Sheffield Children's NHS
NHS Foundation Trust

Initial Management of Febrile Neutropenia or Suspected Bacterial Infection

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Intended Audience

These guidelines have been produced to inform the management of children who are receiving "standard dose" chemotherapy. They should be used by anyone asked to see a child under the care of the haematology and oncology team with fever, or if there are any other concerns regarding infection.

The guidelines are regularly reviewed in relation to the NICE guidelines, local service evaluation of the febrile neutropenia admissions and ongoing review of bacterial isolates from patients on The Haematology & Oncology Unit. A separate SOP (HSCT/038 - CG1029) should be referred to if the child in question has undergone a haemopoietic stem cell transplant procedure.

The 2019 update of these guidelines introduces the option for early step-down in subgroups of patients at low risk of serious illness. Please read carefully.

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1. Introduction

Children receiving cytotoxic drugs are at risk from infection, particularly bacterial. This risk is greatest in those children undergoing intensive treatment such as bone marrow transplantation, high dose chemotherapy with stem cell support or during leukaemia induction treatment. Where leukaemia is concerned the risks are related to the duration of neutropenia which is generally longer for AML than for standard childhood ALL. However some ALL protocols are associated with severe and prolonged myelosuppression.

Children with solid tumours can also become severely pancytopenic, although in general this is for a shorter period. In the majority of these children the blood count nadir usually occurs 10 to 14 days after a course of treatment, and recovery has occurred by day 21.

Prophylactic antibiotics (ciprofloxacin +/- amoxicillin/co-amoxiclav +/- antifungals) are given to children who are expected to have a prolonged period of neutropenia. This includes patients with AML, aplastic anaemia and those undergoing transplantation procedures, see H&O/06/988 and HSCT/038. Other children are not routinely given prophylactic antibiotics, but may occasionally be prescribed these on an individual basis

This guideline gives advice on the initial investigation and management of patients presenting with fever or suspected bacterial infection (sepsis can present with normo- or hypothermia). The majority of patients will be febrile and neutropenic, but the management of an unwell child is the same regardless of actual or anticipated neutrophil count and should not be delayed whilst waiting for laboratory results. **All severely unwell patients and any patient who deteriorates after initial improvement must be discussed urgently with a consultant**

Information about viral or fungal infection can be found in subsequent sections of The Haematology & Oncology Unit Clinical Guidelines, Section 6: Infection, CG856 Management of suspected fungal infection (H&O/06/856) and CG857 Management of suspected viral infection (H&O/06/857). Additional specific guidelines are also available for the management of patients undergoing bone marrow transplantation (HSCT/038 - CG1029).

2. Telephone Triage

If a child at home becomes unwell a parent will usually phone the ward for advice. These calls will be triaged by appropriately trained nursing staff using the national Telephone Triage Tool. Where necessary further clarification will be sought from the treating clinicians. **Any decision not to review a febrile patient must be taken in discussion with a senior doctor from the Haematology/Oncology Team.**

3. Febrile Neutropenia

Fever
Single temperature ≥38.0^{o}C.

Sepsis can present with normal or low temperature (overwhelming sepsis, steroids, Trisomy 21)

Neutropenia
Absolute neutrophil count of ≤0.5 x 10^{9}/L.

Any suggestion of infection in children at risk must be urgently investigated and treated.

Antibiotics should be administered within an hour of presentation to all febrile patients in whom there is an expectation of neutropenia.

Neutropenia should be assumed in the following patients presenting with fever:

- any patient with FBC demonstrating neutrophils ≤0.5x10^{9}/L in last 48 hours
- any patient receiving AML therapy
- severe aplastic anaemia
- any patient within 3 months of BMT
- ALL patients in induction, delayed intensification, Reg B/C consolidation or Capizzi interim maintenance.

Children in the above groups should be cultured and started on antibiotics without waiting for the FBC result if they are febrile on arrival to hospital.

Well children with a history of fever at home, but who are afebrile on admission may be observed for a period pending results of initial bloods to help decide whether antibiotics are required. Antibiotics should be started *after appropriate cultures have been obtained* if neutrophils ≤0.5 x 10^{9}/L, even in the absence of any other signs or symptoms.

However if there is additional history suggestive of bacterial infection, e.g. diarrhoea, rigors or productive cough, then antibiotics should be started *once cultures obtained*.

Children with central lines are at risk from "line infections" even when they are not neutropenic. Immunocompromised children with diarrhoea are at particular risk from gram negative bacteraemia.

Any child receiving chemotherapy who appears unwell but is not febrile or neutropenic may still need treating with antibiotics. If in any doubt as to whether antibiotics should be given it is usually preferable to err on the side of caution and give them. **Discuss with more senior colleague if you are not sure**.

Children who have ***recovered*** normal haematopoiesis after completing all their chemotherapy and radiotherapy, are off any immunosuppression and whose central line has been removed should be investigated according to SC(NHS)FT medical guidelines and treated accordingly.

