ONCOLOGY/BLOOD TRANSPLANT AND CELLULAR THERAPY FEVER OR SUSPECTED SEPSIS – INITIAL MANAGEMENT

PRACTICE GUIDELINE©

DOCUMENT SUMMARY/KEY POINTS

- Infection in paediatric oncology / Blood Transplant and Cell Therapy (BTCT) patients presents most commonly with fever. Some patients with serious infection may present without fever or with hypothermia. **Prompt administration of antibiotics (within 60 minutes of presentation)** will reduce morbidity and mortality[1-6].
- The guideline is designed to provide assistance within the critical first 60 minutes of presentation to hospital and provide further guidance for the following 48 hours.
- Continued re-evaluation of these patients is critical to their successful outcome. The child's treating oncologist or oncologist on call should be contacted as soon as practicable after initiation of treatment[1-3,6].
- Decisions regarding subsequent changes to and duration of antibiotic therapy are beyond the scope of this guideline and are the responsibility of the treating oncologist within the scope of local antimicrobial stewardship programs.

Related Documents

Empiric Guidelines:

Empiric Antibiotic Guidelines- SCH

Central Venous Access Devices (CVAD): Practice Guidelines SCHN

Child Life Therapy: Procedure Support Practice Guideline

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st September 2022	**Review Period**: 3 years
Team Leader:	Senior Staff Specialist	**Area/Dept**: SCH & CHW Oncology

CHANGE SUMMARY

- Mandatory review of guideline
- Inclusion criteria updated
- All patients that present to the SCH or CHW emergency department should be triaged a minimum of category 2
- Gentamicin should only to be given in the clinically unstable or shocked patient.
- Recommendation to not use initial discard volume (up to 3 mL) of blood from CVAD for blood cultures.
- Recommendation for minimum blood culture volumes for peripheral blood cultures based on age/weight of patient.
- IV antibiotics, antiviral and antifungals reviewed and updated
- **14/10/22** - Minor review:
  - Wording changed in flow chart to reflect name of guideline “SCHN Oncology/Blood Transplant and Cellular Therapy Fever or Suspected Sepsis – Initial Management.
  - Link to “Oncology Patient-Fever-Low Risk Management Practice Guideline inserted”
  - Recommended blood volumes for cultures separate paragraph
  - Minor formatting changes.

READ ACKNOWLEDGEMENT

- All clinical staff in SCHN involved in the care of oncology, blood transplant and cellular therapy patients should read and acknowledge they understand the contents of the Guideline.

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Background

Purpose

- This guideline is designed to provide guidance to clinicians in the **initial 60 minutes** of presentation to the Emergency Department or designated inpatient setting in the management of the following patients presenting with fever or reported fever ≥ 38.0°C or who are unwell regardless of their temperature:
    - Patients on treatment for cancer
    - Patients who ceased treatment for cancer within the last 3 months
    - Recipients BTCT within the last 6 months or on immunosuppressive therapy
    - Recipients of immune effector cells (IEC), including chimeric antigen receptor T (CAR-T) cells, virus-specific cytotoxic T-cells (CTLs) or natural killer (NK) cells7,8
    - Oncology, BTCT or non-malignant haematology patients with Central venous Access Device (CVAD) in situ.
    - Non-malignant haematology patients with neutropaenia
    - Patients with Severe Aplastic Anaemia
- It is important to note that most paediatric oncology patients have a CVAD in situ which is a potential source of infection irrespective of neutrophil count.
- Not all patients are at the same risk of acquiring significant infections during episodes of neutropaenia. Clinical assessment and judgement of patients at presentation may not, with complete accuracy, discriminate those with and without significant infection. Patients are divided in two groups[3,6,9-12]:

Patients with Fever and Neutropaenia: The majority of paediatric oncology patients present with fever and neutropaenia and usually do not have an obvious focus of infection. For such patients the morbidity and mortality is reduced with prompt administration of empiric antibiotic therapy.

