediated immunity.

At risk post HCST patients
Haemopoeietic stem cell transplant patients are at risk of VZV irrespective of antibody status and should receive VZIG up to 2 years post procedure and up to 12 months off all immunosuppressive therapy, unless on aciclovir or IVIG prophylaxis (check with the PTC BMT team)

**Figure 1. Algorithm for management of patients post chemotherapy or post haematopoietic stem cell transplant (HSCT) who come into contact with other children with VZV.**

Is contact significant?

Yes

Has the patient received Chemotherapy only or Post HSCT?

Post HSCT

VZV IgG Negative

Give VZIG or alternatives such as HNIG or aciclovir

Post Chemo

Is patient’s VZV IgG positive?

Not known

Test and act on result

VZV IgG Positive

Observe

Observe

Definition of significant exposure to VZV

**Type of VZV infection in index case:**
The risk of acquiring infection from an immunocompetent individual with non-exposed zoster lesions is remote. The issue of VZIG should be restricted to those in contact with:

- Varicella
- Disseminated zoster
- Immunocompetent individuals with exposed zoster lesions
- Immunosuppressed patients with localised zoster on any part of body (viral shedding can be greater in immunosuppressed patients)

**Timing of exposure in relation to onset of rash in index case:**

- Varicella or disseminated zoster - between 48hrs before onset of rash until no new lesions cropping/ crusting of lesions
- Localised zoster – day of onset of rash until crusting of lesions
Closeness and duration of contact:
- Play or direct contact (in the same enclosed space such as house, classroom or 2/4 bedded hospital bay) for ≥15 minutes
- Face to face contact
- In the case of large open paediatric wards/outpatient department, airborne transmission at a distance has occasionally been reported and giving VZIG to all susceptible high-risk contacts should be considered

VZIG or alternate treatment
Dose of VZIG:
0–5 years, 250mg (one vial)
6–10 years, 500mg (two vials)
11–14 years, 750mg (three vials)
15 years or over, 1000mg (four vials).
Given by slow IM injection

Patients with thrombocytopaenia/bleeding disorders who cannot be given an intramuscular injection should be given intravenous normal immunoglobulin (HNIG) at a dose of 0.2g/kg body (i.e. 4ml/kg for a 5% solution) instead. This will produce serum VZ antibody levels equivalent to those achieved with VZIG (Paryani et al., 1984).

If VZIG is not available, alternatives are:
- HNIG or
- High dose oral aciclovir for 14 days starting at Day 7 after exposure (ie from 7-21 days following contact). For doses see Chapter 5.

Re-exposure
Children re-exposed to varicella or zoster (see above for details of significant exposure) after ≥3 weeks of receiving VZIG and who are VZV IgG negative should have further dose of VZIG.

Information to parents after VZIG
Even with VZIG, the child can still develop varicella.
After VZIG, the incubation period of varicella can be prolonged to 28 days.
If the child develops varicella, he/she will need admission for IV aciclovir.
Live vaccines are not to be given within 3 months of VZIG administration.

Treatment of Clinical Varicella/Herpes Zoster

Varicella and herpes zoster can be fatal in immunosuppressed patients. Presentation may be atypical. Patients should receive intravenous aciclovir for 5 days (or until there are no new lesions developing) followed by 5 days of oral aciclovir (check renal function and modify dose if needed). If cropping of new lesions continues the IV aciclovir should be given until no lesions develop and crusting of lesions occurs.

For doses see Chapter 5.

Patients who have clinical reactivation of VZV after allogeneic HSCT should continue on aciclovir prophylaxis for a further 3 months.
Measles

Take an immunisation history from all newly diagnosed patients and their siblings/household contacts.

Prevention of Measles Infection

Vaccination

The majority, but not all children, will have received measles vaccine as part of the universal childhood vaccination programme before their diagnosis of cancer. Measles vaccine is contraindicated in immunosuppressed patients and must not be given to patients once a cancer diagnosis is made and until at least 6 months after completion of chemotherapy or longer post HSCT (see below). Siblings/household contacts may receive the MMR vaccine as vaccine-acquired infection cannot be transmitted.

Post exposure prophylaxis

The need for intervention following measles exposure depends on the vaccination/ past measles infection status of patient and the degree of immunosuppression of the patient. The most immunosuppressed children (i.e. those undergoing HSCT and until at least 12 months after finishing all immunosuppression and patients on treatment for ALL within and until at least six months after completion of immunosuppressive therapy) are termed Immunosuppressed Group A in this guidance. Group A patients are unlikely to develop or maintain antibody levels from past exposure or vaccination. It is recommended that these patients require urgent testing within 3 days of exposure, regardless of a past history or a previous positive measles antibody result (see Table 3).

Immunosuppressed Group B patients are all other patients with malignant disease until at least six months after completion of immunosuppressive chemotherapy or radiotherapy. Group B patients should be able to develop and maintain adequate antibody from any prior successful vaccination or infection and can therefore be managed on the basis of reliable history or antibody screening (see Table 3).

For management following significant measles contact see Table 3. Significant contact is defined as play or direct contact for more than 15 minutes at home or on ward or school with an individual with virologically confirmed measles during the infectious period (4 days before and 4 days after the onset of the rash). Every effort should be made to confirm the diagnosis of measles in the index case.

HNIG should be given within 6 days of exposure, ideally within 3 days of exposure. For immunosuppressed patients where exposure is recognised late or who are found to be antibody negative or equivocal between 6 and 18 days after exposure, discussion with the specialist caring for the individual should take place, and NHIG may be considered in order to attenuate infection. Where a second exposure occurs more than three weeks after a first dose of immunoglobulin, a further dose of immunoglobulin will need to be considered.

Family members of measles seronegative patients that have contact with measles should be given a dose of MMR up to 18 days after exposure.

As neither immunoglobulin nor vaccines are 100% effective in preventing measles, appropriate infection control procedures should be followed, for example in health care settings. Those receiving vaccine, however, may develop a vaccine-associated measles like rash. Carers should be advised, however, that any illness with rash within the 18 days following exposure should be managed as if it is true measles. If such a rash does develop, oral fluid samples should be collected and sent for confirmation and virus typing, ideally within one week of onset, and vaccination dates clearly documented on the request form.
Dose of NHIG
For immunosuppressed individuals intravenous NHIG is recommended and available in most hospital pharmacies. It achieves more rapid, higher levels of measles antibody compared to intramuscular or subcutaneous product. Consult the product literature for information about administration. **The dose is 0.15 g/kg of intravenous normal human immunoglobulin.** If subcutaneous normal immunoglobulin has to be used, the dose is 0.6 ml/kg.


Treatment of Measles Infection

Most immunosuppressed children with measles do not have a rash or clinical measles. Suspect in cases of 'atypical' or 'viral' pneumonia. Send nasopharyngeal aspirate for culture and immunofluorescence and PCR. There is no effective treatment for measles infection, but it may be worth trying HNIG (and/or steroids for measles pneumonia) along with good supportive care.

Measles encephalopathy occurs several months after the original illness. Complex and intractable seizures are usually followed by severe brain damage or death.

Table 3. Managing immunosuppressed contacts of measles

<table>
<thead>
<tr>
<th>Age group</th>
<th>History</th>
<th>Immunosuppressed Group A</th>
<th>Immunosuppressed Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Born before 1970</td>
<td>Of measles infection</td>
<td>Regardless of history and even if known to be measles antibody positive previously, test again at time of exposure</td>
<td>Assume immune</td>
</tr>
<tr>
<td></td>
<td>No measles infection</td>
<td></td>
<td>Test and issue only if measles antibody negative or equivocal</td>
</tr>
<tr>
<td>Born between 1970 and 1990</td>
<td>Of measles infection</td>
<td>Issue immunoglobulin if measles antibody negative or equivocal</td>
<td>Test and issue only if measles antibody negative or equivocal</td>
</tr>
<tr>
<td></td>
<td>No measles infection</td>
<td>If not possible to test within three days of exposure, offer immunoglobulin</td>
<td>Test and issue only if measles antibody negative or equivocal</td>
</tr>
<tr>
<td>Born after 1990</td>
<td>One measles vaccine</td>
<td>Test and issue if measles antibody negative or equivocal. If not possible to test within three days of exposure, offer immunoglobulin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Two measles vaccines</td>
<td>Test and issue if measles antibody negative or equivocal. If not possible to test within three days of exposure, offer immunoglobulin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unvaccinated</td>
<td>Offer immunoglobulin, ideally within three days</td>
<td></td>
</tr>
</tbody>
</table>

* excluding patients who are already on IVIG replacement therapy for either primary immunodeficiency or severe defects of cell mediated immunity.
Pneumocystis Jirovecii Pneumonia (PCP) and other Interstitial Pneumoniae

Causes of interstitial pneumonia in the immunocompromised patient may include Pneumocystis jirovecii (formerly known as Pneumocystis carinii), cytomegalovirus, measles (usually no preceding rash), varicella-zoster (rare), fungal infections (radiology not typical), mycoplasma, legionella. Common respiratory viruses include influenza, parainfluenza, adenovirus and RSV.

Prevention of PCP Infection

Co-trimoxazole (trimethoprim/sulfamethoxazole) prophylaxis is given to all children on ALL chemotherapy according to protocol and to certain intensive solid tumour regimens (e.g. MMT 98, high risk neuroblastoma) or relapsed solid tumour protocols (e.g. Wilms’, Group C).

For patients who cannot tolerate co-trimoxazole e.g. excessive myelosuppression during ALL therapy, PCP prophylaxis should continue with one of the alternative drugs. Data from HIV populations suggests that dapsone is a more effective choice than nebulised pentamidine or atovaquone. **G6PD qualitative assay should be performed before starting dapsone therapy.** For patients who cannot tolerate dapsone, nebulised pentamidine or oral atovaquone is recommended.

For doses, see Chapter 5.

Treatment of Clinical PCP

Clues are cough, fever, tachypnoea, lymphopenia, hypoxia, absence of chest signs on auscultation and bilateral infiltration on chest x-ray. Although unlikely in patients on prophylactic co-trimoxazole, it should be considered in patients with this clinical presentation. It is important to start treatment early at the first suspicion of PCP – discuss with PTC.

**Investigations:**
Cultures for bacteria and viruses (discuss with PTC – may require bronchio-alveolar lavage)
Nasopharyngeal aspirate for immunofluorescence.
Viral and mycoplasma serology.

First line therapy is high dose co-trimoxazole, often with erythromycin or clarithromycin. If no response at 24-48 hours discuss with PTC and consider addition of further antifungal/antiviral cover if not already started. Pentamidine is effective in most non-responders. Steroids may be life-saving in this situation - to be discussed on an individual basis. Consider use of surfactant in non-responders.
Prevention of Infection in Haematopoietic Stem Cell Transplant Recipients

Prophylaxis for PCP

GOSH/UCLH patients
Use standard prophylactic dose of co-trimoxazole (Chapter 5) from the time of engraftment until 6 months post stem cell return for autologous procedures or until immunosuppressive therapy has ceased and the lymphocyte count > 1.0 x10^9/l.

Where recurrent neutropenia becomes a problem then co-trimoxazole may be substituted by monthly nebulised or intravenous pentamidine (see Chapter 5 for doses).

RMH patients
Receive pentamidine on Day +28 if count not recovered. Co-trimoxazole is recommenced at a prophylactic dose twice daily for two consecutive days per week when good counts are established, i.e. neutrophils >1.0 x10^9/l for at least 3 days. Prophylaxis is continued until 6 months post stem cell return or until immunosuppressive therapy has ceased and the lymphocyte count > 1 0 x10^9/l.

If there are problems with cytopenias on co-trimoxazole, monthly nebulised or intravenous pentamidine should be restarted.

Pneumococcal infection

Commence penicillin prophylaxis in all allograft patients from day 30 post-transplant. Give pneumococcal vaccine according to the revaccination schedule (see p 53) but continue lifelong oral penicillin for all patients receiving allografts of any kind.

Dose of penicillin: Age 1-5 yrs, 125 mg twice daily, Age 6-18+ yrs 250 mg twice daily.

In the event of penicillin allergy clarithromycin or azithromycin can be used.

Gram negative infection

At GOSH all patients undergoing allografts receive ciprofloxacin prophylaxis 7.5mg/kg bd during the neutropenic phase. In children at risk of line contamination (typically young children in nappies), ciprofloxacin prophylaxis may be continued until line removal. Routine prophylaxis against gram negative sepsis is not used at RMH.

Fungal prophylaxis

Antifungal prophylaxis should be given in accordance with local policy during conditioning and continued until neutrophils > 1.0 x 10^9/l and whilst on immunosuppressive therapy. Itraconazole is given 2.5mg/kg orally twice daily.

Oral liquid is preferable to capsules as it results in superior drug blood levels. In paediatrics, double the dose if using capsules. It is best to dose adults in terms of body weight as audit showed that patients above 80kg body weight do not always achieve adequate levels with the ‘flat’ dosing of 200mg BD.

If not tolerated, change to voriconazole or posaconazole or liposomal amphotericin B (AmBisome) at 1mg/kg/day – discuss with PTC.
Herpes simplex and VZV reactivation

Aciclovir is used in all patients undergoing allografts to prevent VZV/HSV and in some units also to prevent CMV reactivation. Continued until immunosuppressive therapy has ceased and the lymphocyte count is >1.0 x10^9/l.

Although, not routinely used at the other centres, at UCLH aciclovir prophylaxis may be considered for up to 3 months post autologous procedures.

GOSH policy
Regardless of CMV serostatus:
Aciclovir 300 mg/m^2 po 4 times daily
250 mg/m^2 iv 4 times daily

RMH/UCLH policy
Regardless of CMV serostatus:
Aciclovir 200 mg po 4 times daily if aged < 2 years
200-400 mg po 4 times daily if aged ≥ 2 years

Varicella zoster

The risk period for VZV reactivation continues for up to 2 years post BMT in those who have latent virus with reactivation occurring in up to 50% of patients. A randomised study showed that prophylaxis with acyclovir to 1 year post-allogeneic transplant reduced VZV disease without subsequent rebound infections (Boeckh Blood 2006). Although reactivations occur after this time-point, it is not justified to give prophylaxis beyond 1 year, as if the disease occurs it can be treated promptly and efficiently with IV aciclovir until the disease is controlled (see p47).

Cytomegalovirus

Risk depends on recipient and donor status.
Individual patient prophylaxis will be scheduled by PTC – see under HSV/VZV reactivation.

Surveillance for viral infection/reactivation

For allografts whilst inpatient in PTC and following discharge, in accordance with the local policy, there will be regular, usually at least weekly, monitoring of peripheral blood CMV, adenovirus and EBV PCR peripheral in susceptible patients.

Passive immunisation after HSCT in children

Measles and varicella zoster
Significant contact with measles or with varicella zoster virus infection requires treatment as outlined on p45-49, regardless of antibody status pre HSCT. In patients who are already on aciclovir or IVIG prophylaxis, no further treatment is needed.
This recommendation is applicable for all allogeneic and autologous HSCT patients until at least 1 year post-HSCT (18 months if donor is non-sibling, unrelated or mismatched related donor) and at least 6 months off all immunosuppressive treatment.
Humoral immunodeficiency in the transplant patient
Although not routinely used, in allogeneic recipients with recurrent infections and documented secondary IgG deficiency, monthly IVIG replacement therapy (0.4g/kg) IV may be considered. If in doubt, discuss indications and duration of treatment with PTC.

Vaccinations for Paediatric Patients treated with Standard-Dose Chemotherapy

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 treatment. In view of the diversity of malignant diseases and their treatment protocols, it is difficult to propose different vaccination schedules for each disease. Rather it is pragmatic to divide into children treated with standard-dose chemotherapy and children treated with high-dose chemotherapy (+/- radiation) followed by allogeneic or autologous HSCT.

Standard-Dose Chemotherapy

Use these guidelines for vaccination of all patients treated with standard-dose chemotherapy.

General Principles

- Avoid administration of all live vaccines to patients on chemotherapy and within 6 months following completion of chemotherapy.
- Avoid administration of live vaccines, except MMR (Measles/Mumps/Rubella), VZV (Varicella Zoster Virus) and Rotavirus vaccines, to siblings of patients on chemotherapy (or within 6 months following completion of chemotherapy).
- VZV vaccine should be offered to healthy susceptible siblings/older family members of patients receiving chemotherapy.
- Inactivated influenza vaccine should be offered to all patients receiving chemotherapy, within 6 months of completion of chemotherapy and to HSCT recipients. It should also be offered to household contacts of patients (NB household contacts of patients undergoing HSCT should not be given the live attenuated intranasal influenza vaccine).
- Update primary health care records if vaccination takes place in hospital.

Vaccination Schedules

Vaccinations for Patients Receiving Standard-Dose Chemotherapy (or within 6 months of completion)

- Consider following timing and content of routine childhood vaccination programme, using only non-live vaccines provided child’s general condition is stable and is expected to stay so for 3 weeks from vaccination.
- Avoid vaccination during period patient is receiving steroids (the immune response will be suboptimal) or when patient is neutropenic.
- Inactivated influenza vaccine is recommended (see above, General Principles)
Vaccination Schedule for Patients 6 months after Completion of Standard-Dose Chemotherapy

Booster doses of:

- Diphtheria, Tetanus, acellular Pertussis, IPV, Hib-conjugate (DTaP/IPV/Hib) [Pediacel®]
- Meningococcal C-conjugate vaccine (Men C) [NeisVac® or Menjugate®]
  - Or Men ACWY-conjugate vaccine [Menveo®] for at risk children (such as children whose treatment could have resulted in splenic dysfunction/ asplenia or patient has underlying splenic dysfunction/ asplenia or complement deficiency)
- 13-valent Pneumococcal conjugate vaccine (PCV13) [Prevenar 13®]
- MMR [Priorix® or MMRVaxPRO®]: If patient only received one 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 situations.
- Human Papilloma Virus vaccine (HPV) for eligible girls [Gardasil®]: Girls that did not start or complete the course of HPV vaccination should be given 3 doses of HPV vaccine at 6, 8 and 12 months after completion of chemotherapy. For girls that did complete the course, a booster dose should be given.

Routine booster immunisations on the national schedule will not be necessary if scheduled to be given within one year of the above booster doses.

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 vaccinate according to local policy.

Vaccination of Close Contacts of Patients Receiving Standard-Dose Chemotherapy (or within 6 months of completion)

Avoid administration of live vaccines to siblings/ close family contacts of patients on chemotherapy or within 6 months following completion of chemotherapy. The exception is MMR, VZV, shingles vaccine (Zostavax®), live attenuated influenza vaccine (LAIV) and rotavirus vaccines.

- MMR Vaccine should be given to contacts as per the national vaccination schedule.
- VZV vaccine ([Varivax®] should be offered to healthy susceptible siblings of VZV seronegative patients and to adult family members without a history of chickenpox (see VZV section).
- Shingles vaccine (Zostavax®): 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 Zostavax® should avoid direct contact with the patient until the rash is dry and crusted.

Rotavirus vaccine (Rotarix®): 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 faecal-oral route for at least 14 days post-vaccination. 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 of Rotarix.

Annual influenza vaccine (see above, under General Principles)

### Travel Abroad

Discuss with PTC. 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.

### Vaccinations in Children Treated with High-Dose Chemotherapy and HSCT

The aim in HSCT recipients is to commence re-vaccination as soon as it is safe and a protective immune response can be achieved. The patient must be off immunosuppressive therapy. Potentially vaccination can be as early as 6 months after HSCT for some patients but in most published studies vaccination schedules are 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 as detailed below.

Re-vaccination should commence:

- 12 months after any HSCT

**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 – discuss with BMT team.
Table 4. Re-Vaccination Schedule for HSCT Recipients

<table>
<thead>
<tr>
<th>Time after HSCT</th>
<th>Age under 10 years</th>
<th>Age over 10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vaccine</td>
<td>Vaccine</td>
</tr>
<tr>
<td>Every autumn (start 6 months after transplant)</td>
<td>Inactivated influenza&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Inactivated influenza&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>12 Months</td>
<td>DTaP / IPV / Hib&lt;sup&gt;2&lt;/sup&gt; (Pediacel) PCV13</td>
<td>dTaP / IPV (Repevax) Hib / Men C (Menitorix) PCV13 HPV&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>13 Months</td>
<td>DTaP / IPV / Hib&lt;sup&gt;2&lt;/sup&gt; (Pediacel) Men C</td>
<td>dTaP / IPV (Repevax) HPV&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>14 Months</td>
<td>DTaP / IPV / Hib&lt;sup&gt;2&lt;/sup&gt; (Pediacel) PCV13</td>
<td>dTaP / IPV (Repevax) Hib / Men C (Menitorix) PCV13</td>
</tr>
<tr>
<td>18 Months</td>
<td>MMR&lt;sup&gt;4&lt;/sup&gt;</td>
<td>MMR&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>24 Months</td>
<td>MMR&lt;sup&gt;5&lt;/sup&gt;</td>
<td>MMR&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Men ACWY PCV13 or PnPS23</td>
<td>Men ACWY PCV13 or PnPS23</td>
</tr>
<tr>
<td>48 Months</td>
<td>DTaP / IPV (Infanrix-IPV) Hib / Men C (Menitorix)</td>
<td>dTaP / IPV (Repevax) Hib / Men C (Menitorix)</td>
</tr>
<tr>
<td>School leaver booster</td>
<td>dT / IPV Men C</td>
<td>dT / IPV Men C</td>
</tr>
</tbody>
</table>

<sup>1</sup>The intranasal live-attenuated influenza vaccine should not be used in post-HSCT patients. 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.

<sup>2</sup>Can be given as Pediacel (for <10 years age at administration) or Repevax and Menitorix (for ≥10 years age)

<sup>3</sup>HPV vaccine should be offered to girls ≥12 years old: 3 doses of HPV vaccine (Gardasil) should be given at 0, 1-2 and 6 months from starting re-vaccination.

<sup>4</sup>1<sup>st</sup> dose of MMR should be given at 18 months provided patient is at least 12 months off all immunosuppressive treatment, fulfills criteria as above

<sup>5</sup>The 2<sup>nd</sup> dose of MMR is usually given 6 months after the 1<sup>st</sup> dose, but can be given 3 months after the 1<sup>st</sup> or even earlier (1 month after 1<sup>st</sup> dose) in outbreak situations

**Other Vaccines**

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

There are not much 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 NOT to be given to HSCT recipients**
- BCG (see above)
- Rotavirus
- Intranasal live attenuated Influenza vaccine
- VZV vaccine
- Yellow fever
- Live attenuated Typhoid vaccine
- MMR (until at least 18 months post HSCT – see above)

**Vaccination of close contacts of HSCT recipients**
Avoid administration of live vaccines to siblings/ close family contacts of patients on chemotherapy or within 6 months following completion of chemotherapy. The exception is MMR, VZV, Shingles vaccine (Zostavax®) and Rotavirus vaccines. If any patient specific issues discuss with BMT consultant.

- MMR Vaccine should be given to contacts as per the national vaccination schedule.
- VZV vaccine (Varivax®) should be offered to healthy susceptible siblings (and adult family members without a history of chickenpox) of VZV seronegative patients (see VZV section).
- Shingles vaccine (Zostavax®): Is offered to adults aged 70-79 years old, so the patient’s grandparents will 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 Zostavax® should avoid direct contact with the patient until the rash is dry and crusted.

Rotavirus vaccine (Rotarix®): 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 faecal-oral route for at least 14 days post-vaccination. 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 of Rotarix.
5.
DRUGS USED IN THE TREATMENT OF INFECTIONS
## 5. Drugs used in the treatment of infections

The drug details given in this chapter are necessarily brief, but reflect the dosages commonly used in immunocompromised patients. If in doubt, consult published formularies and discuss with microbiologists and/or the PTC. Always check doses for neonates and children with hepatic or renal failure with published formularies. Be aware of drug interactions.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Route</th>
<th>Dose</th>
<th>Frequ./day</th>
<th>Maximum per dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aciclovir</td>
<td>Herpes simplex treatment and Chicken Pox and Shingles and Herpes simplex treatment</td>
<td>po</td>
<td>1 month-2 years 200mg, 2-18 years: 400 mg</td>
<td>X5</td>
<td></td>
<td>IV doses in obese patients should be calculated on the ideal weight for height to avoid excessive dosing.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>iv</td>
<td>1-3 months 10-20mg/kg, 3 months-12 years: 500mg/m², 12-18 years: 10 mg/kg</td>
<td>X3</td>
<td></td>
<td>Start iv until cropping ceases. At least 10 days total.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>po</td>
<td>1 month-2 years: 200 mg, 2-6 years: 400 mg, 6-12 years: 800 mg, 12-18 years: 800 mg</td>
<td>X4</td>
<td></td>
<td>Continue for 2 days after crusting of lesions</td>
</tr>
<tr>
<td>Liposomal</td>
<td>Pyrexia of unknown origin, suspected or proven fungal infection, all BMT patients needing amphotericin, hepatosplenic candidiasis, toxicity with conventional amphotericin</td>
<td>iv</td>
<td>Test dose 0.1mg/kg (max 1mg) then 1-5mg/kg</td>
<td>x1</td>
<td>Usually 3-5mg/kg</td>
<td>Now treatment of choice for PUO/suspected/proven fungal infection</td>
</tr>
<tr>
<td>Amphotericin</td>
<td></td>
<td>iv</td>
<td>Initially 15mg/kg then adjust according to serum amphotericin concentration</td>
<td>X1</td>
<td>1500mg</td>
<td>According to local policy. Monitor trough. Discuss if renal impairment. Reduce dose in neonates. GOSH uses 20mg/kg for children &gt; 1 month. Trough prior to 2nd dose and then every 3 days</td>
</tr>
<tr>
<td>Benzyl penicillin</td>
<td></td>
<td>iv</td>
<td>50mg/kg</td>
<td>x4-6</td>
<td>2400mg</td>
<td></td>
</tr>
<tr>
<td>Caspofungin</td>
<td>Proven/suspected invasive fungal infection</td>
<td>iv</td>
<td>&lt;3 months 25mg/m², 3 months – 1 year 50mg/m², 1-18 years 70mg/m², 50mg/m² on day 1 then 50mg/m²</td>
<td>X1</td>
<td>70mg</td>
<td>Reduce dose in moderate to severe hepatic impairment</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td></td>
<td>iv</td>
<td>50mg/kg</td>
<td>X3</td>
<td>2000mg</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td></td>
<td>po</td>
<td>Neonate 15mg/kg, 1 month-18 years: 20mg/kg</td>
<td>X2</td>
<td>750mg</td>
<td>Infuse over 30-60 mins</td>
</tr>
<tr>
<td></td>
<td></td>
<td>iv</td>
<td>Neonate 10mg/kg, 1 month-18 years: 10mg/kg</td>
<td>X2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Frequ./day</td>
<td>Maximum per dose</td>
<td>Comments</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-----------------------------------------</td>
<td>-------</td>
<td>---------------</td>
<td>------------</td>
<td>------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td></td>
<td>po</td>
<td>7.5mg/kg</td>
<td>x2</td>
<td>500mg</td>
<td>Check drug interactions.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>iv</td>
<td>7.5mg/kg</td>
<td>x2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>PJP prophylaxis (formerly known as PCP)</td>
<td>po</td>
<td>SA 0.5-0.75m²</td>
<td>x2</td>
<td></td>
<td>On 2 consecutive days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>po/iv</td>
<td>SA 0.76-1.0m²</td>
<td>x2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SA &gt;1.0m²</td>
<td>x2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PJP treatment</td>
<td></td>
<td>60mg/kg</td>
<td>x2</td>
<td>240mg</td>
<td>Start with iv treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>360mg</td>
<td>For 14-21 days</td>
</tr>
<tr>
<td>Dapsone</td>
<td>PJP prophylaxis (2nd line) (formerly known as PCP)</td>
<td>po</td>
<td>2mg/kg</td>
<td>x1 weekly</td>
<td>100mg</td>
<td>Check patient’s G6PD status before starting</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4mg/kg</td>
<td></td>
<td>200mg</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td></td>
<td>iv</td>
<td>12.5mg/kg</td>
<td>x4</td>
<td>1g</td>
<td>Double dose in severe infections (to max 1g/dose). Check drug interactions.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>po</td>
<td>12.5mg/kg</td>
<td>x4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flucloxacillin</td>
<td></td>
<td>po</td>
<td>25mg/kg</td>
<td>x4</td>
<td>1g</td>
<td>Double dose in severe infections. Reduced frequency in neonates.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>iv</td>
<td>25mg/kg</td>
<td>x4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>Prophylaxis/mucosal candidiasis</td>
<td>po</td>
<td>3mg/kg</td>
<td>x1</td>
<td>400mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment of systemic candida infection</td>
<td>po</td>
<td>3mg/kg</td>
<td>x1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>iv</td>
<td>6-12mg/kg</td>
<td>x1</td>
<td>800mg</td>
<td>12mg/kg for at least 48 hours, then 6mg/kg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6-12mg/kg</td>
<td>x1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ganciclovir</td>
<td>CMV prophylaxis in BMT</td>
<td>iv</td>
<td>5mg/kg</td>
<td>x2</td>
<td></td>
<td>14-21 days treatment</td>
</tr>
<tr>
<td></td>
<td>CMV treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>In patients with impaired renal function, dosage adjustments based on creatinine clearance are required</td>
</tr>
<tr>
<td>Gentamicin</td>
<td></td>
<td>iv</td>
<td>7mg/kg</td>
<td>x1</td>
<td></td>
<td>In obese child, consider dosing by ideal weight for height</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reduce dose in neonates.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Give over 30min infusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Monitor trough levels prior to 2nd and then every 3 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Discuss if renal impairment.</td>
</tr>
<tr>
<td>Granulocyte Colony</td>
<td>Prophylaxis</td>
<td>iv/sc</td>
<td>5-10 microgram/kg</td>
<td>x1</td>
<td></td>
<td>Always name product on prescription eg Filgrastim, Lenograstim</td>
</tr>
<tr>
<td>Stimulating Factor</td>
<td>Severe sepsis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(GCSF)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Frequency/day</td>
<td>Maximum per dose</td>
<td>Comments</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------------------------------------------------</td>
<td>-------</td>
<td>-------------------------------</td>
<td>---------------</td>
<td>------------------</td>
<td>----------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Human Normal Immunoglobulin</td>
<td>Measles prophylaxis</td>
<td>iv</td>
<td>0.15g/kg of IVIG</td>
<td></td>
<td></td>
<td>Most effective if given within 72 hours but can be effective if given within 6 days.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>sc</td>
<td>0.6ml/kg of HNIG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imipenem (with cilastatin)</td>
<td></td>
<td>iv</td>
<td>1-3 months 20mg/kg</td>
<td>X4</td>
<td>1000mg</td>
<td>Restricted use - discuss with microbiologist.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 months - 1 year 25mg/kg</td>
<td>X4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itraconazole</td>
<td>BMT prophylaxis</td>
<td>po</td>
<td>2.5mg/kg (liquid)</td>
<td>X2</td>
<td>200 mg</td>
<td>Double the dose if using capsules. RMH monitor levels and adjust doses (no maximum dose).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(UCLH and GOSH)</td>
<td>Ensure this is not given 48 hours before or after vincristine/vinka alkaloid.</td>
</tr>
<tr>
<td>Linezolid</td>
<td>Multi-resistant gram positive infections</td>
<td>iv/po</td>
<td>&lt;7 days: 10mg/kg</td>
<td>x2</td>
<td>600mg</td>
<td>No dosage adjustments required for renal or hepatic impairment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;7 days – 12 yrs: 10mg/kg</td>
<td>X3</td>
<td></td>
<td>Restricted use – discuss with microbiologist.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;12 yrs: 600mg</td>
<td>X2</td>
<td></td>
<td>Monitor liver function. Use with caution in hepatic impairment or if receiving other hepatotoxic drugs.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Continue for at least 14 days.</td>
</tr>
<tr>
<td>Micafungin</td>
<td>Proven/suspected invasive fungal infection</td>
<td>iv</td>
<td>&lt;40kg</td>
<td></td>
<td>200mg</td>
<td>Restricted use - discuss with microbiologist. Monitored function.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2mg/kg increase to 4mg/kg if inadequate response</td>
<td></td>
<td></td>
<td>Use with caution in hepatic impairment or if receiving other hepatotoxic drugs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;40kg</td>
<td></td>
<td></td>
<td>Continue for at least 14 days.</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Severe, resistant infection</td>
<td>iv</td>
<td>&lt;50kg: 20mg/kg</td>
<td>x3</td>
<td>1000mg</td>
<td>Restricted use, discuss with microbiologist.</td>
</tr>
<tr>
<td></td>
<td>Resistant meningitis</td>
<td></td>
<td>&gt;50kg: 1g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>iv</td>
<td>40mg/kg</td>
<td>x3</td>
<td>2000mg</td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td>C. diff toxin - positive diarrhoea</td>
<td>po</td>
<td>7.5mg/kg</td>
<td>x3</td>
<td>400mg</td>
<td>Well ventilated room. Minimise exposure to bystanders.</td>
</tr>
<tr>
<td></td>
<td>Anaerobic infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reduce dose in renal impairment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>po</td>
<td>7.5mg/kg</td>
<td>x3</td>
<td>400mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>iv</td>
<td>7.5mg/kg</td>
<td>x3</td>
<td>500mg</td>
<td></td>
</tr>
<tr>
<td>Pentamidine isothionate</td>
<td>Prophylaxis</td>
<td>inhaled</td>
<td>300mg</td>
<td>monthly</td>
<td></td>
<td>Well ventilated room. Minimise exposure to bystanders.</td>
</tr>
<tr>
<td></td>
<td>Treatment of PJP - resistant to co-trimoxazole</td>
<td></td>
<td>4mg/kg</td>
<td>every 2-4 weeks</td>
<td>x1</td>
<td>Reduce dose in renal impairment.</td>
</tr>
<tr>
<td></td>
<td>(formerly known as POP)</td>
<td>iv</td>
<td>4mg/kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenoxymethyl penicillin</td>
<td>Prophylaxis in BMT</td>
<td>po</td>
<td>Under 1 year 62.5mg</td>
<td>X2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1-5 years 125mg</td>
<td>X2</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5-18 years 250mg</td>
<td>X2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piperacillin/ Tazobactam</td>
<td></td>
<td>iv</td>
<td>&gt;1 month 90mg/kg</td>
<td>X4</td>
<td>4500 mg</td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Frequency/day</td>
<td>Maximum per dose</td>
<td>Comments</td>
</tr>
<tr>
<td>--------------------</td>
<td>-------------------------------------</td>
<td>-------</td>
<td>-------------------------------------------</td>
<td>---------------</td>
<td>------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Teicoplanin</td>
<td></td>
<td>iv</td>
<td>1 month-18 years 10mg/kg 12 hourly for 3 doses, then 10mg/kg once daily</td>
<td></td>
<td>400 mg</td>
<td>Reduce dose in neonates</td>
</tr>
<tr>
<td>Valaciclovir</td>
<td>HSV prophylaxis</td>
<td>po</td>
<td>&gt;3 months-12 years 20mg/kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CMV prophylaxis in at risk transplant patients</td>
<td>po</td>
<td>&gt;3 months – 1 year 34mg/kg</td>
<td>X2</td>
<td>500 mg</td>
<td>Round dose to the nearest half or quarter tablet</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 year - 12 years 40mg/kg</td>
<td>X4</td>
<td>2g</td>
<td>Reduce dose in renal impairment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt; 12 years 2g</td>
<td>X4</td>
<td>2g</td>
<td>(Taken from GOSH guidelines)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td></td>
<td>iv</td>
<td>15 mg/kg</td>
<td>x3</td>
<td>Maximum total daily dose 2000 mg</td>
<td>Infuse over at least 1 hour (do not exceed 10mg/min for doses &gt;500mg) Monitor trough levels and adjust dose accordingly</td>
</tr>
<tr>
<td>Varicella Zoster Immune Globulin</td>
<td>VZV prophylaxis</td>
<td>im</td>
<td>0-5 years 250mg</td>
<td>once</td>
<td></td>
<td>Ensure adequate platelet count before injection. Repeat upon subsequent exposure if &gt; 3 weeks after first dose has elapsed. Potentially infectious up to 28 days following contact if ZIG given.</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>Suspected/proven invasive fungal infection</td>
<td>po</td>
<td>2-12 yrs 9mg/kg</td>
<td>X2</td>
<td>350 mg</td>
<td>Discuss with PTC if child &lt;2 years since experience is limited Monitor liver function Care in moderate-severe renal dysfunction if IV Doses may be adjusted according to response/tolerance For a maximum of 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;50kg dose as for 2-12yrs</td>
<td>X2</td>
<td>150mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;50kg dose as for 15-18yrs and &gt;40kg</td>
<td>X2</td>
<td>300 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>15-18yrs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;40kg 200mg for 2 doses then 100mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;40kg 400mg for 2 doses then 200mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2-12 yrs 9mg/kg for 2 doses then 8mg/kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12-15yrs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;50kg dose as for 2-12 yrs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;50kg dose as for 15-18 yrs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>15-18yrs 6mg/kg for 2 doses then 4mg/kg</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
6.

ONCOLOGICAL EMERGENCIES
6. Oncological Emergencies

Introduction
Neutropenic sepsis is the commonest oncological emergency and it is the most common cause of morbidity and mortality amongst children receiving chemotherapy for malignant conditions. Neutropenic sepsis is covered comprehensively in Chapter 3.

Most episodes of uncomplicated febrile neutropenia are managed effectively at a POSCU; on the other hand, the majority of other oncological emergencies require urgent transfer to a PTC for further management. However, it is important for POSCU’s to understand this chapter because these emergencies are often recognised & diagnosed at the POSCU. After commencing initial management, it is vital for the POSCU to liaise with the PTC early to facilitate urgent transfer of these patients.

Ecthyma gangrenosum/Necrotising fasciitis
Cutaneous infection usually characterised by discoloured lesions or areas of skin (eg dusky, purple or black) in an immunocompromised patient. The commonest site is perineal skin, although this infection can occur in other parts of skin. Highly suspicious of Gram negative infection, particularly Pseudomonas aeruginosa. Send blood cultures, local swabs and stool culture.

Ecthyma gangrenosum requires urgent treatment with intravenous antibiotics covering Pseudomonas and Gram negative organisms. (iv p iptazobactam and aminoglycosides as per neutropenic sepsis protocol is appropriate) Patients should be discussed with PTC for urgent transfer to PTC, surgical review and consideration of debridement.

Tumour lysis syndrome
Tumour lysis syndrome (TLS) is a very serious and potentially life threatening complication of children with a malignancy. Rapid cancer cell death (cytolysis) releases large amounts of uric acid, phosphate and potassium into the circulation. A secondary hypocalcaemia may result from hyperphosphatasaemia. End result being urate nephropathy and acute renal failure.

Whilst the onset of TLS is a true emergency, it can usually be prevented or treated, providing it is correctly anticipated. Prevention is the aim of management, using hyperdiuresis (via hyperhydration) together with allopurinol or rasburicase. TLS usually starts after induction of appropriate treatment; uncommonly TLS can also occur prior to chemotherapy. Duration depends on severity and supportive measures in place, but on average lasts for approximately 48 to 72 hours from start of treatment.
**Figure 2. Tumour lysis syndrome flow chart 1: Prior to starting treatment/chemotherapy**

TLS Flowchart 1: Prevention of Tumour Lysis Syndrome (TLS) – prior to starting treatment

**At presentation – can be initiated at POSCU**

**Low risk for TLS AND**
- Normal U&E & urine output (eg WCC <20x10⁹/L)
  - i) no need to hyperhydrate
  - ii) maintenance (oral with or without intravenous fluids combined total)
  - iii) Start Allopurinol 100mg/m²/dose 8 hourly by mouth
  - iv) Prior to start of treatment, only need once daily bloods (TLS* & FBC).