4. Initial Management

All patients should undergo a rapid clinical assessment to determine whether they are "well" or "unwell". A full history and examination should then be completed, alongside immediate treatment if required. Be sure to specifically document any symptoms such as diarrhoea or cough or the presence of focal signs of infection such as skin sepsis. **There is a proforma for admissions with suspected febrile neutropenia which should be used – ask the nursing staff if you do not know where these are kept.**

Well children should be managed in line with the advice in Section 3.

Unwell children should **ALWAYS** be given antibiotics irrespective of their count.

Unwell children may have tachycardia, tachypnoea or poor perfusion.

Hypotension is a late sign and suggests critical illness.

This is not an exhaustive list – if your overall impression or gut feeling suggests the patient is unwell, treat them as such.

Remember that nursing staff on The Haematology & Oncology Unit know the patients well and are used to providing fairly high dependency nursing; if they feel a child is significantly unwell they will tell you and you should take note, ensuring a rapid and thorough assessment is undertaken.

Initial management should proceed as per PLS/APLS guidelines with the early involvement of senior members of the Haematology/Oncology team. Escalation to PCCU may be required immediately, or following inadequate response to resuscitation and should be arranged in line with current hospital guidelines.

If you are unfamiliar with the resuscitation of critically ill children you should not be managing a septic Haem/Onc patient on your own – get senior help immediately.

Whilst they are on their way ensure the following actions are being taken:

- Administer oxygen therapy via an appropriate mask to maintain saturations > 95%
- Give 10ml/kg bolus of 0.9% Sodium Chloride if haemodynamically compromised (e.g. tachycardia not explained by fever, delayed capillary refill, hypotension); can repeat as necessary to restore normal physiological parameters
- Ensure appropriate cultures obtained (providing no delay)
- Start "first line" antibiotics unless alternative documented on EDMS alert system (e.g. drug allergy, known to be colonised with resistant organism)

Severely unwell patients should be given antibiotics prior to collection of blood cultures if the central line will not bleed back. Peripheral cultures should be taken when a cannula is sited. Central cultures can be attempted again when the patient has been resuscitated. Do not wait for urine cultures in unwell children.

Ongoing management

- Monitor vital signs including urine output closely. Catheterisation may be required.
- Further fluid boluses should be given as required. Discuss with PCCU if a second bolus is required and they are not already aware of the patient.
- Beware of children who remain cardiovascularly unstable or who deteriorate after initial improvement. Antibiotics should be changed to Meropenem and Teicoplanin to cover the possibility of resistant organisms, without waiting for culture results.

5. Initial Investigations

Blood Cultures	From central line (all lumens individually) Ideally aerobic and anaerobic set (blue and purple). Aim for 8-10 ml per bottle (increased volume = increased detection). Smaller volumes may be acceptable in younger children and infants. Paediatric bottle (yellow) only if infant or small volume sample anticipated. Label samples from multiple lines / lumens correctly
Urine	Send for M,C+S. Do not delay antibiotics waiting for this if unwell. Label form with method of collection.
Stool	If history of diarrhoea. Send for MC+S, C. difficile, virology
NPA/Throat swab	NPA or viral throat swab - If upper or lower respiratory symptoms Bacterial throat swab – if symptoms of pharyngitis and/or evidence of Candida
Swabs	All clinically infected lesions Remember to check line site (bacterial swab) Look for rash esp. vesicular (bacterial and viral swabs) Look inside mouth for candida, HSV, ulceration (bacterial and fungal, viral)
CRP	Can be stored and analysed in working hours. Only useful for subsequent management; not required for decision making
CXR	Not required on admission unless respiratory signs/symptoms
LP	**Not to be performed unless requested by Haem/Onc Consultant**

6. First Line Antibiotics (both should be prescribed)

Drug	**Dose**	**Notes**
Ceftazidime	50 mg/kg 8 hourly	Max 2g/dose
Gentamicin	Once daily dose see Appendix I for details	NB serum level monitoring

Patients who have previously grown multi-resistant gram negative bacteria may require alternative first line antibiotics. This will usually be Meropenem. If an alternative first line antibiotic regime is required this will be documented in the Alert section on EDMS. Other antibiotics may be also be given in the presence of specific focal signs, e.g. clarithromycin or high dose co-trimoxazole, if there are respiratory signs – discuss with a senior colleague.

Prophylactic antibiotics (other than co-trimoxazole which should always continue) are stopped if IV antibiotics are given.

Patients with / at risk of impaired renal function

Patients with impaired renal function or at risk of renal toxicity due to concomitant use of nephrotoxic drugs e.g. some chemotherapy or anti-virals. If such patients are clinically well,

Piperacillin/Tazobactam could be considered as alternative first line therapy after discussion with consultant on call. Unwell patients in this group should receive single agent Meropenem.

Patients having high dose methotrexate

Penicillins and aminoglycosides should be **avoided** when patients are receiving high dose methotrexate. Meropenem should be used in these patients.

7. Subsequent Management – See Appendix II

Initial Assessment for Suitability for Outpatient Febrile Neutropenia Management

Following the first dose of IV antibiotics, patients should, where appropriate, be assessed for suitability for ongoing febrile neutropenia management as an outpatient. Low risk, clinically well patients, may be eligible for discharge home under parental care with oral antibiotics if they fulfil all necessary criteria. If there is any doubt, a patient should remain in hospital on IV antibiotics pending consultant review.