Unwell Oncology/BTCT patients regardless of temperature or neutrophil count: Patients may have significant infections without fever and/or neutropaenia. In this group clinical significance may not be recognised, leading to inappropriate or delayed management. These guidelines recommend that these patients are managed initially in the same way as febrile patients who are neutropenic.

- The treatment plan for these patients must always incorporate an initial assessment and physical examination but, administration of antibiotics should not be delayed.

Infection in paediatric oncology/BTCT patients presents most commonly with fever. Some patients with serious infection may present without fever or with hypothermia.

Prompt administration of antibiotics (within 60 minutes of presentation) will reduce morbidity and mortality.

Key Points in the recognition and management

- Do not wait for topical anaesthetic to take effect to access Implantable Venous Access Access Device (CVAD) or insert a peripheral cannula.
- Do not wait for laboratory test results before starting antibiotics
- CVADs with or without neutropaenia are a significant source of infection.
- Patients who become febrile within 12 hours of CVAD access should be considered at high risk of infection/sepsis.
- Patients who have recently received CAR-T (chimeric antigenic receptor T) cell infusion are at high risk of toxicity including Cytokine Release Syndrome (CRS) and must be assessed following local guidelines for the Management of Immune Effector Cell Toxicity[7,8]
- The full blood count can change rapidly within 24-48 hours if patient is receiving chemotherapy. Results of blood counts taken more than 24 hours prior to presentation may not be indicative of the degree of neutropaenia.
- Mucositis is a common complication in oncology patients presenting with fever and neutropaenia and requires appropriate consideration and management.
- Fever in paediatric oncology patients may be secondary to drugs (Cytarabine, Bleomycin), transfusion of blood products or viral infection. It is not possible to rule out bacterial infection in these patients and hence prompt administration of antibiotics is indicated in such situations.
- Fever may be absent in some paediatric oncology patients with infection, particularly those with profound neutropaenia and those receiving corticosteroids. The presence of infection in this setting may be detected only by attention to seemingly minor complaints from the patient or by subtle physical findings.

  For example:

  - abdominal pain may signify an evolving intra-abdominal infection (enterocolitis, appendicitis)
  - erythema and tenderness along a subcutaneous catheter tunnel track may indicate the presence of a deep seated soft-tissue infection
  - diarrhoea may be the only symptom of infection

- fainting may be the sole manifestation of sepsis

- Children with sepsis may present with hypothermia.
- Some children present with history of fever at home, but are afebrile on presentation to the hospital. These patients must be treated in the same way as patients with fever.
- After accessing the CVAD and administration of antibiotics there may be acute deterioration due to septic shower/endotoxin release. It is vital that the child is closely observed and monitored for deterioration.

Definitions

Fever and neutropaenia

- **Fever** - a single temperature ≥38.0°C by any route (axillary, oral, at home or on presentation). Tympanic temperatures are not recommended due to inaccuracy.
- **Neutropaenia** - An absolute neutrophil count <0.5x10^9/L OR <1.0x10^9/L with a predicted decline to <0.5x10^9/L over the next 48 hours. Patients who have received chemotherapy within the preceding 14 days are likely to have a falling neutrophil count. **Do not wait for blood results to commence antibiotics**.

Sepsis (international definition from CEC)

'life-threatening organ dysfunction caused by dysregulated host response to infection.'

Septic Shock (international definition from CEC)

'A subset of sepsis where underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.'

