Infection in the Immunocompromised Patient

INTRODUCTION

. **INFECTION IS THE MAJOR AVOIDABLE CAUSE OF DEATH IN CHILDREN WITH CANCER. FATAL INFECTIONS OFTEN OCCUR IN CHILDREN WHOSE CANCER IS POTENTIALLY CURABLE**
PLEASE DO NOT HESITATE AT ANY TIME, WHEN TREATING A CHILD WITH FEBRILE NEUTROPAENIA, TO DISCUSS MANAGEMENT WITH YOUR NEW ZEALAND CHILD CANCER SERVICE
Fiji with Christchurch and Samoa/Tonga with Starship, Auckland

Risk Factors

Clinical

The risk and pattern of infection in children with cancer and/or neutropenia depends on the primary diagnosis and the type, duration and intensity of the treatment. Some or all of the following factors may influence the type and risk of infection:

- Duration and severity of neutropenia
- Associated gut toxicity due to cytotoxic drugs

Disease-related

Acute Lymphoblastic Leukaemia (ALL) during 'continuing chemotherapy'

- measles, varicella zoster and pneumocystis carinii

Important points

1. The symptoms and signs of infection may be minimal or absent in the presence of neutropenia due to the paucity of the neutrophil mediated inflammatory response. The majority of patients who present with febrile neutropenia have few clinical findings apart from fever. In this setting there is no certain way of telling which febrile neutropenic patients have a potentially life-threatening infection; therefore, all such patients require prompt investigation and empirical treatment with antibiotics.
2. The most frequent blood culture isolates are Staph. epidermidis, various Streps, Gram negative bacilli, Staph. aureus but the most rapidly lethal are E coli, Klebsiella and Pseudomonas. Hence empirical antibiotic therapy is often weighted towards Gram negative organisms.
3. The origin of most bacterial sepsis in neutropenic patients is from the host themselves ie. not from transmission by contact with an infected individual.
4. The risk of viral infection eg. chickenpox is independent of the neutrophil count and more related to lymphocyte number and function. Any child receiving chemotherapy is at risk regardless of their neutrophil count.

Prevention Of Infection

The following measures may be taken in an attempt to avoid infection:

- minimising exposure to contacts especially chickenpox
- passive immunisation after exposure to varicella zoster or measles
- dietary advice
- protecting mucosal and epithelial barriers
  - mouth care (see Symptom Care chapter)
  - avoidance of rectal medications or procedures if patient is neutropenic
  - care with Intravenous sites
  - avoidance of routine surgical procedures when patient is neutropenic eg. dental extractions
- prophylactic antibiotics
  - cotrimoxazole to prevent pneumocystis carinii pneumonia (PCP) in ALL and high-risk solid tumours

FEVER IN THE NEUTROPENIC PATIENT

Persistent fever in the neutropenic child whether at home or in hospital requires immediate attention, meticulous assessment and early commencement of broad-spectrum antibiotics.
Note that all children on chemotherapy with a fever regardless of the neutrophil count must be assessed. They should present directly to the Paediatric Ward, and not be triaged via the Emergency Department

Definitions

Neutropenia

Absolute neutrophil count < 0.5 $x10^{9}$/litre

Leukaemia at diagnosis often have dysfunctional neutrophils .

Neutrophils counts may drop rapidly, particularly with sepsis, so that a count > 0.5$x10^{9}$/l in the morning may have plummeted by that evening. A neutropenic child with a neutrophil count < 0.2 x 10^{9} and fever > 38^{0} C has 70% chance of bacteraemia.

Fever

$\geq 38.5^{0}$ C at any time, or
> 38.0 deg C on two consecutive occasions > 2hours apart

These are guidelines; patients may be septic at lower temperatures particularly those receiving steroids.
All in-patients with a new fever must be reviewed by the Registrar immediately.
Patients fulfilling the above criteria at home must be admitted to hospital.

Types of Infection

Viruses:
Respiratory viruses, enteroviruses, CMV, EBV, HSV, VZV measles
Bacteria:
Gram +ve: Staph aureus, Staph epidermidis, Streptococcal and pneumococci
Gram -ve: Ecoli, Klebsiella, Enterobacter, Citrobacter, Pseudomonas
Fungi: Candida sp, Aspergillus
Others: Atypical pneumonias, Pneumocystis carinii pneumonia (PCP)
The likely organism depends upon the site of infection.
However it is very common for febrile neutropenia to be culture negative. Febrile Neutropenia is the diagnosis and antibiotics should be commenced and continued as indicated below.
The most common bacterial isolates are G+ve especially Staph epidermidis but the most lethal are the G-ve organisms.