First calculate the AUS-rules score (Table 1) and then review the Eligibility for Out-patient FN Management Criteria (Table 3).

Due to access to consultant level review, there are differences between which patients can be discharged out of hours and which can be discharged during normal working hours.

Table 1: AUS Score Calculation

AUS-rules variables	Yes	No
Chemotherapy more intensive than ALL maintenance*	☐ 1	☐ 0
Total WCC <0.3x10^9/L	☐ 1	☐ 0
Platelets <50x10^9/L (irrespective of recent transfusion)	☐ 1	☐ 0

Table 1

*All chemotherapy regimes are considered more intensive than ALL maintenance with the exceptions of:

- LCH maintenance
- Weekly vinblastine alone

Calculate Total Score (minimum = 0, maximum = 3)

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Table 2: AUS Score Interpretation

Score	
0	This patient is very-low risk for a bacterial infection. If they are clinically stable and fulfil the Eligibility for Out-patient FN Management Criteria then discharge home under parental care after a minimum of 4-8 hours observation Any patient discharged home out of hours must be discussed with the 1st on-call consultant for oncology (or haematology ST3+ if on-call)
1	This patient is low risk for a bacterial infection. If they are clinically stable and fulfil the Eligibility for Out-patient FN Management Criteria the patient may be discharged home under parental care after at least 4-8 hours observation **and** consultant review. Patients admitted out of hours will have consultant review and decision re: suitability for outpatient management on the ward round the following morning.
2	This patient is moderate risk for a bacterial infection. If they are clinically stable and fulfil the Eligibility for Out-patient FN Management Criteria then consider discharge home under parental care after a minimum of 24 hours inpatient observation
3	This patient is higher risk for a bacterial infection. If they are clinically stable and fulfil the Eligibility for Out-patient FN Management Criteria then consider discharge home under parental care after a minimum of 48 hrs inpatient care and a minimum of 24 hours without fever

Table 2

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Table 3: Eligibility Criteria for Outpatient Febrile Neutropenia Management

Any responses in a shaded box mean the patient is **NOT ELIGIBLE** for outpatient febrile neutropenia management.

Criteria	Yes	No
Disease Status Within 6 weeks of first diagnosis or confirmation of relapse	☐	☐
Higher risk disease Is the patient in any of the following groups: ▪ ALL in induction ▪ Infant ALL (except maintenance therapy) ▪ AML ▪ Allogeneic HSCT within 3 months of transplant or still on immune suppression ▪ Autologous HSCT within 3 months of transplant ▪ Down Syndrome ▪ Any patient <12 months of age ▪ Aplastic Anaemia ▪ Congenital Immunodeficiency	☐	☐
Confirmed focus of infection requiring in-patient care*	☐	☐
Medical complication requiring in-patient care**	☐	☐
Severe sepsis at presentation***	☐	☐
Penicillin allergy****	☐	☐
History of seizures	☐	☐
Availability of 24 hour care provider at home	☐	☐
Good education of patient and carer regarding reportable symptoms	☐	☐
Availability of a working telephone	☐	☐
Lives within 1 hours drive of Sheffield Children's Hospital and has own transport	☐	☐
Treating team prefer to manage as inpatient	☐	☐
History of non-compliance with medical care	☐	☐

Table 3

* Including, but not limited to, central venous access device (CVAD) site infection, cellulitis, perianal cellulitis or pain, significant pneumonia, infection with multi-drug resistant bacteria.

** Including, but not limited to, pain requiring intravenous analgesia, poor oral intake or excessive loss requiring intravenous hydration; respiratory distress or oxygen requirement.

*** Severe sepsis includes any of (i) altered conscious state, (ii) inotrope requirement, (iii) fluid bolus requirement or (iv) respiratory support requirement

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****Patients with a penicillin allergy require a combination of oral antibiotics that can cause significant QTc prolongation. This is particularly a risk if they are on concomitant medications that also affect the QTc. These include, but are not limited to, ondansetron, azole antifungals and tyrosine kinase inhibitors. Penicillin allergic patients can only be considered for outpatient management after review by a Haematology or Oncology consultant and medication review by a haematology/oncology pharmacist. This will rarely be possible outside routine working hours.

Management of Low Risk Patients with Febrile Neutropenia as Outpatients

Children who, based on the above criteria are suitable for outpatient management of febrile neutropenia should be observed in the haematology and oncology clinic or in an appropriate inpatient area for the time specified in Table 2 (above). If they remain well at this point, they can be discharged according to the following pathway.

Prior to discharge home, the patient must:

- Be reviewed by an Advanced Nurse Practitioner or ST2 or above doctor.
- During working hours, the patient must be reviewed by a haematology or oncology consultant, ST4+ haematology/oncology trainee or a clinical fellow
- Out of hours, all patient being discharged before the morning ward round must be discussed with the 1st on-call consultant for oncology or a haematology/oncology specialty trainee if one is on call.
- Have tolerated one dose of oral antibiotics in the hospital
- Parents must have received appropriate education and information leaflet and demonstrated good understanding of it.