Clinical Presentation

Toxicity: altered conscious state (lethargy, irritability, floppiness, weak cry); colour pale or mottled; cool peripheries; grunting; rigors

Clinically stable	Clinically Unstable	Septic Shock
ALL of the following **1.** No signs of toxicity **AND** 1 Yellow or No Red Zone criteria	**ALL of the following** **1.** No signs of toxicity **AND** Two or more of the following in Yellow Zone: respiratory rate, respiratory distress, O2 saturation, heart rate **AND** Normal blood pressure, capillary refill and level of consciousness If any signs of cold or warm shock elevate to severe sepsis/shock pathway	**ANY ONE of the following** **1.** Any sign of toxicity Three or more of the following in Yellow Zone: respiratory rate, respiratory distress, O2 saturation, heart rate Any parameter in Red Zone Signs of cold shock: diminished pulses, prolonged capillary refill (>3 seconds),hypotension Signs of warm shock: bounding pulses, flash (very rapid) capillary refill, wide pulse pressure (diastolic BP less than 50% of systolic BP)

Hypotension is not necessary for the clinical diagnosis of septic shock;
however, its presence in a child with clinical suspicion of infection is confirmatory.

Initial Presentation/Triage Algorithm

An oncology/ BTCT patient with fever or reported fever ≥38°C or unwell regardless of the temperature
(eg: abdominal pain, erythema and tenderness along subcutaneous catheter, diarrhoea, fainting)

- Patients on treatment for cancer
- Patients who ceased treatment for cancer within the last 3 months
- Recipients of Blood Transplant and Cellular Therapy (BTCT) within the last 6 months or on immunosuppressive therapy
- Recipients of immune effector cells (IEC), including CAR-T cells, CTLs or NK cells **[management of IEC Toxicity Guideline]**
- Oncology, BTCT or non-malignant haematology patients with Implantable venous Access Device (CVAD) in situ
- Non-malignant haematology patients with neutropenia
- Patients with severe aplastic anaemia

NO → **Escalate as per LOCAL CERS**

YES → Do they have an active CAR T Cell Status?

NO → Are they currently being treated with Intravenous Antibiotics as per the "SCHN Oncology/Blood Transplant and Cellular Therapy Fever or Suspected Sepsis – Initial Management"?

YES → Contact consultant for treatment advice

YES → **Refer to LOCAL CAR T CELL THERAPY PROCESSES**

NO → **Emergency Department:**
- Patients should receive a minimum category 2 triage,

Inpatient Areas:
- Clinically stable patients activate **Clinical Review**
- Clinically unstable and/or suspicion of severe sepsis/shock activate a **Rapid Response**

Do Not Wait for local anaesthetic to take effect (eg to access CVAD or insert peripheral line)
Access CVAD or establish peripheral IV and collect **Blood Cultures, FBC, VBG (Lactate & Glucose), EUC, Group & hold**
DO NOT WAIT FOR BLOOD RESULTS TO START ANTIBIOTICS

RECOGNISE

DOES THE PATIENT HAVE ANY SIGNS OF SHOCK OR TOXICITY?
COLD SHOCK: Diminished pulses, prolonged capillary refill (>3 seconds), hypotension
WARM SHOCK: bounding pulses, flash (very rapid) capillary refill, wide pulse pressure (diastolic BP less than 50% of Systolic BP)
TOXICITY: altered conscious state (lethargy, irritability, floppiness, weak cry); colour pale or mottled; cool peripheries; grunting; rigors

NO → DOES THE PATIENT HAVE **2 OR MORE YELLOW OR ANY RED ZONE OBSERVATIONS?**

NO → CLINICALLY STABLE

YES → **DOES THE PATIENT HAVE**

***TWO* of the following *YELLOW ZONE* Observations**
Respiratory Rate, Respiratory Distress, O_2 Saturations, Heart Rate/BP

OR

ANY RED ZONE OBSERVATION / SIGNIFICANT STAFF CONCERN OR **ADDITIONAL CRITERIA**
3 or more simultaneous Yellow Zone observations or **ANY** RED ZONE CRITERIA

YES → **CLINICALLY UNSTABLE**

YES → **SEPTIC SHOCK**

RESPOND AND ESCALATE

CLINICALLY STABLE
Administer antibiotics within **60 minutes**
Piperacillin-Tazobactam
Consult with oncology team before commencing other antibiotics