Clinical Assessment of Febrile Neutropenia

History

In addition to the usual history;

- Determine what treatment the child has recently had and check out where they are on their treatment protocol.
- If child recently on steroids, consider Addisonian crisis if septic (see Emergencies chapter)
- Determine how long patient has been neutropenic and check most recent FBC
- Any history of contacts especially chicken pox, measles, diarrhoea and vomiting illnesses.
- Systematic inquiry especially ENT, respiratory, abdominal and urinary symptoms
- Any history of pain

Clinical examination

The usual signs of localised sepsis such as redness and swelling may be absent - pain may be the only feature so pay special attention to localised pain**.**

1. General assessment: level of consciousness, heart rate, BP, capillary perfusion time, jaundice, anaemia, lymph nodes
2. Skin: metastatic abscess, infarcted lesion with central blackness suggestive of Pseudomonas (or occasionally fungus). Exanthem of VZV, measles, parvovirus.
3. recent puncture sites - venipuncture, LP, BMA
4. ENT: examine ears and palpate mastoid bones. An inflamed tympanic membrane may be aural mucositis in association with severe oral mucositis rather than otitis media. Pain from oral mucositis may be referred to the ears without evidence of a reddened tympanic membrane. Examine mouth carefully - chemotherapy-induced mucositis causes pallor of the membranes first, then diffuse redness sometimes with sloughing. Look for evidence of thrush, ulceration and gingivitis.
5. Respiratory system: observe for tachypnoea +/- indrawing as this may be the only sign of respiratory infection. Cough &/or tachypnoea demands a CXR. Pulse oximetry for tachypnoea.
6. CVS: heart rate, BP and capillary perfusion. Cardiac size and murmurs.
7. Abdomen: hepatomegaly, splenomegaly, localised tenderness, ascites, distension, masses, bowel sounds.
   Post-chemotherapy gut (ileus) is usually distended, reduced bowel sounds, generally mildly tender. Extreme pain in the RIF suggests typhlitis (ileocaecal transmucosal infection). Examine perianal region but never do a PR on a neutropenic patient - pain on defaecation or tenderness around anus must be taken seriously.
8. CNS: focal signs, meningism. Acute bacterial meningitis is very unusual in neutropenic patients but can occur.
9. Musculoskeletal: examine generally. Signs of bone and joint infection may be subtle.

Sequential Approach To Investigation And Treatment Of Febrile Neutropenia

Hour 0

At presentation of febrile neutropenic patient

Investigations

1. Blood cultures - peripheral
2. FBC, biochemistry (liver function)
3. CRP (if readily available)
4. Culture other sites as clinically indicated

5. Chest XRay/urine/faeces as clinically indicated
6. Sputum/NPA as clinically indicated

Children with fever and neutropenia may have any of the following and should all be admitted to hospital

1. Septic shock – hypotension, poor capillary refill, thready fast pulse
2. Oral or perianal mucositis
3. Soft tissue infection – localised pain with defaecation, even without much erythema or tenderness, should raise suspicion.
4. Dehydration and/or vomiting
5. Haemorrhage
6. Patient < 3 years old
7. Leukaemia during induction or reinduction therapy
8. Abdominal pain or tenderness
9. Pneumonia or CXR suggestive of infective change (a CXR need not be done unless there is clinical suspicion of a LRTI)
10. SaO_2 < 96%
11. Dexamethasone – patient either on this medication or (a) within 2 days of completing 5 day course or (b) within a week of completing a course longer than 5 days
12. Concern regarding social circumstances- eg: family have no transport to return to the hospital

(British Journal of Haematology 2001, **112**, 832-837)

RISK GROUPS

	LOW RISK	***HIGH RISK***
Absolute neutrophil count (ANC)	**0.1 - 0.5**	**<0.1**
DURATION NEUTROPENIA	**< 7 DAYS**	**>7-10 DAYS**
COMORBIDITY	**NIL**	**TOXIC**

Hospital Treatment of children with fever and neutropenia

- Stop cotrimoxazole.
- Continue mouth care. Start fluconazole if mucositis moderate/severe and patient not receiving a triazole (either fluconazole or itraconazole)

- Stop chemotherapy , except during ALL induction treatment
- Start antibiotics as per risk group

Antibiotic availability will vary from country to country.