Oral Antibiotic Choice and Duration

Patients should be discharged with a combination of **oral Co-amoxiclav and Ciprofloxacin**, dosed as per BNFc.

Penicillin allergic patients should receive **Ciprofloxacin and Clarithromycin**, dosed as per BNFc. [Note the need for consultant and pharmacist review prior to commencing oral antibiotics and discharge].

If there is a history of severe beta lactam allergy or known resistant bacteria, the patient should be discussed with microbiology and not discharged out of hours without a consultant review.

Duration of Antibiotics

All patients will be discharged with 5 days of antibiotics. Patients/carers will be informed under what circumstances they should re-present urgently and that a member of the team will contact them daily.

Antibiotics will be stopped in any patient with negative blood cultures after being apyrexial for at least 24 hours, if clinically well, unless an alternative cause for pyrexia has been found.

Any patient who remains febrile after 5 days will be reviewed.

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Discharging Nurse Responsibilities

1. Provide patient/parent education and ensure parents know under what circumstances they should return urgently.
2. Ensure families have the correct contact details for the hospital.
3. Advise families to take temperature 4-6 hourly during waking hours and to record it on the provided chart (*H&O Form 854 003 FN home obs chart – Parent*)
4. Advise families that a member of the team will contact them daily and to have the temperature chart available to discuss.
5. Add patient name to ward list in handover book and on ward whiteboard

Medical Team responsibilities

1. Keep an up to date list of all patients being managed as outpatients for febrile neutropenia
2. Check blood culture results at least daily: antibiotics may need to be changed depending on these results. The microbiology lab should be phoned on Day 1 to ensure blood cultures have been received and again after 48 hours if no report is available on ICE
3. Daily phone call to parents/carer and completion of *H&O Form 854 002 FN home obs chart – Hospital* until antibiotics stopped.
4. Once antibiotics stopped, ensure *H&O Form 854 002 FN home obs chart – Hospit*al is sent for filing on EDMS

Appointments Schedule

Day	Appointment/Intervention
0	Bloods & clinical review prior to hospital discharge Telephone appointments arranged Patient information given
1	Telephone follow up Documentation of temperatures and symptoms at home on *H&O Form 854 002 FN home obs chart – Hospit*al Ensure blood cultures received by lab, review culture results and action as required
2-4	Telephone follow up Documentation of temperatures and symptoms at home on *H&O Form 854 002 FN home obs chart – Hospit*al Review of culture results and action as required Stop antibiotics if blood cultures negative, patient well and afebrile for >24 hours Send completed *H&O Form 854 002 FN home obs chart – Hospital* for scanning on EDMS once antibiotics stopped
5	If remains febrile, patient to attend hospital for medical review, repeat blood cultures and decision to be made whether for readmission or to continue out-patient based treatment.

Reasons for Medical Review following initial discharge

- Ongoing fever (>72 hours from presentation) or new fever after being afebrile for 24 hours
- Feeling unwell/new symptoms and signs
- Parental concern
- Significant decrease in oral intake or significant increase in output (vomiting and diarrhoea)
- Positive blood culture or new infection identified after transfer home
- Severe or persistent pain
- Chills/rigor/shaking
- Not afebrile by day 5 of home-based care

Reasons for Readmission

- Fever > 38^{o}C beyond 5 days from the start of the febrile neutropenic episode
- Clinically unwell / unstable
- Infection requiring in-patient care

If readmission is 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 consider antifungal therapy once patient is febrile >96 hours from the start of the febrile neutropenic episode.

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Ongoing Management of Patients who Remain an Inpatient on Intravenous Antibiotics

12-24 hours after starting antibiotics	Check gentamicin level. Refer to Appendix I for further details.
If afebrile **and** well at 48 hours, **and** all cultures **negative**	If child well, stop antibiotics and discharge home. Withhold third dose of gentamicin if well, afebrile and 48 hour culture not yet available at point this is due.
If still febrile at 48 hours **but** cultures negative	Stop gentamicin
If still febrile at 96 hours	Start caspofungin according to H&O 06 856 - Management of Suspected Fungal Infection SOP Potential sources of fungal infection should be investigated according to the above SOP within 24-48 hours of starting antifungals
If cultures **positive** (may take up to 48 hours to confirm)	Change antibiotics if necessary as dictated by cultures. Gentamicin may be stopped if appropriate alternative available – discuss with microbiologist. Systemic antibiotics should be given for a minimum of 5 days – discuss with microbiologist. In some situations, e.g. if *S. aureus* isolated, a more prolonged course of systemic antibiotics will be needed. Consider removal of central line if *S. aureus* or *Candida* isolated. Antibiotic "locks" may be needed after a course of systemic antibiotics, e.g. if *coagulase negative staphylococcu*s repeatedly isolated from central line. (See Appendix III)
In case of acute deterioration after a period of stabilisation	Change to Meropenem and Teicoplanin to cover resistant organisms. Consider early addition of Antifungals and Aciclovir

NB Consider need for daily blood cultures in children who remain febrile.