CLINICALLY UNSTABLE
Administer antibiotics within **30 minutes**
GENTAMICIN* AND Piperacillin-Tazobactam
Add Vancomycin (if indicated)
Give Sodium Chloride 0.9% 20 mL/kg Bolus

SEPTIC SHOCK
Administer antibiotics
IMMEDIATELY
GENTAMICIN *
AND
Piperacillin-Tazobactam
AND
VANCOMYCIN
Escalate as per Local CERS
Resuscitate as clinically indicated

If the patient deteriorates further or has an elevated lactate (=2mmol/L) escalate as per local CERS, Resuscitate as clinically indicated and ADD Vancomycin

Discuss the management plan with the patient and the family
Notify Haematologist / Oncologist as soon as possible

*** Gentamicin: Only to be given as first line treatment in Clinically Unstable and Shock.**

SEE NEXT PAGE FOR ANTIBIOTIC INFORMATION

Table 1: First Dose of Empirical Antibiotics[1,2,4,6,10,12-17]

TREATMENT		Clinically Stable	Clinically Unstable	Septic Shock
EMPIRICAL ANTIBIOTIC REGIMEN*		**Piperacillin + Tazobactam** 100 mg/kg/dose IV 6 hourly (max. dose 4 g Piperacillin component)	**Gentamicin *** (dose based on lean body weight for obese patients) 7.5 mg/kg/dose IV (max. dose 320 mg) Single dose only **then** **Piperacillin + Tazobactam** 100 mg/kg/dose IV 6 hourly (max. dose 4 g Piperacillin component) ADD **Vancomycin^** if clinically indicated 15 mg/kg/dose IV 6 hourly (max. initial dose 750 mg)	**Gentamicin *** (dose based on lean body weight for obese patients) 7.5 mg/kg/dose IV (max. dose 320 mg) Single dose only **then** **Piperacillin+Tazobactam** 100 mg/kg/dose IV 6 hourly (max. dose 4 g Piperacillin component) **AND** **Vancomycin** 15 mg/kg/dose IV 6 hourly (max. dose 750 mg)
ALLERGY	Non-severe penicillin hypersensitivity	**Cefepime** 50 mg/kg/dose IV 8 hourly (max. dose 2 g)	**Gentamicin *** (dose based on lean body weight for obese patients) 7.5 mg/kg/dose IV (max. dose 320 mg) Single dose only **AND** **Cefepime** 50 mg/kg/dose IV 8 hourly (max. dose 2 g)	**Gentamicin *** (dose based on lean body weight for obese patients) 7.5 mg/kg/dose IV (max. dose 320 mg) Single dose only **AND** **Cefepime** 50 mg/kg/dose IV 8 hourly (max. dose 2 g) **AND** **Vancomycin** 15 mg/kg/dose IV 6 hourly (max. dose 750 mg)
	Severe Penicillin Hypersensitivity not known to tolerate Cephalosporins /Meropenem safely	**Ciprofloxacin** 10 mg/kg/dose IV 8 hourly (max. dose 400 mg) **AND** **Vancomycin** 15 mg/kg/dose IV 6 hourly (max. dose 750 mg)	**Gentamicin *** (dose based on lean body weight for obese patients) 7.5 mg/kg/dose IV (max. dose 320 mg) Single dose only **AND** **Ciprofloxacin** 10 mg/kg/dose IV 8 hourly (max. dose 400 mg) **AND** **Vancomycin** 15 mg/kg/dose IV 6 hourly (max. dose 750 mg)	**Gentamicin *** (dose based on lean body weight for obese patients) 7.5 mg/kg/dose IV (max. dose 320 mg) Single dose only **AND** **Ciprofloxacin** 10 mg/kg/dose IV 8 hourly (max. dose 400 mg) **AND** **Vancomycin** 15 mg/kg/dose IV 6 hourly (max. dose 750 mg)
MODIFICATIONS		Add **Metronidazole** 12.5 mg/kg/dose IV 8 hourly (max. dose 500 mg) if Cefepime or Ciprofloxacin used AND evidence of abdominal/perineal infection	Use **Meropenem** rather than Cefepime or Piperacillin/ Tazobactam if colonised with a multi-resistant GNR (e.g. ESBL) Add **Metronidazole** 12.5 mg/kg/dose IV 8 hourly (max. dose 500 mg) if Cefepime or Ciprofloxacin used and evidence of abdominal/ perineal infection	Use **Meropenem** rather than Cefepime or Piperacillin/Tazobactam if colonised with a multi-resistant GNR (e.g. ESBL) Add **Metronidazole** 12.5 mg/kg/dose IV 8 hourly (max. dose 500 mg) if Cefepime or Ciprofloxacin used AND evidence of abdominal/perineal infection

