Adult neutropenia, fever and sepsis

This is a key point summary of the e-learning module – Adult Neutropenia, Fever and Sepsis. To review the complete module, please visit eviQ Education.

This module reviews the epidemiology, clinical manifestations and strategies for managing fever and neutropenia in adult cancer patients.

Topic 1 General principles and definitions

What is febrile neutropenia?

In patients with neutropenia, fever is often the only sign of an underlying infection. This is because neutrophils are required to produce the usual infective signs and symptoms including redness, swelling and pus formation.

Neutrophil nadir

The neutrophil nadir refers to the point at which the Absolute Neutrophil Count (ANC) is at its lowest point after chemotherapy, approximately 7-14 days post chemotherapy.

There are two key components to consider; the depth of the nadir and the recovery period, both of which contribute to the overall risk of infection.[4] The risk of infection and febrile neutropenia is greatest during the neutrophil nadir period.

There are various definitions for fever and neutropenia exist in the literature and hospital guidelines.

What definitions are used in your local policy and guidelines?

Topic 2

Host defences against infection

The immune system is complex and comprised of first and second line of defence against infection.

Skin

The skin acts as the first line defence against microbial invasion. Breaches in skin integrity can lead to local or systemic infection with skin, gut or even environmental organisms.(6)

One of the most significant disruptions to skin integrity is from the use of vascular access devices. Approximately 4000 central line associated blood stream infections occur in Australian ICU's each year.[11]

Mucous membranes

The mucosal surfaces acts as the first line of defence against microbial invasion. Two of the most common complications of cancer treatment are mucositis or stomatitis.

Causes of mucosal disruption include chemotherapy, targeted therapies, surgery, radiotherapy, direct invasion from the cancer, graft versus host disease, infections and endotracheal, nasogastric and urinary catheters.[10]

Spleen

The spleen acts as a mechanical filter and produces antibodies to encapsulated bacteria. Patients may have impaired splenic function due to graft versus host disease, asplenia, or as a side effect of cancer treatment.

GI system and nutrition

In addition to providing a physical barrier, the cells lining the GI tract secrete acids and antibodies that serve as a potent defence against potential enteric pathogens. Viruses such as herpes simplex virus (HSV) and cytomegalovirus (CMV) and bacteria such as Clostridium difficile. Profound neutropenia can also cause a severe form of colitis known as Typhlitis or neutropenic enterocolitis.[12]

Neutrophils

When the first line of defence is breached (i.e. the mucous membranes and skin), the second line of defence is activated (i.e. the neutrophils). Patients with defects in the number and/or function of neutrophils are at increased risk of serious bacterial and fungal infections.[13]

Lymphocytes

The B and T lymphocytes form the adaptive host response.

Defects in immunoglobulin synthesis leads to increased risk of infection with encapsulated bacteria such as Streptococcus pneumoniae, Haemophilus Influenzae Type B and Neisseria Meningitidis.

Lymphopenia and impaired cell mediated immunity persists for many months after completion of chemotherapy or stem cell transplant. This is in contrast to neutropenia, which recovers within days to weeks.

How is anti-cancer treatment impairing a patient's host defences against infection?

What are the common pathogens associated with neutropenia fever? How do these pathogens impair a human host defence?

Topic 3

Cause of fever during neutropenia

The cause of fever during neutropenia includes:

Unexplained fever

An unexplained fever is fever in the absence of microbiological or clinical evidence of infection. For example, clinical signs are absent due to profound neutropenia or appropriate investigations are not done (i.e. not enough blood taken for cultures).

Fever not related to infection

Fever not related to microbiological or clinical evidence of infection, is a diagnosis of exclusion. Causes may include drug-fever, disease-related fever, bone marrow recovery and blood-transfusion reactions.

Bacteraemia

Bacteraemia refers to the presence of bacteria in the blood.
Approximately 80% of identified infections arise from the patient's endogenous flora.