For advice about appropriate antibiotics for a child with continuing fever and negative cultures, discuss with Consultant Microbiologist. If a source of suspected bacterial infection is strongly suspected, then appropriate antibiotics should be **added** to ensure adequate cover of possible organisms. Consult the hospital antibiotic policy (section 2.3 Medical Staff Guidelines) in consultation with microbiology. **DO NOT ASSUME THE CAUSE OF INFECTION**; always continue broad spectrum antibiotics until a positive culture is isolated, or patient has been afebrile and well for at least 24 hours.

8. Additional Antibiotics

Antibiotic	Dose	Administration	Notes
Teicoplanin Age ≥ 2 months	10mg/kg	12 hourly IV x 3 doses then every 24 hrs	If treating a Coagulase negative staphylococcal line infection can change to vancomycin "lock" after 48 hrs Maximum single dose 800mg
Vancomycin Age ≥ 1 month	15mg/kg	8 hourly IV age ≥12 6 hourly IV age <12 Infusion over 1 hour (rate not > 10mg/min)	Monitor drug levels* Reduce doses if renal impairment Maximum starting dose 2g/day Total daily dose may be increased if indicated by drug levels
Flucloxacillin	50mg/kg	6 hourly IV bolus or short infusion	Max 2 g qds
Meropenem Age ≥ 1 month	20mg/kg (1g if > 50kg)	IV 8 hourly	40 mg/kg if life threatening sepsis or CNS infection Maximum dose 2g 8 hourly Adjust dose if renal impairment
Clarithromycin	1 month – 11 years: 7.5mg/kg >12 years: 500mg	IV 12 hourly Infuse over 1 hour Do not give as a bolus	**Maximum dose 500mg 12 hourly**
Metronidazole Age ≥ 2 months	7.5mg/kg	8 hourly IV Infuse over 20-30 minutes	**Maximum dose 500mg 8 hourly**
Piperacillin/ Tazobactam Age ≥ 1 month	90mg/kg	6 hourly IV	**Maximum dose 4.5g 6 hourly**

*A trough vancomycin level should be taken 24 hours after starting, ie, before the 4th dose, for TDS dosing and the 5th dose for QDS dosing, which should then be given, and doses adjusted from the 5th or 6th dose respectively.

Target levels are 10-15 for standard infections and 15-20 for CNS infections.

If the level is subtherapeutic on the first level, the dose should remain the same and the frequency increased to every 6 hours. If the level remains subtherapeutic or is toxic at any point, pharmacy advice should be sought.

9. Patients on Oral Chemotherapy

Many patients will be taking oral chemotherapy, including mercaptopurine, methotrexate, thioguanine, temozolamide, procarbazine, etoposide or imatinib, at home.

When admitted to hospital with possible infection the decision whether to suspend or continue these drugs will need to be made by a senior member of the Haem/Onc team (ST4+ or Consultant). This decision may depend partly on the blood count but also how unwell the child is and which part of the chemotherapy protocol they are on

Oral chemotherapy drugs are only given during the day. Patients admitted in the evening prior to that days dose should be discussed at time of admission. Patients admitted after they have taken their evening dose or overnight should be identified at handover for discussion with the relevant consultant on the morning ward round prior to the drug being written up or administered. See The Haematology & Oncology Unit guidelines, Section 4: Chemotherapy Administration section for further information.

10. Advice for Shared Care Centres

All patients and their parents are asked to contact The Haematology & Oncology Unit if they become unwell. Parents will usually be advised to bring their child to SCH(NHS)FT or their local shared care centre for review. If they are felt to be severely unwell parents will be asked to dial 999 and request an emergency ambulance. On occasion parents may also dial 999 without contacting The Haematology & Oncology Unit first and in both these situations the patient is likely to be taken to Accident and Emergency at their local hospital.

These guidelines have therefore been written to be equally applicable to Haematology/Oncology patients who present to designated shared care centres (or other referring district general hospitals within our cancer network).

The following additional advice for Shared Care centres should also be noted:

- Ensure early liaison with the Consultant on Call for paediatric Oncology
- If haemodynamic compromise present or develops contact Embrace urgently
- Avoid rectal route of drug administration in neutropenic patients
- Use peripheral access if nobody immediately available to access central line. Take peripheral blood cultures if possible when cannula is sited, and label as such. Central line cultures can be obtained later. Do not delay treatment waiting for them.
- Patients should not be discharged with oral antibiotics according to the low risk febrile neutropenia protocol without discussion with a haematology/oncology consultant at SC(NHS)FT to ensure suitability and appropriate follow up.
- After initial investigation and emergency management, patients should be transferred from the POSCU/DGH to the PTC if:

  i. The POSCU does not have in-patient shared care arrangements
  ii. The patient is clinically unstable and may require PICU care
  iii. There is a strong suspicion of fungal infection or need for surgical intervention
  iv. The patient remains febrile after 96 hours of antibiotics