NOTES:

All Antibiotic doses are based on actual body weight except Gentamicin.

Gentamicin: Dose based on lean body weight for obese patients – see *guideline for* method for calculating lean body weight in obese children. **Indications for Vancomycin**: Obviously infected vascular devices (erythema/tenderness along subcutaneous track or purulent exit site discharge), MRSA carriers with clinical instability, High dose Cytarabine (>2g/m^2/day) recipients with clinical instability. For clinically stable patients the decision to continue Gentamicin beyond the first dose must be made after discussing with treating oncologist, but is not recommended by the Australian Therapeutic Guidelines – Antibiotic 2015 due to the lack of proven benefit and potential for toxicity. Subsequent antibiotic choice/dose (i.e. after first dose) may need modification based on patient's renal function, clinical stability and history of colonisation with multi-drug resistant organisms. These decisions must be made after discussing with treating oncologist. For patients continuing Gentamicin, drug level must be monitored just prior to second dose. For patients continuing Vancomycin, drug level must be monitored just prior to 5th dose.

Initial Assessment of Fever or suspected infection in paediatric oncology patients is considered a medical emergency and therapy must be initiated promptly.

Children who have received BTCT within the previous 6 months and those who remain on immunosuppressive therapy (e.g. CIclosporin, steroids, Tacrolimus) should be considered at risk of infection regardless of their blood count.

Parental concerns must always be considered.

Remember that not all septic patients will be febrile.

If parents are concerned the child should be clinically assessed and discussed with a senior medical officer.

Emergency Departments

All patients presenting to SCH or CHW Emergency Department should receive a minimum of a Category 2 triage

Inpatient Units

Escalation **MUST** occur for all inpatient oncology patients with a new fever or suspected infection.

Clinically Stable and no signs of toxicity: Clinical review

Clinically Unstable, Septic Shock: Rapid Response

Initial priority must be rapid assessment of the following:

- **Airway**
- **Breathing:** Respiratory rate, effort, SpO2, colour
- **Circulation**: Heart rate, rhythm and pulse strength, blood pressure, capillary refill, colour, consider cardiac monitoring if appropriate
- **Disability**: Mental status, (GCS/AVPU), pain assessment
- **Exposure:** Axillary temperature (tympanic temperatures are not accurate in children), rashes
- **Fluid:** Hydration status inclusive of urine output, mucous membranes
- **Glucose**: Blood glucose level

The selection of a management pathway most appropriate for the patient is done by rapid clinical assessment. This includes looking for signs of toxicity (Alertness, decreased arousal or activity; pale or mottled colour; cool peripheries; weak cry; grunting; rigors; bounding pulses; wide pulse pressure).

All patient parameters must be recorded either:

- Electronically on the Between the Flags (BTF) Chart **OR**
- In the event of a downtime or where eMR BTF Charts are not available patient on the age appropriate:

- Standard Paediatric Observation Chart (SPOC)
- Paediatric Emergency Department Observation Chart (PEDOC)

CLINICAL PRESENTATION

The most common initial manifestation of infection in paediatric oncology patients is fever. The NSW Health Observation trigger for high temperature starts at 38.5°C. As 'Fever' within this patient population is defined as a single temperature of ≥ 38.0°C by any route these patients should be escalated as per local CERS at this lower threshold.