It is important that each institution knows at any one time what is immediately available.

Each institution will need to know :

- What is their first line antibiotic?
- What are the second line antibiotic/s?
- What are the third line antibiotic/s?
- Is Amphotericin-B available?

With the above information- treatment plan below will need to be modified

INITIALTREATMENT: LOW RISK

CEFTAZIDIME 150mg/kg/day divided 8 hourly (max 6G/day)

Evaluate after 48 hours:
If **afebrile** with negative cultures and still neutropenic
Change to once daily IV Ceftriaxone 80mg/kg/day
(max 2G/day) until neutrophil and platelet counts start to increase or until ANC>0.5 then discharge home.

.
If still **febrile** see below.

INITIAL TREATMENT: HIGH RISK

AMIKACIN/TIMENTIN or GENTAMICIN/PIPERACILLIN or PIPTAZOBACTAM

AMIKACIN (AMIKIN) 600mg/m2/day in 3 doses 8 hourly (or 7.5mg/kg/dose for infants <12months)

TICARCILLIN/CLAVULANATE (TIMENTIN) 300mg/kg/day (ticarcillin content) in 4 doses 6 hourly - max 12G/day

Evaluate after 48 hours:
If **afebrile** with negative culture and still neutropenic for once daily:
Ceftriaxone (80mg/kg, max 2G) and **Amikacin** (20mg/kg).

Antibiotics to continue until ANC>0.5

Investigations to be repeated whilst patient in hospital

Daily

1. Blood cultures while febrile. Repeat even more frequently if patient remains febrile and unwell. If blood culture positive, continue with daily cultures until clear regardless of whether patient febrile or not.
2. Transfuse red cells if septic keep Hb >100g/l
3. Transfuse platelets (to keep >20) if febrile
4. Biochemistry (ensure renal function normal whilst receiving nephrotoxic antibiotics)
5. **Check Microbiology results daily**

Twice weekly

1. swabs, stool and urine if febrile
2. Antibiotic levels. Check peak and trough initially - if satisfactory, then only trough levels.

Hour 48 with continuing fever >38^{0}C

Investigation

chest X-ray.

Treatment

with negative cultures, reassess and reculture and add
Vancomycin 60mg/kg/day divided 6 hourly, max 2G/day.
Stop Vancomycin after 72 hours if cultures negative.

96 hours continuing fever >38^{0}C

Treatment

Substitute gentamicin/amikacin and piptazobactam/timentin with meropenem 20mg/kg 8 hourly. (60mg/kg/day).

Would be helpful at this point to discuss with NZ child cancer service.

Febrile at 5 days

Consider addition of an antifungal agent: Amphotericin-B- discuss with NZ child cancer service.

Continued fever

Consider:

1. Ultrasound for abscesses
2. If available-CT scan sinuses, chest, abdomen and pelvis
3. Antibiotic fever
4. Consider dental sepsis- may be occult
5. ? Add acyclovir

Endpoints

Blood culture +ve

Treat for 7 days after clearance of organism from blood culture regardless of neutrophil count.

Blood culture -ve

1. no continuing focus of infection - if neuts (ANC) >0.5 and afebrile, stop all antibiotics

Patients With Fever And Specific Symptoms , Signs or Causes

Fever with abdominal pain, diarrhoea or vomiting

Diarrhoea in the febrile, neutropenic patient is usually due to chemotherapy-induced gastrointestinal mucositis. This is often characterised by a distended abdomen, generalised tenderness, reduced bowel sounds and intermittent cramps. In this setting, avoid abdominal X-rays which often shows air-fluid levels, and metronidazole which often makes the diarrhoea worse. In addition to the above investigations:
Stool for viral studies, C. difficile toxin and culture, parasites including giardia and cryptosporidium antigens

Clostridium difficile enterocolitis

- If feasible, discontinue antimicrobials
- Do not allow patient to mix with other patients until toxin negative – barrier nurse
- Pay meticulous attention to handwashing and toilet hygiene
- Treat for 10 days with:
    - oral/IV metronidazole preferably, or
    - oral vancomycin:
        1. oral vancomycin not absorbed much but beware in patients with renal failure
        2. efficacy of IV vancomycin uncertain in this setting
        3. increasing concern about selection of VRE (vancomycin resistant enterococci)
        4. more expensive than metronidazole