11. References

11.1 ALSG. APLS manual 7th edition, 2021

11.2 Ammann RA, Hirt A et al. Identification of children presenting with fever in chemotherapy induced neutropenia at low risk of severe bacterial infection. Med Paed. Onc. 2003; 41:436-443

11.3 Children's Cancer and Leukaemia Group (CCLG). Managing Febrile Neutropenia in the UK in 2020.Proposed New Management Pathway. V1.01 April 2020. Available at www.cclg.org.uk

11.4 Sheffield Children's NHS Foundation Trust (2016) Clinical Guideline for Once Daily Gentamicin in Infants and Children. SCH Guideline (CG893)

11.5 Freifeld AG, Bow EJ et al 2010 update Clinical Practice Guideline for the use of Antimicrobial Agents in Neutropenic Patients with Cancer. Clin Infectious Dis. 2011; 52: 427-431

11.6 Jackson TJ, Napper R, Haeusler GM, et al. Can I go home now? The safety and efficacy of a new UK paediatric febrile neutropenia protocol for risk-stratified early discharge on oral antibiotics. Archives of Disease in Childhood 2023;108:192-197.

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Appendix I: Administration of Once Daily Gentamicin

(Note: this is not the full SC(NHS)FT Gentamicin Policy – available at http://staff.sch.nhs.uk/documents/3-clinical-guidelines/447-once-daily-gentamicin-in-infants-and-children-guidelines-for)

Dosage and Monitoring

Dose:

35 weeks gestation to 1 month = 5mg/kg per dose
> age 1 month = 6mg/kg per dose
If obese, calculate dose using SCH guidelines for prescribing in Obesity (available on Intranet)

Administration:

Slow IV infusion over 15 – 20 minutes
Dilute with sodium chloride 0.9% or glucose 5% (volume not critical)

Monitoring:

- Initially prescribe one dose only (on the regular medication section of the treatment chart), wait for levels before further doses are prescribed
- Only **trough** levels should be monitored
- Take level **12 – 24 hours** after the start of the infusion
- Record the following on the drug card and laboratory request form (labels available);
  1. Exact time dose given
  2. Exact time sample taken

Thereafter take level:

- twice weekly if stable, 12 - 24 hours after last dose
- if renal function fluctuating, take level 12 to 24 hours after each dose
- Whenever possible, send levels to microbiology during normal working hours, always mark request forms with '**Once daily'** gentamicin

Renal function :

- Monitor serum creatinine when starting gentamicin and then daily thereafter
- If renal function impaired, consider alternative treatment
- If gentamicin used must seek guidance from Microbiology or Pharmacy

Contra-Indications and Warnings

- The narrow spectrum of activity of gentamicin must be kept in mind as used alone it provides no cover for streptococci or anaerobes.
- Patients should be well hydrated during therapy.
- Extra caution in neonates with urinary outflow problems (bladder obstruction, urinary retention) in case of renal impairment, dehydration or concomitant nephrotoxic chemotherapy (including high dose methotrexate and platinum agents). Discuss with consultant on call if unsure.

Side Effects

Nephrotoxicity and ototoxicity can occur if optimum blood levels are exceeded.

- Monitor renal function in **all** children receiving gentamicin.
- **Extra caution in child receiving other nephrotoxic drugs e.g. ciclosporin, ifosfamide or cisplatin.**

(See over for "Interpretation of Gentamicin Levels"