Microbiologically defined infection (MDI)

MDI is defined as an infection that is clinically detectable and microbiologically proven.
Although bacteraemia is the most common MDI in patient with cancer, other important infections include urinary tract infections (UTIs) and pneumonia.

Clinically defined infection (CDI)

CDI is defined as a site of infection that is diagnosed but its microbiological pathogenesis either cannot be proven or is inaccessible to examination.
Patient should undergo a thorough clinical examination at least once a day for the duration of the FN episode as new symptoms or signs may emerge.

What are the causes of fever in neutropenic patient that you seem in your workplace?

What is the difference between microbiologically defined infection and clinically defined infection?

Topic 4

Sepsis recognition and treatment in the first hour

Adults with cancer are at increased risk of severe sepsis and septic shock.[19]

Key Message for Sepsis - Recognise, Resuscitate, Refer.

For more information please read Sepsis Kills.[19]

The sepsis kills program has been developed to reduce preventable harm to patients with sepsis through early recognition, resuscitation and referral. While the program has been developed for all people with sepsis, the key message of early recognition, early antibiotics, and adequate fluid therapy, is particularly relevant for patients with fever and neutropenia.

What are the signs of sepsis?

What are the key treatments in the first hour of sepsis patient with febrile neutropenia?

After sepsis resuscitation has been commenced, which medical teams should be refer to?

RECOGNISE
the signs of sepsis and patients at high risk of developing sepsis. Febrile neutropenia is a medical emergency.

RESUSCIATE
with IV fluids and IV antibiotics as clinically indicated.

REFER
to primary treating team or specialist AFTER sepsis resuscitation has commenced.

NOTE: Please refer to your local or state sepsis guideline/pathway.

Topic 5

Empiric Antibiotics for management of febrile neutropenia

Empiric antibiotics for FN should provide broad-spectrum cover against Gram positive and Gram negative bacteria, including Pseudomonas aeruginosa.[23]

Monotherapy
Monotherapy has been shown to be safe and effective for clinically stable patients with FN.

Dual therapy
Addition of a second antibiotic is recommended for patients who are clinically unstable (i.e. severe sepsis or septic shock).

Others
The empiric addition for a glycopeptide are used for patient has a proven or suspected infection with resistant Gram positive bacteria, or has an allergy to penicillin/beta lactams.

The addition of vancomycin should be considered for patients who are clinically unstable (i.e. severe sepsis), cellulitis, infected vascular devices or with known MRSA colonisation.[23, 24]

Where can you locate your locally endorsed empiric antibiotic guideline?

In what clinical circumstance, will patient require an additional antibiotic therapy?

Check with your local guidelines or Infectious Disease expert for further information.[23, 24]

For more information, see eviQ Clinical resourses - Immediate management of neutropenic fever and Use of empiric antimicrobial therapy in neutropenic fever. Australian Consensus Guidelines 2011 Steering Committee

Topic 6 Risk assessment

Not all patients with cancer and FN are at equal risk of severe infection and medical complications.

A risk assessment directs the approach to therapy:

- High risk patients always require hospital admission and IV antibiotics.
- Low risk patients may be suitable for oral antibiotics and close supervision as an outpatient.[25]

Identifying patients at low risk

The Multinational Association for Supportive Care in Cancer Risk Assessment Index is a validated tool that can be used to measure the risk of neutropenic fever related medical complications. The score was developed to select patients for therapeutic strategies that could potentially be managed in the ambulatory setting.[28]

Please refer to MASCC febrile neutropenic risk index score for more information.

Implementing ambulatory management at low risk patient with FN

Ambulatory management of patients with low-risk FN in a structured and supported program has shown to be safe, improve quality of life and is cost effective.

Patient identified as low-risk should be assessed for suitability of home-based management and oral antibiotics prior to discharge home.

For more information, see National Centre for Infections in cancer low risk fever neutropenia program toolkit.

Does your facility utilise any risk assessment to direct the approach for febrile neutropenia management?