Fever may be the first and only manifestation often without any localising symptoms.

It is important to recognise that the "usual" presenting symptoms and signs of infection in paediatric oncology patients may not be obvious in the absence of an inflammatory response. Furthermore fever in this group of patients may be secondary to drugs (Cytarabine, Bleomycin), blood products or viral infection (usually respiratory viruses). It is not possible to rule out bacterial infection in these patients and hence prompt administration of antibiotics is indicated.

Localised infection (pain and signs of inflammation) may occur in the absence of fever. For example, neutropenic patients with intra-abdominal sepsis may complain only of localized pain despite significant intra-abdominal pathology (e.g. perforated bowel). Thus, in an afebrile patient with local pain, haemodynamic instability, prompt initiation of empiric antibacterial therapy is indicated.

Clinical scenarios of localised infection which require prompt antibiotic administration include (but not limited to) the following:

Local Infection of CVADs: This can present as

- Warmth, tenderness, erythema at exit site, and/or
- Swelling and fluctuation around the subcutaneous catheter hub with signs of inflammation or cellulitis of the overlying skin, and/or
- Tunnel infection which is characterized by spreading cellulitis in the subcutaneous tissues along the tunnel tract of the catheter.

Ear infection: Paediatric oncology patients can develop the same repertoire of infectious disease as immune-competent patients. Clinical findings suggesting an ear infection range from the classic complaints (e.g. ear pain, drainage, fever, irritability) to minimal findings (e.g. slight tympanic erythema) in profoundly neutropenic children.

Lower respiratory tract infection: These patients may present with cough, respiratory distress, hypoxia with or without fever. Initial chest x-ray changes could be minimal due to the absence of neutrophils.

Intra-abdominal infection: e.g. typhlitis (also known as neutropenic enterocolitis) can present with abdominal pain, diarrhoea with or without fever in profoundly neutropenic patients.

Infectious meningitis in paediatric oncology patients is uncommon but is associated with significant morbidity and mortality. Symptoms may not include headache or photophobia. Neck stiffness may be absent. Meningitis in paediatric oncology patients can be subtle in

presentation and signs and symptoms of CNS dysfunction should alert the clinician to this possibility. Children with intra-ventricular shunts and CSF access reservoirs are at high risk for development of CNS infection and early CSF collection for microscopy and culture should be considered.

Initial Management

All paediatric oncology, BTCT, non-malignant haematology patients with neutropaenia or patients with severe aplastic anaemia presenting with fever, reported fever or unwell should be managed as if they have neutropenic fever and receive prompt empiric antibiotics.

Venous access should **not be delayed** waiting for anaesthetic cream to take effect

Antibiotic commencement should **not be delayed** for confirmation of neutrophil count.

Antibiotic management can be modified based on clinical features & laboratory results if neutrophil count is normal.

Clinically stable	Clinically Unstable	Septic Shock
Patients should receive antibiotics within **60 minutes** of presentation after collection of blood cultures and blood samples	Patients should receive their first antibiotic dose within **30 minutes** of presentation after the immediate collection of blood cultures, blood samples and initiation of fluid support	Patients should receive their first antibiotic dose **immediately** and resuscitation commenced as clinically indicated

Low Risk Management patients presenting to ED

Refer to Oncology Patient-Fever- Low Risk Management

Low Risk Management Patients presenting to the ED should be assessed and managed as per usual practice for managing fever or suspected sepsis in the oncology / BTCT patient

Patients on IV antibiotics via an infusor:

a. Disconnect infusor, collect bloods including blood culture and manage as per guideline

b. Transfer from HITH to inpatient hospital

Patients on oral antibiotics

Patients on oral antibiotics at home who present to ED should have their oral antibiotics ceased and IV therapy commenced as per the febrile neutropaenia pathway.