*TLS bloods = urate, U&E, K, Ca, Phos

**Intermediate risk AND**
- Normal U&E & urine o/p (eg WCC 20-100x10⁹/L)
  - i) Consider hyperhydration 0.45% saline/2.5% glucose 2.5 - 3 L/m²/day. Discuss with PTC
  - ii) Allopurinol (oral) 100mg/m²/dose tds
  - iii) Prior to start of treatment, only need 12 to 24 hourly bloods (TLS* & FBC)

**High risk for TLS**
- High cell count leukaemia (>100 x10⁹/L)
- Burkitt's type lymphoma (BNHL)
- Large tumour bulk
- Bulky T cell lymphoma (mediastinal mass)
- Bulky LPD/PTLD
- Evidence of renal infiltration with tumour
- Renal impairment with abnormal U&E
- Consider insertion of permacath during first GA

---

**On presentation start following:**

i) Hyperhydration 0.45% saline/2.5% glucose 3 L/m²/day. can be ↑ to 4L/m²/day if there is no evidence of fluid overload. Caution with hyperhydration in children with very low Hb and high WCC count. (Risk of haemodilution and dropping Hb further). Discuss with PTC for plan of hyperhydration.

ii) Ensure urine output >3ml/kg/hour. Frusemide PRN. For patients at risk of leukostasis, discuss with PTC before giving frusemide. (Dehydration may worsen leukostasis)

iii) Start IV rasburicase** (ideally document G6PD status in patients who are at risk of G6PD deficiency before starting rasburicase)

200 microgram/kg/dose once daily.

iv) If rasburicase is unavailable at POSCU, start allopurinol, then switch to rasburicase on arrival to PTC.

v) If TLS bloods normal; repeat 8 hourly with FBC

**Rasburicase can trigger haemolysis in G6PD deficiency.**
Figure 3. Tumour lysis syndrome flow chart 2: After starting appropriate treatment/chemotherapy

TLS Flowchart 2: Prevention and treatment of Tumour Lysis Syndrome (TLS) – after starting treatment

Low risk for TLS AND
Normal U&E & urine output
12-24 hrs prior to starting treatment:
Allopurinol
Hyperhydration

Intermediate risk AND
Normal U&E & urine o/p
12-24 hrs prior to starting treatment:
Allopurinol
Hyperhydration

High risk for TLS
Prior to starting treatment:
Rasburicase
Hyperhydration

After starting appropriate treatment/chemo – usually at PTCs

8 - 12 hourly TLS bloods
FBC minimum 24 hourly
Strict fluid balance/urine o/p
Ensure urine output >3ml/kg/hour.
Frusemide PRN.

6 to 8 hourly TLS
FBC minimum 24 hourly
Strict fluid balance/urine output
Ensure urine output >3ml/kg/hour.
Frusemide PRN.

4 to 6 hourly TLS & FBC
Clinical review 4 hourly: include review of fluid balance/urine output/evidence of fluid overload etc.
Ensure urine output >3ml/kg/hour.
Frusemide PRN. (Caution if high WCC: risk of leukostasis, discuss with PTC consultant)

If urate remains high or urate start to escalate despite 24 hourly rasburicase, consider administering additional doses of rasburicase at 200micrograms/kg/dose minimum time interval 12 hourly (discuss with PTC consultants)

If no evidence of fluid overload, consider increasing hyperhydration can be ↑ up to 4L/m²/day

If concerns with deteriorating TLS bloods +/- urine output +/− fluid overload despite frusemide, contact PTC consultant/ renal team/PICU to consider haemofiltration or dialysis

If developing signs of TLS,
Change to rasburicase & high risk arm

If no evidence of TLS
• 48hrs to 72hrs after start of treatment /chemo, consider starting to wean off hyperhydration and frequency of blood tests.
• If on rasburicase, after 2 to 3 days from start of treatment: if no evidence of TLS, consider switching from rasburicase to allopurinol
• Complete 5 to 7 days in total of allopurinol (+/− rasburicase) from the start of treatment/chemo.
TLS may occur:

a) spontaneously (e.g. post-surgery)
b) as part of “unintentional” treatment (e.g. steroids given to a child with wheeziness caused by anterior mediastinal tumour, which has been misdiagnosed as ‘new asthma’; or steroids given during general anaesthesia) or
c) following intentional therapy for a malignant tumour

### Recognition of Risk

<table>
<thead>
<tr>
<th>RISKS</th>
<th>Examples</th>
<th>Typical prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High risk of TLS</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Bulky, highly chemosensitive malignancies | • Leukaemia with total white cell count usually in excess of 100 x10^9/L  
• Non-Hodgkin’s lymphoma - B or T cell (e.g. large anterior superior mediastinal mass)  
• Large tumour bulk (e.g. large organomegaly)  
• Bulky lymphoproliferative disease (LPD) or post-transplant lymphoproliferative disease (PTLD)  
• Evidence of renal infiltration with tumour (e.g. on ultrasound) +/- Evidence of renal impairment (urea & creatinine) | Urate oxidase (Rasburicase) |
| **Intermediate risk of TLS** | | |
| Widespread, chemosensitive malignancies | * Leukaemia with total white cell count usually between 20 to 100 x 10^9/L – in the absence of large tumour bulk or renal impairment | Allopurinol |
| **Low risk of TLS** | | |
| Widespread, chemosensitive malignancies | * Leukaemia with total white cell count usually less than 20 x 10^9/L – in the absence of large tumour bulk or renal impairment  
* Non-bulky NHL, LPD or PTLD with normal renal function | Allopurinol |
| **Unusual to develop TLS** | | |
| Most other tumours | * Solid malignancies  
* HLH | None |

### Diagnosis

Defining the criteria for the diagnosis of TLS is considerably less important than following the practical management plan outlined here. All the biochemical components may not be present initially and many of these measures can be instituted early to prevent progression to full blown TLS.

In patients who develop TLS, the biochemical abnormalities usually start to become evident 4 to 6 hours after initiation of appropriate treatment for the malignancy. The risk of TLS developing usually lasts until approximately 48 hours after starting appropriate treatment; after this time, the chance of TLS developing becomes much lower.
Initial management = Prevention (Figure 2 and Figure 3)

1. Hyperdiuresis/Hyperhydration

   a. Acute leukaemia with WCC less than $20 \times 10^9/L$, low disease bulk and in the absence of renal impairment: in terms of hyperhydration, there is no need to hyperhydrate too early, as the risk of iatrogenic complications outweighs the benefit of preventing TLS in these patients. Allopurinol can be started and it is usually sufficient for this sub-group of patients to receive maintenance fluid (orally and/or intravenously) before starting chemotherapy. Hyperhydration should be started 12 to 24 hours prior to start of steroids or chemotherapy.

   b. WCC between 20-100 $\times 10^9/L$, early initiation of hyperhydration can be considered and this should be discussed with PTC at the time of referral.

   c. High risk for TLS: hyperhydration should be started early (e.g. start at POSCU)

   d. Caution with hyperhydration in patients with high count leukaemia and low haemoglobin - hyperhydration can cause further haemodiluation (i.e. lowering haemoglobin count). Remember packed red cell transfusion is a relative contraindication in high count leukaemia & leukostasis. Discuss with PTC.

   0.45% NaCl / 2.5% Dextrose at between 2.5 - 3 litres/m²/day. DO NOT add KCl (potassium chloride).

   If there is no evidence of fluid overload, greater rates up to maximum of 4 litres/m²/day may be required for increasing metabolic disturbance.

2. Allopurinol 100mg/m²/dose orally 3 times per day. Ideally this should be started at least 12 hours before commencement of chemotherapy and can be started before patient is transferred to PTC. Continue until 5 to 7 days after starting treatment.

   Or Urate oxidase (Rasburicase) 0.2mg/kg/dose IVI over 30 mins once every 24 hours. In established TLS, the frequency can be increased to 18 hourly to a maximum of 12 hourly (at same dosage). Rasburicase usage should be reviewed on daily basis. If rasburicase is unavailable at POSCU, start allopurinol, then switch to rasburicase on arrival to PTC.

   Note: ideally document G6PD status in patients who are at risk of G6PD prior to starting rasburicase. (Risk of rasburicase triggering haemolysis in G6PD deficient patients.) In exceptional cases, discuss with PTC consultant.


   Ensure urine output of at least 3ml/kg/hour. Give furosemide if poor urine output and/or fluid overload. Note: furosemide is contraindicated in patients at risk of leukostasis.

4. Monitor trend of electrolytes regularly - “TLS bloods”

   a. Urate
   b. Potassium
   c. Urea & Creatinine
   d. Calcium & Phosphate

   Suggested guideline for frequency of TLS bloods:

<table>
<thead>
<tr>
<th>TLS risk group</th>
<th>Before starting treatment</th>
<th>After starting treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>8 hourly</td>
<td>4 to 6 hourly</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>12 to 24 hourly</td>
<td>6 to 8 hourly</td>
</tr>
<tr>
<td>Low risk</td>
<td>24 hourly</td>
<td>8 to 12 hourly</td>
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</table>
Established tumour lysis

- Discuss and urgent transfer to PTC for further management as patient may require haemofiltration or haemodialysis via a permacath or vascah.

- Apply cardiac monitor (looking for evidence of peaked T waves and widened QRS complex of hyperkalaemia, and prolonged QT interval of hypocalcaemia).

- Clinical review - 4-hourly (looking for signs of hypocalcaemia such as vomiting, cramps, seizures, spasms, altered mental state and tetany; and of hyperkalaemia such as weakness and paralysis).

In particular circumstances, after discussion with PTC, it may be appropriate to:

- Catheterise patient if anuric or oliguric (ensures bladder is empty and accuracy of future measurements)

- Replace allopurinol with rasburicase (0.2mg/kg IVI over 30 mins x 1/day). However, this should be avoided if patient known to have G6PD deficiency. Discuss with PTC

Emergency management of hyperkalaemia
(see also chapter 13: fluid & electrolytes, p182)

- Urgent repeat of biochemistry (blood gas machine for immediate result and urgent formal laboratory sample) Ensure free flowing venous sample. Special caution in high count, avoid excessive shaking of sample or pneumatic chute delivery system leading to artificially haemolysed samples.

- Discuss with PTC/renal physicians/intensive care retrieval team urgently. The measures outlined below should only be used under the guidance of PTC and renal physicians, as these measures will only transiently reduce the potassium level. Patients in established TLS with true hyperkalaemia require urgent haemofiltration or haemodialysis.
  - If ECG changes: Calcium gluconate 10% 0.5ml/kg = 0.1mmol/kg IV, maximum 20ml slow bolus over 5-10 minutes. (Central access: give neat. Peripheral access: Dilute 1ml in 4ml 0.9% NaCl.)

  - Give insulin & dextrose AND salbutamol TOGETHER (40-50% of patients are non-responders to salbutamol alone so avoid monotherapy)
    - Insulin @ 0.05-0.1units/kg/hr with 10% dextrose in 0.9% NaCl@5ml/kg/hr. Titrate to keep blood glucose >6mmol/l. If blood glucose <6mmol/l give 5ml/kg bolus of 10% dextrose in 0.9% NaCl before starting infusions.
    - Salbutamol:
      If self-ventilating nebulised salbutamol: Age <2.5yrs = 2.5mg; >2.5yrs = 5mg
      If not self-ventilating salbutamol 4micrograms/kg iv over 5 min (Central neat, peripheral dilute 1mg in 2ml 0.9% NaCl). Repeat dose until ECG & K normalised.
Leukostasis and Hyperleukocytosis

Patients with high count leukaemia (hyperleukocytosis) are at risk of death or serious complications due to leukostasis/hyperviscosity syndrome, coagulopathy, or tumour lysis syndrome. High count leukaemia is considered a haemato-oncological emergency. Hyperleukocytosis occurs in approximately 10-20% of acute leukaemia and the greater the white cell count, the greater the risk.

Recognition of risk/definition of “high count” in leukostasis:
Generally high count leukaemia is defined as a white cell count of >100 x 10^9/l.
In monocytic AML (FAB type M5), high count is defined as >50 x 10^9/L as the malignant cells are large, tend to aggregate, and cause coagulopathy more readily.

Pathological definition: “Morphological evidence of intravascular accumulation of leukaemic blasts occupying most or all of the vascular lumen, with or without the presence of fibrin”. It is thought that “sludging” of leukaemic blasts in capillary vessels lead to diffuse cerebral, pulmonary and renal microcirculatory failure, therefore tissue hypoxia, infarct or haemorrhage can occur as a result.

Diagnosis:
There are no diagnostic tests or criteria for leukostasis. Clinicians must have a high index of suspicion in patients who are at risk as defined above. Respiratory and CNS status must be reviewed regularly. Discuss with PTC consultants early if leukostasis is suspected.

<table>
<thead>
<tr>
<th>Early signs include (CNS):</th>
<th>Early signs include (Respiratory):</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Headaches</td>
<td>• Dyspnoea</td>
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<tr>
<td>• Retinal haemorrhages</td>
<td>• Tachypnoea</td>
</tr>
<tr>
<td>• Papilloedema</td>
<td>• Oxygen desaturation</td>
</tr>
</tbody>
</table>

Progressing to:

| • Fluctuating / depressed CNS mental status | • Pulmonary infiltrates – diffuse, bilateral |
| • Focal CNS abnormalities                  |                                             |
| • Seizures                                 |                                             |

And ultimately:

| • Intracranial haemorrhages                | • Respiratory failure                     |

Coagulopathy, thrombosis & haemorrhagic stroke
Pro-coagulant molecules plus interaction with vascular endothelium may result in a consumptive coagulopathy, or frank thrombosis. Thus patients are at risk of haemorrhagic stroke.

Management
1) Prompt & URGENT transfer from POSCU to PTC
2) If very high count (suspected) AML: (e.g. above WCC 50x10^9/L, especially AML M4/5 and APML) liaise with PTC consultant urgently. *PTC consultant to consider urgent transfer to PICU (directly from POSCU) for exchange transfusion or leukopheresis (not recommended for APML). If PTC consultant deems the patient is at high risk of leukostasis and requires an exchange transfusion or leukopheresis, then the POSCU consultant will need to arrange immediate intensive care (CATS/STRS) transfer. The patient should arrive at PICU within 2 hours of referral to PTC.
If a PTC is unable to accommodate or accept a patient in this situation, there should be a PTC consultant to PTC consultant referral to ensure prompt transfer of the patient from the POSCU to an appropriate PTC.

**Exchange transfusion/Leukophoresis** is usually performed on PICU. This is usually not recommended for APML (AML M3) as this may worsen DIC.

3) **CAUTION: AVOID Red Cell transfusion**

Packed Red Cells are very viscous with a high haematocrit (~70%) and transfusion may lead to clinical exacerbation of leukostasis; especially it may precipitate cerebral infarction and respiratory distress. Generally transfusion is avoided or very limited until the white cell count has been reduced to safe levels. **Only administer Packed Red Cells after discussion with PTC consultant.** If PTC consultant agrees to red cell transfusion, patients should not receive more than 5ml/kg in a single transfusion, given over 4 hours. **It is rarely needed to raise Hb to above 6g/dL by Pack Red Cell transfusion.** If further blood transfusion is required, discuss with PTC consultant first.

\[
\text{Volume (ml) of Packed Red cells} = \text{Desired rise in Hb (g/dL)} \times 3 \times \text{weight (kg)}.
\]

4) **Tumour lysis syndrome:** management, rasburicase (if indicated check G6PD before starting), hyperhydration and biochemistry monitoring as per GOSH Tumour Lysis Protocol.

5) Monitor FBC, coagulation and TLS bloods 4 to 6 hourly

6) **Platelets** - Maintain platelet count above 50 x10^9/L in the presence of active bleeding or coagulopathy, otherwise maintain platelets above 30 x10^9/L.

7) **Coagulopathy** – Coagulopathy is more common in AML than ALL, but may occur in any leukaemia. In the presence of prolonged PT or APTT (>3 seconds above normal range) 10-15mls/kg of FFP should be given. Fibrinogen (aim for >1g/L) should be maintained with cryoprecipitate (5mls/kg). Further clotting tests should be sent following administration of FFP or cryoprecipitate. Should the clotting screen still be deranged, please discuss with consultant haematologist. In the event of active bleeding and coagulopathy, FFP and cryoprecipitate should be given according to the clotting parameters. Discuss with a consultant haematologist in this situation.

8) **Children may deteriorate after starting cytotoxic therapy** – a patient’s respiratory and neurological status sometimes will initially worsen after starting cytotoxic chemotherapy, due to pro-coagulants released from dying cells. Close observation is mandatory.

9) **Pulmonary infiltration and respiratory distress** – Clinical signs of pulmonary infiltration/leukostasis include tachypnoea, dyspnoea and hypoxia. Clinically and radiologically, it is often difficult to differentiate pulmonary infiltration/leukostasis from fluid overload from hyperhydration. Fluid balance assessment, twice daily weight and careful clinical examination are important.

**Furosemide should NOT be given as a routine** - Avoid dehydration/volume depletion, as this may exacerbate leukostasis. Liaise with PTC consultant if patient is fluid overloaded.

10) **Neurology** - careful monitoring of neurological status. Clinical signs of CNS leukostasis include stupor, delirium, dizziness, altered mental status, tinnitus, ataxia, visual blurring, visual disturbance, papilloedema, retinal vein distension, retinal abnormalities. Clinical signs of abnormal neurology and raised intracranial pressure (headache, vomiting, neck stiffness, focal neurology, abnormal pupil reactions, deranged GCS etc.) may indicate cerebral infarction and/or intracranial haemorrhage. Careful and regular clinical assessment is mandatory. Inform consultant if patient develops neurological abnormalities.

11) **Ophthalmology** – very high risk patients with coagulopathy are at risk of retinal haemorrhage. Ophthalmology review should be considered when patient has stabilized.
The definitive treatment and prevention of leukostasis is to commence chemotherapy urgently. Leukophoresis/exchange transfusion will only transiently reduce white cell count. Starting chemotherapy is a PTC consultant decision.

* Decision on whether patients need PICU & leukophoresis/exchange transfusion is multifactorial & beyond the scope of this protocol. This paragraph triggers the need of a PTC consultant experienced in managing these very high risk patients to consider the risks, pros & cons of PICU leukophoresis & exchange transfusion.

**Anterior mediastinal masses & Superior Vena Cava (SVC) obstruction**

Children with an anterior mediastinal mass are a haematological-oncological emergency. This group of patients may experience serious and potentially fatal complications at presentation or during sedation/general anesthesia, usually as a consequence of extrinsic compression of the airway, obstruction to the venous return or obstruction to the output of the heart. With modern chemotherapy regimens, the majority of children with an anterior mediastinal mass have an excellent long term prognosis. Instigation of appropriate initial management can lead to avoidance of unnecessary morbidity and mortality.

**Recognition**

The undiagnosed child with a large anterior mediastinal mass may present in many ways and the classical features of SVC obstruction, signified by swelling of the upper thorax, head and neck with overlying superficial prominent & distended collateral veins, being infrequently observed. More often the anterior or middle mediastinal mass presents with respiratory & neurological symptoms or signs (see below). Posterior mediastinal masses rarely cause SVC or respiratory compromise.

**Symptoms that should raise concern in any child with a mediastinal mass include:**

<table>
<thead>
<tr>
<th>Respiratory</th>
<th>Neurological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td>Headaches</td>
</tr>
<tr>
<td>Cough</td>
<td>Dizziness</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>Syncope</td>
</tr>
<tr>
<td>Orthopnoea</td>
<td>Episodic confusion &amp;/or anxiety</td>
</tr>
<tr>
<td>Stridor</td>
<td></td>
</tr>
</tbody>
</table>

Careful clinical assessment should be made since airway obstruction has been reported in up to 60% of patients presenting with mediastinal masses. Furthermore, a third of asymptomatic patients have a significant reduction in tracheal dimensions when assessed by CT.

**Signs to be alert to:**

<table>
<thead>
<tr>
<th>Respiratory</th>
<th>Neurological</th>
<th>Cardiovascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachypnoea</td>
<td>Papilloedema</td>
<td>Facial oedema</td>
</tr>
<tr>
<td>Cyanosis</td>
<td></td>
<td>Facial plethora</td>
</tr>
<tr>
<td>Wheeze</td>
<td></td>
<td>Distended veins</td>
</tr>
<tr>
<td>Reduced breath sounds</td>
<td></td>
<td>Pulsus paradoxus</td>
</tr>
<tr>
<td>Hypoxia</td>
<td></td>
<td>Hypertension</td>
</tr>
</tbody>
</table>

Not infrequently pleural and pericardial effusions may be associated with the mediastinal mass (typically T cell lymphoma / leukaemia). Pleural effusions may be bilateral and further compromise the child’s respiratory status.
Diagnosis
BEWARE – inappropriately requested investigations may result in worsening respiratory compromise, rapid clinical deterioration and cardio-respiratory arrest!

CXR  include PA/AP and lateral to establish size of mass and whether the mass is anterior or posterior.

Chest CT Only perform if it is safe for the patient. This test is not mandatory. If significant mass on CXR and/or significant respiratory symptoms: Avoid sedation or general anaesthesia, this may precipitate respiratory failure leading to death. If respiratory symptoms deteriorate on lying supine, unsedated chest CT in supine position should be avoided. This may also precipitate acute respiratory failure. If patient can tolerate lying prone or lateral without worsening of symptoms, CT chest may be considered in these positions. Discuss with PTC consultant.

Chest USS If unable to perform chest CT, consider discussing with radiologist for chest/mediastinal ultrasound scan to assess mediastinal mass.

Blood tests Baseline blood investigations (FBC, blood film, U&E, Phosphate, Urate, LDH, AFP & HCG) and urinary catecholamines should be performed as indicated and in discussion with PTC.

No further invasive investigations until the patient has been assessed by PTC consultant.

Management
• Urgent transfer to PTC – if significant mass on imaging and/or significant respiratory symptoms. Consider intensive care retrieval to PICU.

• Close monitoring of the child is mandatory including respiratory rate and saturations. Any child with hypoxia, orthopnoea, dyspnoea, stridor or marked tachypnoea requires anaesthetic review, urgent transfer to a PTC and potential PICU support, as in these situations emergency (empirical) chemotherapy or radiotherapy may be required.

• AVOID sedation and/or GA for any further investigations and contact PTC regarding transfer of the patient. A chest CT at this stage is contra-indicated in children with any respiratory or cardiac symptoms. These children should be referred to a tertiary centre on clinical suspicion; a CT is NOT required.

• DO NOT give steroids at this stage as there is a risk of initiating significant tumour lysis.

• If T-NHL / T-ALL suspected then follow tumour lysis syndrome section.

• If evidence of SVC obstruction – avoid hyperhydration via upper limb, as there is a risk of exacerbation of facial swelling and cerebral oedema in SVC obstruction. Hyperhydrate via lower limb cannulae only.

• On arrival to PTC, review by PTC consultant to decide whether empirical treatment should be initiated immediately without tissue diagnosis.

Other causes of SVC obstruction
Superior vena cava obstruction is associated with:
Obstruction of the SVC secondary to an anterior mediastinal mass (lymphomas – typically NHL, leukaemia – typically T-ALL, thymoma and teratoma), complicates approximately 10% of mediastinal mass presentations.

Thrombosis within the SVC (usually related to central venous catheters).

The child with a known malignancy and on active treatment whom presents with SVC obstruction is likely to have a central venous catheter related thrombus. In these situations the central line is likely to have stopped functioning adequately, which may be the initial presenting symptom. Alternatively, the child may present with classical features of SVC obstruction (swelling of the upper thorax, head and neck with overlying superficial prominent & distended collateral veins). Investigations that would be recommended and may have been performed in coming to the diagnosis are a CXR and Echocardiogram. Screening for prothrombotic tendencies may be requested although baseline bloods and a clotting screen will usually suffice until the child is seen at the PTC.

In these situations the child will require transfer to the PTC for removal of the catheter +/- thrombus excision, followed by anticoagulation.

Spinal cord compression (SCC)

Spinal cord compression is relatively uncommon, but requires urgent attention to avoid irreversible sequelae. It complicates 4-7% of all childhood malignancies from presentation to completion of treatment. In the majority of SCC cases, presentation is in the terminal phases of relapsed or progressive malignancy, but 25% of cases are in undiagnosed children during their first presentation. Other causes of spinal cord compression include infection (osteomyelitis, paraspinal/spinal abscesses), vertebral collapse and haematomas/infarction, which may occur in oncology patients during their treatment phase.

Approximately half of all SCC cases are caused by neuroblastoma or Ewing's tumours. Thereafter, rhabdomyosarcoma, other soft tissue sarcomas and osteosarcoma account for the majority of the remaining incidences, although almost any metastatic tumour can result in SCC. Compression typically results from direct tumour extension through the intervertebral foramina to impinge upon the spinal cord (the so called 'dumb-bell' tumour), although primary/intramedullary CNS tumours of the spinal canal may present in a similar fashion.

Recognition

Classical symptom triad:
In older children/adolescents, back pain is typically the first symptom and will precede neurological dysfunction by hours to months. Weakness is usually symmetrical (presenting with an unsteady gait through to paraplegia or quadriplegia) and may be associated with sensory dysfunction, and the insidious onset of loss of sphincter control. Signs are appropriate for the level of the SCC with a sensory level, muscular weakness, increased tone, clonus and extensor plantar reflexes. Tenderness to palpation is often present. A palpable bladder is a sinister sign in this context!

Particular care must be taken in assessing possible spinal cord compression in young, pre-ambulatory children when the signs may be subtle. It is particularly important to distinguish loss of motor milestones (i.e. regression) from developmental delay since the former is considerably more concerning for spinal pathology. In older children, whilst weakness of the lower limbs may be due to Guillain-Barré Syndrome, spinal cord compression must also be considered and MRI spine is advised.

**Diagnosis**
- **The investigation of choice is an MRI of the spine.** This may be requested from the POSCU in discussion with the PTC as it may result in less delay before definitive treatment (chemotherapy, radiotherapy or neurosurgical decompression) is commenced. A CT may reveal paraspinal pathology; however a *normal spinal CT does not necessary exclude intraspinal pathology*. Liaise with PTC.
- **Standard initial investigations as determined locally with FBC and film, Biochemistry and Clotting screen.** Additional serum for AFP/HCG, LDH and urinary catecholamines may be required, although is likely to be performed at the PTC since there should be minimal delay in transferring the patient.

**Management**
- **Contact PTC** to arrange early transfer and further investigations.

- Start dexamethasone 0.25-0.5mg/kg PO/IV x4/day **URGENTLY.** The only proviso to this is that there should be no other features suggestive of lymphoma (anterior mediastinal mass on CXR/lateral or CT, hepatosplenomegaly & peripheral blood film with blasts present), although it should be remembered that this is rare. If in doubt discuss with PTC.

- Commence appropriate analgesia for the presenting pain and discomfort (refer to Chapter 12 – Basic principles of symptom management for further guidance).

**Raised intracranial pressure**

Primary CNS tumours are not discussed in any great detail throughout the supportive care guidelines since the referral pathway is via the neurosurgeons. The management of raised intracranial pressure should be in discussion with the neurosurgeons and depends upon local policy, as this complication is neither specific nor peculiar to oncology patients.

However, cerebral herniation may result from an expanding mass within the fused skull vault, or from obstruction of the CSF channels. This may occur in primary CNS or metastatic extracranial tumours but also in cases of intracranial haemorrhage, thrombosis, infarction or abscess formation, which may also occur in the oncological patient.
Recognition

Be aware of this complication in children presenting with headache, nausea and vomiting (particularly effortless early morning vomiting that relieves the headache), a stiff neck and papilloedema. Impending cerebellar herniation may be suggested by impaired conscious level, focal neurological signs (particularly abnormal extraocular movements and unequal pupils with sluggish light reflexes), and hypertension with bradycardia (the Cushing Reflex).

Management

- Discuss with appropriate neurosurgical unit and involve local anaesthetic team. Urgent time-critical neurosurgical transfers will have to be performed by the local anaesthetic team, discuss urgently with neurosurgeons and CATS/STRS. Less urgent cases will be transferred by CATS/STRS.

- Head CT or MRI urgently

- AVOID strong opiate analgesia, since this makes monitoring of the child more difficult and will affect papillary reflexes prior to intubation. Once the child is anaesthetised and ventilated it is appropriate to use morphine to maintain sedation whilst transferring a child to PICU and will not mask papillary responses. It is essential to monitor papillary signs in these patients frequently (5-15 minute intervals).

- In discussion with PICU/anaesthetic support and neurosurgeons consider elective intubation and normocarbia (target pCO2 4-5kpa), osmotherapy (mannitol 0.5-1gm/kg IVI over 20-30 mins or hypertonic saline 2.7% 3-5ml/kg over 5 minutes) and/or dexamethasone 0.5mg/kg PO/IV x4/day)

Seizures and status epilepticus

As per local or APLS guidelines for any child presenting with seizures. See also Chapter 12 – Basic principles of symptom management for further guidance.

Acute hypertension and hypertensive encephalopathy

This is dealt with in detail in Chapter 11 – Drug treatment of hypertension. Hypertension is not an uncommon problem and may be seen as part of the presenting features for certain tumours (particularly neuroblastoma, phaeochromocytoma and nephroblastoma), or as a consequence of treatment (especially steroids during induction chemotherapy for ALL). Maintaining a normal blood pressure with intermittent oral anti-hypertensives is essential to avoid complications associated with prolonged hypertension and precipitation of an acute hypertensive crisis or encephalopathic illness (hypertensive or posterior reversible leukoencephalopathy syndrome).

The acute hypertensive crisis is best dealt with using IV anti-hypertensives, and requires anaesthetic/PICU support in many cases. Discuss urgently with the PTC.
**Intestinal obstruction and typhlitis**

Gastro-intestinal tract (GIT) obstruction, pseudo-obstruction and ileus are infrequent problems and rarely precipitate acute emergency situations. Mucositis and constipation are much more common problems and have been discussed at length in Chapter 10 Mucositis and Chapter 12 – Basic principles of symptom management: constipation section.

On occasions a child presenting with acute intussusception is diagnosed with abdominal lymphoma (usually Burkitt's type) or rarely another malignancy. The management of intussusception typically precedes the diagnosis of malignancy (although suspicions are raised in older children with irreducible or recurrent problems) and the medical management is unchanged by the underlying cause.

Acute or sub-acute/pseudo bowel obstruction may follow chemotherapy, or be as a consequence of abdominal surgery after tumour resection and usually settles with conservative treatment i.e. nil by mouth, large bore NG tube on free drainage, IV hydration +/- IV antibiotics. It may be necessary to alter drug doses with future chemotherapy courses (notably vincristine), so please inform the PTC. If the patient has undergone recent abdominal surgery, transfer back to the paediatric surgeons may be required.

**Typhlitis**

This is neutropenic enterocolitis. It most commonly occurs in the caecum and typically follows a prolonged course of neutropenia, resulting in benign mucosal ulceration, bacterial invasion and bowel perforation & peritonitis.

*Recognition/Diagnosis*

The symptoms suggest inflamed bowel with any/all of: abdominal pain, nausea & vomiting, bloody/watery diarrhoea being present. There may be absent bowel sounds, high fevers and the child may be clinically shocked due to sepsis.

♦ BEWARE – the symptoms are masked by steroids and the presence of a rigid board like abdomen typical of peritonitis will not necessarily be present. Hence the child in the latter half of induction chemotherapy for ALL may present atypically. Investigations should include those for febrile neutropenia, along with AXR and erect CXR looking for pneumatosis coli or evidence of perforation and an ultrasound of the abdomen.

*Management*

- Treatment is initially conservative (as per bowel obstruction above)

- Broad spectrum antibiotics are required immediately to cover the sepsis (as per febrile neutropenia policy, but add in metronidazole as well for anaerobic cover).

- If the child is significantly unwell (hypotensive not responding to fluid bolus then transfer to the PTC or PICU may be warranted for inotropic support – please discuss).

- If the symptoms do not settle rapidly, surgical intervention may be required, so liaison with the PTC and paediatric surgeons is necessary, not least as the mortality due to typhlitis is high!
Pancreatitis

This is an uncommon but important cause of abdominal pain in haematology-oncology patients, usually (but not exclusively) caused by the use of asparaginase. Other drugs such as steroids may also be risk factors.

Recognition

Classically the pain is epigastric, of sudden onset, gradually intensifying, then becoming constant and radiating through to the back. Clearly, however, it is rare to obtain such a history in children and the index of suspicion should be high in any child post-asparaginase presenting with abdominal pain. There may be associated nausea or vomiting, fever, tachycardia and, in severe cases, tachypnoea. There is usually upper abdominal tenderness, with or without guarding, abdominal distension and reduced bowel sounds. The Grey Turner and Cullen signs are very rare in children.

Diagnosis

Initial investigations should include a blood gas, glucose, amylase and lipase. The lipase is much more specific than the amylase, and levels more than 3x the upper limit of normal are usually due to pancreatitis. It should be borne in mind, though, that both the amylase and the lipase can fall in the later stages of worsening pancreatitis and can even be within the normal range. Further investigations should therefore be carried out if there is a clinical suspicion of pancreatitis even if the enzyme levels are normal.

The definition of pancreatitis used in UKALL 2011 trial is provided here as reference (UK clinical guidelines; - Gut 2005, 54)

For the purpose of UKALL2011 trial, pancreatitis is defined on the basis of at least two of the following features,

1. Abdominal pain strongly suggestive of acute pancreatitis
2. Serum amylase and/or lipase ≥3 times the upper limit of normal (lipase is preferred over amylase due to greater specificity)
3. Characteristic imaging findings of acute pancreatitis (ultrasonography is often unhelpful but contrast enhanced CT or MRI/MRCP may be useful for both confirming the diagnosis, determining severity, assessing complications, and for guiding potential percutaneous interventions).

Management

- Patients should be managed in the PTC, with close input from the gastroenterologists and pain team.
- Initial treatment comprises fluid resuscitation as appropriate, bowel rest and appropriate analgesia.
- A nasogastric tube (NGT) should be sited for symptom relief and IV fluids commenced.
- Close attention to fluid balance.
- It is often necessary to administer PN whilst waiting for the symptoms to settle.
- Ketamine is preferred to morphine for pain relief.
- In severe cases octreotide can be helpful. Discuss with gastroenterologists.
Strictly speaking, antibiotics are not beneficial for pancreatitis. However, it is usually appropriate for them to be prescribed, as children with pancreatitis are often very unwell and neutropenic, therefore sepsis cannot be excluded.

As symptoms settle, feeds can be slowly reintroduced. In mild cases it may be possible to reinstitute feeds via the NGT in the form of easily digestible medium chain triglycerides (MCT). In more severe cases, feeds should be given via a nasojejunal tube (NJT).

Complications, such as severe haemorrhage, intestinal obstruction/necrosis and pseudocyst formation are very rare, but should be looked out for.

Repeat imaging and referral to the paediatric surgeons may occasionally be required.

Coagulopathy/DIC
There are many reasons for acute haemorrhage in oncology patients before or during treatment, some of which are shown below:

<table>
<thead>
<tr>
<th>Problem</th>
<th>Possible causes</th>
<th>Products to be considered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>Lack of production (e.g. bone marrow infiltration or suppression, Fanconi’s anaemia or TAR syndrome)</td>
<td>Platelet pool (10-15mls/kg over 20-30 mins)</td>
</tr>
<tr>
<td></td>
<td>Increased destruction (e.g. sepsis syndrome, ITP or TTP)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sequestration (e.g. hypersplenism)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hereditary (e.g. Wiskott-Aldrich or Bernard-Soulier syndrome)</td>
<td></td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>Increased consumption of clotting factors such as DIC (e.g. sepsis syndrome or AML-M3) &amp; Fibrinogen depletion (asparaginase therapy)</td>
<td>Cryoprecipitate (5-10ml/kg over 20-30 mins) &amp;/or FFP (10-15ml/kg over 20-30 mins)</td>
</tr>
<tr>
<td></td>
<td>Decreased production of clotting factors (e.g. liver dysfunction or infiltration)</td>
<td>Vitamin K 0.3mg/kg IV slowly (max. 10mg) +/- FFP (10-15ml/kg over 20-30 mins)</td>
</tr>
<tr>
<td>Acquired anticoagulants</td>
<td>Inhibitors against coagulation factors (e.g. antiphospholipid antibodies)</td>
<td>Prolonged APTT, but propensity to acute thrombosis (call PTC)</td>
</tr>
<tr>
<td>Acquired von Willebrand’s disease (vWD)</td>
<td>Wilms’ tumour associated</td>
<td>As per hereditary vWD (call PTC)</td>
</tr>
<tr>
<td>Direct effects</td>
<td>Erosion of blood vessels (e.g. by tumour or fungus) &amp; venepuncture (insertion of central venous catheter)</td>
<td>Local haemostasis</td>
</tr>
</tbody>
</table>
Investigation
Check FBC, clotting screen, D-dimers (for DIC), acquired anticoagulants, clotting factors as appropriate.

Management
In most cases the bleeding can be controlled with appropriate blood product support and also, where appropriate, local haemostasis (e.g. ENT nasal packing for epistaxis). Please see chapter 2 on the 'Use of Blood Products', for details on appropriate transfusions, indications and dosing. Coagulation and FBC should be monitored regularly, 6-8 hourly, and acted on accordingly until transfer of the patient to the PTC. Ultimately, correction of the coagulation disorder requires treatment of the underlying cause, which may include:

- Chemotherapy
- Appropriate antimicrobials if sepsis syndrome
- Vitamin K for liver failure

As previously mentioned, coagulopathy is occasionally associated with hyperleukocytosis or tumour lysis syndrome. Additionally, it is a potentially life threatening complication of AML-M3 (Acute Promyelocytic Leukaemia) at presentation or following induction chemotherapy, and is the commonest cause of induction deaths in APL.

- All children thought to have Acute Leukaemia, should have a clotting screen performed promptly.
- Where APL is considered platelet counts should be kept above 30x10^9/l
- Coagulopathy should be anticipated in high count leukaemia
- Please discuss with PTC, but in established coagulopathy, platelets, FFP and cryoprecipitate are likely to be required (see Chapter 2).

Cardiac dysfunction & tamponade
Congestive heart failure (CHF) is a rare initial presentation in some children with cancer due to profound anaemia or as a consequence of treatment (anthracycline-induced myocyte damage).

Recognition
The presentation is no different to any other child in heart failure with breathlessness (poor feeding in infants), weight loss/failure to thrive and sweating. There may be associated anaemia, tachypnoea, respiratory distress, elevated venous pressure and hepatomegaly.

Diagnosis
Typical investigations include:
- Baseline bloods
- CXR (enlarged cardiac shadow)
- ECG (various non-specific abnormalities seen in CHF +/- low voltages may be seen in anthracycline induced cardiomyopathy)
- Echocardiogram will determine cardiac function and is used to monitor response to treatment.
Management

- Discuss with PTC and paediatric cardiologists – urgency for transfer for assessment will depend upon underlying aetiology, clinical state and response to treatment.

- Initial treatment is with diuretics in CHF (however, if secondary to profound anaemia a top up transfusion and usual management for a new patient with malignancy is advocated, although diuresis may still be required).

- **Cardiogenic Shock** – this is a rare cause of shock in haemato-oncological patients. However, it is important to remember that the standard treatment for shock (with septic shock being the commonest in haem/onc patients) with fluid boluses and volume expansion will lead to clinical deterioration and worsening cardiac failure in patients with known heart failure. Clinicians must discuss with cardiologists the management of shock in a patient with known cardiac failure.

**Cardiac tamponade**

Cardiac tamponade is an exceptionally rare complication of malignancy despite the relative frequency of pericardial effusions at presentation.

**Recognition:**

Clinical features at presentation may relate to the underlying malignancy but also with evidence of CHF as documented above. Additional features may include chest pain, cough, hiccups, non-specific abdominal pain and pulsus paradoxus.

**Diagnosis:**

- **CXR** reveals the enlarged ‘boot-shaped’ cardiac shadow
- **ECG** low voltages with flattened or inverted T waves
- **Echocardiography** is diagnostic.

**Management:**

- Discuss with PTC and paediatric cardiologists since percutaneous drainage is the treatment of choice for symptomatic relief. Additionally, the effusion may be diagnostic if tumour cells are identified on cytology &/or cytopsin with immunophenotyping. Definitive treatment is the appropriate treatment for the primary tumour!

- Diuretics may have a limited role to provide some symptom relief, thereby enabling transfer – discuss with PTC.
Veno-occlusive disease

Veno-occlusive disease (VOD) of the liver (or sinusoidal occlusion syndrome [SOS] as it is also known) is a serious regimen-related toxicity that typically follows bone marrow and stem cell transplantation. However, it can be seen following traditional chemotherapeutic schedules. Regimens including thiopurines, (typically thioguanine during the intensification blocks) may predispose to a typically more insidious but nonetheless significant form of VOD. Actinomycin D may also precipitate VOD.

Recognition/diagnosis

Classical clinical findings are a triad of weight gain, ascites and tender hepatomegaly. This may be associated with abnormal LFTs, thrombocytopenia, which tends to be refractory to platelet transfusions and reversal of portal blood flow on ultrasonography. (The latter is not required to make the diagnosis, since this is a very late feature of the syndrome). If clinical and/or ultrasound findings are consistent with this, then thioguanine, actinomycin D or presumed precipitant should be stopped and re-exposure avoided.