- As many as 20% of patients experience recurrence after discontinuation of therapy. In addition to antimicrobial therapy above, consider:

    oral Intragam (see section on Rotavirus below)

Typhlitis

Typhilitis is a specific abdominal condition that presents in neutropenic patients. Because of broad-spectrum antibiotics, it is an unusual diagnosis to make nowadays. Typhlitis is heralded by fever, vomiting, diarrhoea and abdominal tenderness which then localises to the right iliac fossa. Fullness may be felt in the RIF. Pathologically, there is infection and necrosis in the wall of the caecum. The most frequent organism is Pseudomonas aeruginosa but infection is usually polymicrobial. Plain abdominal X-ray and CT scan are helpful in diagnosis. Management includes gram negative and anaerobic antibiotic cover and G-CSF. Severe cases perforate and need surgical intervention.

Remember - appendicitis may occur in cancer patients

If fever and diarrhoea persist, it is worthwhile asking microbiology to look at stool commensals and their pattern of antibiotic sensitivity because it is much more common for a commensal to be implicated in a febrile neutropenic episode than a known pathogen that infects non-immunocompromised GITs.

Fever with respiratory tract symptoms

Radiological evidence may be minimal so take any infective changes seriously.

Localised infection

- sputum for M,C+S, and viral and PCP immunofluorescence
- nasopharyngeal aspirate
- Mycoplasma IgM
- Empirical Gram positive cover.

Interstitial pneumonitis

Aetiology

Viral	parainfluenza, adenovirus, RSV, influenza, VZV (usually preceding rash), CMV, measles (usually no preceding rash)
Bacteria	Mycoplasma, Legionella
Parasites and fungi	PCP, Candida, aspergillus

Investigation of interstitial pneumonitis

Sputum/cough swab M,C+S for bacteria, fungi and viruses

Management

Commence high-dose IV cotrimoxazole (Trimethoprim component of cotrimoxazole dose 30mg/kg/dose 6 hourly IV)

Consider empirical antifungal therapy

Pneumocystis carinii pneumonia

PCP occurs in ~20% of patients with ALL who are not on prophylaxis. It is very unusual in patients taking cotrimoxazole.

PCP rarely occurs in those compliant with cotrimoxazole. The risk of PCP is related to chronic immunosuppression and lymphocytopenia, not to the severity of neutropenia.

Clinical features

Clues include fever, cough, tachypnoea (very characteristic rapid shallow breathing), absence of signs on auscultation (unless patient is fluid-overloaded), hypoxaemia, lymphopenia and, on CXR diffuse bilateral shadowing (this may be quite subtle in the early stages). Patients may have clinical signs without changes on CXR

At risk patients presenting with clinical signs of a pneumonitis must be considered as likely to have PCP.

Investigations

As above as other opportunistic organisms can present similarly.

Treatment

Commence high-dose cotrimoxazole (see Drug Dose chapter) for 2 weeks with a minimum of 5 days intravenously. Should deterioration occur despite high-dose cotrimoxazole, carefully control fluid balance - dry patient out +/- frusemide. If that fails commence dexamethasone and consider adding pentamidine intravenously. Respiratory failure requiring ventilation may benefit from surfactant.

Mycoplasma pneumoniae

Mycoplasma is a frequent cause of pneumonia, including sometimes an interstitial picture, in children with ALL in remission. It may be indolent with a chronic non-progressive course and recur following cessation of treatment with erythromycin. Diagnose with raised specific IgM titres.

Whooping Cough

Always consider possibility in patient or contact with chronic cough. Oncology patients should receive prophylactic clarithromycin for 10 days following confirmed contact. Beware interaction between macrolides and vincristine but the effects are diminished with clarithromycin compared with erythromycin.

Influenza

Influenza A occurs more frequently and is more virulent than influenza B. The incubation period is 1 – 7 days, usually 2 – 3 days. Uncomplicated influenza presents with cough, malaise, fever/chills, headache, nasal congestion, sore throat and myalgia. In our experience with influenza (both A and B) in immunocompromised children, the most common complications include pneumonitis and/or hepatitis.

Bacteraemia

Gram positive bacteraemia

The initial antibiotic regimen is directed against Gram negative flora and is not optimal for proven Gram positive septicaemia. Where blood cultures are shown to have Gram positive cocci, whether staphylococcus or streptococcus, add vancomycin.