The Oncology team is responsible for reviewing the patient in ED after the ED assessment is complete. The oncology team (medical or nursing) must notify HITH of any patient on the low risk program presenting to the hospital.

Investigations/Diagnostic Tests

The investigations aim to maximise the chance of detecting systemic bloodstream infection by bacteria or fungi. The following laboratory tests are crucial at initial presentation to assess the aetiology of the episode and guide further treatment. **HOWEVER** antibiotics administration should **NEVER** be delayed beyond 30-60 minutes if there are difficulties collecting the required samples.

To minimise cross contamination and ensure accurate results, the blood samples should be collected and follow the recommended "order of the draw'. A vacutainer device should be used to minimise contamination

First collect Aerobic and anaerobic blood cultures

In usual practice, more isolates are grown from aerobic rather than anaerobic culture bottles. Therefore it is recommended that the aerobic blood culture bottle be inoculated with the recommended blood volume. Where there is a limiting volume of blood that has been collected it is preferable to inoculate the aerobic blood culture bottle with an appropriate volume rather than splitting a small volume between the aerobic and anaerobic blood culture bottles.

CVAD *IN SITU*: If a patient has a CVAD take a blood culture sample from each lumen as per the CVAD practice guideline or local CVAD guidelines. It is important to note that culturing CVAD lock solution and/or the blood occupying the CVAD dead space volume reduces the ability to identify systemic blood stream infection. The discard volume (up to 3ml) from the Implantable venous lines should **not** be used for blood cultures.

Peripherally collected blood cultures **are not required** in patients who have had cultures taken through a CVAD.

NO CVAD or CVAD Blocked / Not bleeding: If CVAD access is not available obtain peripheral cultures, when collecting a peripheral sample an appropriate volume of blood should be collected and inoculated into each blood culture bottle.

Blood Volumes: When collecting the sample the age of the child and size of the blood culture bottle should be taken into consideration. For children ≥1 year aim to collect 1ml blood per year of age up to a maximum of 20ml.

Age of Patient	Volume
<12 months	up to 1 mL
12 months- 5 years	1-5 mL
5-15 years	5 -15 mL
> 15 years	20 mL

	Recommended Minimum Volume	Recommended Maximum Volume
Paediatric Bottles	0.5-2mL*	4-5mL*
Adult Aerobic Bottles	5-8mL*	10mL*
Adult Anaerobic Bottles	5mL-8mL*	10mL*

* Please refer to local pathology services and local guidelines for more information about minimum and maximum volumes

Then obtain additional blood for:

i. Electrolytes/urea/creatinine (EUC) and Liver Function Tests (LFT's)
ii. Full blood count
iii. Group and Hold +/- Crossmatch
iv. Venous Blood Gas (includes Lactate & glucose)
    a. 1 mL slip tip- minimum 0.4 mL
    b. 3 mL luer lock- minimum 1.5 mL
v. Ammonia (only if indicated)
vi. Lactate (if indicated NB: VBG will give lactate result)
vii. Coagulation profile (only if indicated)
    a. Micro- (do not under fill, mix gently 4-5 times)
    b. Adult- 2.7 mL (do not under fill, mix gently 4-5 times)

In general all blood samples unless otherwise listed should be filled to the "fill line" and the sample mixed gently 8-10 times to prevent clotting.

Other

- Urine microscopy and culture
- Chest x-ray (in patients with respiratory symptoms / signs)
- Swab any sites of concern for culture

First Dose Antibiotic regimen

First dose antibiotic therapy for all patients is as per Table 1

Gentamicin: Only to be given as first line treatment in Clinically Unstable and Septic Shock. For all other patients, gentamicin should only be given after consultation with the admitting Oncologist

- **Clinically Stable:** First dose antibiotic therapy includes 1 antibiotic (Piperacillin+Tazobactam)
- **Clinically Unstable:** First dose antibiotic therapy includes 2 antibiotics (Gentamicin and Piperacillin+Tazobactam)
- **Septic Shock:** First dose antibiotic therapy includes 3 antibiotics (Gentamicin and Piperacillin+Tazobactam, Vancomycin)

The first dose of antibiotic for some patients may be different, due to a history of allergy or colonisation with multidrug resistant organisms.