Management

General recommendations for the supportive care of VOD are as follows:

♦ Discuss with PTC, patients with suspected VOD should be transferred to PTC for further management.
♦ Careful monitoring of fluid balance (including twice daily weights and abdominal girths) and avoidance of sodium loads.
♦ Fluid restriction.
♦ Diuretics as indicated (excessive positive balance or weight gain) aiming for equilibrium.
♦ Opiate analgesia as indicated (i.e. right upper quadrant pain).
♦ BEWARE - patients with severe VOD and multi-organ failure are at increased risk of infection. Therefore if clinical concerns or fever, commence antibiotics as per febrile neutropenia protocol.
♦ PN is likely to be required, and should this be instigated, lipids should be avoided due to the likelihood of increasing liver damage.
♦ Should ascites cause respiratory compromise, paracentesis may be appropriate, but should be performed with caution and careful attention to coagulation parameters.
♦ Careful observation in severe cases for ensuing renal and pulmonary failure requiring haemodialysis and mechanical ventilation – Liaise with PICU as required.
♦ Use of defibrotide (discuss with PTC consultant).

Extravasation

Should a known vesicant extravasate (anthracyclines or vinca alkaloids) prompt action must be taken. This is covered in detail in Chapter 8 – Extravasation.
7. CARE OF CENTRAL VENOUS ACCESS DEVICES
7. Care of Central Venous Access Devices

Summary of Care of Central Venous Access Devices
Hickman®, Broviac® and Hickman type catheters, Bardport®, Implantable Ports, Peripherally Inserted Central Catheters (PICCs) and Haemodialysis/Apheresis Catheters

A central venous access device (CVAD) is a catheter inserted into the central venous system, with the internal tip sitting within the superior/inferior vena cava or right atrium. The PTC use different suppliers for some devices. If a child is discharged to you and the care that their CVAD requires differs from the advice given here, the PTC will let you know.

CVAD maintenance care should adhere to the ‘Saving Lives programme’ High Impact Intervention number 1, central venous catheter care bundle (DOH 2007).

All personnel who use venous access devices must have knowledge of, be trained and competent in the use and care of these devices.

Aseptic Non-Touch Technique (ANTT)

The main focus of ANTT is to minimise the introduction of micro-organisms, which may occur during preparation, administration and delivery of IV therapy. Furthermore, ANTT is basic in nature and clearly defined, focusing on the essentials of all IV therapy, regardless of intravenous device, administration route or clinical condition (Rowley, 2001). The theory behind ANTT focuses on the basic principles of infection control, such as effective hand washing, the wearing of non-sterile gloves (Dougherty, 2000), maintaining asepsis of equipment and environment, and the use of alcohol based solutions for decontamination with adequate cleaning and natural evaporation of the alcohol. If alcohol based products are not allowed to dry naturally, then the antibacterial properties of the agent will be ineffective, placing the patient at risk of developing an infection (Rowley et al 2010; RCN 2010).

Diagrams taken from UCLH Central Venous Catheter Policy 2009
The EPIC 2 guidelines recommend that an aseptic non-touch technique (ANTT) must be used for catheter site care and for accessing the venous system (Pratt et al 2007).

Key Parts

- Key parts – the aseptic parts of the procedure include equipment that needs to have direct contact with aseptic key-parts of the patient, or any liquid infusion. If contaminated, key-parts provide a direct route for transmission of pathogens between the procedure and the patient (Rowley et al 2010).

  - Key parts include:
    - Needles (any part of the actual needle itself and the inside of the sheath)
    - Syringe hubs
    - Any solution to be given via the catheter e.g. sodium chloride, heparin, IV medication.
    - Either the exposed end of the IV catheter or the end of the cap that the syringe connects to.

ANTT involves the essential practice of identifying, cleaning effectively and optimally protecting the key-parts at all times during a procedure. For example, in IV therapy, syringe tips should always be protected by dedicated caps, capped needles or the inside of syringe packets (Rowley et al 2010). When cleaning an intravenous needle free access device, introduce the port tip into the centre of a large 70% alcohol/2% chlorhexidine impregnated wipe. Scrub the tip of the needle free access device hard generating friction for 30 seconds. Use different parts of the wipe in order to clean away as well as kill any harmful organisms. The rest of the port and lumen is then cleaned working away from the tip (Rowley et al 2010).
Care of Tunneled and Non-Tunneled CVAD’s

Infection Prevention & Management

- Infection is the most common complication associated with CVAD’s and one of the most serious
- Decontaminate hands before and after each patient contact using correct hand hygiene procedure
- Always use ANTT when accessing the CVAD
- Regularly inspect for signs of infection (at least daily if patient is in hospital)

Assessing Patency

NB Always use ANTT when accessing the CVAD

- Do not administer chemotherapy, drugs or fluids unless the line is fully patent
- Test for flashback of blood before administering IV Medication by attaching a 10ml syringe with 0.9% sodium chloride to the catheter, flush a couple of mls into the line and then withdraw. As soon as you see a trace of blood in the catheter or syringe just flush the rest of the sodium chloride into the line
- Refer to Flushing table in appendix (page 102) for volumes

Flushing

NB Always use ANTT when accessing the CVAD

Before Flushing:
- If there are infusional vasoactive drugs in the lumen, withdraw prior to flushing to avoid bolus dose

Technique:
- Brisk push-pause technique with positive pressure finish

What to flush with:
- 0.9% sodium chloride between incompatible drugs / infusions and after blood sampling
- Prior to blood sampling (Lipids usually turned off for a minimum of 2 hours depending on local policy) when TPN is running, with 5-10mls Sodium Chloride 0.9%
- Refer to Flushing table in appendix (page 102) for volumes

Frequency of flushing:
- Flush unused lumens of CVADs once or twice a week to maintain patency.

Exit Site Care

NB Always use ANTT for exit site care

Cleaning:
- Clean site at dressing changes using 2% chlorhexidine in 70% isopropyl alcohol solution (Chloraprep) using a 30 second back and forth friction rub. Allow to dry
- If there is loose blood or exudate present, this should be removed first using sterile gauze and 0.9% sodium chloride

Dressings:
- Exit Site:
**Post insertion:** gauze under transparent dressing for 1 day or until bleeding stops

**After 1 day:**
- Sterile semi-permeable transparent dressing e.g. IV3000 or Tegaderm. Change every 7 days (or sooner if dressing becomes wet, soiled or detached).
- If patient cannot tolerate Tegaderm, try a plain transparent dressing with or without Biopatch. Change every 7 days (or sooner if dressing becomes wet, soiled or detached).
- If patient cannot tolerate a transparent dressing at all, use gauze-type dressing (eg Mepore) with or without Biopatch. Mepore dressings require changing every 3 days. Inspect and change daily if patient at high risk of exit site infection. (Change sooner if dressing becomes wet, soiled or detached).
- **After 21 days:**
  - Choose between continuing with same dressing or no dressing if appropriate for patient

**Bathing, showering & Swimming:**
- **Bathing:** Patient should not submerge exit site in bathwater
- **Showering:** If transparent dressing is intact patient can shower., If patient has dry dressing or no dressing, he/she can shower after 21 days as follows:
  - Remove dry dressing (if any) immediately before or after showering
  - Dry exit site after showering using sterile gauze and not-touch technique
  - Clean exit site as usual and apply new dressing if used
- **Swimming:** Not generally advised because of the infection risk

**Removal**
- CVAD’s must be removed as soon as possible if they are not needed
- Only staff qualified to do so may remove a CVAD

**Care of Implantable Ports**

**Infection Prevention & Management**
- Infection is the most common complication associated with Port’s and one of the most serious
- Decontaminate hands before and after each patient contact using correct hand hygiene procedure
- Always use ANTT when accessing the Port
- Regularly inspect for signs of infection (at least daily if patient is in hospital)

**General Points**
- **NB Always use ANTT when accessing the Port**
  - Only access port using a dedicated non-coring needle with integral extension set with clamp/stopcock
  - If patient undergoes MRI scan, inform scanning personnel about the Port
  - If patient requires defibrillation do not place paddles directly over the Port
  - The Port should never be used for power-injection of contrast medium as this may cause the catheter to split (unless the patient has a CT-rated Port)
Inserting the Non-coring Needle

NB Always use ANTT when accessing the Port

- Numb the skin over the Port if required using topical anaesthetic (before skin preparation)
- Prepare skin over the Port using 2% chlorhexidine in 70% isopropyl alcohol solution (Chloraprep) using a 30 second back and forth friction rub. Allow to dry. Do not touch the proposed needle insertion site again.
- Prime needle and/or giving set with 0.9% sodium chloride
- Hold the Port firmly with thumb and two fingers and stretch skin taut during insertion of the needle to prevent the port sliding out of the way of the needle, and to reduce the risk of the port becoming dislodged within the subcutaneous pocket
- Insert needle swiftly and firmly until it is felt to contact the back of the port
- Verify correct position by flushing with 5-10 mls of 0.9% Sodium Chloride and checking for aspiration of blood
- If there is any local discomfort and/or oedema in the tissues around or over the port this may indicate incorrect position of the needle. Remove needle and re-insert. (You can use the same needle for up to 2 attempts as long as it has not become contaminated or damaged)
- If the port flushes easily without any local discomfort/oedema but there is no flashback of blood, this suggests that the needle position is correct but that the catheter itself is not fully functional.

Assessing Patency

NB Always use ANTT when accessing the Port

- Do not administer chemotherapy, drugs or fluids unless the line is fully patent
- Test for flashback of blood before administering IV Medication by attaching a 10ml syringe with 0.9% sodium chloride to the catheter, flush a couple of mls into the line and then withdraw. As soon as you see a trace of blood in the catheter or syringe just flush the rest of the sodium chloride into the line

Flushing

NB Always use ANTT when accessing the Port

Non-accessed ports:

- Flush at least every four weeks according to PTC guidance or Trust Policy.

Accessed Ports:

- Technique: Brisk push-pause technique

What to flush with:

- 0.9% Sodium Chloride between incompatible drugs/infusions and after blood sampling
- If needle to be removed: lock with 5 mls Heparinised saline 100U/ml
- Refer to Flushing table in appendix (page 102) for volumes

Removing the Needle:

- Lock port with heparinised saline. Ideally remove the needle while injecting the last ml to achieve positive pressure finish. NB you will need to ask the patient or a third party to inject because you will need two hands for removing the needle. If this is not possible, you can achieve a positive pressure finish by clamping the infusion set while injecting the final ml of flush and then remove the needle (UCLH 2010)
- Stabilise the port with one hand during needle withdrawal to avoid trauma to tissues. Take care to avoid a needle-stick injury
- Apply gentle pressure to needle site with sterile gauze until minor bleeding has ceased. A plaster may be applied if necessary/desired.
Exit Site Care

**Frequency of needle change:**
- If port in constant use for more than a week, change needle weekly using different puncture site

**Dressings:**
- **Non-accessed Ports:**
  - No dressing or exit site care required
- **Accessed Ports:**
  - Pad needle with sterile gauze if necessary and cover with sterile semi-permeable transparent dressing e.g. IV3000 or Tegaderm. Needle site should be visible for inspection
  - Tape tubing firmly to skin to prevent pulling on the needle
  - Inspect needle site at least daily
  - Advise patient to report any discomfort or swelling at the puncture site immediately

Bathing, Showering & Swimming

- **Non-accessed Ports:** Patient may bath, shower or swim freely once wound has healed
- **Accessed Ports:**
  - **Bathing:** Patient should not submerge exit site in bathwater
  - **Showering:** Patient may shower if needle site is completely covered with an occlusive dressing, taking care not to dislodge needle
  - **Swimming:** Not advised while needle is in situ

Removal

- Implantable ports are usually removed in Interventional Radiology

Care of PICC’s (Peripherally Inserted Central Catheters)

**Infection Prevention & Management**

- Infection is the most common complication associated with PICC’s and one of the most serious
- Decontaminate hands before and after each patient contact using correct hand hygiene procedure
- Always use ANTT when accessing the PICC
- Regularly inspect for signs of infection (at least daily if patient is in hospital)

**General Points**

**NB Always use ANTT when accessing the PICC**

- Assess external length of PICC before use
- Take care at all times not to pull the PICC out as some will not have sutures
- Avoid compression to vein containing the PICC. Do not use blood pressure cuff on the arm with PICC in situ. Any bandage/tubular dressing must be loose.
- Never use PICC for administering contrast medium as this will cause the PICC to split (unless the patient has a CT-rated PICC).
Assessing Patency

**NB Always use ANTT when accessing the PICC**

- Do not administer chemotherapy, drugs or fluids unless the line is fully patent
- Test for flashback of blood before administering IV Medication by attaching a 10ml syringe with 0.9% sodium chloride to the catheter, flush a couple of mls into the line and then withdraw. As soon as you see a trace of blood in the catheter or syringe just flush the rest of the sodium chloride into the line

### Flushing

**NB Always use ANTT when accessing the PICC**

Make sure you are aware of the type of PICC inserted. Open-ended PICC’s may require heparin. Valved PICC’s only require sodium chloride 0.9%.

**Technique:**

- Brisk push-pause technique with positive pressure finish

**What to flush with:**

- 0.9% sodium chloride between incompatible drugs/infusions or after blood sampling
- Lock with a further 5-10 mls 0.9% sodium chloride
- Refer to [Flushing table in appendix (page 102)](#) for volumes

**Frequency of flushing:**

- PICC’s need flushing at least once a week to maintain patency. Increase to twice weekly if there are patency problems

### Exit Site Care

**NB Always use ANTT when accessing the PICC**

**Securement:**

- Always fix catheter to patient’s skin using steri-strips/statlock/griplock and a transparent dressing

**Cleaning:**

- Clean site at dressing changes using 2% chlorhexidine in 70% isopropyl alcohol solution (Chloraprep) using a 30 second back and forth friction rub. Allow to dry
- There is no need to clean the actual PICC itself. This is unnecessary and risks dislodging the PICC
- If there is loose blood or exudate present, this should be removed first using sterile gauze and 0.9% sodium chloride

**Dressings:**

- **Post insertion:** gauze, steristrips and statlock/griplock dressing under a transparent dressing for 1 day.
- **After 1 day:**
  - Statlock/Griplock dressing under sterile semi-permeable transparent dressing e.g. IV3000 or Tegaderm. Change every 7 days (or sooner if dressing becomes wet, soiled or detached).
  - If patient cannot tolerate Tegaderm, try a plain transparent dressing with or without Biopatch. Change every 7 days (or sooner if dressing becomes wet, soiled or detached).
  - If patient cannot tolerate a transparent dressing at all, use gauze-type dressing (eg Mepore) with or without Biopatch. Inspect and change daily if patient at high risk of exit site infection. (Change sooner if dressing becomes wet, soiled or detached).
Bathing, Showering & Swimming:
- **Bathing & Showering**: Patient should not get the dressing wet. If possible provide a waterproof covering for bathing and showering
- **Swimming**: not advised unless using completely waterproof cover

**Removal**
- PICC’s must be removed as soon as possible if they are not needed
- Only staff qualified to do so may remove a PICC

### Permcath® or Vascath – Dialysis Catheters

**N.B.** Before using Permcath® and other haemodialysis/apheresis catheters the **indwelling heparin must be aspirated with a minimum of 2-3mls blood** from the catheter and lumen(s) and flushed with 10mls 0.9% Sodium Chloride. This is to prevent systemic heparinisation and to remove any clots present.

Permcaths® need flushing at least once a week to maintain patency. For most children it is practical to flush:
- Before and after drug administration with 3-5 mls Sodium Chloride 0.9%
- After withdrawing blood or flushing off TPN, with 5-10mls Sodium Chloride 0.9%
- Prior to blood sampling (Lipids usually turned off for a minimum of 2 hours depending on local policy) when TPN is running, with 5-10mls Sodium Chloride 0.9%
- At the end of each access with the **specific volume of Heparin Sodium 1000 units per ml**.

This specific volume varies dependent on the internal volume of the catheter. It is usually written on each lumen exactly how much to flush with – e.g. 0.8cc’s = 0.8mls. It is vital that the correct amount of heparin sodium is instilled as too much can lead to problems with clotting due to the strength of the heparin. If in doubt, check with PTC caring for patient.

**N.B.** Sterile white caps are also recommended instead of needle-free access devices on the end of dialysis catheters as a prompt to always withdraw the heparin prior to use.

### Needle-free Access Devices

The hub of the external catheter should always be protected with a needle-free access device. PTC’s and hospitals have different contracts with suppliers. Whichever type of needle-free access device is used, it should be changed according to the manufacturers recommendations (MHRA, 2008).

#### Changing the Needle-free access device

**NB Always use ANTT when accessing the CVAD**

- Ensure the catheter is clamped.
- Remove the old needle-free access device
- Clean the end of the catheter with a single patient use 2% chlorhexidine in 70% isopropyl alcohol wipe Allow to dry. (Visibly check the area) this is essential in order to achieve effective cleansing (Dougherty, 2000; Rowley, 2001).
- Apply a new needle-free access device, ensuring not to touch the end of the catheter or the part of the
General Principles of Care

Use of aseptic, non-touch technique (ANTT) whenever the CVAD is accessed and during procedures involving exit sites is essential to prevent infection. There is a strong correlation between bacteraemia and the presence of a CVAD (Haller and Rush 1992).

Regularly inspect for signs of infection (at least daily if patient is in hospital) including inspection of exit site and monitoring of temperature, pulse and blood pressure at least daily when the patient is in hospital.

Take action immediately if there are signs of CVAD related infection. These include:
- Pyrexia, rigor, malaise
- Tenderness, inflammation and/or pain at exit site

Wear gloves when carrying out any procedure related to the CVAD. Gloves are worn to prevent descaling of bacteria into key parts (Rowley 2001).

Cap off the catheter with a needle-free access device when not in use. This will minimise interruptions to the closed system. Manufacturers’ instructions vary for each device and should be adhered to (Pratt et al 2007, MHRA, 2008, RCN 2010). The risk of contamination increases with every interruption to the closed system (Haller & Rush 1992).

Whenever the needle-free access device is removed from the catheter, it must be replaced with a new one. The needle-free access device should also be changed immediately if the integrity of the device is compromised or residual blood is present.

When accessing the catheter through the needle-free access device, always decontaminate the device using chlorhexidine 2% in alcohol and using ANTT. The device should be cleansed each time using a 30 second vigorous friction rub and allowed to dry before inserting a sterile syringe-tip

If the catheter possesses an integral clamp, keep it closed when not in use -The clamp will prevent air entry and bleeding, should the needle-free access device become unattached.

Assessing Patency

- Do not administer chemotherapy, drugs or fluids unless the line is fully patent. By fully patent we mean that:
  - The line can be flushed easily
  - There is flashback of blood

Testing for patency:

- When first accessing the CVAD, gentle pressure must first be used to assess the patency of the catheter.
- Attach a syringe containing 10 mls 0.9% Sodium Chloride, flush a couple of mls into the line and then withdraw. As soon as you see a trace of blood in the catheter or syringe just flush the sodium chloride into the line.
If obtaining blood cultures aspirate before flushing as you will need this initial 3-5mls for the culture.

Before administering vesicant drugs/fluids the catheter should be flushed to determine any resistance and brisk, free flowing blood return into an empty syringe is seen (Hadaway, 2007; Dougherty and Lister, 2008). A flash back of blood into a syringe of saline is not an adequate assessment when administering vesicant drugs (Sauerland et al 2006).

**The importance of syringe size**

Syringe size has a significant impact on the risk of catheter damage. The basic principle is that smaller syringes generate higher internal pressures, with very little force than larger syringes when flushing the device (Hadaway 2006).

Smaller syringes can exceed 25 pounds per square inch (psi) which can cause venous damage and catheter rupture. Exerting normal pressure on a 10 ml syringe produces 11 psi, while a 3 ml produces 29 psi and a 1 ml produces >100 psi. CVAD’s can burst above 25-40 psi (Bard Access Systems 2008).

10 ml syringes or larger will need to be used when first accessing any CVAD. The back pressure from an occlusion may not be felt when using a small syringe until damage to the catheter has occurred (Conn 1993). Catheter fracture/rupture can be internal or external. A total break can result in the catheter dropping further into the venous system resulting in possible catheter emboli.

Smaller syringes can be used once catheter patency has first been established using a 10 ml syringe (Hadaway 1998).

**Turbulent flush** – a pulsating, push-pause flush allows turbulent flow to remove any medication or blood components, thereby decreasing the risk of fibrin and platelets becoming adhered to the internal wall of the CVAD (Dougherty & Lamb 2008), creating less chance for lumen occlusion (Hadaway 2006).

**Volume of flush required to properly lock the catheter** depends on the priming volume of the catheter plus any add-on devices. The Infusion Nurses Society (INS) Standards of Practice call for the minimum volume to be equal to twice the internal volume of the catheter system (INS 2006; RCN 2010).

**Positive Pressure** – use of positive pressure when flushing off (locking) a CVAD helps to maintain the patency of the catheter (RCN 2010, Dougherty & Lamb 2008). The use of positive pressure helps to prevent a vacuum forming after completion of the flush, preventing blood being sucked back into the catheter. This will help to prevent catheter occlusion. For CVAD’s, Ports and open-ended PICC’s, positive pressure is achieved by closing the clamp whilst flushing.

- For valved PICC’s, continue to flush the PICC, whilst removing the leur-slip syringe from the needle free access device – do not use a leur-lock syringe.

**Heparin versus sodium chloride 0.9%**

There are currently two standard flushing solutions used most frequently on CVAD’s. These are heparin and sodium chloride 0.9%. No alternative solutions are commercially available at the present time. Low dose heparin flushes are frequently used to fill the lumens of a CVAD between use in an attempt to prevent thrombus formation and to prolong the duration of catheter patency. However, the efficacy of this practice is unproven (Pratt et al 2007; Bishop et al 2007).

A recent review of the evidence on heparin flushes by UK Medicines Information indicates that the evidence for heparin flushes is unclear and inconclusive (UK Medicines Information 2012).
Some clinicians and manufacturer's recommend heparin flushes when CVAD’s are infrequently accessed (e.g. implanted ports) or are used for blood processing (i.e. apheresis or haemodialysis) (Pratt et al 2007).

Apheresis/haemodialysis catheters are commonly flushed with heparin 1,000-5,000 units per ml to maintain patency.

The requirement for heparin over 0.9% sodium chloride may be a function of catheter bore, as large bore catheters (i.e. apheresis/haemodialysis catheters) allow faster back-tracking of blood up the lumen (Bishop et al 2007).


A rapid response report issued by the NPSA in April 2008 advised organisations to review local policies in order to minimise the use of heparin flush solutions for all vascular access devices (NPSA 2008) Since the publication of the National Patient Safety Agency Rapid Response Report (NPSA, 2008) highlighting the risks associated with heparin flushes some NHS Trusts have elected to stop using heparin to flush CVAD’s (Bravery, 2010). The use of heparin vs Sodium chloride 0.9% for flushing CVAD's remains controversial. In practice some centre's based on their own experience have chosen to use sodium chloride 0.9% to flush tunnelled and non-tunnelled CVC’s and PICC’s.

There is a lack of research in children on the efficacy of heparin flushes. Whilst changing from heparin to sodium chloride 0.9% flushes for CVAD’s would result in cost savings and more importantly a reduction in risks of inadvertent administration of an overdose of heparin, current research does not appear to support such a withdrawal of heparin.

Indeed it is not known whether withdrawing heparin from use in CVAD's would lead to an increase in occlusion and premature removal of such devices (Toft 2007).

Other studies have demonstrated an increase in infections when changing from heparin to sodium chloride 0.9% (Jacobs et al 2004; Schilling et al 2006)

**Exit Site Care**

- Maintaining the dressing site is important to reduce the risk of infection and to minimise the risk of CVAD dislodgement, fracture or accidental removal
- CVAD and PICC dressings need to be changed the day after the insertion as any blood left underneath the dressing increases the risk of infection (RCN 2010). After this time, CVAD dressings are changed weekly, unless the exit site has bled or oozed or the dressing is not secure.
- The CVAD exit site should be cleaned with a single patient use application of alcoholic chlorhexidine based cleaning solution, preferable 2% chlorhexidine gluconate in 70% isopropyl alcohol (Pratt et al 2007). Alcohol based cleaning solutions have demonstrated good activity against bacteria, viruses and most fungi. A solution of 2% will reduce the likelihood of resistance developing.
Loose blood, exudate or other debris which might provide a focus for infection or might impair inspection of the wound may be gently removed by cleaning with sterile 0.9% Sodium chloride prior to cleaning with 2% Chlorhexidine (Oliver, 1997)

2% chlorhexidine in 70% isopropyl alcohol should not be used on the skin of pre-term infants under 35 weeks gestational age. It can be used with caution in children under 2 months of age. However, if there is any evidence of skin reaction in this age group, discontinue its use and consult the PTC

NB Alternative antiseptic solutions that may be used:

- 0.5% chlorhexidine gluconate in 70% denatured ethanol B
- Providone-iodine 10%

**Dressing Selection**

The first choice for a CVAD dressing should be a sterile semi-permeable transparent dressing e.g. IV3000 or Tegaderm (Pratt et al 2007; RCN 2010). Gauze dressings are not waterproof and require frequent changing in order to inspect the catheter site. Sterile transparent, semi-permeable dressings, reliably secure the CVAD and Port needle, permits continuous visual inspection of the catheter site, allows patients to bathe and shower without saturating the dressing, and requires less frequent changes than that required for standard gauze dressings, thus also saving personal time. It also provides a sterile barrier, yet is permeable to water vapour from the skin in order to reduce the growth of local microflora.

- Dressings may remain in situ for up to one week.
- Sterile wound closure strips can also be used to provide extra fixation if preferred.
- No dressing may be suitable for some patients with tunnelled CVAD’s from 21 days post insertion once the tissues have fibrosed around the cuff and in the absence of exudate or signs of infection.

Self-adhesive island non-woven dressings e.g. Mepore, need to be used if there is any oozing from the exit site to absorb any exudates. Remnant exudate on the site increases the risk of infection (RCN 2010). The dressing needs to be changed daily if exudate is present and the exit site reviewed. The dressing can be left for 48 hours if there is no ooze. Any dressing change will need to be documented and should include comments of the condition of the exit site. Sodium Chloride 0.9% or aqueous chlorhexidine 0.05% may be used if the site is cleaned daily as 2% chlorhexidine in 70% isopropyl alcohol will sting and daily use may irritate the skin

If an allergy to any dressing is suspected a barrier film, such as Cavilon, may be used to protect the skin prior to a dressings’ application for sensitive skin or those with mild reactions.

A soft silicone adherent dressing (e.g. Mepiform or Mepilex) can be used as an alternative if the child/young person has a severe allergy to the above dressings. This is generally used for dermatology patients. The adhesive is silicon based and less likely to cause reactions. These should only be used if clinically indicated and after discussion with the PTC.

**Antimicrobial dressings**

Antimicrobial dressings such as BioPatch can be used if supported by the PTC. Please discuss with the PTC for more guidance and information.

**Bathing, Showering and Swimming**

There is very little literature to support guidelines. The following principles should be taken into account when advising patients.
21-days post-insertion, the patient's tissues should have adhered to the cuff, creating a physical barrier to ascending bacteria (Wickham et al, 1992; Wilson, 1994).

Patients may be advised that they can shower after this time as long as they remove any dry gauze-type dressing immediately before or after showering, and dry the skin thoroughly afterwards using sterile gauze and a non-touch technique. Cleaning of the exit site in the usual way should follow and a new dressing applied.

If the patient is using an IV dedicated transparent dressing, then there is no need to change the dressing after showering, as long as the dressing remains occlusive and no water has seeped underneath the dressing. If the dressing has come adrift it must be removed immediately and the exit site cleaned and redressed using ANTT.

If the patient wishes to have a bath, he/she should be advised to keep the exit site out of the water and not to let the catheter ends hang in the bath water, even if it is covered with an occlusive dressing.

Troubleshooting

Oclusion

Urokinase (Syner-kinase®) has recently been licensed for use as a thrombolytic for occluded CVAD’s and would be the preparation of choice where available, as it is the only thrombolytic licensed for this indication. The licensed dose is 5,000-25,000 units held in the line for up to 4 hours. The recommended dose for unblocking lines remains 5,000 units made up with sodium chloride 0.9%.

Urokinase is still available as an unlicensed preparation from Germany via IDIS and Alteplase may also be used to unblock lines where Urokinase is not available.

Please contact Principle Treatment Centre (PTC) if unable to obtain Urokinase or you have any queries.

Withdrawal Occlusion or Total Occlusion may be due to one of the following:

- Catheter tip malposition
- Intraluminal clot
- Intraluminal medication precipitate
- Catheter kink (external and internal to body)
- “Pinch-off”
- Catheter related thrombosis (intra and extraluminal)
- Suture constriction
- Fibrin sheath/tail/flap
- Malposition/dislodgement of implanted port needle
- Fibrin in port reservoir
- Other

If a thrombolytic used correctly fails to restore function, contact the PTC for further advice. A chest x-ray should be carried out to check the position of the line. If a chest x-ray shows that the catheter is correctly placed, it may be worth investigating further using fluoroscopy which may reveal a fibrin sheath. This may need to be performed in the PTC.
**Protocol for Urokinase Administration**

- Arrange prescription
- Make up Urokinase as per instructions or local policy:

<table>
<thead>
<tr>
<th>UCLH</th>
<th>Marsden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reconstitute 10,000 unit vial with 2 mls water for injection and dilute further to 4 mls. Use 2 mls (5,000) units per lumen</td>
<td>Reconstitute 10,000 units with the priming volume of the CVAD (PICC 0.5 mls, skin tunneled catheter 1 ml, Port 3 mls) plus additional 1.5 mls of 0.9% sodium chloride</td>
</tr>
<tr>
<td>Install into each lumen of the CVAD and wait 2 hours (or preferably longer if possible)</td>
<td>Draw up solution in a leur lock syringe. Remove extension set and needle free access device</td>
</tr>
<tr>
<td>Assess the CVAD again – use 0.9% sodium chloride and flush the line to ensure it is cleared of the blockage. There is no need to worry that you are flushing the Urokinase into the patient as small doses can be flushed into the patients without any danger unless the patient has deranged clotting</td>
<td>Inject solution into CVAD to the priming volume + 0.5 mls (1st lock) Lock the solution into the CVAD and leave the syringe attached to the lumen. Wait 10 mins Inject a further 0.5 mls of solution and lock again (2nd lock). Wait a further 10 mins Inject another 0.5 mls of solution and lock again (3rd lock) Wait 10 mins then aspirate CVAD lumen and flush with 0.9% sodium chloride to establish flow</td>
</tr>
<tr>
<td>If full function has not been restored – instil the urokinase again and leave it in situ for a longer period of time (several hours or overnight if possible)</td>
<td>If unblocking a dual lumen catheter then inject 10,000 units down each lumen</td>
</tr>
<tr>
<td>For total occlusion – instil urokinase using a 3 way tap</td>
<td>For total occlusion – instil urokinase using a 3 way tap</td>
</tr>
</tbody>
</table>

**Any queries contact the PTC supervising the child’s care**

**Total occlusion:**
If the line is blocked i.e. it will not infuse or aspirate, please contact the PTC supervising the child’s care. Do not attempt to unblock totally occluded catheters unless trained to do so.
N.B. Risk of catheter rupture, catheter embolus

**Withdrawal occlusion:**
If the line will not withdraw (sample blood) give urokinase if you have been trained to do so.
Protocol for Alteplase Administration (Used at GOSH)

Alteplase is a fibrinolytic that acts as a thrombolytic by activating plasminogen to form plasmin, which degrades fibrin and so breaks up thrombi. Vials contain 4 mg in 4 mls Alteplase. Different trusts may decant into smaller amounts.

<table>
<thead>
<tr>
<th>Catheter</th>
<th>Amount to give</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripherally inserted central catheter (4Fr/5Fr)</td>
<td>give 0.5 mls (0.5mg)</td>
</tr>
<tr>
<td>Single lumen CVC (Broviac®) 2.7Fr/4.2 Fr/6.6Fr</td>
<td>give 0.5 mls (0.5 mg)</td>
</tr>
<tr>
<td>Single lumen CVAD (Hickman®) 9.6Fr</td>
<td>give 1.0 ml (1mg)</td>
</tr>
<tr>
<td>Dual lumen CVAD (Hickman®) 7fr/9fr</td>
<td>give 1.0 ml down each required lumen (1mg)</td>
</tr>
<tr>
<td>Triple lumen CVC (Hickman®) 10Fr/12Fr</td>
<td>give 1.0 ml down each required lumen (1mg)</td>
</tr>
<tr>
<td>Implantable Port's</td>
<td>give 1.5 mls (1.5mg)</td>
</tr>
<tr>
<td>Low profile Port</td>
<td>give 1 ml (1mg)</td>
</tr>
<tr>
<td>Central venous access (Temporary) for extracorporeal therapies (Gamcath®/Vascath®) various sizes</td>
<td>The amount instilled must be the equivalent of the volume of the dead space of the catheter</td>
</tr>
<tr>
<td>Central venous access (permanent/cuffed) for extracorporeal therapies (Kimal/Gambro/Tyco/Permcath® Various sizes</td>
<td>The priming volumes for the catheter are printed on the catheter or clamps itself and in the insertion leaflet</td>
</tr>
</tbody>
</table>

**Total occlusion:**
If the line is blocked i.e. it will not infuse or aspirate, please contact the medical team or PTC for telephone advice. Do not attempt to unblock occluded catheters unless trained to do so.
N.B. Risk of catheter rupture, catheter embolus.

**Withdrawal occlusion:**
If the line will not withdraw (sample blood) give Alteplase if you have been trained to do so.
Port Pocket Infection

If needle not in situ

<table>
<thead>
<tr>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>• If possible avoid accessing the Port</td>
</tr>
</tbody>
</table>

If needle is inserted through the skin into the Port, infection may be introduced into the Port and catheter. If child’s condition dictates or no other venous access available it may be preferable to access the Port. If this action is taken ensure blood cultures are obtained and IV antibiotics are commenced. Follow febrile neutropenia protocol. Contact Medical team at the PTC supervising the child’s treatment if advice is needed re antibiotic therapy.

• Culture any purulent discharge
• If Port is not accessed give IV antibiotics via peripheral cannula for 48 hours.
• Assess the Port after 48 hours. If the infection is responding to IV antibiotics the Port may be accessed and antibiotics continued via Port.

Once infection is treated Port may be used. This is advisable if skin infection has cleared to treat any infection that may have entered the Port
• Check Port site daily for signs of skin breakdown.

To identify Port erosion. If Port erosion occurs, contact the PTC supervising the child’s treatment as device may require removal.

If needle in situ

<table>
<thead>
<tr>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do not remove the needle</td>
</tr>
<tr>
<td>It has provided a conduit for the infection, which may already have entered the port.</td>
</tr>
<tr>
<td>Continue to give IV antibiotics via the port for 48 hours</td>
</tr>
<tr>
<td>If no improvement after 48 hours remove the needle and continue IV antibiotics peripherally</td>
</tr>
<tr>
<td>If improvement in the condition of the skin - continue to treat through the port</td>
</tr>
</tbody>
</table>

Port erosion

If skin breaks down over the port reservoir seek advice from the PTC supervising the child’s care. Once Port erosion occurs the device usually requires removal.
**Catheter Damage**

| Child will need referral to the PTC supervising the child’s care for catheter repair unless repair kit is available locally and local staff are trained and experienced to repair the catheter |

**Action**

- Clamp the catheter between the patient and the damaged area with a smooth-edged, atraumatic clamp (use 2 clamps if possible) or fold the catheter between the patient and the damaged area and tape it together.
- Seal damaged area with a sterile occlusive dressing.
- Determine the site of damage and the size and type of catheter.
- Repair catheter (ONLY IF TRAINED TO DO SO).
- Take cultures from all lumens.
- Ensure the child/young person/parents are familiar with the clamping/taping procedure if damage should occur at home.