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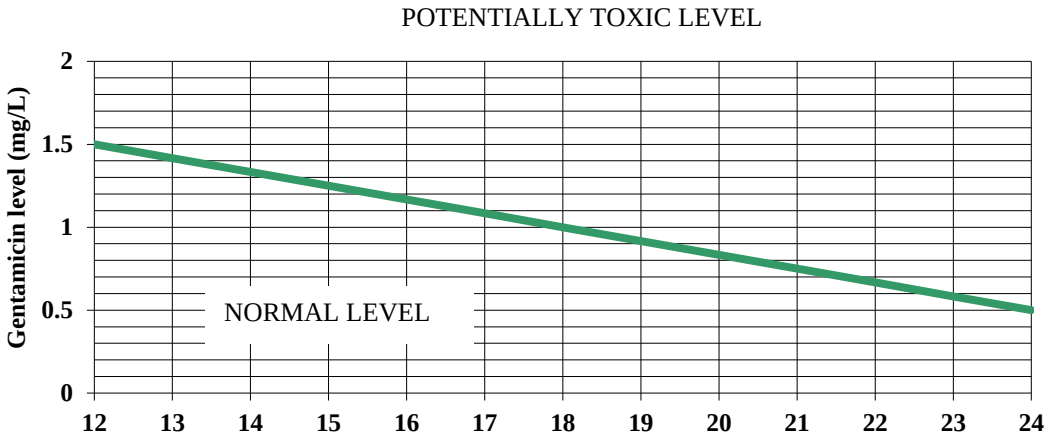
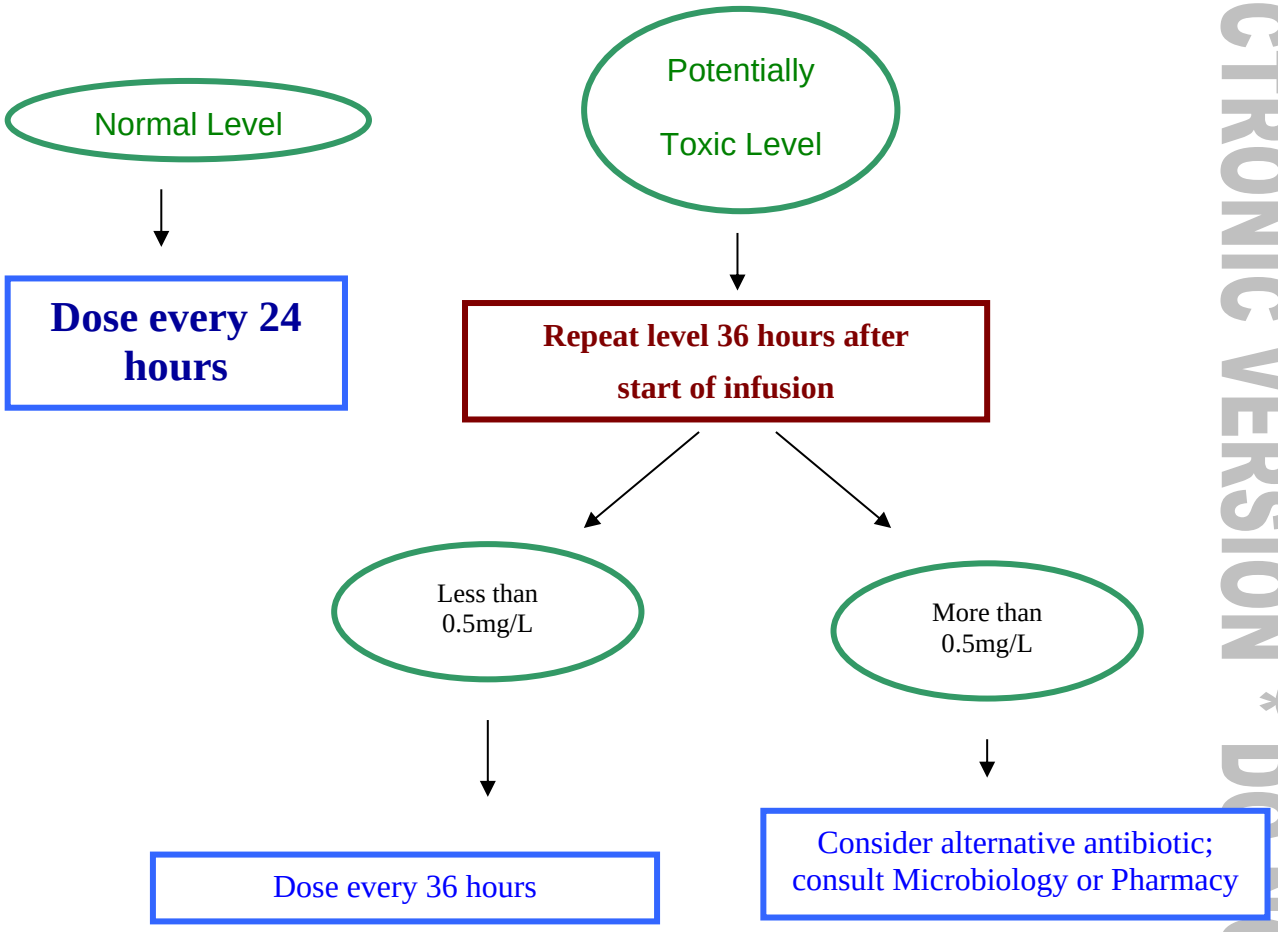
Interpretation of Gentamicin Levels:





NB. The dosage and monitoring regimen in this protocol are different from those in 'BNFc' and decisions regarding changes in therapy should follow the recommendations above. Any deviations from the protocol should only be made on the advice of senior medical staff, microbiology or pharmacy and these should be documented.