Please refer to the Paediatric Injectable Medicine Handbook for administration advice.

Modification to First Dose Empiric Therapy for Patients with Allergies

Some patients may need modification of the therapy as follows:

- Non-severe penicillin hypersensitivity (i.e. rash): Usually **Cefepime** (in specific circumstances **Meropenem** may be substituted) and **Gentamicin**.
    - ADD M**etronidazole** if features of abdominal or perineal infection and **Cefepime** is selected
- Severe hypersensitivity reaction to penicillin: **Ciprofloxacin + Vancomycin and Gentamicin**
    - ADD **Metronidazole** if features of abdominal or perineal infection
- Non-severe Vancomycin allergy (i.e. rash): If Vancomycin would otherwise be indicated, replace with **Teicoplanin** (10mg/kg/dose IV 12 hourly (max. dose 400mg) for 3 doses followed by 10mg/kg/dose IV 24 hourly (max. dose 400 mg))
- Severe Vancomycin allergy: If Vancomycin would otherwise be indicated, consult an infectious diseases physician or clinical microbiologist and oncologist urgently. Options include **Linezolid** (1 month - 12 years 10mg/kg/dose IV 8 hourly (max. dose 600 mg), (greater than 12 years 600mg IV 12 hourly) or **Daptomycin** (Paediatric dose 7-12mg/kg Adult dose is 6-10 mg/kg IV once daily.

Modification to First Dose Antibiotics for Patients with History of Colonisation with Drug Resistant Organisms

The information about colonization with drug resistant organisms is found under Problems, Alerts and diagnoses tab on power chart.

- If a clinically unstable (severe sepsis/shock) patient is known to be colonised with a multi-drug resistant gram negative bacilli (such as an ESBL producing gram negative bacilli) use **Meropenem**
- If the patient is known to be colonised with a Carbapenem-resistant gram negative bacilli (e.g. MBL-enterobacteriaceae) seek urgent infectious disease/microbiology advice and use the aminoglycoside **Amikacin instead of Gentamicin**
- If the patient is known to be colonised by a Van–B type Vancomycin-resistant enterococci (VRE), replace the Vancomycin with **Teicoplanin.** If the VRE is Van A type consult an infectious disease physician/clinical microbiologist urgently. Options include **Linezolid** or **Daptomycin.**

Indications for Vancomycin use

- Sepsis/Shock
- Obviously infected CVAD (erythema/tenderness along subcutaneous track, or purulent exit site discharge) pending cultures
- MRSA carriers who are clinically unstable
- If the episode follows treatment with high dose cytarabine (> 2 g/m^2/day) and/or severe mucositis

Patients with Features of Abdominal or Perineal Infection

- ADD Metronidazole (if receiving Cefepime or Ciprofloxacin as first line)
- Piperacillin+Tazobactam or Meropenem will provide adequate anaerobic cover, if required, other than for suspected or proven *Clostridium difficile*-associated diarrhoea or colitis

Antifungal Therapy

Antifungal therapy in the first 24 hours is rarely indicated unless the patient is already receiving antifungal therapy, in which case it should be continued.

Subsequent modifications to the regimen will depend on clinical response and isolates which is beyond the scope of this guideline.

Psychosocial aspects and family centred care

- Ensure that the patient and parents/carers receive appropriate education on recognition of the unwell child, the signs of infection and when to seek medical attention.
- Commence treatment promptly with the aim that the patient will recover from the infectious episode with minimal complications.
- Discuss with the patient and parents/carers the ongoing treatment plan.
- Engage Child Life Therapy for any procedures and/or refer to Child Life Therapy: Procedure Support Practice Guideline for advice.
- Refer the family to the social worker if available.

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