**Fluid Leakage from Catheter Exit Site**

<table>
<thead>
<tr>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flush catheter with 10 mls of 0.9% Sodium Chloride and observe for signs of fluid extravasation under the skin. Pain, swelling at vein insertion site (neck), tunnel tract (chest wall) and exit site.</td>
</tr>
<tr>
<td>Refer to PTC supervising the child’s treatment</td>
</tr>
</tbody>
</table>
### Flushing Table: Flushing Guidelines for Central venous Access Devices

(Ensure you make sure you know the type and size of device in situ prior to use)

<table>
<thead>
<tr>
<th>Device</th>
<th>Action</th>
<th>GOSH</th>
<th>UCLH</th>
<th>MARSDEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin Tunneled</td>
<td>To assess patency</td>
<td>1-2mls 0.9%</td>
<td>10mls 0.9% sodium</td>
<td>10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td>2.7Fr, 4.2Fr, 6.6Fr Single Lumen</td>
<td>In between/after IV medication</td>
<td>1-2mls 0.9%</td>
<td>10mls 0.9% sodium</td>
<td>2-5mls 0.9% sodium chloride or 5% Dextrose</td>
</tr>
<tr>
<td></td>
<td>Frequently accessed catheters (3x daily or more) after each use as a lock</td>
<td>1-2mls 0.9%</td>
<td>10mls 0.9% sodium chloride followed by a further 10mls 0.9% sodium chloride</td>
<td>2-5mls 0.9% Sodium Chloride</td>
</tr>
<tr>
<td></td>
<td>Infrequently accessed catheters (once or twice week) after each use as a lock</td>
<td>1-2mls 0.9%</td>
<td>10mls 0.9% sodium chloride followed by a further 10mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride followed by 10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td></td>
<td>To lock the catheter (weekly)</td>
<td>1.5mls Heparinised saline 10 units/ml</td>
<td>10mls 0.9% sodium chloride followed by a further 10mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride followed by 3-5ml heparinised saline 10 units/ml</td>
</tr>
<tr>
<td></td>
<td>To flush after blood sampling</td>
<td>2-3mls 0.9%</td>
<td>10mls 0.9% sodium</td>
<td>5-10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td>Implanted Port (Large)</td>
<td>To assess patency</td>
<td>2-3mls 0.9%</td>
<td>10mls 0.9% sodium</td>
<td>10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td></td>
<td>In between/after IV medication</td>
<td>2-3mls 0.9%</td>
<td>10mls 0.9% sodium</td>
<td>2-5mls 0.9% sodium chloride or 5% Dextrose</td>
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<td>2-3mls 0.9%</td>
<td>10mls 0.9% sodium chloride followed by a further 10mls 0.9% sodium chloride</td>
<td>If remained accessed 10mls 0.9% sodium chloride followed by 4-5mls heparinised saline 10 units/ml</td>
</tr>
<tr>
<td></td>
<td>To lock the catheter (weekly)</td>
<td>2.5mls Heparinised saline 10 units/ml</td>
<td>10mls 0.9% sodium chloride followed by a further 10mls 0.9% sodium chloride</td>
<td>If remained accessed 10mls 0.9% sodium chloride followed by 4-5mls heparinised saline 10 units/ml</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>saline 10 units/ml</td>
<td>4-5mls heparinised saline 100 units/ml</td>
<td>10mls 0.9% sodium chloride followed by 4-5mls heparinised saline 100 units/ml</td>
</tr>
<tr>
<td>To lock the catheter (Monthly)</td>
<td></td>
<td>2.5mls heparinised saline 100 units/ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>To flush after blood sampling</td>
<td></td>
<td>5-10 mls 0.9% Sodium Chloride</td>
<td>10mls 0.9% sodium chloride</td>
<td>5-10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td>Implanted Port (Low Profile)</td>
<td>To assess patency</td>
<td>1-2mls 0.9% sodium Chloride</td>
<td></td>
<td>10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td></td>
<td>In between/after IV medication</td>
<td>1-2mls 0.9% sodium Chloride or dextrose 5%</td>
<td></td>
<td>2-5mls 0.9% sodium chloride or 5% Dextrose</td>
</tr>
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<td></td>
<td>Frequently accessed catheters (3x daily or more) after each use as a lock</td>
<td>1-2mls 0.9% sodium Chloride</td>
<td></td>
<td>10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td></td>
<td>Infrequently accessed catheters (once or twice week) after each use as a lock</td>
<td>1-2mls 0.9% sodium Chloride followed by 2mls heparinised saline 10 units/ml</td>
<td>If remained accessed 10mls 0.9% sodium chloride followed by 4-5mls heparinised saline 10 units/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td>To lock the catheter (weekly)</td>
<td>2mls heparinised saline 10 units/ml</td>
<td></td>
<td>If remained accessed 10mls 0.9% sodium chloride followed by 4-5mls heparinised saline 10 units/ml</td>
</tr>
<tr>
<td></td>
<td>To flush after blood sampling</td>
<td>3mls 0.9% sodium chloride</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin tunnelled CVC 9.6Fr (single lumen), 7Fr, 9Fr, 10Fr, 12Fr (double lumen)</td>
<td>To assess patency</td>
<td>2-4mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td></td>
<td>In between/after IV medication</td>
<td>2-4mls 0.9% sodium Chloride or dextrose 5%</td>
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</tr>
<tr>
<td>Infrequently accessed</td>
<td>after each use as a lock</td>
<td>2-4mls 0.9% sodium chloride followed by 2.5mls heparinised saline 10 units/ml</td>
<td>10mls 0.9% sodium chloride followed by a further 10mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride followed by 3-5ml heparinised saline 10 units/ml</td>
</tr>
<tr>
<td>To lock the catheter</td>
<td>(weekly)</td>
<td>2.5mls heparinised saline 10 units/ml</td>
<td>10mls 0.9% sodium chloride followed by a further 10mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride followed by 3-5ml heparinised saline 10 units/ml</td>
</tr>
<tr>
<td>To flush after blood</td>
<td>sampling</td>
<td>5-10mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride</td>
<td>5-10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td>PICC (valved) 3Fr, 4Fr</td>
<td>To assess patency</td>
<td>1-2mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride</td>
<td>5-10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td>(single lumen) and 5Fr</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(double lumen)</td>
<td>In between/after IV medication</td>
<td>2mls 0.9% sodium chloride or dextrose 5%</td>
<td>10mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride or 5% Dextrose</td>
</tr>
<tr>
<td>To lock the catheter</td>
<td>(weekly)</td>
<td>3mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride followed by a further 10mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td>To flush after blood</td>
<td>sampling</td>
<td>3mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td>PICC (open ended)</td>
<td>To assess patency</td>
<td>1-2mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride</td>
<td>5-10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td></td>
<td>In between/after IV medication</td>
<td>1-2mls 0.9% sodium chloride or dextrose 5%</td>
<td>10mls 0.9% sodium chloride</td>
<td>2-5mls 0.9% sodium chloride or 5% Dextrose</td>
</tr>
<tr>
<td>Frequently accessed</td>
<td>after each use as a lock</td>
<td>1-2mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride followed by a further 10mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride</td>
</tr>
<tr>
<td>Infrequently accessed</td>
<td>after each use as a lock</td>
<td>1-2mls 0.9% sodium chloride followed by 2mls heparinised saline 10 units/ml</td>
<td>10mls 0.9% sodium chloride followed by a further 10mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride followed by 3-5mls heparinised saline 10 units/ml</td>
</tr>
<tr>
<td>To lock the catheter</td>
<td>(weekly)</td>
<td>2mls heparinised saline 10 units/ml</td>
<td>10mls 0.9% sodium chloride followed by a further 10mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride followed by 3-5mls heparinised saline 10 units/ml</td>
</tr>
<tr>
<td>To flush after blood</td>
<td>sampling</td>
<td>2-3mls 0.9% sodium chloride</td>
<td>10mls 0.9% sodium chloride</td>
<td>2-5mls 0.9% sodium chloride</td>
</tr>
</tbody>
</table>
Using a Thrombolytic in a Completely Blocked Catheter using a 3-way tap

- Attach 3-way tap and syringes. NB 3-way taps are now contraindicated for routine IV use but are still recommended for this procedure. Always use a 3-way tap without an extension set.
- Open clamp if there is one.
- Open stopcock to the empty syringe and the blocked catheter.
- Pull back on the plunger of the empty syringe to create a vacuum in the catheter. You will need to pull quite forcibly.
- Maintain suction with one hand and with the other hand turn stopcock so it is closed to the empty syringe and open to the syringe containing thrombolytic, which will be sucked into the catheter. Don’t worry if it seems that very little thrombolytic is sucked in: even a tiny volume will reach several cm into the catheter.
- Leave for several hours or overnight. Do not clamp catheter as this will prevent the thrombolytic from penetrating into the line.
- After this time, assess the catheter by attempting to flush it with 0.9% sodium chloride in a 10 ml syringe. Do not use excessive force. It is best not to try aspirating before flushing at this stage as you may block the catheter again.
- If the catheter is still completely blocked, repeat the procedure: sometimes you will need to repeat it several times before it works. Sometimes leaving the thrombolytic in overnight seems to help.
- Once the catheter can be flushed, and only then, check for flashback.
References


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United Kingdom Medicines Information (2012) Should Heparin based flushing solutions be used in preference to saline to maintain the patency of indwelling intravascular catheters and cannulae? Available at: https://www.evidence.nhs.uk/search?q=%22Should+heparin+based+flushing+solutions+be+used+in+preference+to+saline%22 (Accessed 15th August 2013).


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8.
EXTRAVASATION
8. Extravasation

All Trusts should have a local extravasation policy which should be followed.

If a PTC or POSCU has a robust referral pathways for any extravasation injury then this should be followed at all times.

For those POSCU's whose plastics team is off site and the referral pathway is not robust in terms of treating paediatric oncology patients (i.e. ability to access Portacath’s, no haem/onc speciality), please discuss with the PTC Haematology or Oncology Registrar for advice. This should be done immediately and must not cause a delay in the treatment of the extravasation injury.

If it would be more appropriate for the patient to be seen by the Plastics Team at the PTC, then the PTC Registrar will facilitate this.

All extravasation or suspected extravasation injuries should be reported to the patient’s PTC.

All staff involved in the administration of chemotherapy must be fully trained and aware of local Trust policies.

What is Extravasation?

Extravasation is the inadvertent leakage of a vesicant solution from its intended vascular pathway (vein) into the surrounding tissue (Infusion Nurses Society, 2006; European Oncology Nursing Society, 2007; Dougherty and Lister 2008; Doellman et al, 2009; Royal College of Nursing, 2009).

A vesicant refers to any medicine or fluid with the potential to cause blisters, severe tissue injury (skin/tendons/muscle) or necrosis if it escapes from the intended venous pathway (Sauerland et al, 2006; Hadaway, 2007; Doellman et al, 2009).

The degree of injury ranges from mild skin reaction to severe necrosis (European Oncology Nursing Society, 2007).

In severe cases extravasation injury may lead to amputation (Roth, 2006; Hadaway, 2007; Doellman et al, 2009).

There has been little research into extravasation (due to ethical considerations limiting controlled research) and most evidence is based on small, uncontrolled trials or case reports (Hadaway, 2007; Doellman et al, 2009).

A PLASTIC SURGEON REFERRAL SHOULD BE SOUGHT IMMEDIATELY WHERE LARGE VOLUMES OF INFILTRATE HAVE ACCUMULATED.

Infiltration

Infiltration is the inadvertent leakage of a non-vesicant solution from its intended vascular pathway (vein) into the surrounding tissue (Infusion Nurses Society, 2006; European Oncology Nursing Society 2007; Dougherty and Lister 2008; Doellman et al. 2009; Royal College of Nursing 2009).

Infiltration is increasingly seen as a benign event as it generally does not lead to tissue necrosis; however a large volume of infiltrate can cause compression of nerves and acute limb
compartment syndrome (ALCS) resulting in long term disability (Roth, 2006; Doellman et al, 2009).
If this is the case then surgical intervention e.g. fasciotomy may be required to prevent nerve compression and compromise of arterial circulation (Hadaway, 2007).

**Flare**
Flare is a local inflammatory reaction characterised by local erythema, venous streaking and pruritus along the injected vein. This is distinguishable from extravasation by the absence of pain and swelling and the presence of a blood return.

Vein irritation is seen as erythema or dark discolouration along the blood vessel with aching and tightness. **Neither of these two scenarios is considered an extravasation.**
Vesicant drugs and solutions reported to cause extravasation injury:

<table>
<thead>
<tr>
<th>Antimicrobials</th>
<th>Vasocompressive agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>Dobutamine</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Dopamine</td>
</tr>
<tr>
<td>Aciclovir, Ganciclovir</td>
<td>Epinephrine (Adrenaline)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Norepinephrine (Noradrenaline)</td>
</tr>
<tr>
<td>Nafcillin</td>
<td>Vasopressin</td>
</tr>
<tr>
<td>Amphotericin</td>
<td></td>
</tr>
<tr>
<td>Cefotaxime</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Concentrated electrolyte solutions</th>
<th>Cytotoxic agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium chloride 5.5%</td>
<td>Cisplatin</td>
</tr>
<tr>
<td>Calcium gluconate 10%</td>
<td>Dactinomycin</td>
</tr>
<tr>
<td>Potassium chloride 7.45%</td>
<td>Daunorubicin</td>
</tr>
<tr>
<td>Sodium bicarbonate 4.2% or 8.4%</td>
<td>Doxorubicin</td>
</tr>
<tr>
<td>Sodium chloride 10%</td>
<td>Epirubicin</td>
</tr>
<tr>
<td></td>
<td>Idarubicin</td>
</tr>
<tr>
<td></td>
<td>Mechlorethamine</td>
</tr>
<tr>
<td></td>
<td>Melphalan</td>
</tr>
<tr>
<td></td>
<td>Mitomycin</td>
</tr>
<tr>
<td></td>
<td>Paclitaxel</td>
</tr>
<tr>
<td></td>
<td>Vinblastine</td>
</tr>
<tr>
<td></td>
<td>Vincristine</td>
</tr>
<tr>
<td></td>
<td>Vinorelbine</td>
</tr>
<tr>
<td></td>
<td>Vindesine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hyperosmolar agents</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total parenteral nutrition</td>
<td>Radiographic contrast media</td>
</tr>
<tr>
<td>&gt; 10% dextrose</td>
<td>Promethazine (Phenergan)</td>
</tr>
<tr>
<td>Mannitol 15%</td>
<td>Diazepam</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Digoxin</td>
</tr>
</tbody>
</table>

This is not an exhaustive list; there are many more.
**Risk factors for infiltration and extravasation**

Risk factors include device related, drug related, patient related and clinician related (Sauerland et al. 2006). See table below

### Device related

**Peripheral cannula**
- Metal/steel needles (butterfly)
- Large gauge cannula relative to vein size
- Inadequately secured cannula
- Undesirable cannula site location (e.g. antecubital fossa, dorsum of hand or wrist rather than forearm, areas of joint flexion and use of dominant hand)
- Clot formation above cannula site

**Central venous access device (CVAD)**
- CVAD surgically placed in an area prone to movement; difficult to secure
- Inadequately secured needle in implanted port
- Inadequately secured catheter
- Inappropriate needle length for IVAP (i.e. too short to reach back of reservoir)
- Development of fibrin sheath / thrombus at catheter tip
- IVAP (port) / catheter separation, catheter fracture or catheter dislodgement
- Flushing with a small gauge syringe

### Drug related

- Vesicant potential
- Volume of drug/fluid infiltrated
- Concentration of vesicant drug/fluid
- Repeated use of the same vein for vesicant administration
- pH of drug/fluid (extremes of pH i.e. acid or alkaline - pH < 5 or >9)
- Osmolarity of drug/fluid (osmolarity can influence the degree of tissue damage e.g. hypertonic drugs/solutions e.g. 10% Dextrose and parenteral nutrition solutions)
- Vasoconstrictive potential (extravasation of vasoconstrictive substances e.g. dobutamine, dopamine, epinephrine, norepinephrine and vasopressin can cause ischaemic necrosis)
- Cytotoxicity (drugs that bind to DNA can cause greater damage and may remain in the tissues causing further damage)

### Patient related

- Age (very young or old)
- Patients with small, fragile or thrombosed veins
Impaired communication - unable to communicate due to young age or confusion, sedation, inability to speak or language issues

Compromised circulation

Altered sensory perception

Poor understanding of risk related to anxiety or fear, cultural barriers, or medicines

Active patient

Lymphoedema

**Clinic related**

- Lack of knowledge
- Lack of intravenous therapy skills
- Unfamiliarity with CVAD use and management
- Interruptions or distractions during drug administration

(Sauerland et al, 2006; Dougherty 2008; Doellman et al, 2009)

**Recognition of infiltration / extravasation**

It is important for the nurse to be able to recognise the early signs and symptoms of infiltration and extravasation (Dougherty, 2008). See Table below.

<table>
<thead>
<tr>
<th>Infiltration</th>
<th>Extravasation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coolness or blanching at the cannula insertion site</td>
<td>As for infiltration, plus:</td>
</tr>
<tr>
<td>Swelling</td>
<td>• Burning, stinging pain</td>
</tr>
<tr>
<td>Tenderness/discomfort</td>
<td>• Redness may occur followed by blistering, tissue necrosis and ulceration</td>
</tr>
<tr>
<td>Taut or stretched skin</td>
<td></td>
</tr>
<tr>
<td>Leakage of fluid at the insertion site</td>
<td></td>
</tr>
<tr>
<td>Inability to obtain blood return (not always present)</td>
<td></td>
</tr>
<tr>
<td>Change in quality and flow of the infusion or injection</td>
<td></td>
</tr>
<tr>
<td>Numbness, tingling or &quot;pins and needles&quot;</td>
<td></td>
</tr>
</tbody>
</table>

(Hadaway, 2007; Dougherty, 2008)
Prevention of infiltration/extravasation

Device related:

**Peripheral IV access**

- Place cannula in muscled area in forearm when possible
- Use the smallest gauge plastic cannula feasible
- Avoid joints (e.g. wrist, antecubital) and limbs with impaired arterial, venous or lymphatic circulation
- Stabilise & secure the cannula in place using dressing that does not obscure the site (i.e. transparent)
- Confirm blood return prior to vesicant administration

**Central IV access**

- Preferred route of administration
- Confirm blood return prior to vesicant administration
- IVAP: ascertain correct needle placement in septum
- IVAP: stabilise & secure the needle in place using dressing that does not obscure the site (i.e. transparent)
- If catheter tip is questionable, assess prior to vesicant administration (i.e. through a CXR)

Patient related:

- Instruct the patient & family about the risks of vesicant administration
- Instruct the patient & family to notify a health care professional if the child/young person experiences any pain/burning/change in sensation at the cannula or port site; this includes non-verbal assessment also
- Instruct the patient & family not to disturb or dislodge the cannula or port needle and to take care when mobilising
- The patient & family should be able to understand these points

(Sauerland et al, 2006)

**Nursing responsibilities when administering intravenous medicines**

Intravenous therapy is now an integral part of the majority of nurses' professional practice (RCN, 2009). Any nurse involved in the administration of intravenous therapies must be competent to undertake the procedure and act in accordance with the NMC Code and maintain knowledge and skills (NMC, 2008a).

The nurse has a duty of care to the patient to monitor the patient and their response throughout the duration of intravenous medication administration (RCN, 2009; NMC, 2008b).

The Trust medication policy must be adhered to when administering intravenous medications and fluids. Any member of nursing staff deemed competent in IV therapy may administer a non-cytotoxic vesicant drug or infusion via peripheral and central venous access devices. However, the nurse must undertake all safety precautions and assessments and close monitoring must be continued throughout the infusion.

Only staff deemed competent to administer cytotoxic medication may administer a cytotoxic vesicant drug or infusion via peripheral and central venous access devices.
Monitoring of the infusion

The access device should be well secured (Sauerland et al, 2006; Dougherty, 2008)

The pressure of the infusion pump must be monitored & documented at least hourly, along with the signature of the person doing so, on the child’s fluid chart.

The infusion site must be inspected every 30-60 minutes and documented when in use and if extravasation or infiltration is suspected (Masoorli, 2003).

The port needle entry site should be observed before administering vesicants or irritant solutions (Sauerland, 2006).

The suggested maximum pressure alarm setting for an infusion pump is 15–25mmHg for vesicant drugs.

More frequent checks may be necessary in some instances depending on the patient, infusate, vascular integrity and the vascular access device being used (15–30 minutes).

The pressure alarm limit must be set when a vesicant infusion is commenced & rechecked at the beginning of each shift, if still running.

Record pump pressures and site monitoring on the fluid balance charts as per hospital policy.

A rise in pressure must be investigated.

The pressure reading should not be the sole indicator for an extravasation (Sauerland et al, 2006).

Bandages are not recommended for use when administering bolus vesicant therapy and should be used with caution for infusions. Never cover the insertion site as this compromises effective monitoring (Roth, 2006; EONS, 2007).

Patient & family queries about pain, discomfort or swelling must be investigated; they should also have been informed of signs and symptoms (Sauerland et al, 2006)

Management of infiltration and extravasation

Early intervention and identification of the first signs and symptoms of infiltration and extravasation is crucial, in order to prevent serious adverse outcomes (Doellman, 2009).

Compliance with guidelines is essential to minimise the complications associated with extravasation or infiltration (Roth, 2006).

THIS IS A MEDICAL EMERGENCY ANYTIME OF THE DAY OR NIGHT

The recommended immediate management is

- Immediately stop the infusion/injection (Doellman et al 2009)
- Explain the procedure to the child & family.
- Aspirate as much of the residual drug as possible (to minimise the injury caused by the residue of the drug)
- Under no circumstances should the device be flushed.
- Leave the cannula/port needle in situ (in case plastic surgeon wants to use to facilitate treatment and administration of any antidote(s)).
- Mark the extravasated area with a soft tipped pen.
- Disconnect administration set or syringe containing drug but retain it to determine amount of drug extravasated/infiltrated.
Subsequent Action

This may include:

- **Monitoring** – the site will be observed, elevated and monitored to determine whether further treatment is required.
- **Conservative management** – this may involve the use of hot or cold compresses or antidotes (if possible).
- **Surgical management** – this involves a saline washout, a procedure that dilutes the extravasated drug in the tissue (Wickham *et al.*, 2006). The “Flush Out” technique should only be performed by an experienced member of staff.

Further management as indicated

The SpR should prescribe pain relief as required. 
Administer analgesia as required/prescribed.
If a limb is affected it should be elevated.

For All Vesicant Cytotoxic Drugs: Early referral to a Plastic Surgeon should be considered. Any extravasation injury that occurs in a POSCU must be discussed with the PTC Registrar who will then discuss with the PTC plastic’s Team. If the patient needs to be seen by the Plastics Team, then the PTC Registrar will facilitate this.

Document the incident and any actions taken in the child’s health care records and complete an incident form.

Inform child & family of the following:

- That an extravasation is suspected/has occurred
- The possible cause of the extravasation
- What action / treatment will be required
- Any follow-up arrangements
- That an incident form will be completed
- Allow time for any questions and/or queries

Documentation of the process is essential if litigation were to occur (Masoorli, 2003; Roth, 2006).

This documentation will be done by nurses and doctors.

In accordance with the NMC (2009) record keeping is not an option it is an integral part of nursing and is essential to the provision of safe and effective care.
Extravasation Kit

Extravasation kits should be available in all areas where vesicant drugs are administered.

Contents of kits vary from Trust to Trust, however the basic contents may include:

- Hyaluronidase
- Lidocaine
- Scalpel blade
- Sterile field
- Normal giving set
- 500 ml bag of NaCL 0.9%
- Blunt large bore needle
- Syringes of varying size
- Needles of varying size
- Sterile gauze
- Gelonet dressing
- Paraffin gauze packs
- Extravasation Policy
- Extravasation documentation forms

Saline washouts (Flush out Technique)

The flush out technique should only be performed by a trained member of staff. Good results have been achieved with this technique when used at an early stage with adults & children.

It should be initiated as soon as possible following the extravasation injury and must be performed within 12 hours. For young people and children, ideally they should be taken to theatres for the flush out technique. If this is not possible then adequate analgesia must be administered or sedation where appropriate. The age of the child & the extent of the injury will determine if a local or general anaesthetic will be required.

Antibiotic prophylaxis may be recommended in some patients depending on the severity.

In a saline washout the injured area is:

- Injected with the enzyme hyaluronidase into the subcutaneous tissues under the area of damaged skin
- Peripheral incisions are made around the "clock face" of the injury
- Using an atraumatic cannula the area is perfused with 0.9% sodium chloride
- Fluid entering through the needle should flow freely through the stab incisions. Excess fluid can also be massaged out of the tissues by gentle manipulation.
- The washout efflux may be tested for decreasing concentrations of toxin
- Dressing applied post-operatively and the limb elevated for 24 hours

(Gault, 1993)
Follow up treatment

If the plastic surgery team have been involved follow their management plan, if not, follow the plan from the child's/young person's medical team.
Further surgical intervention may be required.
The child/young person may need their injury to be reviewed as an outpatient.
If no action is required observe the extravasation site for:
  - Colour
  - Sensitivity
  - Swelling

This should be done as often as required by the condition of the child/young person until the site regains its normal appearance.
If limb involvement, elevate it (if appropriate, monitor the limb mobility of the child/young person).
If the extravasation site deteriorates or its condition does not improve another referral must be made to the Plastic Surgery Team.

References/Bibliography


Nursing and Midwifery Council (2008b) Standards for medicine management

Nursing and Midwifery Council (2009) Record keeping: Guidance for nurses and midwives


9.
NUTRITION INTERVENTION IN PAEDIATRIC ONCOLOGY & HAEMATOLOGY PATIENTS
9. Nutrition intervention in Paediatric Oncology & Haematology Patients

The promotion and maintenance of good nutritional status is an important part of the supportive care for patients undergoing treatment. Well-nourished patients are thought to better tolerate their treatment (1,2). As treatment protocols are refined and prognosis improves, we are now also dealing with nutritional issues such as obesity and long term disturbance in eating patterns.

The aims of nutritional support in paediatric oncology patients are

- To reverse the malnutrition seen at diagnosis by involvement with the patient and family as soon as possible
- To promote/maintain normal growth and development
- To prevent nutritional depletion/malnutrition associated with treatment
- To meet the needs of an increasing demand for nutrients during treatment
- To aim to decrease the incidence of infection by improving return to immune competence
- To maintain gut wall integrity

Causes of nutritional problems in oncology patients

- Loss of appetite
- Nausea / Vomiting (including anticipatory vomiting)
- Sore throat/mouth
- Taste changes/ loss of taste
- Pain/Fatigue
- Dry mouth/ reduced secretions
- Malabsorption/ Diarrhoea
- Intermittent constipation
- Metabolic disturbances
- Food aversion/ Behavioural issues associated with food/Physiological factors
- Steroid therapy

Nutritional screening and referral

Nutritional screening is essential to identify patients who are already malnourished or at risk of becoming so (NICE, 2006). The child’s height and weight should ideally be documented in the medical notes at the initial medical consultation and plotted on the appropriate RCPCH UK-WHO growth charts. Any weight loss should also be documented as a percentage weight loss. Further nutritional screening is undertaken on their initial admission to the ward and weekly thereafter, using a locally agreed nutrition screening tool (e.g. STAMP/NST).

Referrals for patients identified as ‘at risk’ should then be made to a dietitian as indicated by the screening tool/growth chart/percentage weight loss.

Children identified as being “at risk”

Children identified as being “at risk” should have a nutritional assessment by a dietitian, which should include documentation in the medical notes of:

- Anthropometrical measurements:
  - Weight* and height (and the growth chart centiles)
  - Identification of percentage weight loss/centile reductions
Biochemical data for signs of deficiencies, hydration status, and to monitor for re-feeding syndrome

Clinical information including signs and symptoms such as diarrhoea, vomiting and mucositis, and relevant medications likely to impact on nutritional status.

Dietary history including qualitative/quantitative information utilising food record charts and verbal information gathered from the child and their carers.

Estimation of energy, protein and fluid requirements

A clear plan of action with realistic goals agreed with the doctors, the patient and the carer.

*Tumour mass/ascites/oedema needs to be considered in these measurements

**Nutritional strategies**

May include any or a combination of the following:

- Maximizing oral intake through food fortification and the addition of nutritional supplements and sip feeds
- Enteral tube feeding
- Parenteral nutrition (PN)

**Oral Intake**

The reasons for possible suboptimal intake may be multifactorial. It is important to maximise the nutritional quality of any food eaten. Advice can be given on increasing energy and protein. Copies of a patient/parent information booklet ‘Helping your child to eat’ are available from the CCLG (4)

**Nutritional Supplements & Sip feeds**

The dietitian at the PTC will usually advise which nutritional supplement is best for the child. In complex cases please discuss with PTC dietitian when making decisions locally. These can be useful in patients who are maintaining some oral intake, but do not require enteral feeding.

**Table 5. Types of supplements (prescription only)**

<table>
<thead>
<tr>
<th>Types of supplements</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy &amp; Protein supplements (not nutritionally complete) (milkshake type drinks)</td>
<td>Scandishake / Calshake / Enshake / Aymes shake (care must be taken when using these products with younger children: seek advice from the dietitian)</td>
</tr>
<tr>
<td>Sip Feeds (not nutritionally complete) (juice type drinks)</td>
<td>Paediasure juice For older children (8+): Provide extra, Ensure plus juice style, Fortijuice</td>
</tr>
<tr>
<td>Energy Supplements</td>
<td>Glucose Polymers, Maxijul / Polycal / Vitajoule Fat emulsions (Calogen, Liquigen) Combined fat and glucose (Duocal) (These products should be prescribed with instructions for use provided by the dietitian)</td>
</tr>
</tbody>
</table>

*Not an exhaustive list

**Alternative /Complimentary diets**

**Vitamin and Mineral Supplements**

These are not routinely prescribed and are not usually needed by patients receiving enteral tube feeding. Whilst such supplements may be desirable for those on a restrictive diet, palatability and size of tablet often limit their use. Most of the widely available ‘chewable’ supplements contain a
very limited number of vitamins. Before embarking on a course of vitamin/mineral supplements or herbal supplements, parents should contact the hospital pharmacy to check for potential drug-nutrient interactions.

**Enteral Feeding**

Enteral feeding should be considered if there is a reduction of appetite and loss of weight, despite offering supplements, and where this reduction in appetite is likely to continue for more than one week. For patients with more than ≥10% weight loss on admission, enteral feeding may be considered as a first line intervention, in conjunction with oral nutritional support strategies. However, patients with a large tumour mass may require early enteral feeding, despite presenting with no apparent weight loss. Younger patients are more likely to require enteral feeding. Placement of an enteral feeding tube may ultimately reduce stress for both patients and carers, as it allows for not only the provision of nutrition support but also a route for the administration of medicines and water.

Enteral feeds can be administered via nasogastric tube or gastrostomy tube. Ideally any nasogastric tubes that are placed should be of the longer lasting polyurethane / silicone type to minimise repeated tube replacement. Placement of a gastrostomy should be considered in patients expected to have lengthy treatment regimens e.g. those undergoing treatment for Medulloblastoma following the PACKER chemotherapy regime, or Milan protocol. Post-pyloric feeding (naso-jejunal tube/gastrostomy with jejunal extension/jejunostomy) should be considered for children with gastric dysmotility, acute pancreatitis, severe vomiting or high risk of aspiration.

The main advantage of enteral feeding is that the parents can be taught to administer feeds at home. Ready made preparations for enteral feeding are commercially available and can meet the specific requirements of the individual child. The feed is introduced gradually and the child assessed each day in terms of tolerance with regard to diarrhoea, nausea or vomiting. In some cases the feed may be given overnight, which allows the child to take part in normal activities and may encourage oral intake during the day.

**Table 6. Types of Enteral Feeds**

<table>
<thead>
<tr>
<th>Feed</th>
<th>Age (Weight)</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paediasure (1kcal/ml)</td>
<td>1 – 10 yrs (8-30kg)</td>
<td>Feed suitable as an enteral feed</td>
</tr>
<tr>
<td>Nutrini (1kcal/ml)</td>
<td>1 – 6 yrs (8-30kg)</td>
<td></td>
</tr>
<tr>
<td>Paediasure Plus (1.5 kcal/ml)</td>
<td>1 – 10 yrs (8-30kg)</td>
<td></td>
</tr>
<tr>
<td>Nutrini Energy (1.5 kcal/ml)</td>
<td>1 – 6 yrs (8-30kg)</td>
<td></td>
</tr>
<tr>
<td>Ensure (1.0 kcal/ml)</td>
<td>&gt;6 years</td>
<td>Feed suitable as an enteral feed</td>
</tr>
<tr>
<td>Tentrini (1kcal/ml)</td>
<td>7-12yrs (21-45kg)</td>
<td></td>
</tr>
<tr>
<td>Tentrini Energy (1.5kcal/ml)</td>
<td>7-12yrs (21-45kg)</td>
<td></td>
</tr>
<tr>
<td>Jevity Plus (1.2 kcal/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osmolite (1.0kcal/ml)</td>
<td>&gt; 12 yrs (&gt;45kg)</td>
<td>As above for the older child</td>
</tr>
<tr>
<td>Nutrison (1.0kcal/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fresubin Original (1.0kcal/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osmolite plus (1.2kcal/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osmolite 1.5 (1.5kcal/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jevity (1.1kcal/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jevity1.5 (1.5kcal/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutrison Energy (1.5kcal/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fresubin Energy(1.5kcal/ml)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Not an exhaustive list

In cases of severe diarrhoea or suspected malabsorption, a specialist hydrolysate feed should be considered; examples of such feeds can be found in Table 7. Ideally consult the dietitian for guidance on the feed that best suits the patient.
Table 7. Semi elemental/ elemental/peptide based feeds*

<table>
<thead>
<tr>
<th>Feed</th>
<th>Age (weight)</th>
<th>Nutritional aspects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pepti junior</td>
<td>&lt;1 year</td>
<td>Semi-elemental, peptide based feeds.</td>
</tr>
<tr>
<td>Pepdite</td>
<td>&lt;1 year</td>
<td>Variable fat composition and content</td>
</tr>
<tr>
<td>Pepdite 1+</td>
<td>&gt;1 year</td>
<td></td>
</tr>
<tr>
<td>Nutrini peptisorb</td>
<td>1-6 years (8-20Kg)</td>
<td></td>
</tr>
<tr>
<td>Peptamen junior</td>
<td>&gt;1 year</td>
<td></td>
</tr>
<tr>
<td>Peptamen Junior Advance</td>
<td>1-10 years</td>
<td></td>
</tr>
<tr>
<td>Peptosorb</td>
<td>&gt;6 years</td>
<td></td>
</tr>
<tr>
<td>Perative</td>
<td>&gt;10 years</td>
<td></td>
</tr>
<tr>
<td>Peptamen</td>
<td>&gt;6 years</td>
<td></td>
</tr>
<tr>
<td>Neocate</td>
<td>&lt;1 year</td>
<td>Amino acid based 'elemental feeds’</td>
</tr>
<tr>
<td>Neocate Advance</td>
<td>&gt;1 year -10 years</td>
<td></td>
</tr>
<tr>
<td>Elemental 028</td>
<td>&gt;1 year</td>
<td></td>
</tr>
</tbody>
</table>

*Not an exhaustive list

Hydrolysate feeds, e.g. Pepdite 1+ and Pregestimil should be considered before using elemental feeds.

**Parenteral Nutrition**
Traditionally, Paediatric Oncology patients often have central venous access, and therefore Parenteral Nutrition (PN) was the nutrition treatment of choice.

However, PN should only be used when the gut is not functioning e.g. severe mucositis, severe vomiting (on anti-emetics) or ileus, and if the duration is estimated to be for an extended period, i.e. > 5-7 days.

The pharmacist and dietitian in collaboration with the multidisciplinary team should assess parenteral nutrition requirements. If possible, trophic feeds should be maintained (small volume e.g. 5mls an hour) to help maintain gut wall integrity and reduce the chance of bacterial translocation.

**Healthy eating**
It should be remembered that a large proportion of children undergoing treatment for cancer, and especially some of the haematological cancers, are unlikely to suffer from weight loss and under nutrition. For this patient group, nutritional advice should focus on the promotion of an appropriate weight for height and general principles of healthy eating.

**Excessive weight gain and poor eating habits**
Some patients, particularly those undergoing treatment composing of regular steroid use, may experience excess weight gain and erratic eating patterns. Early referral to the dietitian for weight maintenance advice and regular monitoring is advisable. Parents may also need guidance on the importance of maintaining regular food patterns and in avoiding an overdependence on high calorie ‘snack’ foods and confectionary, both during and after treatment.

**References**
4. Contact for ‘Helping your child to eat’ booklet, CCLG tel:01162494460, email:info@cclg.org.uk website www.cclg.org.uk
10.
MOUTH CARE PROTOCOL
AND MUCOSITIS
10. Mouth Care Protocol and Mucositis

Introduction
The mouth is important for eating, drinking, speech, communication, taste, breathing and defence. Oral hygiene is an integral part of total care. Assessment and planned interventions can help prevent, minimise or reverse changes in the oral cavity (Gibson and Nelson, 2002).

The principle objective of oral care is to maintain the mouth in good condition. It specifically aims to:

- Keep the oral mucosa clean, soft, moist and intact, thus preventing infection
- Keep the lips clean, soft, moist and intact
- Remove food debris / dental plaque without damaging the gums
- Alleviate pain / discomfort, thus enhancing oral intake
- Prevent halitosis and freshen the mouth
- Decrease the risk of oral and systemic infection
- Increase general well-being

Mucositis is a painful inflammation and ulceration of the mucous membrane and is one of the most common side effects of cancer treatment (Glenny et al 2004). The terms mucositis and stomatitis are often used interchangeably. There are however some general distinctions – mucositis describes a toxic inflammatory reaction that affects the gastrointestinal tract from the mouth to the anus, as a result of cytotoxic chemotherapy or ionising radiation. It appears as an erythematous, burn-like lesion or as random, focal-to-diffuse ulcerative lesions. However, stomatitis refers to any inflammatory reaction affecting the oral mucosa, with or without ulceration (National Cancer Institute, 2000).

Mouth care within paediatric oncology is an important aspect of care with the principle objective of ensuring the child’s mouth is clean, moist and free from infection. Regular and thorough mouth care is vital in all children, even if they are not eating. The majority of children will encounter few oral problems during their treatment but diagnosis (and therefore cancer treatment) will determine the level of intervention for each child. Evidence-based guidelines have been developed for national use and are now available at www.cclg.org.uk.

ALL CHILDREN SHOULD CLEAN THEIR TEETH TWICE DAILY

Oral and dental Assessment
At Diagnosis:
Assessing the oral cavity involves a thorough and systematic approach. This is essential so that any changes are monitored and appropriate treatment implemented.

- Ideally oral and dental assessment at diagnoses should be by a dentist or dental hygienist linked to the cancer centre
- Any treatment required should be undertaken by a consultant or specialist paediatric dentist
- If there is not a paediatric dental unit liaising with the cancer centre there should be clear communication between the cancer centre and the routine dental provider.

During Oncology Treatment:

- Ideally by a dentist linked to the cancer centre (retain registration and communication with usual dental provider)
- Any treatment required should be undertaken ideally by dentist linked to the cancer centre.
- If not available, then by usual dental provider with clear communication and guidance from the cancer centre.
Post Treatment:

- By usual dental provider with clear communication and guidance from the cancer centre

See Oral Assessment Guide (OAG) and score sheet, algorithms and evidence based guideline summary (attached)

Implementation

To enable appropriate mouth care to be implemented, a through oral assessment is required. Use of an oral assessment instrument such as the OAG is recommended (Gibson et al 2010). The assessment procedure should be explained to the child and family, including why the assessment is necessary and what it entails. A patient information leaflet about mouth care is available from the GOSH website: http://www.ich.ucl.uk/goshfamilies/informationsheets/chemotherapymouthcare/chemotherapymouthcarefamilies.html

Wherever possible the child should be involved in the assessment. When assessing the mouth of a young child it is advisable to have a second adult present to support the child’s head.

A good source of light is required to examine the oral cavity.

Standard universal precautions should be adopted and non-sterile gloves worn

Toothbrushes:

A small headed, soft, nylon bristled toothbrush, and with round ended filaments should be used to brush / clean teeth (British Dental Health Foundation, 2005; Department of Health, 2009).

Toothbrushes should be changed every 3 months or sooner if the bristles become splayed (British Dental Health Foundation, 2010; UKCCSG-PONF Mouth Care Group, 2006).

The toothbrush should be for the sole use of the child. It should be changed following oral infection (UKCCSG-PONF Mouth Care Group, 2006).

Electric toothbrushes have a rotation, oscillating and vibratory action, which are effective against short and long term decay. Brushes that work with a rotation oscillation action remove more plaque and reduce gingivitis more effectively than a manual toothbrush (Robinson et al, 2005). However the bristles of electric toothbrushes are harder than manual toothbrushes and not advisable for children with a fragile mucosa.

Foam Cleaning Sponges:

These can be used as a temporary measure or combined with a toothbrush to remove debris and cleanse the mouth when a child is unable to brush their teeth effectively or spontaneous bleeding occurs (either before or during oral hygiene).

Basic oral Care:

- Brush teeth well twice a day using fluoride toothpaste containing at least 1,000 parts per million (ppm) (Scottish Intercollegiate Guidelines Network, 2005) and a soft toothbrush
- Whilst in-patient, oral assessment using OAG and score recorded. Frequency of assessment determined by individual need. (refer to algorithm 1)
- OAG score >8 means increased risk of oral complications (refer to algorithm 2)
- Use of additional aids e.g. floss, fluoride tablets and electric toothbrushes – by recommendation of dental team only. Chlorhexidine is not recommended except; if unable to brush teeth, clean mouth with oral sponges moistened with water or diluted chlorhexidine
Analgesia:
Although a variety of approaches to pain management are used, analgesics still form the backbone of any strategy.

In most situations analgesics of gradually increasing strength are used, according to the WHO analgesic ladder (see below). However if a child presents in severe pain then the first steps of the ladder may need to be by-passed. It is essential that analgesics on all steps are given regularly, and that compliance is checked before moving on to the next step of the ladder.

WHO analgesic ladder
Refer to chapter 12 – Basic Principles of Symptom Management: Pain and Analgesia sections

Pain relief may be necessary to relieve the pain of mucositis for children and young people with cancer. Pain associated with mucositis can be severe and opiates should be used to control such pain (UKCCSG-PONF Mouth care group, 2006).

If the OAG score is >8 a pain assessment instrument should be introduced. This will allow for more detailed self-reporting of pain, which when added to observation from parents and clinicians, will provide a more complete picture of the symptom. (Gibson et al, 2006).

Supportive Therapies

Gelclair™

Gelclair™ has been shown to reduce the pain of oral conditions in adults following cancer therapy (Berndtson, 2001) and in palliative care (Innocenti et al, 2002). It was the focus of a preliminary clinical study that GOSH was involved in (study results awaiting publication). It has also been used, by children with oral pain after chemotherapy and bone marrow transplant within the Children’s Cancer Unit at GOSH.