Enterococci are best treated with high-dose intravenous amoxicillin.

Fungal infection

The 2 most commonly diagnosed fungal infections are candidiasis and aspergillosis.

Patients at risk of systemic fungal infection are those with prolonged severe neutropenia on broad-spectrum antibiotics.

Mucositis is a risk factor for Candida.

Candida albicans and other Candida species

Candida may cause skin and/or mucosal infection, severe oesophagitis or systemic disease with fever, jaundice and pulmonary infiltrates. A recently recognised syndrome is the hepato-splenic syndrome with fever, mild jaundice and raised liver enzymes (particularly alkaline phosphatase), and increasing hepatomegaly and sometimes splenomegaly. The symptoms and signs of the syndrome often become evident only with recovery of the neutrophil count.

Invasive candidiasis can be largely avoided by giving mouth care and prophylactic treatment with chlorhexidine mouthwashes, nystatin or triazoles. However, some Candida species are inherently resistant to fluconazole - glabrata and kruzei - so if candidal overgrowth occurs despite fluconazole prophylaxis, ask for typing of the subspecies and substitute fluconazole with either high-dose oral nystatin or IV/oral amphotericin B depending on site of culture. Oral amphotericin is not absorbed so there is no risk of toxicity. A combination of amphotericin with an azole prevents the emergence of resistant candida species in neutropenic patients.

Aspergillus species

Aspergillus usually presents with pulmonary infiltration (best seen on CT scan), sinus infiltration or occasionally focal CNS signs. This infection is often fatal.

Aspergillus is inherently resistant to fluconazole. Itraconazole covers both Candida and aspergillus and there is increasing data to indicate that itraconazole is as least as effective as fluconazole for antifungal prophylaxis.

Empirical antifungal therapy is essential in patients where there is strong clinical suspicion of infection eg. failure to respond to broad-spectrum IV antibiotics after 96 hours in the febrile neutropenic patient.

Perineal and perianal infections

This may present with painful defaecation +/- tenderness in the perianal region only ie. little or no redness/swelling. So take pain/tenderness seriously. Rectal examinations, suppositories and enemas must be avoided in patients who are/shortly will become neutropenic. High suspicion of Gram negative/anaerobic infection. Ensure local swabs and stools sent to lab.

Treat with Amikacin/Timentin or Piperaciliin/Gentamicin, or meropenim and vancomycin.

Review in light of local microbiology results.

Stomatitis/oesophagitis

The commonest cause is chemotherapy. Send swabs for bacterial, fungal and viral culture. Continue mouth care and prescribe fluconazole.

Fluconazole can be effective if given intravenously if problems with oral intake as the drug is secreted in the saliva.

Analgesia – use the analgesic ladder (see section on Palliative Care)

Metronidazole is not to be used empirically.

Acyclovir should be given when the oral ulceration is focal/discrete and the patient is known to be HSV IgG +ve (do not recheck HSV status as it will be +ve from prior blood transfusions!) or the viral culture is positive for HSV. However, a positive culture for HSV does not necessarily mean that the virus is the cause (may be asymptomatic shedding) so do not stop the other antimicrobials.

If there is specific reddening of the gums around the teeth in the febrile neutropenic patient, anaerobic and gram positive cover should be prescribed – piperacillin, gentamicin and vancomycin would be a good choice in this situation.

Pain on swallowing is often directly chemotherapy-induced. Occasionally it may be due to candida or CMV.

Nasal discharge/rhinosinusitis

Viral URTI is still the commonest cause.

Aspergillus may present with nasal/sinus infection in patients with prolonged neutropenia and antibiotic therapy. Features are facial/ocular pain and/or nasal discharge. The symptoms/signs may be strikingly unilateral, and the nasal

discharge profuse but clear.

Send nasopharyngeal swab for M, C+S, fungal and viral culture

Neutropenic and febrile patients - X-ray sinuses (if appropriate for age) are notoriously unreliable so preferably CT scan sinuses. Treat with amphotericin-B, in addition to broad-spectrum antibiotics.

Hepatitis

Consider drugs and infections:

CMV, Hepatitis viruses (A,B & C), EBV and some respiratory viruses eg. influenza may be implicated.

Hepatosplenic candidiasis is an unusual cause.

Hepatic veno-occlusive disease may be confused with viral hepatitis. It can occur in Wilms tumour patients receiving actinomycin D, and those receiving high-dose cyclophosphamide.