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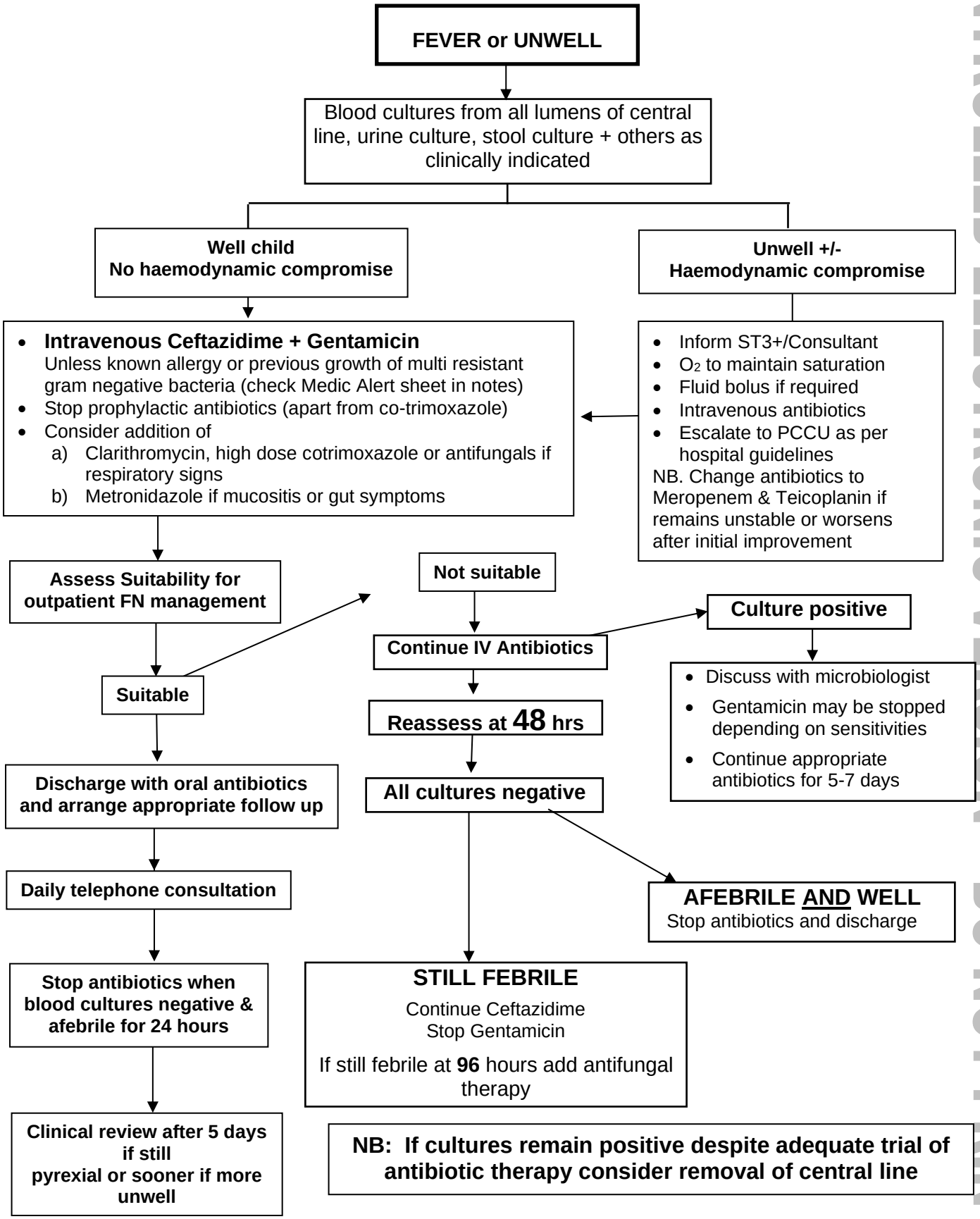
Appendix II: Summary of Management of Neutropenic Fever



Appendix III: Antibiotic Locks

If a line infection is suspected, i.e. organism such as *coagulase negative Staphylococcus* cultured, or there is repeated infection with the same organism then it may be helpful to use an antibiotic lock once the child has received systemic treatment for a minimum of 48 hours (longer if the child is neutropenic or unwell).

If there is a further episode of suspected infection within 1 month of a proven infection, the line should be treated with urokinase 5000 units in 2ml 0.9% sodium chloride for 2 hours each day for 3 days to remove any fibrin sheath from within the line. See The Haematology & Oncology Unit Guidelines, section 7: Central Line Care, CG986 Central Venous Access Device Management (H&O/07/986). Please contact the pharmacist for further advice if urokinase is not available.

Antibiotic locks are prepared by pharmacy in pre-filled syringes, except for gentamicin for which there is insufficient stability data. The lock should be diluted to a volume of 2mls with sodium chloride 0.9% (whether for a Broviac line or portacath). This gives a concentration well above the systemic concentration achieved with systemic drug dosages used on the ward. Normally both lumens are treated in children with double lumen central access even if only one has a positive culture, to ensure that cross contamination from sampling has not occurred.

Drugs that are normally administered by IV bolus injection do not need to be removed before the next lock is administered, e.g. ceftazidime, teicoplanin, unless the child is under 1 year or 10kg when the dose could become significant. Drugs normally administered slowly or by infusion should be aspirated before flushing, e.g. vancomycin, gentamicin or ciprofloxacin.

The line should then be flushed with 2-5mls sodium chloride 0.9% before the next lock is applied. Antibiotic locks are to be used for a minimum of 7 days and usually treatment is given for 14 days in the case of *Coagulase Negative Staph* infections and for up to 21 days for gram negative organisms.

Drug	Dose	Frequency of application
Vancomycin	20mg/2ml	Once daily
Ceftazidime	100mg/2ml	Once daily
Gentamicin	3mg/2ml	Once daily
Ciprofloxacin	4mg/2ml	Once daily
Meropenem	40mg/2ml	8 hourly* *Unstable after 8 hours at 37°c.

Flucloxacillin and teicoplanin are not suitable for preparing line locks. To prepare gentamicin locks dilute 0.3mls of the paediatric injection (20mg/2ml) to 2mls with 0.9% sodium chloride immediately before use.