Gelclair™ is accepted as a Class 1 device as it is not pharmacologically active within the EU and by the MHRA and is listed in the Drug Tariff Part IXA appliances as an oral film-forming agent. Some pharmacy departments are experiencing difficulty obtaining Gelclair™, as it is not approved on the formulary. It may be possible to obtain Gelclair™ locally or from an outside pharmacy. For more information about how to use and obtain Gelclair™ please contact your local pharmacy department.
Prophylactic Mouth care For The Child With A Malignancy

Algorithm 1

**Soft toothbrush and fluoride toothpaste twice a day for all children regardless of diagnosis**

- Pre-assessment indicates febrile neutropenia?
  - YES: Daily OAG until neutropenia resolves
  - NO: Baseline oral assessment indicates deviation from normal?
    - YES: Daily OAG until deviation resolves
    - NO: Is the child’s diagnosis included in Table 1?
      - YES: Continue with daily OAG and 3x/day oral hygiene (cleaning sponge for babies with no teeth)
      - NO: OAG >8

**Table 1**

<table>
<thead>
<tr>
<th>High Risk Neuroblastoma</th>
<th>Infant ALL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapsed ALL</td>
<td>AML</td>
</tr>
<tr>
<td>Philadelphia +ve ALL</td>
<td>Osteosarcoma</td>
</tr>
<tr>
<td>Allogeneic + Autologous BMT</td>
<td>ALL (only whilst receiving anthracyclines or during Capizzi)</td>
</tr>
<tr>
<td>T-cell NHL</td>
<td>Extracranial Rhabdoid Tumours</td>
</tr>
<tr>
<td>B-cell NHL</td>
<td>Ewings (only whilst receiving anthracyclines)</td>
</tr>
<tr>
<td>High Risk Rhabdomyosarcoma</td>
<td></td>
</tr>
<tr>
<td>Infant Ependymoma</td>
<td></td>
</tr>
</tbody>
</table>
Algorithm 2

Introduce individualised nursing care plan Consult with medical staff and discuss:
- Pain assessment tool
- Viral/bacterial/fungal swabs
- Analgesia Topical/Systemic
- Consider increasing oral hygiene to 3 times a day

- Commence fluid balance chart
- Monitor weight
- Liaise with dietitian
- Consider analgesic spray, e.g. benzydamine 0.15% spray

When brushing:
- Is a toothbrush in use?
- Is it being used correctly?
- Consider referral to dentist

Discontinue using toothbrush on gums & consider:
- **Option 1** – Toothbrush for teeth only & cleaning sponge for gums
- **Option 2** – Cleaning sponge
  - Reintroduce toothbrush when able

Ensure oral anti-fungal agent (e.g. fluconazole,itraconazole or ketoconazole) is prescribed
**Oral Assessment Guide for Children and Young People**

<table>
<thead>
<tr>
<th>Category</th>
<th>Method of assessment</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Swallow</strong></td>
<td>Ask the child to swallow or observe the swallowing process. Ask the parent if there are any notable changes.</td>
<td>Normal. Without difficulty</td>
<td>Difficulty in swallowing</td>
<td>Unable to swallow at all. Pooling, dribbling of secretions</td>
</tr>
<tr>
<td><strong>Lips and corner of mouth</strong></td>
<td>Observe appearance of tissue</td>
<td>Normal. Smooth, pink and moist</td>
<td>Dry, cracked or swollen</td>
<td>Ulcerated or bleeding</td>
</tr>
<tr>
<td><strong>Tongue</strong></td>
<td>Observe the appearance of the tongue using a pen-torch to illuminate the oral cavity</td>
<td>Normal. Firm without fissures (cracking or splitting) or prominent papillae. Pink and moist</td>
<td>Coated or loss of papillae with a shiny appearance with or without redness and/or oral Candida</td>
<td>Ulcerated, sloughing or cracked</td>
</tr>
<tr>
<td><strong>Saliva</strong></td>
<td>Observe consistency and quality of saliva</td>
<td>Normal. Thin and watery</td>
<td>Excess amount of saliva, drooling</td>
<td>Thick, ropy or absent</td>
</tr>
<tr>
<td><strong>Mucous membrane</strong></td>
<td>Observe the appearance of tissue using a pen-torch to illuminate the oral cavity</td>
<td>Normal. Pink and moist</td>
<td>Reddened or coated without ulceration and/or oral Candida</td>
<td>Ulceration and sloughing, with or without bleeding</td>
</tr>
<tr>
<td><strong>Gingivae</strong></td>
<td>Observe the appearance of tissue using a pen-torch to illuminate the oral cavity</td>
<td>Normal. Pink or coral with a stippled (dotted) surface. Gum margins tight and well defined, no swelling.</td>
<td>Oedematous with or without redness, smooth</td>
<td>Spontaneous bleeding</td>
</tr>
<tr>
<td><strong>Teeth</strong> (If no teeth score 1)</td>
<td>Observe the appearance of teeth using a pen-torch to illuminate the oral cavity</td>
<td>Normal. Clean and no debris</td>
<td>Plaque or debris in localised areas</td>
<td>Plaque or debris generalised along gum line</td>
</tr>
<tr>
<td><strong>Voice</strong></td>
<td>Talk and listen to the child. Ask the parent if there are any notable changes</td>
<td>Normal tone and quality when talking or crying</td>
<td>Deeper or raspy</td>
<td>Difficult to talk, cry or not talking at all</td>
</tr>
</tbody>
</table>

**NB if score >8 introduce pain assessment instrument**

### Oral Assessment Sheet (Score between 1 - 3)

<table>
<thead>
<tr>
<th>Date</th>
<th>Swallow</th>
<th>Lips</th>
<th>Tongue</th>
<th>Saliva</th>
<th>Mucous Mem</th>
<th>Gingiva</th>
<th>Teeth</th>
<th>Voice</th>
<th>Total</th>
<th>Comments</th>
<th>Pain Score</th>
<th>Signature</th>
</tr>
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<tbody>
<tr>
<td></td>
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</table>
**Mouth care for children and young people with cancer: Evidence based guidelines**

### BASIC ORAL CARE

#### AT DIAGNOSIS & DURING TREATMENT

- Brush teeth well twice a day using fluoride toothpaste and soft toothbrush.
- Whilst in-patient, oral assessment using OAG and score recorded. Frequency of assessment determined by individual need.
- **OAG score >8 means increased risk of oral complications.**
- Use of additional aids e.g. floss, fluoride tablets and electric toothbrushes – by recommendation of dental team only. Chlorhexidine is not recommended unless – see below.

(If unable to brush teeth, clean mouth with oral sponges moistened with water or diluted chlorhexidine)

### DENTAL CARE / TREATMENT

#### AT DIAGNOSIS: Oral & dental assessment

- Ideally by a dentist or dental hygienist linked to the cancer centre.
- Any treatment required should be undertaken by a consultant or specialist paediatric dentist.
- If there is not a paediatric dental unit liaising with the cancer centre there should be clear communication between the cancer centre and the routine dental provider.

#### DURING ONCOLOGY TREATMENT: Dental assessment every 3 – 4 months

- Ideally by a dentist linked to the cancer centre (retain registration and communication with usual dental provider).
- Any treatment required should be undertaken ideally by dentist linked to the cancer centre.
- If not available, then by usual dental provider with clear communication & guidance from the cancer centre.

#### POST TREATMENT

- By usual dental provider with clear communication & guidance from the cancer centre.

### ORAL COMPLICATIONS

<table>
<thead>
<tr>
<th></th>
<th>PREVENTION</th>
<th>TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MUCOSITIS</strong></td>
<td>• Basic oral care (as above).</td>
<td>• Basic oral care (as above). • Appropriate pain control.</td>
</tr>
<tr>
<td><strong>CANDIDIASIS</strong></td>
<td>• Basic oral care. • If antifungal agent is to be used please choose one that is absorbed from the GI tract. Drug of choice – fluconazole. • Check treatment protocols. • Nystatin is not recommended.</td>
<td>• Basic oral care, plus • Prescribe antifungal agent that is absorbed from the GI tract. Drug of choice – fluconazole. • Check treatment protocols. • Nystatin is not recommended.</td>
</tr>
<tr>
<td><strong>XEROSTOMIA</strong></td>
<td>• Basic oral care</td>
<td>• Basic oral care. • Consider saliva stimulants/artificial saliva (see BNF)</td>
</tr>
<tr>
<td><strong>HERPES</strong></td>
<td>• Basic oral care • Aciclovir is only recommended as a preventative strategy for herpes simplex in patients undergoing high dose chemotherapy with stem cell transplant / BMT</td>
<td>• Basic oral care, plus Mild and/or non progressive lip lesions: topical aciclovir. Moderate/severe and/or progressive lip lesions &amp; for Mild/Moderate oral lesions: oral aciclovir. Severe oral lesions or if oral cannot be tolerated: IV aciclovir. (for doses see BNF – Children)</td>
</tr>
</tbody>
</table>
References:


11. DRUG TREATMENT IN HYPERTENSION
11. Drug Treatment of Hypertension

Hypertension is a reasonably common problem in children with cancer and maybe related to the disease itself (e.g. neuroblastoma, Wilms’ tumour or tumours causing obstructive nephropathy), side effects of treatment (e.g. steroids) or occasionally related to an underlying disorder (e.g. neurofibromatosis). An important distinction is between:

- “standard” hypertension
- acute hypertensive crisis – a medical emergency

The medical management of hypertension can be complicated owing to the large number of available drugs. Choice of therapy depends on the severity of the hypertension and its underlying cause. It is very useful to get acquainted with a limited number of drugs, to know their effects and side effects profile. Treatment is often started with a short acting drug and then if needed continued with a more long acting. The main groups to use are calcium channel blockers, diuretics and ACE inhibitors with beta-blockers as third line drugs. Discuss with PTC.

Measurement of Blood Pressure

Accurate measurement of BP is essential for the diagnosis of hypertension and during use of antihypertensive agents. The cuff used must encircle the upper arm and its width should cover two-thirds of the distance from the shoulder to the elbow. If an abnormal BP is expected or detected by doppler measurement this should be confirmed by a manual sphygmomanometer. Automated measurements may be inaccurate. The level of hypertension at which treatment is instituted must be defined and correlated with age and height. Blood pressures consistently above the 95th centile for age should normally be treated (Table 8 and Table 9).

Classification of normal and abnormal blood pressure in children and adolescents

<table>
<thead>
<tr>
<th>Classification of blood pressure</th>
<th>SBP or DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;90th percentile</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>90th or &lt; 95th centile or &gt; 120/80 in adolescents</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>95th to 99th centile + 5 mm Hg</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>&gt; 99th centile + 5 mm Hg</td>
</tr>
</tbody>
</table>

SBP – Systolic BP
DBP - Diastolic BP

The term malignant hypertension should be avoided. Severe hypertension has recently been defined as a BP elevation that fulfils (and usually exceeds) the definition of stage 2 hypertension and is accompanied by severe symptoms. Physical examination and/or laboratory findings of accelerated hypertension are frequently also present.

Medical management of hypertension

**Mild to Severe “Standard” Hypertension**

Diuretics are first line drugs in all children with fluid overload and should be used in children with salt and water retention that occurs with the use of peripheral vasodilators and steroids. Children with hypertension can be managed effectively with single agent amlodipine or nifedipine. Amlodipine has the advantage of once-daily dosing and nifedipine can be used to adjust BP...
Acute. ACE inhibitors such as Enalapril and Trandolapril should be used if fluid retention is not the cause of the hypertension. For third line, a beta-blocker, e.g. atenolol, may be a useful addition but not in children with contra-indications such as asthma or poor cardiac function (check ECHO). Additional agents such as hydralazine or doxazosin as a vasodilator can be considered if an IV agent is required (see Table 10 for doses of drugs). If in doubt, discuss with PTC or nephrologists. Steroid induced or tumour associated (neuroblastoma or Wilms) hypertension should be treated in the same way. However it is important to rule out whether there is a major component of fluid overload or not.

**Catecholamine Excess Hypertension**

In catecholamine excess states associated with hypertension (e.g. neuroblastoma, phaeochromocytoma) start with phenoxybenzamine and later add a beta blocker like atenolol if required. (see Table 10 for doses) Nifedipine also has a role in this situation.

Phenoxybenzamine should be commenced a week before any surgery is undertaken to provide alpha blockade.

**Hypertensive Crisis/Acute Hypertensive Encephalopathy**

*Discuss with paediatric oncology centre urgently*

This is an emergency and the patient should be managed in a high dependency or PICU. Transfer after emergency management after discussion with PTC.

Emergency management is indicated when the level of BP is a threat to life or to the function of vital organs. The aim of treatment is to bring the blood pressure steadily back to normal over about 72 hours, avoiding sudden hypotension. A useful target is to aim to reduce the BP by one third of the total required reduction in the 1st 24 hours of treatment.

It is necessary to use drugs with a rapid action but these require careful administration to prevent sudden hypotension and resulting failure of auto regulation mechanisms. Drugs which can be infused intravenously to finely control BP during the critical early phase of management are preferred. Labetalol and sodium nitroprusside are both effective. Hydralazine may be used in milder cases particularly if high dependency care is not available. Alternatively Labetalol or Sodium Nitroprusside may be considered. When commencing an IV drug, always have a saline infusion set-up and connected, to enable immediate saline bolus if the BP drops too quickly. All patients should have frequent observations for neurological status and should be treated in a high dependency unit.

Oral/sublingual hypotensive agents or diuretics are contraindicated in the initial management of hypertensive crisis. These are best reserved until the blood pressure is safely controlled. If the child is having a convulsion a suitable anticonvulsant should be administered intravenously in addition to steps being taken to reduce blood pressure.

**Important**

Repeated checks on visual acuity and pupillary reactions to light are essential because the risk of infarcting the optic nerve heads of children with accelerated hypertension is considerable. The loss of vision or pupillary reaction to light as the BP is reduced is an emergency that justifies raising the BP by intravenous saline or plasma. Dexamethasone maybe required.
Table 8. Blood pressure levels for the 90th and 95th percentiles of blood pressure for boys age 1 to 17 years by percentiles of height.

<table>
<thead>
<tr>
<th>Age BP†</th>
<th>Systolic BP (mm Hg)</th>
<th>Diastolic BP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5%</td>
<td>10%</td>
</tr>
<tr>
<td>1 90th</td>
<td>94</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>98</td>
<td>99</td>
</tr>
<tr>
<td>2 90th</td>
<td>98</td>
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<tr>
<td></td>
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<td>102</td>
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<tr>
<td>3 90th</td>
<td>100</td>
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<td></td>
<td>104</td>
<td>105</td>
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<tr>
<td>4 90th</td>
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<td></td>
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<td>107</td>
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<td>5 90th</td>
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<td>108</td>
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<tr>
<td>6 90th</td>
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<tr>
<td>7 90th</td>
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<td>8 90th</td>
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<td></td>
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<td>112</td>
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<tr>
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<td>12 90th</td>
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<td>120</td>
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<tr>
<td>13 90th</td>
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<tr>
<td>15 90th</td>
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<tr>
<td>16 90th</td>
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<td></td>
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<td>130</td>
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<tr>
<td>17 90th</td>
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<td>129</td>
</tr>
<tr>
<td></td>
<td>132</td>
<td>133</td>
</tr>
</tbody>
</table>

*Height percentiles determined by standard growth curves.
†Blood pressure percentiles determined by a single measurement.
Table 9. Blood pressure levels for the 90<sup>th</sup> and 95<sup>th</sup> percentiles of blood pressure for girls age 1 to 17 years by percentiles of height.

<table>
<thead>
<tr>
<th>Height Percentiles*</th>
<th>Systolic BP (mm Hg)</th>
<th>Diastolic BP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP†</td>
<td>5% 10% 25% 50% 75% 90% 95%</td>
<td>5% 10% 25% 50% 75% 90% 95%</td>
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<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90&lt;sup&gt;th&lt;/sup&gt;</td>
<td>97 98 99 100 102 103 104</td>
<td>53 53 53 54 55 56 56</td>
</tr>
<tr>
<td>95&lt;sup&gt;th&lt;/sup&gt;</td>
<td>101 102 103 104 105 107 107</td>
<td>57 57 57 58 59 60 60</td>
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<td>2</td>
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<tr>
<td>90&lt;sup&gt;th&lt;/sup&gt;</td>
<td>99 99 100 102 103 104 105</td>
<td>57 57 58 58 59 60 61</td>
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<tr>
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<td>102 103 104 105 107 108 109</td>
<td>61 61 61 62 62 63 64</td>
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<tr>
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<td>100 100 102 103 104 105 106</td>
<td>61 61 61 62 63 63 64</td>
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<tr>
<td>95&lt;sup&gt;th&lt;/sup&gt;</td>
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<td>65 65 65 66 66 67 68</td>
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<td>63 63 64 65 65 66 67</td>
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<td>67 67 68 69 69 70 71</td>
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<td>67 67 68 69 69 70 71</td>
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<td>69 69 69 70 71 72 72</td>
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<td>73 73 73 74 75 76 76</td>
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<td>116 116 118 119 120 121 122</td>
<td>75 75 76 76 77 78 78</td>
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<tr>
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<td>79 79 80 80 81 82 82</td>
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<td>82 82 83 83 84 85 86</td>
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<td>79 79 79 80 81 82 82</td>
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<tr>
<td>95&lt;sup&gt;th&lt;/sup&gt;</td>
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<td>83 83 83 84 85 86 86</td>
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<td>79 79 79 80 81 82 82</td>
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<td>95&lt;sup&gt;th&lt;/sup&gt;</td>
<td>126 126 127 129 130 131 132</td>
<td>83 83 83 84 85 86 86</td>
</tr>
</tbody>
</table>

*Height percentiles determined by standard growth curves.
†Blood pressure percentiles determined by a single measurement.
### Table 10. Drugs used in the treatment of hypertension

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Age</th>
<th>Dose</th>
<th>Frequency</th>
<th>Maximum Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amlodipine</td>
<td>po</td>
<td>1 month – 12 years</td>
<td>100-200mcg/kg (up to 400mcg/kg)</td>
<td>Once daily</td>
<td>10mg</td>
<td>If necessary increase at intervals of 1-2 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-18 years</td>
<td></td>
<td></td>
<td>10mg</td>
<td></td>
</tr>
<tr>
<td>Atenolol</td>
<td>po</td>
<td>1 month- 12 years</td>
<td>0.5-2mg/kg</td>
<td>Once daily</td>
<td>50mg</td>
<td>May be given in 2 divided doses. Doses higher than 50mg daily rarely necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 -18 years</td>
<td>25-50mg</td>
<td></td>
<td>50mg</td>
<td></td>
</tr>
<tr>
<td>Captopril</td>
<td>po</td>
<td>1 month- 12 years</td>
<td>100-300micrograms/kg</td>
<td>2-3 times a day</td>
<td>150mg daily in divided doses</td>
<td>Test dose must be given 100micrograms/kg (max 6.25mg), monitor blood pressure carefully for 1-2 hours.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 -18 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12.5-25mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2-3 times a day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enalapril</td>
<td>po</td>
<td>1 month- 12 years</td>
<td>100micrograms/kg (up to 1-2mg/kg)</td>
<td>Once daily</td>
<td>Up to 1mg/kg in 1-2 divided doses</td>
<td>Monitor blood pressure carefully for 1-2 hours after initial dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 -18 years</td>
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<td></td>
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<td>2.5-20mg</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1-2 divided doses</td>
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<td></td>
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<tr>
<td>Frusemide</td>
<td>po</td>
<td>1 month- 12 years</td>
<td>0.5-2mg/kg</td>
<td>2-3 times a day</td>
<td>80mg daily</td>
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<tr>
<td></td>
<td></td>
<td>12 -18 years</td>
<td></td>
<td></td>
<td>80-120mg daily</td>
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<tr>
<td></td>
<td>iv</td>
<td>1 month- 12 years</td>
<td>0.5-1mg/kg</td>
<td>Every 8 hours</td>
<td>2mg/kg (max 40mg) every 8 hours</td>
<td>IV –do not exceed 0.5mg/kg/min, max 4mg/min.</td>
</tr>
<tr>
<td></td>
<td>iv</td>
<td>12 -18 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Route</td>
<td>Age</td>
<td>Dose</td>
<td>Frequency</td>
<td>Maximum Dose</td>
<td>Comments</td>
</tr>
<tr>
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<td>-------------------------------</td>
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<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>po</td>
<td>1 month-12 years</td>
<td>250-500 micrograms/kg</td>
<td>Every 8-12 hours</td>
<td>7.5 mg/kg daily (max 200 mg daily)</td>
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</tr>
<tr>
<td></td>
<td>po</td>
<td>12-18 years</td>
<td>25 mg</td>
<td>Twice daily</td>
<td>50-100 mg twice daily</td>
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</tr>
<tr>
<td></td>
<td>iv</td>
<td>1 month-12 years</td>
<td>100-500 micrograms/kg</td>
<td>Every 4-6 hours</td>
<td>3 mg/kg (60 mg daily)</td>
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<tr>
<td></td>
<td>iv</td>
<td>12-18 years</td>
<td>5 mg</td>
<td>prn</td>
<td>3 mg/kg daily</td>
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</tr>
<tr>
<td></td>
<td>continuous</td>
<td>1 month-12 years</td>
<td>12.5-50 microgram/kg/hour</td>
<td>Every 4-6 hours</td>
<td>3 mg/kg daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>infusion</td>
<td>12-18 years</td>
<td>3 mg/hour</td>
<td>prn</td>
<td>3 mg/kg daily</td>
<td></td>
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<tr>
<td>Labetalol</td>
<td>iv</td>
<td>1 month-12 years</td>
<td>250-500 micrograms/kg</td>
<td>As a single dose</td>
<td>20 mg</td>
<td>Should only be given in an area that can carry out all the necessary checks.</td>
</tr>
<tr>
<td></td>
<td>iv</td>
<td>12-18 years</td>
<td>50 mg</td>
<td>Repeat after 5 mins if necessary</td>
<td>Max. total dose 200 mg</td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td>po</td>
<td>1 month-12 years</td>
<td>200-300 micrograms/kg</td>
<td>Three times a day</td>
<td>3 mg/kg daily or 90 mg daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>po</td>
<td>12-18 years</td>
<td>5-20 mg</td>
<td>Three times a day</td>
<td>90 mg daily</td>
<td></td>
</tr>
<tr>
<td>Sodium Nitroprusside</td>
<td>continuous infusion</td>
<td>1 month-18 years</td>
<td>500 nanograms/kg/min</td>
<td>-</td>
<td>Increase in steps of 200 nanograms/kg/min to max 8 micrograms/kg/min (4 micrograms/kg/hour if used &gt;24 hours)</td>
<td>Should only be given in an area that can carry out all the necessary checks.</td>
</tr>
<tr>
<td>Spironalactone</td>
<td>po</td>
<td>1 month-12 years</td>
<td>1-3 mg/kg</td>
<td>1-2 divided doses</td>
<td>9 mg/kg daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>po</td>
<td>12-18 years</td>
<td>50-100 mg</td>
<td>1-2 divided doses</td>
<td>400 mg daily</td>
<td></td>
</tr>
</tbody>
</table>
12. BASIC PRINCIPLES OF SYMPTOM MANAGEMENT
12. Basic principles of symptom management

Introduction

Symptom management embraces the management of acute symptoms throughout the acute phase of active treatment, and then extends into the palliative/non-curative supportive care. It is essential, as research has shown, that the suffering experienced from treatment and its side effects will be what families remember. For those children and young people who unfortunately cannot be cured, palliative care, including rigorous attention to symptom management, will help to provide as good a quality of life as possible for the time that remains.

Each child/young person and their family respond to their symptom experience differently. The wide spectrum of cognitive ability and chronological age amongst this patient group necessitates an individualised approach to assessment and management. In addition, consideration of the best setting in which the child/young person may be assessed and managed is required. The advantages and disadvantages of each intervention must be carefully considered. The treatment must be appropriate to the symptom and the stage of illness and the chances of improving the symptom must then be balanced against the inconvenience and any discomfort caused.

It is helpful to approach the management of any symptom systematically:

```
<table>
<thead>
<tr>
<th>History and Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify cause</td>
</tr>
<tr>
<td>Choose treatments</td>
</tr>
<tr>
<td>Regular review</td>
</tr>
</tbody>
</table>
```

When choosing pharmacological treatments in the management of symptoms for children and young people, it is important to remember that some drugs are used ‘off licence’ or ‘off-label’ and there is sometimes little data to support use in the younger age groups. A lack of clinical trial data within this patient population means that some drugs within this document reflect the experiences of individual centres rather than published evidence. Close collaboration and communication amongst health and allied healthcare professionals is essential. Advice will be available as required from the specialist palliative care team – paediatric oncology outreach nursing team, symptom control or the adult palliative care team. In addition standard texts such as the BNFC and APPM formulary should be used.

This chapter will discuss the pharmacological management of common symptoms the child/young person may experience. However it is very important to also consider non-pharmacological strategies for example: distraction therapy, hypnotherapy, physiotherapy and occupational therapy.

Dosages and preparations of drugs discussed under each section within this chapter are given in Table 12.
Nausea and Vomiting

Identifying the cause of nausea and vomiting, which may be multifactorial, can help in making the logical choice of antiemetics.

**Causes of nausea and vomiting**

- **Cancer related causes**
  - Irritation of the upper GIT
  - Blood in stomach
  - Gastric outflow obstruction
  - Constipation
  - Abdominal mass
  - Anxiety
  - Uraemia
  - Cough
  - Pain
  - Raised intracranial pressure

- **Treatment related causes**
  - Radiotherapy
  - Drug therapy e.g. opioids, chemotherapy, corticosteroids (IV), carbamazepine, NSAIDs, Monoclonal antibodies

---

**Diagram:**

- Anxiety, sensory stimuli
- Motion sickness, vascular neuritis
- Drugs, uraemia, hypercalcaemia, infection, tumour, toxins
- Gastrointestinal tract (GIT) stimulation, radiation colitis
- Cerebral cortex
- Vestibular apparatus
- Chemoreceptor trigger zone (CTZ)
- Vagal and sympathetic afferents

**Vomiting centre**
**Antiemetics and sites of action**

<table>
<thead>
<tr>
<th>Anti-emetics</th>
<th>Site of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclizine</td>
<td>Vomiting centre</td>
</tr>
<tr>
<td>Hyoscine</td>
<td></td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>ctz, vomiting centre</td>
</tr>
<tr>
<td>Dopamine antagonists e.g.</td>
<td>ctz</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>ctz, GIT</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>ctz</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>ctz, GIT</td>
</tr>
<tr>
<td>Domperidone</td>
<td>ctz</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>ctz</td>
</tr>
<tr>
<td>5 HT₃ antagonists e.g.</td>
<td>ctz, GIT</td>
</tr>
<tr>
<td>Ondansetron</td>
<td></td>
</tr>
<tr>
<td>Granisetron</td>
<td></td>
</tr>
</tbody>
</table>

**Nausea and vomiting during therapy**

Managing nausea and vomiting aggressively from the start helps to gain the confidence of the child and parents, and reduces the difficult problem of anticipatory vomiting. All therapy — chemotherapy, radiotherapy and surgery have the potential to trigger nausea and vomiting and as such should be assessed and treated appropriately. The emetogenic potential of different chemotherapy agents varies (see Table 11) although susceptibility to these side effects varies from child to child. Nausea and vomiting caused by chemotherapy is generally mediated centrally via the chemoreceptor trigger zone (ctz) and peripherally via the gastrointestinal tract (GIT). Anticipatory vomiting is less common in the younger child. Anti-emetics can be given in advance of chemotherapy so that an effective blood level has been established before the chemotherapy is given and consideration should be given to anti-emetics being given at home prior to the chemotherapy. For chemotherapy with a low emetogenic potential a single anti-emetic can be given, if necessary. For those with moderate or high potential, combinations of anti-emetics will be needed. It is important to provide anti-emetics for the child to take home after chemotherapy for use until the symptoms subside (usually 2-3 days).

**Nausea and vomiting in palliative care**

Cyclizine and levomepromazine are commonly used for nausea and vomiting associated with raised intracranial pressure. Short pulses of dexamethasone can also be of benefit in this situation and haloperidol is a useful second line choice if cyclizine or levomepromazine are ineffective. Haloperidol and levomepromazine (should generally not be used together) may also be effective for nausea/vomiting secondary to metabolic disturbance e.g. renal failure. Nausea and vomiting due to bowel obstruction requires specialist advice, and treatment may include steroids or chemotherapy/ radiotherapy to reduce the obstruction, as well as anti-emetics, and potentially include Octreotide (to reduce secretions) for inoperable bowel obstruction (if needed discuss with PTC before starting). (Cyclizine, levomepromazine and haloperidol are all compatible with morphine for subcutaneous/intravenous infusions).
### Table 11. Cytotoxic agents and emetic risk

<table>
<thead>
<tr>
<th>CYTOTOXIC AGENTS</th>
<th>POTENTIAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin*</td>
<td>HIGH</td>
</tr>
<tr>
<td>Cyclophosphamide &gt;1000mg/m²*</td>
<td></td>
</tr>
<tr>
<td>Ifosfamide*</td>
<td></td>
</tr>
<tr>
<td>Melphalan*</td>
<td></td>
</tr>
<tr>
<td>Actinomycin</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Amsacrine</td>
<td></td>
</tr>
<tr>
<td>Busulphan</td>
<td></td>
</tr>
<tr>
<td>Carboplatin*</td>
<td></td>
</tr>
<tr>
<td>Chlorambucil</td>
<td></td>
</tr>
<tr>
<td>Cladribine</td>
<td></td>
</tr>
<tr>
<td>Clofarabine</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide &lt;1000mg/m²</td>
<td></td>
</tr>
<tr>
<td>Cytarabine &gt;150mg/m²</td>
<td></td>
</tr>
<tr>
<td>Dacarbazine</td>
<td></td>
</tr>
<tr>
<td>Daunorubicin</td>
<td></td>
</tr>
<tr>
<td>Daunorubicin liposomal</td>
<td></td>
</tr>
<tr>
<td>Docetaxel</td>
<td></td>
</tr>
<tr>
<td>Doxorubicin</td>
<td></td>
</tr>
<tr>
<td>Epirubicin</td>
<td></td>
</tr>
<tr>
<td>Idarubicin</td>
<td></td>
</tr>
<tr>
<td>Irinotecan</td>
<td></td>
</tr>
<tr>
<td>Lomustine</td>
<td></td>
</tr>
<tr>
<td>Methotrexate &gt;1g/m²</td>
<td></td>
</tr>
<tr>
<td>Mitozantrone</td>
<td></td>
</tr>
<tr>
<td>Nelearabine</td>
<td></td>
</tr>
<tr>
<td>Procarbazine</td>
<td></td>
</tr>
<tr>
<td>Temozolamide</td>
<td></td>
</tr>
<tr>
<td>Topotecan</td>
<td></td>
</tr>
<tr>
<td>Treosulfan</td>
<td></td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>LOW</td>
</tr>
<tr>
<td>ALG/ATG</td>
<td></td>
</tr>
<tr>
<td>Bleomycin</td>
<td></td>
</tr>
<tr>
<td>CD45 antibodies</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide &lt;300mg/m²</td>
<td></td>
</tr>
<tr>
<td>Cytarabine &lt;150mg/m²</td>
<td></td>
</tr>
<tr>
<td>Etoposide</td>
<td></td>
</tr>
<tr>
<td>Fludarabine</td>
<td></td>
</tr>
<tr>
<td>Gemcitabine</td>
<td></td>
</tr>
<tr>
<td>Gemtuzamab</td>
<td></td>
</tr>
<tr>
<td>Mercaptopurine</td>
<td></td>
</tr>
<tr>
<td>Methotrexate &lt;1g/m²</td>
<td></td>
</tr>
<tr>
<td>Thioguanine</td>
<td></td>
</tr>
<tr>
<td>Thiotepa</td>
<td></td>
</tr>
<tr>
<td>Vinblastine</td>
<td></td>
</tr>
<tr>
<td>Vincristine</td>
<td></td>
</tr>
<tr>
<td>Vindesine</td>
<td></td>
</tr>
<tr>
<td>Vinorebine</td>
<td></td>
</tr>
</tbody>
</table>

*Delayed Emesis Risk
Constipation

A decrease in frequency of the passage of stools caused by either a complete or incomplete action of the bowels (Selwood et al 1999); constipation is most likely to occur as a side effect of drug treatment. Other factors such as intra-abdominal disease, poor fluid intake, inactivity, poor nutrition, cord compression, hypercalcaemia and hypokalaemia should also be considered. These underlying causes should be treated where appropriate/possible.

Prophylaxis or treatment for constipation should start with Movicol (lactulose is less effective), although as a single agent this is frequently insufficient and other oral stimulants and softeners are often required.

Doses of laxatives should be titrated up rather than always adding in a new laxative. Codanthyramer should only be used in children/young people with non-curative disease and should be used with caution in those who are incontinent, catheterised or in nappies as skin excoriation may occur. Occasionally rectal preparations may be needed provided the patient is not neutropenic or thrombocytopenic and all oral measures have been tried (see box).

**Pathway for treatment of constipation**

1. **Consider and treat underlying cause**
   - Side effects of Vincristine
   - Side effects of analgesia
   - Poor fluid intake
   - Inactivity
   - Poor diet
   - Poor nutrition
   - Hypercalcaemia
   - Hypokalaemia
   - Intra-abdominal disease

   **Is the rectum impacted with hard faeces on abdominal palpation/x-ray?**

   **Yes**
   - Are there signs of obstruction?
     **Yes**
     - Seek medical/surgical advice from PTC. Use softeners only. No stimulant laxative.
     **No**
     - **Is the child thrombocytopenic and/or neutropenic?**
       **Yes**
       - Continue stimulant/softener. Seek further advice from PTC.
       **No**
       - Use suppositories/enema

   **No**
   - **Softening agents**
     - Macrogols (eg Movicol – Half)
     - Macrogols (eg Movicol Paediatric Plain)
     - Lactulose
   - **Stimulant laxatives**
     - Senna (Senosides)
     - Bisacodyl
     - Sodium Picosulphate
   - **Combined softener/stimulants**
     - Co-danthyramer (licensed in palliative care only)
     - Docusate Sodium
   - **Rectal preparations**
     - Rectal impaction – glycerine/Bisacodyl suppositories, phosphate/microlax (or equivalent) enema
     - Colonic impaction – softeners: high arachis oil enema (preferably overnight), stimulants: phosphate enema (post arachis oil enema)
Pain

Pain is a complex sensation related to physical, social, psychological and cultural reasons which all need to be considered in the assessment of a child/young person’s pain to reflect the best choice of treatment. Problems from pain can occur throughout the disease process (see below).

Causes of pain during the disease process

<table>
<thead>
<tr>
<th>Pain</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>at diagnosis</td>
<td>tumour</td>
</tr>
<tr>
<td></td>
<td>infection</td>
</tr>
<tr>
<td>on treatment</td>
<td>procedures (e.g. needles, LP, bone marrows)</td>
</tr>
<tr>
<td></td>
<td>side effects (e.g. mucositis)</td>
</tr>
<tr>
<td></td>
<td>tumour</td>
</tr>
<tr>
<td></td>
<td>other (e.g. pressure areas, infection)</td>
</tr>
<tr>
<td>progressive disease</td>
<td></td>
</tr>
</tbody>
</table>

Assessment of Pain

Pain is a subjective experience and the child/young person’s own opinion is the best guide as to what they are feeling, but this can be limited by their level of understanding and communication skills, i.e. irritability and restlessness, reluctance to be held or unnatural stillness may be misunderstood. Parents are usually able to interpret their child's feelings but may sometimes under or over-estimate the pain experience. Specific pain assessment tools are available, according to the child's age and ability. Body charts are helpful for all ages to locate and identify sites of pain, whilst colour scales, faces, numeric and visual analogue scales can be used to measure severity. When assessing pain it is also important to consider psychological and cultural factors influencing the child and family and their coping skills.

Pain Tools

For those aged under 4 years of age and non-verbal children: FLACC Chart

<table>
<thead>
<tr>
<th>FLACC scale</th>
<th>Scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Face</td>
<td>No particular expression or smile</td>
</tr>
<tr>
<td>Legs</td>
<td>Normal position or relaxed</td>
</tr>
<tr>
<td>Activity</td>
<td>Lying quietly, normal, position moves easily.</td>
</tr>
<tr>
<td>Cry</td>
<td>No cry, (awake or asleep)</td>
</tr>
<tr>
<td>Consolability</td>
<td>Content, relaxed</td>
</tr>
</tbody>
</table>
For 4 years of age and above: Baker-Wong Faces chart or Numerical pain scale

Definitions of pain

Procedure-related pain

Some of the tests or procedures that children have during their treatment may be uncomfortable or painful. The need for appropriate analgesia should be anticipated. Some examples are central line insertions, bone marrow tests or lumbar punctures. The duration of pain/discomfort experienced may be variable from a few hours to a few days and should be managed with a step-wise approach.

Persisting Pain

The WHO persisting pain guidance 2012, defines children with cancer related pain (either from treatment or tumour related causes) as having persisting pain. Persisting pain is therefore considered to be any pain that is not related to a procedure or investigation.

The current WHO guidelines (2012) no longer recommend the use of codeine as a weak opioid for the management of persisting pain. It advocates a two-step approach from simple analgesia eg Paracetamol followed by the use of low doses of strong opioids eg morphine.

Correct use of analgesic medicines will relieve pain in most children with persisting pain due to medical illness and relies on the following key concepts:

• using a two-step strategy
• dosing at regular intervals
• using the appropriate route of administration
• adapting treatment to the individual child

Neuropathic pain

Neuropathic pain is caused by structural damage and nerve cell dysfunction in the peripheral or central nervous system (CNS). Any process that causes damage to the nerves, such as metabolic, traumatic, infectious, ischaemic, toxic or immune-mediated pathological conditions, can
result in neuropathic pain. In addition, nerve compression or the abnormal processing of pain signals by the brain and spinal cord can cause neuropathic pain.

Nerve pain is characteristically associated with an area of altered sensation, and can be burning, stinging or shooting in nature. Children/young people may complain the area is hot or cold and may be relieved by rubbing or squeezing the site of pain. This pain is only partially relieved by opioids, although opioids should still be given as first line. Co-analgesics such as amitriptyline, gabapentin, and/or pregabalin may be helpful in this situation. However these do not provide instant relief and each drug needs to be titrated to maximum benefit. In addition a steroid pulse may also be helpful if the pain is due to nerve compression. Other complex approaches including use of Ketamine, Methadone and local or regional nerve blocks may be used in difficult cases, with advice from the PTC.

Management of Pain

In pain management it can be helpful to combine a variety of approaches. Advice should be sought from the specialist team when pain is complex and unresponsive to treatment.

Approaches to Pain Management

<table>
<thead>
<tr>
<th>Treatment of underlying disease</th>
<th>Non-pharmacological management of pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiotherapy</td>
<td>Education</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>Explanation</td>
</tr>
<tr>
<td>Surgery</td>
<td>Distraction</td>
</tr>
<tr>
<td><strong>Pharmacological management of pain</strong></td>
<td>Relaxation</td>
</tr>
<tr>
<td>Non opioid analgesics</td>
<td>Hypnosis</td>
</tr>
<tr>
<td>Opioid for mild to moderate pain</td>
<td></td>
</tr>
<tr>
<td>Opioid for moderate to severe pain</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td></td>
</tr>
<tr>
<td>Antidepressants ) for neuropathic</td>
<td></td>
</tr>
<tr>
<td>Anticonvulsants ) pain</td>
<td></td>
</tr>
<tr>
<td>Anaesthetic agents</td>
<td></td>
</tr>
<tr>
<td>Local agents e.g. EMLA, Ametop</td>
<td></td>
</tr>
<tr>
<td>Sedating agents</td>
<td>Cold e.g. ice pack</td>
</tr>
<tr>
<td>Inhaled anaesthesia e.g. nitrous oxide</td>
<td></td>
</tr>
<tr>
<td>Regional blocks</td>
<td>Massage</td>
</tr>
<tr>
<td>Epidural</td>
<td>Physiotherapy</td>
</tr>
<tr>
<td></td>
<td>TENS</td>
</tr>
<tr>
<td></td>
<td>Acupuncture</td>
</tr>
</tbody>
</table>

The World Health Organisation (WHO) has recently updated its proposed standard approach to paediatric pain management (see ‘Persisting pain in children with a medical illness’).

**WHO approach to paediatric analgesia**

<table>
<thead>
<tr>
<th>Analgesic drugs</th>
<th>AND</th>
<th>Analgesic therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>- by the ladder</td>
<td>-supportive</td>
<td></td>
</tr>
<tr>
<td>- by the clock</td>
<td>-behavioural</td>
<td></td>
</tr>
<tr>
<td>- by the mouth</td>
<td>-physical</td>
<td></td>
</tr>
<tr>
<td>- by the child</td>
<td>-cognitive</td>
<td></td>
</tr>
</tbody>
</table>
Analgesics

Although a variety of approaches to pain management are used, analgesics still form the backbone of any strategy. The principles of analgesic use are outlined below and doses are given in Table 12.

In most situations, analgesics of gradually increasing strength are used, according to the WHO analgesic ladder (see below). However the recent MHRA recommendations have removed step 2 from the WHO ladder, which in essence means removal of the weak opioid step for non-acute pain. The MHRA guidelines suggests that codeine should not be prescribed in <12 year olds, and should only be prescribed in 12-18 year olds for up to three days with acute pain if pain cannot be relieved by paracetamol / ibuprofen. It is essential that analgesics on all steps are given regularly, and that compliance is checked before moving on to the next step of the ladder. Paracetamol is helpful in mild to moderate pain and has few side effects. The prescriber should be cautious in the use of NSAIDs due to the know effect on platelets. When pain is no longer relieved by regular paracetamol, a strong opioid at a low or standard starting dose is recommended. Anticipated side effects are constipation (laxatives should be prescribed routinely) and an antiemetic should also be prescribed for the first 3 days, due to the risk of nausea and vomiting. In a situation where pain is improving because of other interventions e.g. adjuvant radiotherapy or chemotherapy, analgesics should be reviewed and reduced and/or changed to those on a lower step on the ladder.