A consistent feature of HVOD is platelet refractoriness related to intravascular consumption of platelets, RUQ pain, weight gain and raised bilirubin.

Chemotherapeutic agents and antibiotic-associated hepatitis:

Flucloxacillin may cause an obstructive picture.

L-asparaginase (see Blood Product and Cytokine Support chapter)

Viral Infections

Measles

Take an immunisation history in all newly diagnosed patients, ?measure antibodies as per unit policy.

Potential to transmit measles may occur up to 7days before the rash comes out in the contact, and for 4 days after the rash emerged.

Confidently establish whether the contact does indeed have measles

- most “contacts” do not! Chase the source, diagnosing GP etc.

Following definite exposure regardless of immunisation history

give pooled Normal Immunoglogulin (if available)

Route:

IM 0.5 mls/kg by deep IM injection
or if thrombocytopaenic IVIG (Intragam) should be used (400mg/kg)

Preferably administer within 72 hours of exposure but give up to 14 days of exposure

Encourage vaccination of siblings and playmates; by doing this, there is no established risk to the patient.

Chickenpox

Approximately 7% of immunocompromised patients who developed chickenpox in the pre-acyclovir era died, usually from visceral dissemination particularly pneumonia and encephalitis. Chickenpox is highly contagious.
A significant contact is defined as:

- Play with (or breathing the same air) a child for > 15-20 minutes during the infectious period
- Infectious period is defined as within 72 hour of the rash developing until crusting of all vesicles (+/- 5-7 days)

Parents of at-risk patients need to be advised at the time of diagnosis about the risk and severity of chickenpox while their child is on chemotherapy. It is imperative that the school and friends are informed of the need to report outbreaks of chickenpox. Refer *Draft letter* to parents of fellow school students
The usual incubation period for chickenpox is 10-21 days, but after ZIG the incubation period of chickenpox can be prolonged to 28 days.

Dear Teacher,

Chicken Pox and Measles Awareness
We would like to request you to alert all parents to the need for vigilance with chicken pox and measles.
We suggest you send out a letter such as the one outlined below to all parents asking for their help.

Yours sincerely

Paediatrician

LETTER OUTLINE

Dear Parent,

A classmate of your son/daughter has recently been diagnosed with cancer.
At the present time the child is back at school and doing well.
"The purpose of this letter is twofold."

The first is to make you aware of his/her disease and reassure you that cancer is not contagious.

The second is to request that you please contact the principal (or school nurse or class teacher) if your child comes into contact with chickenpox or measles or develops them.
These illnesses can have serious implications for a person on treatment for cancer and we need to inform the parents so that appropriate action can be taken.

Please feel free to contact me with any questions or concerns.

Thank you for your help.

Yours sincerely
Principal

Chickenpox contact in Immunosuppressed patients

1. It is ideal to know what the patients' serology is, but as this is not always known, these guidelines are for all patients:
   a. on chemotherapy
   b. during 6 months post chemotherapy
   c. Any child who is lymphopenic (< 1.0) or on immunosuppression (steroids > 0.5 mg/kg/day)
2. **Notification of contact within 96 hours:**

ZIG (zoster immune globulin) or **INTRAGAM** if ZIG unavailable

Age	Dose ZIG	Intragam equivalent
0-5 years	200iu	20ml
6-12 years	400iu	40ml
>12 years	600iu	60ml

3. **Notification of contact later than 96 hours or if ZIG/Intrgam unavailable:**
   ACYCLOVIR tabs 80mg/kg/day in 4 divided doses
   commencing day 7 following exposure and continue for 14 days.

Age	Dose Acyclovir
<2 years	200mg qid
2-6 years	400mg qid
>6 years	800mg qid

(Reference : Paediatrics vol 92,no2 , Aug 1993)

ISOLATION:
VZIG and acyclovir recipients still need isolation 7 –28 days post chicken pox exposure
VZIG protection lasts approximately 4 weeks

Chickenpox vaccination (if available) for siblings and close contacts

Patients receiving chemotherapy should not receive the varicella vaccine until at least 6 months off treatment.

However, it may make sense to vaccinate siblings and close contacts of the patient to "ring fence" the immunocompromised individual.

Information from the US indicates that healthy children receiving the varicella vaccine are unlikely to transmit the virus. However, some children developed vesicles between day 5 – 26 following vaccination suggesting the possibility of transmission during this time.