Prescribing analgesia
In most situations pain is constant, and analgesics should be given regularly (‘background analgesia’). Further analgesia should always be prescribed on a p.r.n. basis (‘breakthrough analgesia’) for relief of pain between the regular doses of analgesia. If a patient is requiring multiple doses of breakthrough over a prolonged period (e.g. 48hrs) the dose of background analgesia should be increased. The team at the Paediatric Oncology Centre should be consulted if any problems are encountered.
Opioids

Morphine is still the first line for moderate to severe nociceptive pain. Adjuvants or alternatives may need to be considered, particularly, in neuropathic, bone and abdominal (especially liver) pain. Morphine sulphate should be administered four-hourly (immediate release preparations) for breakthrough pain and on initial commencement of Morphine, and twelve-hourly (slow release preparations) for background pain, calculated from the breakthrough requirement doses. The initial dose should be calculated according to the child's weight and then increased, in increments, to provide adequate analgesia. Commencing 'low dose' morphine rather than standard morphine dosing for the opiate naive either as a step from Paracetamol or to relieve moderate/severe pain, may be considered appropriate. Low dose morphine is usually considered as 50% of the standard morphine cBNF dose. Titration of morphine can occur as usual based on clinical effect. For pain relief there is no ceiling 24hour morphine dose. When using the slow release preparations provide an immediate release preparation for breakthrough pain (10% of the 24hour morphine dose is now considered a more appropriate initial guide to breakthrough dosing).

Side effects of opioids

Opioids have many side effects. The side effect most likely to cause clinical problems is constipation, and laxatives should always be prescribed concomitantly. Nausea and vomiting are less frequent side effects (but can occur in up to 50% of cases) and antiemetics should be prescribed for the first three days. If the nausea and vomiting has dissipated then the antiemetic can be stopped. Drowsiness is also common when initiating opioids or when escalating doses but almost always wears off within two or three days. It is useful to warn child/young person and their parents about this or they may worry that the disease has suddenly progressed. Some children/young people experience itching; this usually also wears off but if not antihistamines or 5HT3 antagonists are helpful. If itch persists then an opioid switch should be considered.

Respiratory depression does not appear to cause problems in children being treated with opioid drugs for pain who are appropriately prescribed and appropriately titrated doses. Children on opioids should be regularly assessed and reviewed. Once established, opioids should not be stopped abruptly as this may cause an acute withdrawal syndrome; the dose should be reduced gradually (whilst monitoring for withdrawal) and then stopped.

Parental concerns about opioids

Sometimes parents are reluctant to consider the use of morphine for their child's pain. In order to overcome this, the reason for their concern needs to be explored. Often it is not the use of morphine itself that is the problem, but the fact that it represents an acknowledgement that the child is actually seriously ill/dying. Parents may also be confused about the risk of addiction and may need reassurance that psychological addiction does not occur in children requiring opioids for pain. It may be helpful to point out that morphine can be reduced and stopped should the pain be relieved by other measures such as radiotherapy.

Familiar analogies to explain dependence, tolerance and addiction (Cooper 2000)

Parents familiar with the habit of drinking coffee in the morning are aware they will experience noticeable effects without usual caffeine intake, and are also aware they can withdraw from coffee by gradual lowering of daily consumption. The fact that their body is used to a certain amount of caffeine at certain times of the day means they are dependent. Many people become accustomed to a certain level of salt for food to taste ‘salty’. After a while they may need to increase their salt intake to ensure food continues to taste the same because the body has adjusted to or now tolerates the previous amount of salt so it no longer has the same effect.
In the same way a child can become tolerant to an opioid dose so they require a higher dose to achieve the same pain reduction. Tolerance and dependence do not equal addiction.

**Alternative Opioids**

If you consider the patient to be intolerant to morphine and need to discuss the use of alternative oral opioids, please contact the Paediatric Treatment Centre (PTC).

**Alternative routes of administration**

If the oral route is not possible, for example because of nausea and vomiting, difficulty swallowing, or gradual loss of consciousness, other routes should be considered:

- **Transdermal**
  Transdermal fentanyl is suitable for children who are on a stable dose of opioid, and who dislike or cannot tolerate oral medication. It is not suitable for children in whom pain is changing and whose analgesic needs are therefore altering on a day-to-day basis. It may not be suitable for children on very high doses of opioids because reliable dose conversion becomes difficult, and in small children the available skin surface area may limit number of patches that can be administered.

- **Rectal**
  During the palliative care phase some children tolerate rectal medication, and may prefer it to routes involving needles. When a child is no longer conscious (or during the last few hours) morphine suppositories can be used (these are not routinely available so would have to be ordered via your pharmacy). The rectal route is not suitable for children during curative chemotherapy who may be neutropenic or thrombocytopenic.

- **Parenteral**
  Analgesics can easily be given parenterally by continuous infusion. If a central intravenous catheter is in situ, this can be used, otherwise a needle can be placed subcutaneously. The site of a subcutaneous needle should be changed according to clinical need to avoid inflammation, and topical anaesthetic such as EMLA/Ametop can be used when the needle is re-sited if required. For the older child/young person a Patient Controlled Analgesia infusion pump (PCA) may be used and for younger children a NCA (Nurse controlled analgesia) may be considered. Community PCAs and PPCAs (patient proxy controlled analgesia) are now available from some specialist services.

- **Epidural**
  Epidural analgesia/anaesthesia can give very effective pain relief but is reserved for pain resistant to other measures and needs specialist management and care.
### Management of acute (procedure-related) and persisting pain ON chemotherapy, targeted therapy or radiotherapy treatment

On treatment includes children & young people on any chemo, targeted therapy or radiotherapy. Each family should be given an appropriate level of education and support regarding pain management supplemented by a patient information leaflet (PIL) on managing pain in children.

#### Step 1

**For out-patients/day case attenders**
- Assess the child, consider the cause of pain
- Check temperature prior to each dose:
  - **Give Paracetamol if:**
    - The child is afebrile but otherwise well
    - Pain assessment score: Mild (1-4) or moderate (5-7) and
    - ANC>0.5 x 10^9/L (due to the theoretical risk that it may mask fever especially in the face of neutropenia)
  
  If ANC < 0.5 x 10^9/L and/or if answer ‘no’ to any of above, then go to **STEP 2.**

It is recommended that regular Paracetamol is not used for longer than 2-3 days without clinical review. A child with pain persisting (for longer than 3 days), should be seen by a trained doctor or nurse practitioner for assessment & further management.

**For in-patients (until discharge)**
- Assess the child, consider the cause of pain
- Check temperature prior to each dose:
  - **Give Paracetamol if:**
    - The child is afebrile but otherwise well
    - Pain assessment score: Mild (1-4) or moderate (5-7) and
    - A child on the ward with ANC <0.5 x 10^9/L may be given Paracetamol regularly provided they are receiving appropriate TPR monitoring and assessment by a trained doctor/nurse practitioner.
    - The child is afebrile but otherwise well

For inpatients who are already on antibiotics as per neutropenic sepsis protocol, child can be given paracetamol as antipyretic or analgesic. In this situation there is no need to withhold paracetamol (irrespective of temperature or neutrophil count).

#### Step 2

**For inpatient, daycare attending and outpatient review**
- **Give Morphine** (or Oxycodone if morphine intolerant) if:
  - The child does not meet the criteria in step 1
  - Pain has not responded to Paracetamol
  - The child’s pain persists beyond 3 days
  - Pain assessment score: severe (8 -10)

For prescribing Morphine, follow the lowest standard starting dose in the BNFc. Some clinicians may want to prescribe ‘low dose’ morphine which is consider to be 50% of the standard start Morphine and then titrate accordingly.

A child, with pain persisting on Opiates for longer than three days, should be seen by a trained doctor or nurse practitioner for assessment and further management.

For patients with bone tumours, **NSAID’s (see page 155)** can be used as second line analgesia instead of low dose oral morphine. Discuss with PTC/UCLH.

**On-going Opiate use >3 days**
- If child requires Morphine/Oxycodone for more than 3 days then the child should have:
  - A clear on-going management plan with regular follow-up should be implemented.
  - A child can only continue on regular opiates with the agreement of the child’s lead consultant (shared care or oncologist)
  - Awareness of indications for immediate release (IR) and Modified release (MR) use, side effects, tolerance, addiction and withdrawal and alternative routes of administration eg transdermal.
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs):
For patients with bone tumours, NSAID’s can be used as second line analgesia instead of low dose oral morphine. Discuss with PTC/UCLH.

Other than UCLH patients with bone tumours, NSAIDs are generally avoided in haematology/oncology patients. This is because of concerns with increased risk of bleeding as a combine result of antplatelet activity of NSAIDs and thrombocytopenia. Once NSAID has been given, and even after discontinuation of NSAID, the antplatelet activity may be ongoing for weeks. Therefore NSAID is generally avoided if a patient is predicted to be thrombocytopenic in the near future (eg if a patient with normal blood counts is due to start a block of chemotherapy). In this situation, NSAIDs are only used at PTC consultant’s discretion or if there is a local policy stating otherwise.

**OFF Treatment (ie with sustained count recovery)**

| Step 1 | -Assess the child and consider the cause of pain  
|        | -Give Paracetamol and/or non-steroidal anti-inflammatory drugs (NSAIDs) eg ibuprofen (see NSAID section at top of this page) if:  
|        | • Pain assessment score : Mild (1-4) or moderate (5-7)  |

| Step 2 | Give Morphine or Oxydone if:  
|        | • The pain does not respond to Paracetamol/NSAIDs  
|        | • Pain assessment score: severe (8 -10)  |

| On-going Opiate use beyond 3 days | If a child requires Morphine/Oxycodone for more than 3 days then the child should be reviewed  
|                                 | • A clear on-going management plan with regular follow up should be implemented.  
|                                 | • A child can only continue on regular opiates with the agreement of the child’s lead consultant (shared care or oncologist)  
|                                 | • Awareness of indications for immediate release (IR) and Modified release (MR) use, side effects, tolerance, addiction and withdrawal and alternative routes of administration eg transdermal.  |

**Management of neuropathic pain**

| For mild pain (pain scale: 1-4) | Consider simple analgesia first  
|                                 | • Paracetamol if not Neutropenic  
|                                 | • Ibuprofen if off treatment (see NSAID section above)  |

| For moderate pain (pain scale: 5-7) or severe pain (pain scale: 8-10) | Consider a neuropathic agent first line  
|                                                                      | • Gabapentin (titrated up to tds dose over 3 days)  
|                                                                      | • Amitriptyline (2nd line agent)  
|                                                                      | NB may take 1-2 weeks to be effective  
|                                                                      | Consider Morphine during neuropathic pain titration. Opioids should be continued until pain score is <4  |

**Bone pain**

Non-steroidal anti-inflammatory (NSAID) drugs are particularly helpful for this type of pain but should be used with caution when the platelet count is already likely to be low, as there is an increased risk of gastro-intestinal bleeding. (refer to NSAIDs section at top of this page) Steroids may also be helpful in bone pain and can be administered as a pulse over 3-5 days. Gastric irritation should be anticipated with NSAIDS and/or steroids and a H2 receptor or a proton pump inhibitor prescribed. Pain from discrete bony metastases is often helped by a short course of palliative radiotherapy.
Headaches

A headache may have a simple underlying cause. However, headaches from central nervous system leukaemia are most effectively relieved by intrathecal chemotherapy.

- **Pain due to raised intracranial pressure**

  Symptoms associated with raised ICP include confusion, personality change, drowsiness, vomiting, focal neurology and headache.

  Headaches associated with raised intracranial pressure from brain tumours or cerebral metastases may be relieved with steroids. Steroids are often useful as a short-term measure but the disadvantages of long-term steroids, such as mood swings and changes in appearance, usually outweigh the advantages, and treatment with standard analgesics is preferable. For vomiting the drug of choice is cyclizine. Special consideration should be given if the child/young person has a shunt in situ as the raised ICP could be due to blockage or infection – seek advice from the PTC or paediatric neurosurgical team.

Dyspnoea

Dyspnoea is not just a symptom of disordered breathing. There is often the combination of physical, psychological, emotional and functional factors. It can impact on a child/young person’s day-to-day activities and if severe can be a very frightening symptom for both the child and the carers. Dyspnoea is common in children/young people who have disease in the chest but may be caused by a wide variety of other factors such as anxiety, anaemia, effusions, metastases, infection, SVC obstruction, PE, cardiac failure, central nervous system tumours and liver enlargement. Treatment of potentially reversible causes (complete or partial) where possible, will help alleviate this symptom. Radiotherapy/chemotherapy may be indicated. If anaemia is a significant factor the benefit of blood transfusion should be considered. If bronchospasm is thought to be a contributory factor, a trial of bronchodilators may be helpful. Furosemide may be of benefit in patients with pulmonary metastases. Low dose morphine (30-50% of the analgesic dose for the individual child) can be very effective in reducing the sensation of dyspnoea. Short pulses of steroids are useful for dyspnoea secondary to some types of obstructive mass. In the palliative care setting, Midazolam (buccal) may be useful for reducing the anxiety component contributing to the child’s breathlessness.

Sweating

Sweating is a common problem for children/teenagers with solid tumours, particularly neuroblastoma, and in children with Hodgkin’s disease. It is often helped by the use of regular ranitidine and/or a NSAID such as ibuprofen. (Due to the anti-platelet effects of non-steroidal drugs the risks and benefits should be discussed before prescribing these agents).

Seizures

Seizures may occur in children/young people with brain tumours or those with metastatic central nervous system disease. Chemotherapy/radiotherapy could trigger a predisposition to seizures. Reversible causes such as electrolyte imbalances should be investigated and treated appropriately. Occasional, short seizure activity may not require medication, although buccal/intranasal midazolam (and/or rectal diazepam) should be available. Regular oral anticonvulsants may be appropriate for children with brain tumours or cerebral/CNS metastases having frequent convulsions over a prolonged period, and levels should be monitored to ensure that they are within therapeutic range. Seizures can become difficult to control in the terminal phase and in these circumstances continuous subcutaneous/ intravenous midazolam may be helpful.
Anxiety and Agitation

Anxiety may reflect a child/young person’s need to talk about their fears and concerns and may improve following discussion and explanation. Pain as an underlying cause should be considered. Non-pharmaceutical measures are often helpful such as psychological intervention by a suitably qualified team member, play therapist or child psychologist/psychiatrist where available (see Approaches to Pain Management). Low dose oral diazepam or sublingual lorazepam may be helpful, particularly for panic attacks, episodic anxiety or for procedures likely to cause anxiety.

Terminal Restlessness

Restlessness and agitation, sometimes termed terminal restlessness, is common in the final stages of life. It can be treated with midazolam, haloperidol or levomepromazine, most are compatible with opioids in subcutaneous/intravenous infusions but the compatibility of drugs should be checked. Levomepromazine lowers the seizure threshold so is not generally used as first line in children with CNS disease. Haloperidol should be considered if there is a significant hallucinogenic or psychosis component to the agitation. Either Haloperidol or Levomepromazine should be considered if escalating Midazolam doses are not effective.

Retained Respiratory Tract Secretions
(Often Termed The Death Rattle)

This is a common symptom in children/young people who lose the ability to swallow secretions, and in those with decreased levels of consciousness in the final stages of life. It can be distressing for parents/carers but not necessarily for the child/young person since they are often unconscious at this stage. Early intervention with anti-secretory agents can be of benefit. A hyoscine hydrobromide (scopoderm) patch provides a non-invasive method of treatment but may not be of benefit as the symptom worsens. Subcutaneous/intravenous hyoscine hydrobromide can be used, although as it crosses the blood–brain barrier it may cause neurological side effects and agitation. Glycopyrronium is a useful alternative and may be used whilst the child/young person is still conscious, as it does not cross the blood–brain barrier and can be given orally or via subcutaneous/intravenous infusions. Non-pharmaceutical methods, such as repositioning to avoid pooling of secretions, can be helpful. Oral/pharyngeal suction is sometimes beneficial however excessive suction should be discouraged as it may stimulate more secretions.

Bleeding

Significant bleeding is uncommon in children/young people. Persistent oozing e.g. bleeding gums can be managed with topical agents such as tranexamic acid or adrenaline 1:1000 applied directly to the bleeding point. If low platelets are a contributory factor, a platelet transfusion should be considered as appropriate.

In the palliative phase a significant bleed is a possibility and this should be explained to the parents. Medication for anxiety (Midazolam), agitation (Midazolam) and breathlessness (Diamorphine/Morphine) should be made available.

Syringe Drivers

A syringe driver is an infusion pump used to give continuous medication parenterally, usually over a 24 hr period. Syringe drivers can deliver medication intravenously (e.g. via central venous catheter) or subcutaneously. It is particularly suitable for children who are unable to tolerate oral medication or who require immediate control of difficult symptoms, unresponsive to other intervention. Although it is a common route to administer medication at the end of life, it can also be used for short periods to gain control of difficult symptoms or when the oral route is temporarily impractical (e.g persistent vomiting).

As recommended by MHRA an anti-syphon extension should be used with any syringe driver.
**Indications for using a syringe driver**

- Inability to absorb, tolerate or take oral medication
- Difficulty in swallowing
- Persistent vomiting
- Bowel obstruction
- Severe weakness/semi-unconscious state
- Alternative routes not appropriate
- Unsatisfactory response to oral routes
- Patient/parent anxieties

**Advantages of using this delivery system are**

- Delivers drugs at an even rate continuously, maintaining plasma concentration without peaks and troughs
- May minimise the number of injections required
- Mobility and independence is maintained
- The ability to deliver complex drug combinations safely

Certain drugs can be mixed together and given in the same syringe driver. Others will require the use of a separate syringe driver. The compatibility of drugs should always be checked. In some situations up to 5 drugs can be mixed in one driver. Advice regarding mixing of 3 or more drugs should be sort from the specialist palliative service.

**Notes on using syringe drivers**

- It is usual practice to change the syringe every 24 hours
- Discuss with specialist palliative team if the mixing of more than three drugs in one syringe is indicated.
- Check with your own pharmacy or specialist service before using any unusual combinations
- Avoid high concentrations of drug combinations especially when using cyclizine
- Never use chlorpromazine, prochlorperazine and diazepam subcutaneously
### Table 12. Drugs and Doses

Drugs and doses should be used in conjunction with standard paediatric text *(Medicines for Children, 2003)*

Dilution advice for I.V and S.C use is not given; Dilute as indicated in package insert. Consult your unit policy regarding drug compatibility in syringe drivers.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Route</th>
<th>Dose</th>
<th>Times daily</th>
<th>Preparations</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenaline 1:1000</td>
<td>Small external bleeds</td>
<td>Topical</td>
<td>See note</td>
<td>Single dose</td>
<td>1:1000 solution</td>
<td>Soak gauze, apply directly to bleeding point.</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>Neuropathic pain</td>
<td>Oral</td>
<td>2-12 years: 200-500mcg/kg (max 25mg) 12-18 years: 10-25mg gradually increasing to 75mg</td>
<td>Nocte</td>
<td>Tablets: 10 mg, 25 mg, 50 mg Oral solution: 25mg in 5 ml 50mg in 5 ml,</td>
<td>Higher doses sedating. May cause urinary retention, constipation and dry mouth. Initial dose may be increased as tolerated if required, up to 2-12 years: 1mg/kg twice daily on specialist advice 12-18 years: doses &gt;75mg daily on specialist advice only</td>
</tr>
<tr>
<td>Baclofen</td>
<td>Start dose Muscle spasm</td>
<td>Oral</td>
<td>1-10yr: 2.5mg &gt;10yrs: 5mg</td>
<td>3</td>
<td>Tablets: 10 mg Liquid: 5 mg in 5 ml</td>
<td>Increase dose every 3 days to maintenance dose. Maximum daily dose 100mg. Preferably with or after food. Can cause sedation on initial commencement of drug Avoid rapid withdrawal: withdraw over 1-2 weeks. Use with caution in epilepsy as lowers seizure threshold. Decrease dose by 50% and frequency to once daily in patients with renal failure. Monitor and review reduction in muscle tone and potential adverse effects on swallow and airway protection.</td>
</tr>
<tr>
<td></td>
<td>Maintenance dose Muscle spasm</td>
<td>Oral</td>
<td>1-2yr: 5-10mg 2-6yr: 10-15mg 6-10yr: 15-30mg &gt;10yr: 15-30mg</td>
<td>2</td>
<td>Tablets: 5 mg</td>
<td></td>
</tr>
<tr>
<td>Bisacodyl</td>
<td>Constipation</td>
<td>Oral/Rectal</td>
<td>4-10yr: 5 mg &gt;10 yrs 5-10mg</td>
<td>Nocte</td>
<td>Tablets: 5 mg Suppositories: 5 mg, 10 mg</td>
<td>Give tablets at night and suppositories in the morning. Stimulant laxative. Doses and frequency can be increased up to 15-20mg once daily. Acts in 12 hr po, 20-60 mins PR.</td>
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<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Route</th>
<th>Dose</th>
<th>Times daily</th>
<th>Preparations</th>
<th>Notes</th>
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<tbody>
<tr>
<td></td>
<td>Start dose</td>
<td>Oral</td>
<td>1month to 12yrs: 2.5mg/kg</td>
<td>2</td>
<td>Liquid: 100 mg in 5ml</td>
<td>Enzyme inducer therefore less commonly used compared with other neuropathic agents</td>
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<td></td>
<td>Nerve pain</td>
<td></td>
<td>12-18yrs: 100-200mg</td>
<td></td>
<td>Tablets: 100 mg, 200 mg, 400 mg</td>
<td>Seek specialist advise Increase starting dose by 2.5mg/kg/dose at weekly intervals.</td>
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<tr>
<td></td>
<td>Maintenanc</td>
<td>Oral</td>
<td>1month to 12 yrs: 5mg/kg</td>
<td>2-3</td>
<td>Modified release tablets: 200mg and 400mg</td>
<td>Doses up to 20mg/kg/day may be required.</td>
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<td></td>
<td>e dose</td>
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<td>12-18 yrs: 200-400mg</td>
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<td>Suppositories: 125mg, 250mg</td>
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<tr>
<td>Code</td>
<td>Moderate</td>
<td>Oral/Rectal</td>
<td>&gt;12yr: 30-60mg</td>
<td>4-6</td>
<td>Syrup: 25 mg/5 ml</td>
<td>Constipating - prescribe with a laxative. Reduce dose in moderate renal failure. Recent advice: not recommended in under 12 years Seek local guidance about alternatives</td>
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<tr>
<td>ine</td>
<td>Pain/</td>
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<td>Maximum dose 240mg/24hours</td>
<td></td>
<td>Tablets: 15 mg, 30 mg, 60mg</td>
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<td></td>
<td>Diarrhoea</td>
<td></td>
<td>NB: should not be used &lt;12 years</td>
<td></td>
<td>Suppositories: 1mg, 2mg, 3mg, 6mg.</td>
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<td>Codeine</td>
<td>Oral/Rectal</td>
<td>&lt;2 year:0.5-1mg/kg</td>
<td>3</td>
<td>Tablets 50 mg</td>
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<td></td>
<td>phosphate</td>
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<td>2-5 yr: 12.5 mg</td>
<td>3</td>
<td></td>
<td>Commonly used for emesis associated with raised intracranial pressure. Maximum single dose &lt; 6yr 25mg &gt;6yr 50mg Maximum dose 150mg/24hrs)</td>
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<td>(now</td>
<td>Moderate</td>
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<td>6-12 yr: 25 mg</td>
<td>3</td>
<td>Injection 50 mg/ml (can be given Orally)</td>
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<td>contrain</td>
<td>Pain/</td>
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<td>&gt;12 yr: 50 mg</td>
<td>3</td>
<td>Suppositories ‘specials’</td>
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<td>Diarrhoea</td>
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<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Route</th>
<th>Dose</th>
<th>Times daily</th>
<th>Preparations</th>
<th>Notes</th>
</tr>
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<tbody>
<tr>
<td>Cyclizine</td>
<td>Nausea and vomiting</td>
<td>Subcutaneous/Intra venous</td>
<td>3mg/kg to a max 150mg/day(adult dose)</td>
<td>Continous over 24 hrs</td>
<td>Injection 50 mg/ml</td>
<td>Commonly used for emesis associated with raised intracranial pressure.</td>
</tr>
<tr>
<td>Danthron (co - danthramer)</td>
<td>Constipation</td>
<td>Oral</td>
<td>&lt;12yr: 2.5-5ml of 25/200</td>
<td>1 - 2</td>
<td>Suspension: 25/200 in 5ml</td>
<td>Stimulant laxative. Acts in 6 - 12 hrs. Increase dose if needed. May make urine red and stain skin. May cause superficial burns to skin: Use with caution in children who are incontinent, have urinary catheters in situ or using nappies Only licensed for use in terminally ill children.</td>
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<td>&gt;12yr: 2.5-20ml of 25/200</td>
<td>1 – 2</td>
<td>Strong suspension: 75/1000 in 5ml Capsule: 25/200 37.5/500</td>
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<td>&lt;12 yr 1-2 capsules(25/200)</td>
<td>1-2</td>
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</tr>
<tr>
<td>Dexamethasone</td>
<td>Raised intracranial pressure:</td>
<td>Oral/subcutaneous/intravenous</td>
<td>1 month-12 yr 250 microgram/kg 12-18 yr: 4mg</td>
<td>2</td>
<td>Tablets: 0.5 mg. 2mg Injection: 4 mg/ml (can be given orally)</td>
<td>Use minimum dose for effect. Short course if possible (eg 3-5 days) and then stop or reduce dose by 25-50% if need to continue. If stopping after prolonged course, tail off dose slowly rather than stop abruptly. Fast s/c or IV can cause sensation of perineal burning to occur. Where dose is divided, give morning and lunch-time as can disrupt night-time sleep. Behavioural changes may occur: this is not dose dependant and varies from individual to individual. Maximum 16mg/24hrs If using high dose, reduce risk of gastritis by co-prescribing proton pump inhibitor. ^For nausea associated with chemotherapy, give dose during chemotherapy and for 48 hrs after chemotherapy finished. Dexamethasone should not be used in the following circumstances unless approved by a consultant: 1. Regimens containing steroids 2. Brain tumour protocols 3. Retinoblastoma protocols ^Bowel obstruction is rare in children and specialist advice should be sought. In this context dexamethasone may help by reducing peri-tumour oedema.</td>
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<tr>
<td></td>
<td>headache</td>
<td></td>
<td>1 month-12 yr: 125-500 microgram/kg 12-18 yr: 4 mg</td>
<td>2</td>
<td>Oral solution: 2mg in 5 ml</td>
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<td></td>
<td>Raised intracranial pressure:</td>
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<td>2</td>
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<td>Other symptom</td>
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<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
<td>Notes</td>
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<tr>
<td>Dexamethasone (continued)</td>
<td>Spinal cord compression</td>
<td>Oral/ Subcutaneous/ Intravenous (slowly over 3-5mins)</td>
<td>2-5yr: 2mg, 6-12yr: 3mg, &gt;12yr: 4-8mg</td>
<td>2</td>
<td>See above</td>
<td>See above</td>
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<tr>
<td></td>
<td>Peripheral nerve compression</td>
<td>Oral/ Subcutaneous/ Intravenous (slowly over 3-5mins)</td>
<td>Birth-18yr: 125-500microgram/kg</td>
<td>2</td>
<td></td>
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<tr>
<td></td>
<td>Nausea associated with chemotherapy</td>
<td>Oral/ Subcutaneous/ Intravenous (slowly over 3-5mins)</td>
<td>1-5yr: 1-2mg, 6-12yr: 2-4mg, &gt;12yr: 4mg</td>
<td>3</td>
<td></td>
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<tr>
<td></td>
<td>Pain</td>
<td>Oral/ Subcutaneous/ Intravenous (Slowly over 3-5mins)</td>
<td>Low dose: 2-5yr: 0.5-1mg, 6-12yr: 1-2mg, &gt;12yr: 2-4mg</td>
<td>2</td>
<td></td>
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<td></td>
<td>High dose: 2-5yr: 2mg, 6-12yr: 3mg, &gt;12yr: 4-8mg</td>
<td>2</td>
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<tr>
<td></td>
<td>Bowel obstruction</td>
<td>Oral/ Subcutaneous/ Intravenous over 3-5mins</td>
<td>200-500micrograms/kg</td>
<td>1</td>
<td></td>
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<tr>
<td>Diamorphine*</td>
<td>Severe pain</td>
<td>Intravenous/ Subcutaneous</td>
<td>20-100 microgram/kg/hr, or convert from Oral morphine sulphate by dividing total 24 hr dose by 3</td>
<td>Continuous infusion over 24hr</td>
<td>Injection: 5 mg, 10 mg, 30 mg, 100 mg, 500 mg for dilution</td>
<td>Used in infusions because much more soluble than morphine. Sleepiness, drowsiness, urinary retention and itching are common after commencing opiates: they normally begin to wear off after 48 hrs. Consider use of antihistamines or Eurax cream.</td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
<td>Notes</td>
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<tr>
<td>Diazepam</td>
<td>Anxiety</td>
<td>Oral</td>
<td>1 month-1yr: 50 microgram/kg&lt;br&gt;2-12yr: 2-3mg&lt;br&gt;&gt;12yr: 2-10mg</td>
<td>2&lt;br&gt;3&lt;br&gt;3</td>
<td>Tablets: 2 mg, 5 mg, 10 mg&lt;br&gt;Syrup: 2 mg in 5 ml, 5 mg in 5 ml&lt;br&gt;Rectal tubes: 2 mg in 1 ml, 5 mg in 2.5 ml, 10 mg in 2.5 ml&lt;br&gt;Suppositories: 10 mg&lt;br&gt;Injection: 10 mg in 2 ml</td>
<td>Usually effective &lt;12 years. Keep daily dose below 10 mg in this category.</td>
</tr>
<tr>
<td></td>
<td>Persistent seizures</td>
<td>Rectal</td>
<td>Birth-1month: 1.25-2.5mg&lt;br&gt;1 month-2yr: 2.5-5mg&lt;br&gt;2-12yrs: 5-10mg&lt;br&gt;&gt;12yr: 2-30mg</td>
<td>single dose</td>
<td>single dose&lt;br&gt;single dose&lt;br&gt;single dose&lt;br&gt;single dose</td>
<td>Diazepam is used for emergency control of seizures; however buccal midazolam is used more often in this setting. Repeat if necessary after 5 mins.</td>
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<td></td>
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<td>Intravenous (over 3-5mins)</td>
<td>Birth-12yr: 300-400 microgram/kg&lt;br&gt;12-18yr: 10-20mg</td>
<td>single dose</td>
<td>single dose&lt;br&gt;single dose&lt;br&gt;single dose</td>
<td>Repeat if necessary after 15 mins</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>Mild/moderate pain, Inflammation</td>
<td>Oral Rectal</td>
<td>6 months-12yr: 0.3-1 mg/kg&lt;br&gt;&gt;12yrs: 25-50mg&lt;br&gt;Maximum 150 mg/24 hrs</td>
<td>3&lt;br&gt;2-3</td>
<td>Tablets: 25 mg, 50 mg&lt;br&gt;Dispersible: 50 mg&lt;br&gt;Slow release tablets/ capsules: 75 mg, 100 mg&lt;br&gt;Suppositories: 12.5 mg, 25 mg, 50 mg, 100 mg</td>
<td>Avoid in children with renal failure. Caution in children with thrombocytopenia.</td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
<td>Notes</td>
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<tr>
<td>Docusate sodium</td>
<td>Constipation</td>
<td>Oral</td>
<td>6-months-12yr: 2.5mg/kg</td>
<td>2-3</td>
<td>Capsules: 100 mg Elixir: 12.5 mg in 5 ml, 50 mg in 5 ml</td>
<td>Stimulant/softener. Large initial dose and reduce. Dilute Oral preparation with milk or orange juice. Oral acts in 1 - 2 days</td>
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<td></td>
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<td></td>
<td>&gt;12yr: 100mg</td>
<td>2-3</td>
<td>2-3</td>
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<tr>
<td>Domperidone</td>
<td>Nausea and vomiting</td>
<td>Oral</td>
<td>1 month-12yr: 200-400 microgram/kg</td>
<td>4</td>
<td>Tablets: 10 mg Suspension: 5mg in 5ml</td>
<td>Before food and at night. Not often used in children &lt; 2 years as extrapyramidal side effects can occur.</td>
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<td>&gt;12yr: 10-20mg</td>
<td>4</td>
<td>4</td>
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<td></td>
<td></td>
<td>Rectal</td>
<td>2-12yr: 15-30mg</td>
<td>2-3</td>
<td>Suppositories: 30 mg</td>
<td>Can repeat rectal doses: &lt;25kg: twice 25-35kg: 3 times &gt;35kg: 4 times</td>
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<td></td>
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<td></td>
<td>&gt;12yr: 30-60mg</td>
<td>2-4</td>
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<tr>
<td>Fentanyl</td>
<td>Pain</td>
<td>Transdermal</td>
<td>Start with 25 microgram/hr patch and monitor closely or convert from Oral morphine dose: see notes</td>
<td>One patch every 3 days</td>
<td>Transdermal patches 12microgram/hr 25micrograms/hr, 50micrograms/hr, 75micrograms /hr, 100micrograms/hr</td>
<td>For stable pain only. Conversion: Fentanyl = total oral morphine/24hr 12mcg/hr= 30-50mg 25microgram/hr = 50-135mg 50microgram/hr = 135-224mg 75microgram/hr = 225-314mg 100microgram/hr = 315-404mg Continue Oral Immediate release preparation for 12hrs after start of first patch. Review dose at each patch change. Wait 24-48hrs before changing dose Avoid exposing patch to excessive heat (sunbathing; hot water bottle etc). Always provide appropriate doses for breakthrough pain. If stopping introduce replacement analgesia gradually. Remember fentanyl will be effective for up to 12hr after removal of the patch.</td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
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<tr>
<td>Fentanyl (continued)</td>
<td>Pain</td>
<td>Lozenge (Actiq®) (with integral oromucosal applicator)</td>
<td>No relationship to dose of background analgesia. Therefore start at 200 microgram and titrate up according to response.</td>
<td></td>
<td>200 microgram, 400 microgram, 600 microgram, 800 microgram, 1200 microgram, 1600 microgram.</td>
<td>Contact PTC team for advice. Useful for breakthrough and incident pain. Form may be acceptable to children. Place lozenge between your cheek and gums. With the handle move the lozenge around cheeks gently (to avoid ulcers) twirling the handle against the buccal mucosa rather than sucking for maximum efficacy. You may take a little water before using Actiq if you have a dry mouth, but do not eat or drink while using Actiq. There are other Fentanyl preparations including buccal and sublingual tablets and intranasal spray. Seek specialist guidance for their use.</td>
</tr>
<tr>
<td>Gabapentin (PTO for maintenance dose)</td>
<td>Starting dose Nerve pain (PTO for maintenance dose)</td>
<td>Oral</td>
<td>2-12yr: 10mg/kg 12-18 years 300mg</td>
<td>See notes</td>
<td>Capsules: 100 mg, 300 mg, 400 mg</td>
<td>Give once daily on day one, twice daily on day two and 3 times daily on day three increasing to maintenance dose or until symptoms improve. Capsules may be opened and contents given in strong flavoured liquid. Avoid abrupt withdrawal reduce gradually over a minimum of one week In renal failure reduce frequency of dose.</td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
<td>Notes</td>
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<tr>
<td>Gabapentin (continued)</td>
<td>Maintenance dose</td>
<td>Oral</td>
<td>2-12yr: 10-20 mg/kg 12-18yr: 300-800mg</td>
<td>3</td>
<td></td>
<td>Target maintenance dose&lt;br&gt;May be effective given twice daily. Doses up to 70mg/kg/day may be required</td>
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<tr>
<td></td>
<td>Nerve pain</td>
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<tr>
<td>Glycopyrronium bromide</td>
<td>Noisy breathing, retained secretions</td>
<td>Intravenous/subcutaneous</td>
<td>1 month-18yr: 4-8 microgram/kg (maximum 200 microgram)</td>
<td>Single dose</td>
<td>Injection 200 microgram in 1ml</td>
<td>Single dose may be repeated up to 4 times in 24hrs</td>
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<td></td>
<td></td>
<td>Subcutaneous</td>
<td>1 month-18yr: 10-40 microgram/kg (maximum 1200 microgram)</td>
<td>Continuous infusion over 24hr</td>
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<td>Oral</td>
<td>1 month-18yr: 40-100 microgram/kg</td>
<td>3-4</td>
<td>Named patient tablets imported through IDIS</td>
<td>Oral dose is ten times parenteral dose.</td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
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<tr>
<td>Granisetron</td>
<td>Nausea and vomiting; opioid induced itch</td>
<td>Oral</td>
<td>1 month-12yr: 20 microgram/kg (maximum 1mg)</td>
<td>2</td>
<td>Tablets 1mg, 2mg.</td>
<td>May cause constipation</td>
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<td>&gt;12yr: 1mg</td>
<td>2</td>
<td>Injection 1mg in 1ml (1ml and 3ml vial)</td>
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<tr>
<td></td>
<td></td>
<td>Intravenous (slowly over 5 minutes)</td>
<td>1 month-12yr: 40 microgram/kg (maximum 3mg)</td>
<td>1</td>
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<td>&gt;12yr: 3mg</td>
<td>1</td>
<td></td>
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<tr>
<td>Haloperidol</td>
<td>Nausea and vomiting</td>
<td>Oral</td>
<td>1 month-12 yrs: 12.5-25 microgram/kg maximum 10mg/24hr</td>
<td>2</td>
<td>Tablets: 1.5 mg, 5 mg, 10 mg, 20mg.</td>
<td>Haloperidol is second line therapy for nausea and vomiting of unknown, non-specific, drug induced and metabolic causes if cyclizine or 5-HT antagonists are ineffective.</td>
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<td>&gt;12 yrs: 0.5-2mg maximum 30mg/24hr</td>
<td>2-3</td>
<td>Capsules: 500 micrograms</td>
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<td>Liquid: 1mg in 1ml, 2mg in 1ml</td>
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<td></td>
<td>Injection: 5 mg in 1ml 20 mg in 2ml</td>
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<td></td>
<td>Subcutaneous</td>
<td>25-50 microgram/kg</td>
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<td></td>
<td>Continuous infusion over 24hr</td>
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<td>Agitation/ anxiety</td>
<td>Oral</td>
<td>2-12yr: 12.5-25 microgram/kg maximum 10mg/24hr</td>
<td>2</td>
<td></td>
<td>Haloperidol is second line therapy for anxiety if benzodiazepines are contraindicated or ineffective.</td>
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<td>&gt;12yr: 1.5-10mg maximum 60mg/24hr</td>
<td>2</td>
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<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
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<tr>
<td>Hyoscine hydrobromide</td>
<td>Noisy breathing, Hypersalivation</td>
<td>Transdermal</td>
<td>&lt;3 yrs: 1/4 patch 3-9yr: ½ patch &gt;9 yrs: 1 patch</td>
<td>Over 72hr</td>
<td>Transdermal: 1.5mg patch released at rate of 1mg over 72 hrs. (Scopaderm patch)</td>
<td>Apply to clean dry hairless area. Can be stuck between shoulder blades, but only 60% absorption. Half a patch between shoulders may be more practical than ¼ patch behind ear. Cover part of patch or cut for smaller doses. Patch may inflame site therefore move site regularly. Use prophylactically at first signs of excess secretions. Crosses the blood-brain barrier, can cause CNS side effects, and Glycopyrronium (which does not cross the blood brain barrier) may be preferable. Can occasionally exacerbate restlessness. Tolerance can develop so patch may need to be changed every 48 hours</td>
</tr>
<tr>
<td>Subcutaneous/ Intravenous</td>
<td></td>
<td>1-12yr: 10 microgram/kg &gt;12yr: 400 microgram</td>
<td>Up to 4</td>
<td>Up to 4</td>
<td>Continuous infusion over 24hr</td>
<td></td>
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<tr>
<td>Subcutaneous/ Intravenous</td>
<td></td>
<td>20-60 microgram/kg Maximum 2.4g/24hr</td>
<td>Continuous infusion over 24hr</td>
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<tr>
<td>Ibuprofen</td>
<td>Pain, inflammation</td>
<td>Oral</td>
<td>1 month-12yr: 5mg/kg Maximum 20mg/kg/day up to 2.4g/24hr &gt;12yr: 200-600 mg Maximum 2.4g/24hr</td>
<td>3-4</td>
<td>Tablets: 200 mg, 400 mg, 600 mg Suspension: 100 mg in 5ml Granules: 600mg per sachet</td>
<td>Modified release preparations available. Avoid in children with renal failure. <strong>Caution in children with thrombocytopenia.</strong> With or after food</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Pain resistant to other measures</td>
<td>Oral, buccal, intravenous, subcutaneous,</td>
<td>See notes</td>
<td></td>
<td></td>
<td>Contact PTC team</td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
<td>Notes</td>
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<tr>
<td>Lactulose</td>
<td>Constipation</td>
<td>Oral</td>
<td>&lt;1yr: 2.5ml</td>
<td>1-2</td>
<td>Solution: 3.1-3.7g/5ml</td>
<td>Osmotic laxative. Titrated according to response. Acts over 24 hrs.</td>
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<td>1-5yr: 5ml</td>
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<td>5-10yr: 10ml</td>
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<td></td>
<td>&gt;10yr: 15ml</td>
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<tr>
<td>Levomepromazine</td>
<td>Nausea and vomiting.</td>
<td>Oral</td>
<td>0.25-1mg/kg (maximum 25mg/24hrs)</td>
<td>3-6</td>
<td>Tablets: 25 mg 6mg as named patient</td>
<td>Sedative at higher doses. May lower seizure threshold.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subcutaneous</td>
<td>100-250 microgram/kg (discuss max dose with PTC)</td>
<td>Continuous</td>
<td>Injection: 25 mg in 1ml</td>
<td></td>
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<tr>
<td></td>
<td>Terminal restlessness</td>
<td>Subcutaneous</td>
<td>350 microgram/kg</td>
<td>Continuous</td>
<td>Continuous infusion over 24hr</td>
<td>For paediatric start at 6-12mg and can increase with symptoms</td>
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<td></td>
<td></td>
<td>Intravenous</td>
<td></td>
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<td>Adult dose: 25-50mg/24 hours increasing to 200mg/24 hours if necessary.</td>
</tr>
<tr>
<td>Loperamide</td>
<td>Diarrhoea</td>
<td>Oral</td>
<td>&lt;12yr: 100-200 microgram/kg 12-18yr: 2-4mg</td>
<td>3-4</td>
<td>Capsules: 2 mg Syrup: 1 mg/5 ml</td>
<td>Maximum adult dose 16mg/24hr</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Anxiety</td>
<td>Oral/Sublingual</td>
<td>25-50 microgram/kg (maximum 1mg)</td>
<td>Single dose</td>
<td>Tablet 1mg (scored). 2.5mg</td>
<td>Most children will not require more than 0.5-1mg as a trial dose. Single dose can be repeated. Tablet can be used sublingually. Maximum 4mg/24 hours</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Nausea and vomiting (slowly over 3mins)/ Subcutaneous</td>
<td>Oral/ Intra</td>
<td>100 microgram/kg</td>
<td>3</td>
<td>Tablets: 5mg, 10 mg Solution: 5mg in 5ml</td>
<td>Dystonic reactions can occur at any dose, reversed with benztropine. Higher doses may be needed with chemotherapy but &lt;12 years should not exceed 500 microgram/kg(max 10mg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intravenous/Subcutaneous</td>
<td>300 microgram/kg</td>
<td>Continuous</td>
<td>Injection: 5 mg in 1ml</td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
<td>Notes</td>
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</tr>
<tr>
<td>Movicol</td>
<td>Chronic constipation</td>
<td>Oral powder</td>
<td>&lt; 1 year 1/2 - 1 sachet daily 1-6 yrs 1 sachet daily (max 4 sachets)</td>
<td>1-2</td>
<td>Movicol paediatric plain</td>
<td>For chronic constipation, adjust dose to produce regular soft stools</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(mix content in 1/4 of a glass of water (approx 60-65 mls); total daily dose to be taken over a 12 hour period)</td>
<td>6-12 yrs 2 sachet daily (max 4 sachets)</td>
<td></td>
<td></td>
<td>For faecal impaction after the start dose, treat until impaction resolves as below.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral powder</td>
<td>&lt; 1 yr 1/2 - 1 daily 1-5 yr 2 sachets on first day 5-12 yr 4 sachets on first day</td>
<td></td>
<td></td>
<td>1-5 yrs 4 sachets daily for 2 days, then 6 sachets daily for 2 days, then 8 sachets daily</td>
</tr>
<tr>
<td></td>
<td>Faecal impaction</td>
<td>Oral powder</td>
<td>&lt; 1 yr 1/2 - 1 daily 1-5 yr 2 sachets on first day 5-12 yr 4 sachets on first day</td>
<td></td>
<td></td>
<td>5-12 years increase in steps of 2 sachets daily to max 12 sachets daily</td>
</tr>
<tr>
<td>Micro-enema (sodium citrate)</td>
<td>Constipation</td>
<td>Rectal</td>
<td>&lt;3yr: ½-1 enema (insert only half nozzle length) &gt;3yr: 1 enema</td>
<td></td>
<td>Enema: 5ml</td>
<td>Do not use in children who are neutropenic or thrombocytopenic. Acts in 15 - 30 minutes.</td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
<td>Notes</td>
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</tr>
<tr>
<td>Midazolam</td>
<td>Urgent control of Seizures</td>
<td>Intravenous (slowly over 3 mins)/Subcutaneous</td>
<td>100-200 microgram/kg</td>
<td>Single dose</td>
<td>Injection: 10mg in 2ml, 10mg in 5ml</td>
<td>See also protocol for status epilepticus in your unit</td>
</tr>
<tr>
<td></td>
<td>Urgent control of Seizures</td>
<td>Buccal/intranasally</td>
<td>Birth-6 months:0.3mg/kg</td>
<td></td>
<td>Buccal Liquid 10mg/1ml</td>
<td>Squirt about half of the prescribed dose between the lower gums and</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6-12 months:2.5mg(2.5ml)</td>
<td></td>
<td></td>
<td>the cheek on one side of the mouth. Squirt the remaining liquid</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1-4 yrs:5mg(5ml)</td>
<td></td>
<td></td>
<td>between the lower gums and the cheek on the other side of the mouth.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5-9 yrs:7.5mg(0.75ml)</td>
<td></td>
<td></td>
<td>For children towards the top of the age range or those with prolonged</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;10yr:10mg(10ml)</td>
<td></td>
<td></td>
<td>seizures a second dose may be administered if no effect is apparent</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>after 10 minutes. A third dose must not be administered sooner than 6</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>hours after giving the second dose. Alternatively it can be administered</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>intranasally into each nostril if there is excessive salivation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intravenous/Subcutaneous</td>
<td>10-300 microgram/kg/hr</td>
<td>Continuous</td>
<td>Infusion over 24hr</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anxiety, Agitation,</td>
<td>Intravenous (slowly over 3 mins)</td>
<td>100-200 microgram/kg</td>
<td>Single dose</td>
<td></td>
<td>Single doses may be repeated as required.</td>
</tr>
<tr>
<td></td>
<td>Terminal restlessness.</td>
<td>Subcutaneous/Intravenous</td>
<td>100microgram/kg</td>
<td>Single dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Terminal restlessness.</td>
<td>Subcutaneous/Intravenous</td>
<td>300-700microgram/kg</td>
<td>Continuous</td>
<td>Infusion over 24hr</td>
<td>Titrate up as necessary</td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
<td>Notes</td>
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<td>-------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Morphine * sulphate</td>
<td>Moderate/severe pain</td>
<td>Oral/ Rectal</td>
<td>See notes</td>
<td>Immediate release: 6</td>
<td>Immediate release: Oral solution (oromorph) 10 mg/5ml, 100 mg/5ml</td>
<td>Co-prescribe laxatives. Start by giving an immediate release preparation at the starting doses shown on a PRN 4hrly basis. Once the child’s dose is stable on immediate release preparations, convert to a sustained release preparation. For the twice daily sustained release preparations (MST, Zomorph and MST granules) the dose should be calculated by adding up the total immediate release dose given in 24 hrs and dividing by 2. Sleepiness, drowsiness, urinary retention and itching are common after commencing opiates; they normally begin to wear off after 48 hrs. Consider use of antihistamines or Eurax cream.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Starting doses:</td>
<td></td>
<td>Tablets immediate release (sevredol) 10mg, 20mg, 50mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 month-1 yr: 80 microgram/kg</td>
<td></td>
<td>Tablet/capsule sustained release (MST) 5 mg, 10 mg, 15 mg, 30 mg, 60 mg, 100 mg, 200 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt; 1 yr: 200-400 microgram/kg</td>
<td></td>
<td>Capsule sustained release (Zomorph) 10mg, 30mg, 60mg, 100mg, 200mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2-12yr: 200-500 microgram/kg</td>
<td></td>
<td>Granules for suspension (sustained release): 20mg, 30mg, 60mg, 100mg, 200mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt; 12 yrs: 10-15 mg</td>
<td>See notes</td>
<td>Suppositories: 10mg, 15mg, 20mg, 30 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>For sustained release</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naproxen</td>
<td>Pain</td>
<td>Oral/ Rectal</td>
<td>5-10 mg/kg</td>
<td>2</td>
<td>Tablets: 250mg, 500mg</td>
<td>Avoid in children with renal failure. Caution in children with thrombocytopenia. With or after food.</td>
</tr>
<tr>
<td></td>
<td>Inflammation</td>
<td></td>
<td>Maximum 1g/24hr</td>
<td></td>
<td>Suspension: 125mg/5 ml-import</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sweating</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ondansetron</td>
<td>Nausea and vomiting; opioid induced itch</td>
<td>Oral</td>
<td>1 - 12yr: 4mg</td>
<td>2</td>
<td>Tablets/melts: 4 mg, 8 mg</td>
<td>Constipation is a common side effect. Give orally after initial IV dose. Continue for up to 5 days after course of chemotherapy. Can be repeated every 8-12 hours during chemotherapy. Can be repeated every 8-12 hours after chemotherapy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt; 12yr: 8mg (max 8mg)</td>
<td>2</td>
<td>Syrup: 4 mg in 5 ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Injection: 4 mg in 2ml, 8mg in 4ml</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Intravenous (slow over 3-5 mins)</td>
<td>1-3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 - 12yr: 5mg/m²</td>
<td>1-3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt; 12yr: 8mg (max 8mg)</td>
<td>1-3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
<td>Notes</td>
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</tr>
<tr>
<td>Paracetamol</td>
<td>Pain</td>
<td>Oral</td>
<td>1-3 months: 20mg/kg 3 months - 1yr: 60-120mg (maximum 80mg/kg/24hrs)</td>
<td>8 hourly</td>
<td>Tablet: 500mg</td>
<td>Maximum total dose in 24 hours: &lt;3 months: 60mg/kg &gt;3 months-12 years: 90mg/kg &gt;12 yrs: 4g Dose related toxicity in hepatic failure; in moderate renal failure (creatinine clearance 10-50ml/min/1.73m²) the minimum interval between doses is 6 hours. In severe renal failure (creatinine clearance &lt;10ml/min/1.73m²) the minimum interval is 8 hrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1-5yr: 120-250mg (maximum 80mg/kg/24hrs)</td>
<td>4-6 hourly</td>
<td>Dispersible tablet: 500mg.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6-12yr: 250-500mg (maximum 80mg/kg/24hrs)</td>
<td>4-6 hourly</td>
<td>Oral solution: 120mg in 5ml.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;12yr: 500mg-1g (maximum 80mg/kg/24hrs)</td>
<td>4-6 hourly</td>
<td>Oral suspension: 120mg in 5ml; 250mg in 5ml.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4-6 hourly</td>
<td>Injection: 500mg/50ml( for children &gt;10kg) 1000mg/100ml</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Paracetamol</td>
<td></td>
<td>Rectal</td>
<td>Birth -1 month: 20mg/kg</td>
<td>8 hourly</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 month -12yr: 20mg/kg (maximum 90mg/kg/24hrs or 4g/24hrs)</td>
<td>4-6 hourly</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;12yr: 500mg-1g (maximum 90mg/kg/24hrs or 4g/24hrs)</td>
<td>4-6 hourly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intravenous</td>
<td></td>
<td></td>
<td>Children weighing 10 - 33kg 15mg/kg</td>
<td>4 hourly</td>
<td></td>
<td>Paracetamol solution is administered as a 15-minute infusion. Minimal interval between each dose is 4 hours. It is recommended when giving paracetamol to patients with severe renal impairment creatinine clearance &lt;30ml/min, that the minimum interval between each administration be increased to 6 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Max daily dose 60mg/kg (without exceeding 2g)</td>
<td>4 hourly</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Children weighing &gt;33kg 15mg/kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Max daily dose 60mg/kg (without exceeding 3g)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Route</td>
<td>Dose</td>
<td>Times daily</td>
<td>Preparations</td>
<td>Notes</td>
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</tr>
<tr>
<td>Senna</td>
<td>Constipation</td>
<td>Oral</td>
<td>&lt;2 yrs: 0.5ml/kg</td>
<td>1</td>
<td>Tablets 7.5 mg</td>
<td>Stimulant laxative. Acts in 8 - 12 hrs.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2-6 yrs, 2.5 - 5 ml or ½ - 1 tablet</td>
<td>1</td>
<td>Syrup 7.5 mg in 5 ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;6 yrs, 5 - 10 ml or 1 - 2 tablets</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Tranexamic acid | Bleeding gums and small bleeds   | Oral  | 1 month-12yr: 25mg/kg  
>12yr: 1-1.5g | 3           | Tablets 500 mg                     | Can use Intravenous solution as mouthwash diluted 1:1 or can apply undiluted intravenous solution directly to bleeding point. Reduce dose in renal failure. Caution in haematuria because of risk of clot retention. |
|             |                                     |       |                                     | 3-4         | Syrup 500 mg in 5 ml      |                                                                      |
|             |                                     |       |                                     |             | Injection 100mg in 1ml    |                                                                      |

*For these preparations, buccal route has been used. Seek specialist advice*
13.
MANAGEMENT OF FLUID AND ELECTROLYTES
13. Management of fluids and electrolytes

Introduction
Management of fluid and electrolyte imbalance forms an important part of the care of paediatric oncology patients. Although some problems are peculiar to patients with malignancies their management follows general paediatric principles. The chapter has been written to provide uniformity of treatment.

In places the document is quite prescriptive. If the particular preparation mentioned is not available in the hospital pharmacy, local guidelines should be used. Where management of electrolyte imbalance becomes very complex and complicating factors like renal impairment are present, always consult the relevant PTC/PICU/renal/endocrine centres for advice and/or patient transfer.

Calculation of electrolyte and fluid deficits is provided in Appendices A and B for the sake of completion. This protocol is in keeping with APLS guidelines. The information about the use of hypertonic (2.7% commercially available; or 3%) saline has been obtained from the South Thames Retrieval Service clinical guidelines section, including the instructions on how to make it up correctly should this be required. It should be stressed that this should only be administered following discussion with a consultant, and, in the case of a critically unwell child, in liaison with the relevant PICU team.

Causes of fluid and electrolyte imbalance in paediatric oncology
Paediatric oncology patients are at high risk of developing fluid balance abnormalities and electrolyte disturbances. These may occur in the following settings:

- During hyperhydration given as part of standard chemotherapy regimens.
- During induction chemotherapy for acute leukaemia, where hyperhydration is essential for the prevention of acute tumour lysis syndrome.
- As part of treatment of tumour lysis syndrome, characterised by hyperkalaemia, hyperphosphataemia, hyperuricaemia and hypocalcaemia.
- Following nephrotoxic chemotherapy (e.g. cisplatin, ifosfamide), which may cause a renal tubular leak, resulting in renal loss of electrolytes, particularly sodium, potassium, magnesium and phosphate.
- As a result of chemotherapy causing vomiting, diarrhoea or mucositis, leading to dehydration, hypokalaemia, hypo- or hypernatraemia, or hypomagnesaemia.
- In post-stem cell transplant patients with gastrointestinal graft-vs-host disease, where fluid and electrolyte loss from the gut may be severe and prolonged.
- In patients with acute septic shock where profound hypotension may require significant fluid resuscitation.
- In febrile patients, in whom insensible fluid losses may be increased.
- In patients with central diabetes insipidus e.g. as a result of a brain tumour (especially craniopharyngioma) or Langerhans Cell Histiocytosis. This may cause dramatic life-threatening intracerebral fluid and sodium shifts unless managed correctly.
- In patients with veno-occlusive disease (VOD) of the liver, most common after stem cell transplant using busulphan-containing conditioning regimens.
- In patients with disseminated malignancy who are at risk of hypercalcaemia.
Some drugs can cause a syndrome of anti-diuretic hormone secretion (SIADH), with hyponatraemia, e.g. vincristine, carbamazepine.

These guidelines discuss the general management of certain fluid and electrolyte disturbances, and some specific scenarios. Topics where the fluid and electrolyte management is covered as part of a section within another chapter of these guidelines have been cross-referenced rather than repeated here. These include: Hyperhydration for the prevention and treatment of tumour lysis syndrome, Septic shock and Veno-occlusive disease.

**Electrolyte Disturbances**

**Sodium**

Sodium is the major extracellular cation. Its movement is, therefore, inextricably linked to that of water. Disorders of sodium are predominantly those of dehydration/under-hydration, or overhydration, and thus management is largely linked to management of fluid balance.

**Hyponatraemia**

**Definition:** Na < 135mmol/l (mild 130-134mmol/l; moderate 127-129mmol/l; severe < 126mmol/l)

**Clinical features:** asymptomatic in mild and sometimes moderate cases; nausea, lethargy, headache, altered level of consciousness, seizures.

**Figure 4. Causes of Hyponatraemia**

- **Dilution / Water Excess**
  - Excess water ingestion / administration
  - Oedema (cardiac failure / renal or hepatic impairment / drugs e.g. imatinib)
  - SIADH (drugs, infection, lung disease)
  - Hyperglycaemia (e.g. patients on steroids)
  - Drugs (e.g. carbamazepine, vincristine, cyclophosphamide, NSAIDs)
  - Infections (e.g. RSV)
  - Increased dose of desmopressin (DDAVP)

- **Sodium Depletion (renal and extra-renal loss)**
  - Diuretics
  - Renal salt-wasting secondary to chemotherapy e.g. cisplatin, ifosfamide, cyclophosphamide
  - Glycosuria
  - Hypotonic fluid replacement of losses
  - High insensible losses, excessive sweating
  - Glucocorticoid insufficiency

- **Pseudohyponatraemia**
  - Severe hypoalbuminaemia / proteinuria
  - Severe hyperlipidaemia
  - Hyperglycaemia
Low Na <135mmol/l

Check paired serum and urine electrolytes and osmolality; blood glucose

CONSIDER use of hypertonic saline UNDER CONSULTANT / PICU GUIDANCE ONLY (dependent on patient's clinical condition): 3% NaCl 3ml/kg iv over 20minutes. This should raise the Na level by 2-3mmol/l; more if there is a large associated diuresis. Monitor Na levels closely. Doses may be repeated if necessary – no maximum number of doses – depends on sodium level response. An acute rise in Na level of no more than 10mmol/l over 24 hours is probably safe. Hypertonic saline can safely be given via a central or peripheral line. (SEE BELOW FOR PREPARATION OF 3% SALINE).

NOTE: Ready-made solutions of 2.7% saline are available (dose also 3ml/kg over 20mins) - use exactly as for 3% saline.

Treat symptoms, e.g. seizures.

Dehydrated / Under-hydrated

- Rehydrate with 0.9% NaCl +/- KCl iv over 24-48hrs to replace existing / ongoing extracellular fluid losses; hyponatraemia will gradually correct.
- If patient on Parenteral nutrition (PN) consider increasing the sodium concentration in PN.

Over-hydrated / Oedematos

- Fluid restrict to 50% of maintenance fluids.
- Use 0.9% NaCl +/- KCL iv if unwell / not drinking.
- If patient on PN consider increasing the sodium concentration in PN.

Normally hydrated, well

- Look for cause (e.g. chronic renal loss).
- Consider oral NaCl supplements.

NOTE: Management of hyponatraemia depends very much on the clinical condition of the patient and the likely underlying cause, rather than merely the absolute sodium value.

Hypertonic saline (2.7% or 3% saline)

In addition to being used for the treatment of severe hyponatraemia or symptomatic hyponatraemic seizures, hypertonic saline is also used for the treatment of cerebral oedema and raised intracranial pressure, with some advantages over mannitol (see chapter 6 on management of raised intracranial pressure).

Intravenous hypertonic saline induces a shift of fluid from the intracellular to the extracellular space across the osmotic gradient it generates. It therefore reduces brain water, increases blood volume and increases plasma sodium. Note that intracellular volume is inversely proportional to plasma sodium concentration.
Figure 6. Preparation of 3% Saline using 30% Saline

**NB!** Use commercial ‘ready-made’ hypertonic saline solutions (2.7%) if available in preference to mixing 3%, to reduce the risk of drug preparation errors. They are almost identical and should be used in the same way.

DO NOT connect the 500ml bag of 3% saline directly to the patient’s iv line (RISK OF SERIOUS ACUTE SODIUM OVERLOAD IF ENTIRE BAG IS ACCIDENTALLY INFUSED.) ALWAYS withdraw the prescribed dose of 3% saline (eg 3ml/kg) and administer to patient separately.

**In case of accidental overdose of 3% saline:**

- Disconnect 3% saline infusion immediately and contact PICU for advice.
- Give 1mg/kg iv frusemide immediately, aiming for a natriuresis of 6ml/kg/hour, which may be enough to keep Na level within the safe range.
- Measure plasma Na every 30-60 minutes for trend. (indications for dialysis include oliguria, anuria or Na level rising rapidly ie >5mmol/hour.)
- **DO NOT** attempt to correct Na with free water or use 0.45% saline (risk of sudden drop in brain osmolality).

**Hypernatraemia**

**Definition:** Na >145mmol/l (and usually not symptomatic/problematic >150mmol/l).

**Clinical features:** symptoms and signs of dehydration; altered level of consciousness, seizures.

**Causes:** Usually due to water loss rather than sodium excess:

- Diarrhoea
- High insensible fluid losses
- Water deprivation
- Diabetes insipidus (central or nephrogenic), omission of desmopressin (DDAVP)
- Obstructive uropathy
- Excess sodium administration / iatrogenic
Potassium

Hypokalaemia

Definition: K< 3.5 mmol/l (with/without ECG changes)

Clinical features: Usually asymptomatic. Muscle weakness, lethargy, paralytic ileus, decreased deep tendon reflexes, rhabdomyolysis.

ECG changes (normally occur when K < 2.5mmol/l): ST segment depression, small T-wave amplitude, U waves, prolonged QT and arrhythmias including ventricular tachycardia, ventricular fibrillation or Torsades de Pointes.

Causes:

- Inadequate intake
- Renal loss e.g. diuretics, renal tubular leak secondary to disease or drugs
- Gastrointestinal loss (diarrhoea & vomiting)
- Sepsis
- Steroids
- Primary or secondary hyperaldosteronism (salt & water are retained)
- Skin loss via excessive sweating / insensible losses
- Shifts from extracellular to intracellular compartments may be caused by alkalosis, hyperglycaemia, insulin, B-adrenergic agonists, e.g. salbutamol.
- Drugs eg penicillins, amphotericin B/liposomal Amphotericin.
- Bicarbonate
In patients receiving hyperhydration for tumour lysis prevention or treatment, low K should not be corrected until symptomatic and even then only on discussion with consultant, since total body potassium is likely to be high rather than low.

*If hypokalaemia is severe, or child unwell, always check acid-base status*

**Figure 8. Management of hypokalaemia**

<table>
<thead>
<tr>
<th>K 2.8-3.4mmol/l</th>
<th>Hypokalaemia (K &lt; 3.5mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>K &lt; 2.8 mmol/l, or symptomatic hypokalaemia, or poor tolerance of enteral supplements?</td>
</tr>
</tbody>
</table>

- Oral supplements preferred unless patient vomiting or has poor gastrointestinal absorption.
- Calculate maintenance requirement + deficit, and adjust dose according to response.
  - Preparations include:
    - KCl syrup = 1mmol/ml
    - Effervescent K = 6.5mmol/tablet
    - Slow K = 8mmol/tablet
- Amiloride (potassium-sparing diuretic) may be used in conjunction with potassium supplements.
  - Children < 20kg use 2.5mg po daily
  - Children ≥20kg use 5mg po daily

- If child on PN, increase potassium concentration in PN.
- Diluted intravenous KCl via a central line is the treatment of choice.
- Calculate potassium deficit + daily maintenance requirement & aim to replace in iv fluids over 24 hrs; more quickly if severe ongoing losses or potassium level severely low.
- Maximum concentration of potassium in iv fluids is 40mmol/l via a peripheral vein, due to irritant nature of iv preparations.
- In the acute situation where it is necessary to raise levels more quickly, 0.2 to 0.5mmol/kg/hr, diluted in the required volume of 0.9% NaCl may be used; ideally give over 2 hours. FASTER RATES MAY CAUSE ARRHYTHMIAS.
- Check K level 6 hours after replacement; earlier check may be in-accurate.

If patient has hypokalaemia AND hypophosphataemia, consider using potassium phosphate instead of potassium chloride. (Be aware potassium phosphate also contains sodium).

Oral: Effervescent phosphate sandoz (per tablet) = 16mmol phosphate, 3mmol potassium, 20mmol sodium

iv: 20ml iv solution = 40mmol phosphate, 30mmol potassium, 30mmol sodium

1 month – 2 yrs: use 0.7mmol/kg/day of phosphate.
**Hyperkalaemia**

**Definition:** K > 5.5mmol/l (with/without ECG changes)

**Clinical features:**
Muscular weakness, reduced deep tendon reflexes, paralytic ileus, abdominal pain, respiratory paralysis, cardiac arrhythmias / arrest (most common at K levels > 7.5mmol/l). Features of the underlying cause, e.g. renal failure, may be apparent.

**ECG changes:** Peaked T-waves > 5mm tall, decreased QT interval, short PR interval (becoming prolonged as K level rises), wide QRS complexes, broad & flat P-waves, ST changes, bradycardia, ventricular fibrillation or asystole.

**Causes:**

- Beware of pseudohyperkalaemia e.g. traumatic haemolysed samples, delay in analysis, contamination with EDTA and tumour lysis with cell breakdown in the sample tube
- Tumour lysis syndrome at start of chemotherapy in haematological emergencies.
- Potassium overload / iatrogenic: in iv fluids, PN, drugs (penicillins), transfusions.
- Reduced potassium excretion e.g. renal failure, adrenal insufficiency, potassium-sparing diuretics (spironolactone, amiloride), drugs (e.g. ciclosporin).
- Catabolic states wherein K is released from cells e.g. haemolysis, acidosis.
- Drugs causing shifts from the extracellular to intracellular fluid compartments e.g. B-blockers, suxamethonium.
- Hyperglycaemia
- Haemolytic Uraemic Syndrome
Figure 9. Management of hyperkalaemia

Generally speaking, a potassium level between 5.0 and 6.0 mmols/l need not be treated acutely but rather monitored closely.

**Hyperkalaemia**
(K > 5.5mmol/l)
If >7mmol – speak to renal team and PICU team early

**Step 1:** Remove potassium from iv fluids, PN etc & stop oral potassium & potassium-sparing diuretics.
Continuous cardiac (ECG) monitoring. Check blood gas-

ECG changes?

- Yes
- No

**Step 2:** Give only if ECG changes:
Onset < 2 minutes
Calcium gluconate 10% 0.5ml/kg = 0.1mmol/kg IV, maximum 20ml slow bolus over 5-10 minutes
(Central access: give neat. Peripheral access: Dilute 1ml in 4ml 0.9% NaCl ).
**FOR CARDIAC ARREST:** Give stat and neat, centrally or peripherally.
Repeat dose in 5 min if no ECG improvement.
If patient on digoxin give over 30min to avoid arrhythmias.
Calcium chloride may be used instead of calcium gluconate. (Avoid calcium chloride if respiratory acidosis or respiratory failure).
Adverse effects: bradycardia, tissue injury when extravasated.

**Step 3:** Insulin & dextrose AND β2 stimulants (salbutamol) TOGETHER
(40-50% of pts are non-responders to salbutamol alone so avoid monotherapy)
**Insulin & dextrose** (Onset 10-30min)
Insulin 0.05-0.1units/kg/hr with 10% dextrose in 0.9% NaCl 5ml/kg/hr.
Tritrate to keep blood glucose > 6mmol/l.
If blood glucose < 6mmol/l give 5ml/kg bolus of 10% dextrose in 0.9% NaCl before starting infusions.

**With Salbutamol** (Onset 5-30min):
If self-ventilating patient: nebulised salbutamol (dose by age):
Age <2.5yrs = 2.5mg ;>2.5yrs = 5mg
Otherwise salbutamol 4micrograms/kg iv over 5 min
(Central neat, peripheral dilute 1mg in 2ml 0.9% NaCl)
Repeat dose until ECG & K normalised
In **CARDIAC ARREST USE ADRENALINE INSTEAD OF SALBUTAMOL:**
Do not use together as they work on the same β2 receptors
Adrenaline 10micrograms/kg iv (0.1ml/kg of 1:10 000 neat). Repeat as needed.
Do not give blood transfusion if K >7mmol/l

**Step 4:** In refractory cases refer for dialysis if necessary (Guy’s or GOSH Renal Unit).

**Step 5:** In refractory cases with metabolic acidosis (pH<7.2) infuse sodium bicarbonate 1mmol/kg/hr for 4-6hrs.
(Single stat dose has no benefit)
**Calcium**

Calculate the corrected calcium for serum albumin concentration:

Corrected Calcium = Measured Calcium + \((40 – \text{serum albumin}) \times 0.02\)

**Hypocalcaemia**

**Definition:** Corrected Ca < 2mmol/l

**Clinical features:** weakness, cramps, tetany, seizures, hypotension, and cardiac arrhythmias.

**ECG changes:** If severe - prolonged QT, pulseless electrical activity (PEA), ventricular fibrillation

**Causes:** May be part of any severe illness, e.g. septicaemia.

- Tumour lysis syndrome
- Pancreatitis (e.g. caused by asparaginase)
- Acute or chronic renal failure
- Citrate infusion (e.g. in massive blood transfusions), post autologous or allogeneic stem cell infusion

**Management:** Treatment should be considered if patient is symptomatic.

_IN THE SETTING OF TUMOUR LYSIS, CALCIUM MUST NOT BE GIVEN AS RENAL FAILURE MAY BE PRECIPITATED._

(Phosphate binders & haemofiltration / dialysis may be required in this situation - discuss with consultant on call and renal team, especially if phosphate >2mmol/l.)

Treat underlying cause.

In an arrest situation calcium gluconate (10%) 0.5ml/kg may be given stat and neat.

Otherwise, give as an intravenous slow bolus: calcium gluconate (10%) 0.07mmol/kg over 5-10 min or as a 24 hr infusion 0.2 mmol/kg/hr (via central line, as it is an irritant.)

Can also use calcium chloride (10%) 0.2 mmol/kg iv slow bolus (<12yrs)

5-10 mmol iv slow bolus (>12yrs)

**Orally:** 0.2 mmol/kg 8 hourly (<12yrs)

4-8mmol 8 hrly (>12yrs)
**Hypercalcaemia**

**Definition:** Corrected Calcium > 2.7mmol/l

**Clinical features:** may be asymptomatic or present with anorexia, malaise, polyuria, abdominal pain, vomiting, weight loss, failure to thrive, renal calculi/colic, hypertension, behavioural disturbances.

**ECG changes:** short QT, other arrhythmias

**Causes:**

- Disseminated malignancy
- Idiopathic / iatrogenic e.g. thiazide diuretics
- Hyperparathyroidism
- Excess vitamins A or D
- Post rhabdomyolysis

**Management:** Isolated hypercalcaemia in the absence of symptoms may not require treatment. Treatment is required if **corrected calcium** level > 2.7 mmol/l and/or patient is symptomatic. Treatment may be inappropriate in patients with progressive refractory malignancy in the palliative care setting.
**Figure 10. Management of hypercalcaemia**

Hypercalcaemia (Corrected Ca > 2.7mmol/l)

- Hyperhydrate with 0.9% saline at 3-4l/m²/day for 24 hours.
- Ensure adequate diuresis of >1ml/kg/hr using 0.5-1mg/kg frusemide iv/po (maximum does 40mg, then assess response) as required.
- Treat underlying malignancy.

Corrected Ca still > 2.7mmol/l after 24 hours of hyperhydration

Assess renal function (governs choice of bisphosphonate). **Seek advice from PTC before starting treatment.**

Creatinine normal or < 1.5x normal for age

**Sodium clodronate**
- Suggested paediatric dose is 20mg/kg in 0.9% saline (as small a volume as possible) iv over 4 hours, to a maximum adult dose of 1500mg in 500ml 0.9% saline.
- Continue IV hydration at 2-3l/m²/day.
- If no response after 7 days, dose should be repeated.

Creatinine > 1.5x normal for age

Discuss with the renal +/- endocrine team

**Disodium pamidronate**

Dose depends on serum corrected calcium level. Suggested paediatric dose is:

- 0.4mg/kg IV over 4 hrs if calcium 2.7-3mmol/l
- 0.8mg/kg IV over 8 hrs if calcium 3.1-4mmol/l
- 1.2mg/kg IV over 8 hrs if calcium > 4mmol/l

Adult (maximum) dose is:

- 30mg IV over 4 hrs if calcium 2.7-3 mmol/l
- 60mg IV over 8 hrs if calcium 3.1-4 mmol/l
- 90 mg IV over 8 hrs if calcium > 4 mmol/l

**Note:** May take 48hrs to have an effect, so dose should not be repeated as there is a risk of hypocalcaemia.

Glucocorticoids and Calcitonin may be considered if hypercalcemia is refractory to above treatment measures.
Magnesium

Hypomagnesaemia

**Definition:** Mg < 0.6 mmol/l +/- ECG changes

**Clinical features:** may be asymptomatic; severity of symptoms may not correlate with serum Mg level. Hypertension, anorexia, nausea, vomiting, lethargy, weakness, muscle cramps, paraesthesiae, irritability, confusion, seizures. Often occurs in conjunction with hypocalcaemia or hypokalaemia.

**ECG changes:** Arrhythmias eg Torsades

**Causes:**
- Diarrhoea
- Renal tubular leak, particularly in post-BMT patients.
- Pancreatitis (e.g. secondary to asparaginase)
- Drugs (e.g. amphotericin, aminoglycosides, cisplatin, ciclosporin, pentamidine, diuretics, laxatives)
- TPN
- Poor magnesium intake

**Figure 11. Management of hypomagnesaemia**

| Well child; adequate enteral absorption: |
| Magnesium glycerophosphate: 0.2mmol/kg po 8hrly (<12yrs) or 4-8mmol po 8hrly (>12yrs) |

| Unwell child; severe hypomagnesaemia or poor enteral absorption: |
| Magnesium sulphate: 0.2mmol/kg IV 12 hourly (<12yrs) or 4mmol IV 12 hourly (>12yrs) over 30min-2 hours (dilute to a 10% solution with 5% dextrose or 0.9% saline) |
Hypermagnesaemia

Definition: Mg > 2mmol/l +/- ECG changes

Clinical features: nausea, muscle weakness, hyporeflexia, sedation, hypoventilation, respiratory acidosis, hypotension (due to vasodilatation), bradycardia, arrhythmias, and respiratory paralysis.

ECG changes: Arrhythmias, bradycardia, heart block

Causes:
- Increased intake of magnesium supplements (especially in renal impairment)
- Rhabdomyolysis
- End-stage renal failure
- Adrenal insufficiency

Management:
Remove cause of elevated Mg levels. Infusion of calcium produces a short-lived reduction in serum Mg, but often improves clinical condition dramatically.

Calcium gluconate (10%) 0.07mmol/kg over 5-10 min or as a 24 hr infusion 0.2 mmol/kg/hr (via central line, as it is an irritant.)

Can also use calcium chloride (10%) 0.2 mmol/kg iv slow bolus (<12yrs) 5-10 mmol iv slow bolus (>12yrs)

Ensure adequate rehydration and force diuresis with frusemide 0.5-1mg/kg (maximum 40mg) if urine output < 1ml/kg/hr. Dialysis may be required if unable to diurese adequately.

Phosphate

(Refer to the tumour lysis management guidelines for the normal serum values of phosphate according to age)

Hypophosphataemia

Definition: Phosphate <1 mmol/l. Clinical symptoms usually starts when level is < 0.64mmol/l). Levels < 0.3mmol/l life threatening.

Clinical features: Irritability, disorientation, tremors, seizures, haemolytic anaemia, reduced myocardial function, potential respiratory failure, potential coma

Causes:
- Inadequate intake,
- Decreased absorption or increased losses from the gastrointestinal tract
- Increased renal phosphate excretion.

Management:
Identify the underlying cause and take steps to correct it.
Replacement is generally done very slowly because the actual serum level may not reflect a deficit in the intracellular compartment. Unless acute symptoms are present, phosphate depletion is treated by enteral administration of phosphorus: up to 6 mmol/kg/day divided into several doses to minimize diarrhoea.

Parenteral administration of phosphates is usually restricted to children with levels below 0.3 mmol/l: 0.15–0.33 mmol/kg as a continuous infusion over at least 6 hours. Either potassium phosphate or sodium phosphate may be used, with the potential associated complications associated with hyperkalaemia or hypernatraemia.

Other adverse effects of phosphate administration include hyperphosphataemia, which may result in hypocalcaemia, and hypotension. It must be well diluted to avoid irritation of the blood vessels, extravasation, or infiltration leading to tissue necrosis. Administration of large quantities of phosphorus may lead to precipitation with calcium if levels are not carefully monitored.

**Hyperphosphataemia**

**Definition:** Phosphate >1.4 mmol/l

**Clinical features:** tachycardia, hyperreflexia, abdominal cramps, nausea, diarrhoea, muscle tetany

An inverse relationship exists between phosphorus and calcium in the extracellular compartment. Therefore in conditions producing hyperphosphataemia, hypocalcaemia also exists. The relationship between these two imbalances accounts for the fact that the clinical signs and symptoms associated with hyperphosphataemia are the same as those found in the child with hypocalcaemia.

**Causes:**

- Chronic renal failure
- Tumour lysis

**Management:**

Adequate hydration/hyperhydration, diuresis
Aluminium antacids
For hyperphosphataemia due to renal failure, sodium bicarbonate may be used.
Correction of hypocalcaemia in children who do not have tumour lysis.
In refractory cases renal dialysis may be required.
Specific Fluid Balance Problems in Oncology Patients

*Diabetes Insipidus*

In paediatric oncology this is seen most frequently in the setting of patients with brain tumours (especially craniopharyngioma) or Langerhans Cell Histiocytosis (LCH). These patients tend to have central rather than nephrogenic diabetes insipidus, as a result of disruption of the hypothalamo-pituitary axis and consequent reduction in vasopressin (ADH) secretion. This results in the production of large volumes of dilute urine, with the risk of developing either hypernatraemic dehydration or hyponatraemia and water intoxication if not appropriately managed.

Treatment is with desmopressin/DDAVP under the expert guidance of a paediatric endocrinologist who should always be consulted at an early stage.

Children with this condition should have strict fluid balance monitoring whilst in hospital, as well as close monitoring of plasma and urine electrolytes and osmolarity. Large positive or negative fluid balances should be avoided. If the child starts producing large volumes of dilute urine with a resultant rise in plasma sodium, or shows a sudden reduction in urine output with a drop in plasma sodium, desmopressin doses are likely to need adjustment. This should always be done under senior / expert guidance.

Starting doses of desmopressin acetate:

**Intranasal:**
- 1 month – 2 years: 2.5-5microgram 1-2 times daily
- 2-12 years: 5-20microgram 1-2 times daily
- 12-18 years: 10-20microgram 1-2 times daily

**Oral:**
- 1 month – 2 years: 10microgram 2-3 times daily
- 2-12 years: 50microgram 2-3 times daily
- 12-18 years: 100microgram 2-3 times daily

*Doses should be adjusted depending on response.*

**NOTE differences between intranasal and oral dosing schedules.**

Hyperhydation for the Prevention and Treatment of Tumour Lysis Syndrome (TLS).