Recommendations from the Center for Disease Control (CDC-USA) states that "if a susceptible, immunocompromised person is inadvertently exposed to a person who has a vaccine-related rash, VZIG need not be administered because disease associated with this type of transmission is expected to be mild".

Treatment of established Chickenpox in Immunosuppressed patients

ACYCLOVIR 1500mg/m2/day in 3 divided doses until afebrile and finished cropping - usually 7-10 days.

If not too unwell give orally

If toxic and unwell give IV Acyclovir.

Need to be isolated

Stop chemotherapy until lesions crusted and blood counts recovered

Viral Gastroenteritis

Rotavirus (and other viruses) can cause severe and/or protracted diarrhoea in immunocompromised patients. Since organisms implicated in enteritis replicate in the GI lumen, it may be feasible to treat using orally administered immunoglobulin. A randomised study in acute rotavirus gastroenteritis showed that those children who received oral immunoglobulin had significantly faster resolution of symptoms and reduced duration of viral excretion.
Dose is 300mg/kg (single dose) of Intragam P to nearest whole vial. Ensure the indication is appropriate – treatment is not cheap (see table below).

Volume	Grams	Cost (NZ$)
50mls	3	170
200mls	4	684

IMMUNISATION POLICY (source STARSHIP)

A) CHILDREN ON MAINTENANCE CHEMOTHERAPY

Influenza vaccination (if available):
Recommended for all children annually provided lymphocyte count > 1.0
If lymphopaenic (lymphocyte count <1.0)
advise influenza vaccination for household members (at a cost to the family).

Defer all other immunisations until off chemotherapy.

Ensure siblings are not given OPV (oral polio vaccination) as this contains live virus and can be infectious to the immunocompromised sibling-the patient.

During treatment and up to 6 months off therapy *CONTACT with:*

Chicken Pox
- *regardless of prior history give VZIG or Intragam within 96 hours of contact or*
- *if >96 hours oral acyclovir 80mg/kg/day in 4 divided doses commencing day 7 following exposure and continue for 14 days.*

Age	Dose Acyclovir
<2 years	200mg qid
2-6 years	400mg qid
>6 years	800mg qid

VZIG and acyclovir recipients still need isolation 7 –28 days post chicken pox exposure
VZIG protection lasts approximately 4 weeks

Measles
- *regardless of prior history give pooled Normal Immunoglogulin for confirmed contact.*
- *Route: IM 0.5 mls/kg*
- *or if thrombocytopaenic IVIG (Intragam) should be used (400mg/kg)*

B) <u>CHILDREN OFF TREATMENT</u>

- When off therapy 6 months check baseline immunisation titres (VZV/measles/rubella/Hepatitis B)

- Then commence reimmunisation schedule
  provided lymphocyte count > 1.0

- **Immune globulin interferes with antibody responses to live vaccines only (MR/Varicella)**
  - see worksheet.

NOTE:
Reimmunisation schedule based on the Immunisation Policy for TONGA.

Details awaited for the Policy for Fiji and Samoa

WORKSHEET FOR REIMMUNISATION OF CHILDREN OFF CANCER THERAPY

Attach Patient sticker **Date:……**

Checklist:

Off therapy > 6 months	
Lymphocyte count >1.0	
Date of last IVIG	
Date of last VZIG	
Baseline end of treatment antibodies:	**Immune + (yes/no)**
Hepatitis B	
Measles	
Rubella	
Varicella Zoster	

+ If 'no' to any of measles/ rubella – reimmunise with MR

Immunise as below omitting any vaccines to which immune

	1st Dose	**+ 6 weeks**	**+ 6weeks**	**+ 6 weeks**	**At age 4-6years**	**At age 15-17 years**
Date given						
	DTP-Hib	**DTP-Hib**	**DTP-Hib**		**DTP**	**Td**
	HepB #	**HepB #**	**HepB #**			
			MR^	**MR^**		
	OPV	**OPV**	**OPV**			
				Varicella *		

Notes:
1. # omit Hepatitis B if immune (>10miU/ml)
2. ^ omit if Measles/Rubella (MR) immune) **These live vaccines must not be given within 5 months of VZIG**
3. * omit if VZV immune) **and 8 months of IVIG**
4. * Varicella vaccination if seronegative or no history of chickenpox
5. Annual influenza vaccination recommended
6. Household contacts -
   recommend annual influenza vaccine -
   varicella vaccine for those non-immune