[See Chapter 6 on Oncological Emergencies](#)

Septic Shock

[See Chapter 3 on Management of Infections](#)

Veno-occlusive disease

[See Chapter 6 on Oncological Emergencies](#)
Appendix A

Normal Daily Electrolyte Requirements

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>2-4 mmol/kg/day</td>
</tr>
<tr>
<td>Potassium</td>
<td>2 mmol/kg/day</td>
</tr>
<tr>
<td>Calcium</td>
<td>3 mmol/kg/day</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0.75 mmol/kg/day</td>
</tr>
</tbody>
</table>

Calculation of Electrolyte Deficit

Deficit (mmol) = (Normal level – actual level) x Weight (in kg) x 0.7

e.g. a 24kg child with serum potassium of 2.5 mmol/l

\[
\text{Deficit} = (4 - 2.5) \times 24 \times 0.7
\]

\[
= 25.2 \text{mmol}
\]

Maintenance = 2 mmol/kg/day

\[
= 2 \times 24
\]

\[
= 48 \text{ mmol}
\]

Thus, total requirement = Deficit + Maintenance

\[
= 25 + 48
\]

\[
= 73 \text{mmol}
\]

i.e. If poor oral intake will need maintenance hydration containing 73 mmol over next 24 hours.

If taking diet, and hence maintenance electrolytes, needs 25 mmol extra potassium over next 24 hours.

General Rules for Intravenous Electrolyte Administration

iv electrolytes may be put in 0.9% Normal saline, 5% dextrose, or 2.5% dextrose + 0.45% saline.

Magnesium sulphate and calcium gluconate or calcium chloride and potassium chloride can all be added to the same iv fluid bag if electrolyte concentrations are low (i.e. some cisplatin regimens + PN). If concentrations are too high, calcium sulphate precipitates. Thus at higher concentrations it is safe to mix only 2 supplements, i.e. CaCl & KCl, CaCl & MgCl, Mg SO4 & KCl, because MgSO4 & Ca preparations precipitate.
Appendix B

Fluid Balance

Calculation of daily fluid balance is important in all paediatric oncology patients, but is essential in those receiving intravenous fluids (especially hyperhydration regimens), post-stem cell transplant patients, those with gastrointestinal losses, those with renal or cardiac abnormalities (e.g. impaired cardiac function following previous anthracyclines), or those who are septic or unwell.

Weight and blood pressure are useful parameters in assisting with fluid balance interpretation. Insensible losses need to be considered in addition to charted fluid losses, so a positive balance on a fluid chart is usually not strictly accurate, as it does not account for these losses. Febrile patients will have higher insensible losses than afebrile patients.

For practical purposes, 1kg of weight = 1 litre of fluid.

No action should usually be taken on the basis of a single parameter. The child should be fully assessed, including BP, heart rate, respiratory rate, capillary refill time, temperature, weight and general condition.

If it is felt necessary to act on a positive fluid balance, a reduction in intravenous fluid rate may be sufficient. Older children can tolerate a larger positive fluid balance than younger ones, and larger patients can tolerate a larger positive fluid balance that smaller patients.

Diuretics should only be used in patients who are in too great a positive fluid balance for their clinical status. The choice of diuretic is frusemide 0.5-1mg/kg intravenously or orally (if intestinal absorption is not impaired) as a single dose, with assessment of subsequent urine output. Adult-sized patients should receive no more than 40mg of frusemide initially, followed by assessment of response. Frusemide may cause renal loss of sodium and potassium; plasma levels should be monitored. Beware of using diuretics in patients who have peripheral oedema but may, in fact, be intravascularly depleted, eg as evidenced by a baseline tachycardia.

Calculation of Fluid Requirements

Normal daily fluid maintenance requirement is calculated on the basis of fluid required to keep a patient well hydrated and passing reasonable amounts of urine. The standard calculation (based on APLS recommendations) includes the following considerations:

1. Baseline maintenance requirements
2. Replacement of insensible losses through sweating, respiration, normal stool loss (usually 10ml/kg in an adult, 20ml/kg in a child & 30ml/kg in a baby <1 year)
3. Replacement of essential urine output (=minimal urine output required for waste excretion)
4. Some extra fluid to maintain a modest state of diuresis

Total daily fluid requirement consists of:

Maintenance + Replacement of deficit (existing/on-going loss) + Resuscitation (if required)
Calculation of Maintenance Fluid Requirement
(Includes 1+2+3+4 above)

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Fluid Requirement per 24 hrs</th>
<th>Fluid Requirement per hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>First 10 kg</td>
<td>100ml/kg/24 hrs</td>
<td>4ml/kg/hr</td>
</tr>
<tr>
<td>Second 10 kg</td>
<td>50ml/kg/24 hrs</td>
<td>2ml/kg/hr</td>
</tr>
<tr>
<td>Each subsequent 1 kg</td>
<td>20ml/kg/24 hrs</td>
<td>1ml/kg/hr</td>
</tr>
</tbody>
</table>

\[
\begin{align*}
e.g. 24kg: & = (100 \times 10kg) + (50 \times 10kg) + (20 \times 4kg) \quad \text{OR} \quad 4 \times 10kg + (2 \times 10kg) + (1 \times 4kg) \\
& = 1000 + 500 + 80 \\
& = 1580\text{ml per 24 hours}
\end{align*}
\]

This shows that either method of calculating fluids is acceptable, giving reasonably close answers for fluids for a 24 kg child over a 24 hour period (indeed, the difference between the 2 methods is less than 2ml/hr).

In addition to the above maintenance fluid requirements, on-going losses (e.g. due to significant gastrointestinal losses i.e. diarrhoea or vomiting, polyuria) need to be considered and replaced. In febrile patients, insensible losses through sweating and respiration will be higher than usual; add +/- 13% extra fluid for each 1 degree C > 37.5 degrees C.

Replacement Fluid (Deficit = existing + on-going losses)

On-going losses, e.g. due to significant diarrhoea or vomiting, may be replaced intravenously on a ml-for-ml basis or as part-replacement if the patient is also tolerating some oral fluids. In practice, this involves adding up the previous 4-6 hours losses and replacing them intravenously, either as a short infusion, or over the subsequent 4-6 hours.

Existing losses (i.e. dehydration)

Percentage dehydration can be estimated clinically using the following parameters: (APLS guidelines)

To calculate Replacement fluids (according to % dehydration):

\[
\text{Fluid deficit (ml)} = \text{Percentage dehydration} \times \text{Weight (kg)} \times 10
\]
Resuscitation fluids

In an acutely unwell / dehydrated or shocked child, resuscitative fluids may be urgently required. Recommendations according to APLS guidelines are to give 20ml/kg of isotonic (0.9%) saline as an initial bolus, and then reassess according to usual clinical criteria. A second 20ml/kg may be given if required, but the need for this should raise the alert that anaesthetic and senior assistance /assessment is required as a matter of urgency. (See separate guidelines on ‘Shock’) 

e.g. A 24 kg child is 7.5% dehydrated, calculate fluid requirement. 
  (Assuming no resuscitation required) 
  Fluid deficit  = 7.5 x 24 x 10
              = 1800ml 
  (OR  7.5/100 x 24 x 1000) 

  Maintenance  = (100 x 10kg) + (50x 10kg) + (20x 4kg)
                    = 1000 + 500 + 80
                    =1580ml 

  Thus Total fluid requirement = Maintenance + Deficit + Resuscitation fluids
                               = 1580ml + 1800ml + 0 
                               = 3380ml over 24 hours 
                               (+ addition for on-going losses on a ml-for-ml basis) 

Electrolyte levels must be considered when considering choice of fluid & speed of rehydration. In a patient with hypernatraemic dehydration (Na>145), rehydration must be slow, i.e. over 48 hours rather than 24 hours. In hyponatraemic or normonatraemic dehydration, rehydration should be over a 24 hour period. (see section on hyper- and hyponatraemia.)

Choice of Fluids

1. Maintenance fluids & replacement of existing deficit
The majority of children may safely receive sodium chloride 0.45% with glucose 5% or sodium chloride 0.45% with glucose 2.5% (both hypotonic solutions). There is currently little evidence to recommend a particular strength of glucose. 
Sodium chloride 0.45% with glucose 2.5% (+ 20mmol KCl per litre of fluid) is normally used as hydration fluids with chemotherapy. Some regimens specify the addition of magnesium. 
Sodium chloride 0.45% with glucose 2.5% (NO POTASSIUM) is normally used in the prevention and management of tumour lysis). 
0.18% NaCl with 4% glucose should be restricted to use in PICU or in a renal unit. 

Some children at high risk of hyponatraemia should preferably receive isotonic solutions (sodium chloride 0.9% with glucose 5%, sodium chloride 0.9% or compound sodium lactate solution (Hartmann’s solution)
• intravascular volume depletion / hypotension; sepsis;
• excessive gastric or diarrhoeal losses;
• central nervous system (CNS) infection;
• head injury;
• bronchiolitis;
• salt-wasting syndromes;
• chronic conditions such as diabetes, cystic fibrosis and pituitary deficits. 

It is important to monitor electrolytes levels and adjust potassium concentration of fluids accordingly. Urine dipstick should be done routinely to monitor for hyperglycaemia.

2. Replacement fluids – on-going losses

Choice of replacement fluids for on-going losses should mirror the fluid being lost, with attention to electrolyte levels. Usually, losses due to diarrhoea or vomiting may be replaced using 0.9 % saline with added potassium (usually 20mmol KCl per litre of normal saline, but adjust according to electrolytes)

3. Resuscitation Fluids

There has been much debate over the years as to whether the resuscitation fluid chosen should be crystalloid, colloid or a combination of both. Current APLS guidelines recommend an initial 20ml/kg bolus of a crystalloid with electrolyte concentrations mirroring those of serum, i.e. 0.9% saline or Hartmann’s solution. If response is inadequate, a 2nd 20ml/kg bolus of the same fluid should be given.

### Features of Commonly used Intravenous Fluids in the UK

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Osmolarity (mOsmol/L)</th>
<th>Sodium content (mequiv/L)</th>
<th>Osmolality (compared to plasma)</th>
<th>Tonicity (with reference to cell membrane)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium chloride 0.9% with glucose 5%</td>
<td>586</td>
<td>150</td>
<td>Hyperosmolar</td>
<td>Isotonic</td>
</tr>
<tr>
<td>Sodium chloride 0.9%</td>
<td>308</td>
<td>154</td>
<td>Isomolar</td>
<td>Isotonic</td>
</tr>
<tr>
<td>Sodium chloride 0.45% with glucose 5%</td>
<td>432</td>
<td>75</td>
<td>Hyperosmolar</td>
<td>Hypotonic</td>
</tr>
<tr>
<td>Glucose 5%</td>
<td>278</td>
<td>-</td>
<td>Isomolar</td>
<td>Hypotonic</td>
</tr>
<tr>
<td>Glucose 10%</td>
<td>555</td>
<td>-</td>
<td>Hyperosmolar</td>
<td>Hypotonic</td>
</tr>
<tr>
<td>Hartmann’s *</td>
<td>278</td>
<td>131</td>
<td>Isomolar</td>
<td>Isotonic</td>
</tr>
<tr>
<td>Sodium chloride 0.18% with glucose 4%</td>
<td>284</td>
<td>31</td>
<td>Isomolar</td>
<td>Hypotonic</td>
</tr>
<tr>
<td>Sodium chloride 0.45% with glucose 2.5%</td>
<td>293</td>
<td>75</td>
<td>Isomolar</td>
<td>Hypotonic</td>
</tr>
<tr>
<td>4.5% human albumin solution</td>
<td>275</td>
<td>100-160</td>
<td>Isomolar</td>
<td>Isotonic</td>
</tr>
</tbody>
</table>

References

- Advanced Paediatric Life Support [http://www.alsg.org.uk/APLS](http://www.alsg.org.uk/APLS)
- Care of the Critically Ill Child. R. MacNab, D. Macrae, R. Henning. Chapter 2.10 Churchill Livingstone
- BNF for Children. 2013/2014
- South Thames Retrieval Service website ([www.strs.nhs.uk](http://www.strs.nhs.uk))
14.
MANAGEMENT OF LATE EFFECTS IN SURVIVORS OF CHILDHOOD CANCER
14. Management of late effects in survivors of childhood cancer

In the UK over 1700 children under the age of 15 years are diagnosed with cancer every year. Survival statistics have highlighted that, at present, over 75% of patients can be expected to be long term survivors. The Pan-Thames London childhood cancer population is served by three principle treatment centres (PTC) and a large number of POSCU across North and South Thames regions. The present estimate is that over 1800 long term follow-up patients are actively seen in the London area. There are a greater number of patients not actively seen, but who may require surveillance.

Long term sequelae can present at the end of treatment but, more importantly, can occur several years later. As a part of the NHS Cancer Reform Strategy the National Cancer Survivorship Initiative was set up in 2008. It outlines a 5 year plan to improve patients’ experience of living with cancer and beyond. The vision sets out that all cancer survivors should have:

- Individualised assessment and care plan
- Support to self-manage their condition
- Information on the long-term effects of living with and beyond cancer
- Access to specialist medical care for complications that occur after cancer treatment

In order to translate this into clinical practice, current management (where possible) should reflect the following pathway:

1. Referral of the survivor to the Late Effects clinic in a PTC, is usually 5 years after completion of treatment, but in certain circumstances (ie post HSCT or following brain tumour treatment) it may be earlier.

2. At referral, a multi-disciplinary meeting (Late effects clinician, endocrinologist, specialist nurse, psychologist and social worker) is held to devise a future plan for follow-up.

3. An individualized Care Plan is drawn up (Appendix A) which includes treatment summary, clinical systems at risk and outlines surveillance guidelines (Appendix B) for late effects, based on therapy received.

4. Either based on the individualized Care Plan or a Level of Care (Appendix C) assigned to a patient; follow-up may be in the PTC or shared with the POSCU. The long term objective is to develop a cost effective service which is patient centred, locally based where possible, age appropriate and takes into account the individuals’ risk of developing late consequences of treatment.

5. If the child is being followed-up in a local POSCU, then at 16 yrs (or in some cases 17-18 years), of age they should return to the Late Effects clinic at the PTC or to the adult long term follow-up clinic at 18 years of age if available locally (e.g in Brighton).

6. Following this, the goal is to prepare patients for transfer to the adult clinic which is done between the ages of 18-24 years depending on local set-up. Gradually, as services get better organised, level 1 and 2 patients will be discharged into primary care for managed self-care. However, provision should be made for surveillance investigations to take place in a timely manner and the PTC database updated annually. If the patient develops problems, they should be able to return to the teenage or adult clinic for review as required.

It must be recognised that the pathway outlined below is dependent on local services and resources.
The aims of long-term follow-up are

The timely diagnosis and treatment of late toxicities which may include:

a. Cardiovascular, neurocognitive, neurological, psychological, audiological, skeletal, dental, metabolic and endocrine late effects.

b. Prevention by identifying and treating pre-symptomatic hormonal abnormalities (growth, pubertal delay or advancement, thyroid or parathyroid over or under activity and cortical deficiency)

2. To provide information to survivors about future late effects eg. CCLG AfterCure booklets (www.aftercure.org), fact sheets and local information sheets.

3. To advise on lifestyle and health education issues, such as smoking and exposure to UV light

4. To discuss job selection, insurance etc.

5. Research: The survivors of childhood cancer provide an extremely important cohort for research into the incidence, natural history of late effects and the effect of treatment intervention. This research then influences the development of new protocols, and provides valuable information for the survivors, newly diagnosed patients and their families.
Survivors of childhood cancer at follow-up should have an opportunity to discuss the following

1. Quality of Life: Relationships, emotional function and sexual function, concerns re physical appearance and function, work performance including employment, insurance and related issues.

2. Compliance with medications, e.g. anti-infective prophylaxis, anti-hypertensives, hormone replacement therapy.

3. Lifestyle choices: smoking, alcohol and other risk behaviour

4. Exercise, diet and bone health

5. School attendance and performance

For the survivor and his/her family, this addresses their primary area of concern and also helps the clinician identify services for additional support in the school or local community.

Below is a brief tabulated summary of clinical history, examination and surveillance investigations which should be considered in long term survivors of childhood cancer. Surveillance is therapy based and individualized Care Plans will highlight specific late effects. Investigations may be carried out locally, based on resources.
Table 13. Summary of clinical history, examination and surveillance investigations

<table>
<thead>
<tr>
<th>Surveillance in clinic</th>
<th>Late Effects to consider</th>
<th>Tests</th>
<th>Advice/Referral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height, Weight, BMI</td>
<td>Obesity</td>
<td>Fasting glucose, lipids, LFT Assess insulin resistance/glucose tolerance if severe</td>
<td>Dietary advice (low GI diet) graded exercise</td>
</tr>
<tr>
<td>Height velocity, sitting height, pubertal stage</td>
<td>Early or late puberty, growth hormone deficiency</td>
<td>Gonadotrophins, sex hormones, thyroid function, bone age</td>
<td>Refer to Late Effects-endocrinology service</td>
</tr>
<tr>
<td>Menstrual history, erectile dysfunction, Tanner stage</td>
<td>Gonadal /germ cell failure or Leydig cell dysfunction</td>
<td>Gonadotrophins, sex hormones, thyroid function. Semen analysis when appropriate</td>
<td>Refer to Late Effects-endocrinology Assisted reproduction service</td>
</tr>
<tr>
<td>Joint pain (hip, knee) gait, fractures</td>
<td>Osteopenia/osteoporosis/ Avascular necrosis</td>
<td>Bone profile, DEXA scan/MRI</td>
<td>Encourage a calcium-rich diet, exercise. Refer to Late Effects-endocrinology service</td>
</tr>
<tr>
<td>Hearing and speech development</td>
<td>Sensori-neural hearing loss</td>
<td>Audiological tests</td>
<td>Refer to Audiology/speech and language therapist</td>
</tr>
<tr>
<td>Vision</td>
<td>Cataracts, dry eyes</td>
<td>Ophthalmoscopy</td>
<td>Refer to Ophthalmology</td>
</tr>
<tr>
<td>Dental Health</td>
<td>Caries, short dental roots, microdontia</td>
<td>Dental and oral mucosa examination</td>
<td>Advice on dental hygiene and refer to dentist/specialist orthodontist</td>
</tr>
<tr>
<td>Skin</td>
<td>Naevi, basal cell carcinoma in irradiation field</td>
<td>Measure number, change in size, pigmentation, surface</td>
<td>Refer to Dermatology</td>
</tr>
<tr>
<td>Exercise tolerance, shortness of breath</td>
<td>Cardiac dysfunction or obstructive/restrictive pulmonary defect</td>
<td>ECHO/ECG and/or pulmonary function tests</td>
<td>Refer to Late Effects-cardiology service</td>
</tr>
<tr>
<td>Renal</td>
<td>Isolated hypertension, glomerular/tubular dysfunction</td>
<td>Blood pressure, U&amp;E, urinalysis for proteinuria and haematuria. Estimate GFR if appropriate</td>
<td>Refer to Late effects-renal service</td>
</tr>
<tr>
<td>New masses, regular breast examination, neck masses, brain tumours</td>
<td>Second malignant neoplasms</td>
<td>Imaging</td>
<td>Refer to Late Effects-biopsy and further management</td>
</tr>
</tbody>
</table>

NB This not an exhaustive list but an illustration of common problems

All long-term survivors should have an identified key worker for clinicians/families to contact with concerns.

At Great Ormond Street Hospital the Long Term Follow Up administrator has been identified as a Keyworker and can be contacted on 0207 813 8127 or ltfu@gosh.nhs.uk. Concerns will then be forwarded to the relevant clinicians. At RMH the key worker who is a clinical nurse specialist can be contacted on 0208-661-3329. The key worker for the TYA service can be contacted on 0208-661-1238. For UCLH the LTFU website has been developed to improve communication and sharing of information. [http://www.ich.ucl.ac.uk/clinicalservices](http://www.ich.ucl.ac.uk/clinicalservices) indexed "long-term follow-up childhood cancer"
### Appendix A

**Individualised Care Plan**

(This document may be modified in the future)

**Treatment Summary and Long Term Follow Up Plan**

<table>
<thead>
<tr>
<th>Name:</th>
<th>Date of birth:</th>
<th>Address:</th>
<th>Hosp/NHS No:</th>
<th>Sex:</th>
<th>Consultant:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Diagnosis Date:</th>
<th>Stage/Group:</th>
<th>Treatment End Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trial/Protocol:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

**Recurrence of Disease**

No

<table>
<thead>
<tr>
<th>Date</th>
<th>Site/s</th>
<th>Management Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Chemotherapy**

Yes

<table>
<thead>
<tr>
<th>Drug Effects to Monitor</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Select</td>
<td></td>
</tr>
<tr>
<td>Select</td>
<td></td>
</tr>
<tr>
<td>Select</td>
<td></td>
</tr>
</tbody>
</table>

**Surgery**

Yes

<table>
<thead>
<tr>
<th>Date</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Radiotherapy**

No

<table>
<thead>
<tr>
<th>Date</th>
<th>Site/s</th>
<th>Total Dose</th>
<th>Fractions</th>
<th>Normal Tissues within Field</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Select</td>
<td>Gy</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td></td>
<td>Select</td>
<td>Gy</td>
<td>/</td>
<td>/</td>
<td>/</td>
</tr>
</tbody>
</table>

**Bone-marrow transplantation/PBSC**

No

<table>
<thead>
<tr>
<th>Type</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Conditioning Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug Effects to Monitor</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Body Irradiation</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Complications during treatment  No

Complications after treatment  Yes

Other Studies  N0

Familial factors and syndromes  N0

Treatment summary completed by:
Print Name  Date  /  /2010
Print Title  Clinical Nurse Specialist
**Systems at Risk and Care Plan**

**Growth Problems:** Should be none.

<table>
<thead>
<tr>
<th>Growth hormone started</th>
<th>Select</th>
<th>Start Date</th>
<th>Finish date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final height (cm)</td>
<td>cm</td>
<td>Date</td>
<td></td>
</tr>
<tr>
<td>Onset of Puberty</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Other growth problems** Select

**Fertility Problems:** Select Discussion with patient

<table>
<thead>
<tr>
<th>Menarche Date</th>
<th>Select</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular Periods?</td>
<td>Select</td>
<td>Date</td>
</tr>
<tr>
<td>Semen analysis Result</td>
<td></td>
<td>Date</td>
</tr>
</tbody>
</table>

**Hormone Problems:** Should be none.

**Heart Problems:** Should be none.

<table>
<thead>
<tr>
<th>Pre-treatment Result</th>
<th>Echo</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-treatment Result</td>
<td>Echo</td>
<td>Date</td>
</tr>
<tr>
<td>Follow-up Result</td>
<td>Echo</td>
<td>Date</td>
</tr>
<tr>
<td>Follow-up Result</td>
<td>Select</td>
<td>Date</td>
</tr>
<tr>
<td>Blood Pressure Result</td>
<td>mmHg</td>
<td>Date</td>
</tr>
<tr>
<td>Other abnormalities</td>
<td>/</td>
<td></td>
</tr>
</tbody>
</table>

**Lung Problems:** Should be none.

<table>
<thead>
<tr>
<th>Pre-treatment Result</th>
<th>Select</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post treatment Result</td>
<td>Select</td>
<td>Date</td>
</tr>
</tbody>
</table>

**Kidney Problems:** Should be none.

<table>
<thead>
<tr>
<th>Pre-treatment GFR Result</th>
<th>Select</th>
<th>mL/min</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post treatment GFR Result</td>
<td>Select</td>
<td>mL/min</td>
<td>Date</td>
</tr>
</tbody>
</table>

| Follow Up GFR Result | Select | mL/min | Date |
| Renal tubular dysfunction | Select | mL/min | Date |

**Problems with Brain/Nerves:** Should be none.

**Problems with other Organs/Tissues:** Should be none.

<table>
<thead>
<tr>
<th>Organ/Tissue</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Audiology</td>
<td></td>
</tr>
</tbody>
</table>

**Psychosocial/school/occupation issues**
Lifestyle
It is important to maintain a healthy lifestyle with a balanced diet, including '5 a day' of fruit and vegetables and taking part in regular exercise. Additionally avoid smoking and limit alcohol intake.

**Offspring (live births and miscarriages)**

<table>
<thead>
<tr>
<th>Information given to Patient/Family</th>
<th>Date given</th>
</tr>
</thead>
<tbody>
<tr>
<td>select /</td>
<td></td>
</tr>
<tr>
<td>select /</td>
<td></td>
</tr>
<tr>
<td>select /</td>
<td></td>
</tr>
</tbody>
</table>

**Follow-Up Plan**

- [ ] Disease Related Follow Up at Disease Related Follow Up at shared care hospital - Select
- [ ] Long Term Follow Up at PTC Long Term Follow Up at shared care hospital - Select
- [ ] Long Term Follow Up with GP

Long Term Follow Up due: Select Year.
Frequency of Long Term Follow Up, every: Select Frequency.
Review of follow-up plan
Name of shared care Consultant: _____
## Surveillance Required

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Start Date</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GENERAL</strong></td>
<td></td>
<td>Every appointment</td>
</tr>
<tr>
<td>Height and weight</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pubertal status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinalysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BLOOD TESTS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full blood count</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urea &amp; Electrolytes (Kidney Function)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver Function Test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipid profile (Cholesterol etc.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior Pituitary function tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonadotrophins (Sex Hormones)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid Function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GFR (Kidney Function)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>OTHER</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest x-ray</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DEXA Bone Scan</td>
<td></td>
<td></td>
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<tr>
<td>Interval MRI Scan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT Scan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Echocardiogram (Heart Function)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG (Heart Function)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung Function Tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Audiometry (Hearing Test)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Long Term Follow Up Care Plan completed by:
Print Name  
Print Title  
Confirmed by MDT
References

Therapy based guidelines are web based, readily accessible and easy to use in clinic, if further guidance is needed.

www.ukccsg.org.uk/public/followup/PracticeStatement/index.html

Therapy based long term follow up: Practice Statement. UK Children’s Cancer Study Group

www.survivorshipguidelines.org

Children’s Oncology Group: Long-Term follow-up guidelines for survivors of childhood, adolescent and young adult cancers

www.Sign.ac.uk/pdf/sign76.pdf

15. SOCIAL AND FINANCIAL SUPPORT AVAILABLE TO FAMILIES
15. Social and Financial Support Available to Families

The experience of coping with a diagnosis of childhood cancer is probably one of the most distressing life events that a family can face. All families with a child undergoing treatment for malignant disease are likely to need considerable emotional and practical support.

As treatment progresses many families become increasingly aware of the impact of the illness on their sick child, healthy siblings, as well as the marital and wider family relationships. Family members may welcome the opportunity to talk about their fears and feelings or seek information about how to access support for themselves, possibly through a parent support group. Apart from the emotional trauma of the illness the practical and financial impact can pose a serious strain on family functioning. Families frequently incur extra expenses travelling to and from treatment centres. In addition they may incur extra costs on heating, diet, childcare expenses, telephone, clothing etc. Frequently the disruption caused by the illness and treatment may hinder parents’ ability to work and this can have an adverse effect upon family finances.

Accessing help

The charity, CLIC Sargent, funds specialist social work posts at all CCLG (except Cardiff, which has LATCH social workers) treatment centres and all specialist TYA centres. CLIC Sargent social workers offer a service to children and young people under the age of 25 years affected by any form of cancer. These social workers are able to offer an assessment of a child and family's emotional, social and practical needs. On-going support may be offered on an individual, family or group basis. CLIC Sargent social workers have a good knowledge of statutory and voluntary support services available and can ensure that families access financial and other practical support appropriately.

Where a social worker is not available a CLIC Sargent or Macmillan nurse or a member of the paediatric community nursing team may be able to offer some advice and signposting to local sources of support.

Supporting patients and families

In 2005 Nice published guidance on how the NHS in England should deliver services to children and young people with cancer. The aim of this guidance was to improve not just clinical outcomes but the holistic experience of care for children and their carers. As a consequence of this guidance a review was set up and led by CLIC Sargent with the aim of developing a model of care which would best meet needs both in hospital and in the community. The key messages from this review “More Than My Illness” are as follows:

- Ensuring children and young people have access to information and are empowered to make informed choices
- The importance of the Key worker role as care co-ordinator
- Assessment and care planning processes at key stages of the treatment pathway
- Tailoring packages of care that are unique to a child and their family and take account of clinical, educational, social, emotional, practical and financial needs

Assessment of a child and family’s psychosocial needs is not a static event, but something that needs to be constantly revisited at key stages of the treatment pathway. Key trigger points for reassessment of a child or family’s needs following initial medical diagnosis might be:

- Any changes of concern in the child’s health and general development, behaviour or mood
- Any changes of concern in a parent or care giver (as above)
Any changes in a parent or care giver’s personal circumstances
- Impact of environmental factors such as housing, finance, employment, schooling etc
- Transitions – i.e. end of treatment, referral to long term effects clinic, transfer to adult care
- Relapse
- Palliative care
- Bereavement

Financial Assistance

Accessing additional financial support to manage the extra costs of care is a major concern for most families. CLIC Sargent social workers have a good knowledge of grant making bodies that may be able to offer financial help to families while treatment is in progress. CLIC Sargent also has a Welfare Advice line that can provide advice across a range of areas including the benefit system, housing, employment etc and how to access these resources.

In the absence of a CLIC Sargent Social Worker on site, specialist financial advice can be obtained online or by telephone from CLIC Sargent or Macmillan Cancer Support (see appendix for details).

Alternatively advice about benefits can be obtained from the local social security office or local citizens advice bureau.

Welfare reform

The benefits system is in the process of major change. The Welfare Reform Act 2012 has introduced a variety of changes to the benefit and tax credit systems. Some have taken effect; others will be rolled out over the next few years.

One of the main changes is the introduction of a benefit called Universal Credit which will replace six income related benefits namely:

- Income support
- Housing benefit
- Child tax Credit
- Working Tax Credit
- Income related Employment and Support Allowance
- Income Based Job seekers Allowance

The benefits listed above will be phased out between October 2013 and 2017. By 2017 the Universal Credit system will be fully operational. Families in receipt of the six benefits named above will be contacted over a period of time to arrange transfer to Universal Credits.

Whilst it is not possible here to list all available state benefits the main benefits that families should consider in relation to a malignant diagnosis are:

**Disability Living Allowance (DLA) for Children**

This benefit is for children under 16 years who have a serious illness or disability that need more help and assistance than other children of a similar age. Normally this help must have been needed for at least 3 months and must be likely to be needed for at least a further 6 months.

Disability Living Allowance has two parts called 'components':
- a care component - if you need help looking after yourself or supervision to keep you safe
- a mobility component - if you are unable to walk or find it very hard to walk, or you need help getting around

Some people will be entitled to receive just one component; others may get both. The care component and mobility component are paid at different rates depending on how their disability affects them.

DLA is not payable as of right. It is assessed on “need for care” after completion of a detailed form, part of which also has to be signed by someone who knows the child well, i.e. a carer, doctor, social worker, etc.

**Personal independence Payment**

Personal Independence Payment (PIP) is a new benefit that helps with some of the extra costs caused by long-term ill-health or a disability for people aged **16 to 64**.

To qualify a person must have a long-term health condition or disability and have difficulties with activities related to ‘daily living’ and or mobility. They must have had these difficulties for **3 months** and expect them to last for at least **9 months**.

Claims for PIP will be assessed by an independent health professional to help DWP work out the level of help needed. This may be a face-to-face consultation.

DWP makes the decision about the claim based on the results of the assessment, the application form and any supporting evidence included.

**Special rules for Disability Living Allowance/PIP**

If it is deemed that a child/young person’s life expectancy may be less that 6 months – it is possible to get these allowances processed more speedily and ensure that the care component of the benefit is paid at the highest rate. To get an application considered under the “special rules” it is necessary for a doctor to complete a DS1500 medical form for inclusion with the application.

Being in receipt of Disability Living Allowance/PIP may increase the amount of other benefits or credits individuals are entitled to such as:

- Income Support
- Income-related Employment and Support Allowance
- Income-based Jobseeker’s Allowance
- Pension Credit
- Housing Benefit
- Council Tax Benefit
- Working Tax Credit
- Child Tax Credit

N.B. note that some of these benefits will in time be replaced by Universal Credit
Disability Living Allowance/PIP is normally ignored as income for working out these income-related benefits and credits.

**Carers Allowance (CA)**

One parent/carer can apply for CA. The benefit is:

- Payable to a person caring for a sick or disabled child, who is in receipt of DLA care component at the middle or higher rate or PIP Personal Independence Payment daily living component
- Payable if the parent/carer does not earn above a certain amount
- This benefit is treated as income.

Further information about benefits is available from The Department of Work and Pensions (www.dwp.gov.uk) or local Citizens Advice Bureau. The latter organisation is particularly helpful for families who are dealing with debt and money management problems that require more specialist input.

**Debt management**

Families of a child undergoing cancer treatment may be more likely to get into debt due to reduced income and higher outgoings associated with treatment costs. However, it may be that they were managing significant debt prior to diagnosis which will have the effect of increasing overall stress levels.

Debt management is a complex topic and families should be encouraged to seek help as soon as possible. The CLIC Sargent welfare advice service and the Macmillan Cancer Support website can provide practical support and advice about how to approach this issue. Alternatively, any local CAB office can put families in touch with accredited money advice services.

**Organisations**

Useful contacts:

1. **CLIC Sargent**
   Horatio House
   77-85 Fulham Palace Road
   London W6 8JA
   Tel 0300 330 0803
   Web site www.clicsargent.org.uk

   Provides funding for care professionals at all CCLG and TYA centres that aim to provide emotional, psychological, social and financial support to children and young people under 25 affected by any form of childhood cancer. CLIC Sargent also has holiday resources for the use of families on treatment.

   CLIC Sargent provides an accredited telephone welfare advice service.
   Tel: 0800 9154439 or emailing welfareadvice@clicsargent.org.uk

   Advisers can give information about benefits as well as support and advice on welfare rights, for example, information about employment, family, debt, consumer and housing rights.
2. Macmillan Cancer Support

89 Albert Embankment
London SE1 7UQ
Tel 0808 808 0000
Email cancerline@macmillan.org.uk
Web site www.macmillan.org.uk

A national charity providing expert treatment and care through specialist Macmillan nurses and doctors. Macmillan also provides grants for patients experiencing financial difficulty.

Macmillan Benefits Advice

Tel 0800 808 0000

This service checks people’s entitlement to benefits and will offer assistance with forms. Is also able to offer advice about employment and debt

3. Childhood Cancer Parent Alliance CCPA (formerly NACCPO)

CCPA
Rachel Olley
Operations Manager
SDVS, 131-141 North Walls
Stafford. ST16 3AD
Web site www.naccpo.org.uk
Tel/Fax 01785 603763
Email ro@naccpo.org.uk

CCPO is an umbrella organisation for parent run groups in the UK. It is a national voice for parents and families, working with the Government, the CCLG CLIC Sargent and other bodies on such issues as education, job security and shared care treatment.

4. Children’s Cancer Recovery Fund

71-75 Shelton Street
London, WC2H 9JQ
Tel 0207 470 8755
www.cancerecovery.org.uk

Provides a fund for emergency payments of utility bills, rent payments, council tax, travels costs, TV licence. Maximum grant £300

5. Kids Cancer Charity – (formerly Christian Lewis)

62 Walter Road
Swansea, SA1 4PT
Tel 01792 480500
Fax 01792 480700
Web site www.kidscancercharity.org

Offers financial grants, crisis break holidays in the UK and an information and advice service to families. They can also assist with organising travel insurance and can help to co-ordinate cost effective all-inclusive travel packages for Euro Disney and Disney World Florida
6. Leukaemia Care Society

One Birch Court
Black Pole East
Worcester WR3 8SG
Tel 01905 755977
Email care@leukaemiacare.org.uk
Web site www.leukaemiacare.org.uk

A national group promoting the welfare of people suffering from leukaemia allied blood disorders. It offers limited financial assistance, travel insurance, support and regional support groups. In addition caravans are available for members' holidays in the UK.

7. Lennox Children's Cancer Fund

Suite D, 7-11 High Street
Romford, Essex RM1 1JU
Tel: 01708 734366
Fax: 01708 749421
Web site www.lennoxccf.org.uk

Provides financial assistance and holiday provision.

8. Lymphoma Association

PO Box 386
Aylesbury
Buckinghamshire
HP20 2GA
Tel 0808 808 5555
Fax 0808 808 5555
Email support@lymphomas.org.uk
Web site www.lymphomas.org.uk

Provides information and emotional support to anyone whose life is affected by Lymphoma. The helpline is staffed by people who have knowledge and understanding of the treatment of Lymphomas. Produces information leaflets


4th Floor, Bridge House,
48-52 Baldwin Street,
Bristol, BS1 1QB
0117 989 7820

National Helpline: 0845 108 2201

This is an umbrella organisation, which is working to improve the standard of care and support, which should be universally available throughout the UK for children with life threatening conditions and their families and professionals, though not specifically focused on malignancy.
10. Action for Sick Children

Action for Sick Children
32b Buxton Road
High Lane
Stockport SK6 8BH
Tel 01663 763004
Helpline 0800 0744519
Web site – www.actionforsickchildren.org

The aim is to ensure sick children obtain the highest standards of care in hospital, at home and in the community.

11. Contact a Family

Contact a Family
209-211 City Road
London EC1V 1JN
Tel 020 7608 8700
Fax: 020 7608 8701
Helpline 0808 808 3555 or Textphone 0808 808 3556 Free phone for parents and families (Mon-Fri, 10am-4pm; Mon, 5.30-7.30pm)
Web site www.cafamily.org.uk

Helping families who care for children with any disability or special needs via telephone help line, local support groups and publications

12. Disability Rights UK

12 City Forum
250 City Road
London EC1 8AF
Tel 020-7250 3222.
Fax 020 7250 0212
Web site www.radar.org.uk
E-mail: enquiriies@disabilityrightsuk.org

National organisation run by and working with disabled people. Gives information and advice on all issues relating to disability. Produces a wide range of publications and fact packs on disability issues

13. Rainbow Trust Children’s Charity

Rainbow Trust Children's Charity
6 Cleeve Court
Cleeve Road
Leatherhead
Surrey KT22 7UD

Tel 01372 363438
Web site www.rainbowtrust.org.uk

Family centred care for children with life threatening illnesses. They offer family support services within the home
14. REACT (Rapid Effective Assistance for Children with Potentially Terminal Illness)

React
St Luke's House
270 Sandycombe Road
Kew, Richmond
Surrey, TW9 3NP
Tel 020 8940 2575
Fax 020 8940 2050
Web site www.reactcharity.org

Supports families through making financial grants or purchasing equipment to facilitate their care at home. Provides holidays for families.

15. SIBLINKS

1 Betjemin Close
Coulsdon,
CR5 2LU
Web site www.siblinks.org.uk

SIBLINKS is a national initiative aimed at providing web based help and support to older siblings (15-25) of children or young people with cancer.

16. The Family Fund

4 Alpha Court
Monks Cross Drive
York. YO32 9WN
Email info@familyfund.org.uk
Tel 08449 744 099*
Text phone 01904 658085
Fax 01904 652625
Web site www.familyfund.org.uk

Their purpose is to ease the stress on families who care for a very severely disabled child under 16, by providing grants and information relating to the care of the child

17. The Youth Cancer Trust

5 Studland Road
Alum Chine
Bournemouth BH4 8HZ
Tel 01202 763591
Fax 01202 769064
Website www.youthcancertrust.org.uk

Aims to provide holiday breaks for young people aged 14-25 with cancer, who can also be accompanied by a sibling or friend.
18. UK Brain Tumour Society

Brain Tumour UK  
Tower House  
Latimer Park  
Chesham HP5 1TU  
Helpline 0845 4500 386  
Admin tel 01494 549 180  
Email enquiries@braintumouruk.org.uk  
Website www.braintumouruk.org.uk

Provides information and support for anyone affected by the diagnosis of a brain tumour.

19 Wessex Cancer Trust

Bellis House  
11 Westwood Road  
Southampton  
Hants  
SO17 1DL  
Tel 0238067 2200  
Fax 0238067 2266  
Counselling service 0238067 2255  
Email wct@wessexcancer.org  
Web site www.wessexcancer.org

A regional cancer charity which raises funds to complement and initiate improvement of cancer care services in Wessex. Services include free counselling, befriending, complimentary therapy services, information leaflets, financial assistance and holiday provision.

Useful Publications

Better care: better lives – improving outcomes and experiences for children, young people and their families coping with life limiting and life threatening conditions - DOH 2008

More than My illness – delivering quality cares for children with cancer - CLIC Sargent 2009

The Impact of Cancer on a Child’s World - - the views of children aged 7-13 living with and beyond cancer – CLIC Sargent 2010

More than my illness: delivering quality care for young people with cancer – CLIC Sargent 2010