The Newcastle upon Tyne Hospitals NHS Foundation Trust

Guideline for initial management of critically ill haematology/oncology patients

This guideline is intended as a quick reference for initial management of haematology/oncology patients admitted to intensive care for organ support.

The vast majority of haematology/oncology patients admitted to critical care have a degree of bone marrow failure. This is likely to be related either to the underlying disease, recently administered chemotherapy or a consequence of chemotherapy given earlier in the course of the disease which has caused long term myelosuppression. A high proportion of patients are likely to have had a haematopoietic stem cell transplant (HSCT) procedure.

Common indications for HSCT (1) include

- Leukaemia
- Lymphoma
- Myelodysplasia
- Sarcoma

HSCT in a Nutshell

Patients are given intensive conditioning chemotherapy +/- radiotherapy to kill residual tumour and make immunological space for engraftment. Patients are immunosuppressed with ciclosporin to reduce the risk of rejection of the patient by the incoming T cells (graft-versus-host disease). Both graft and patient are usually further T cell depleted using Campath (a monoclonal antibody) to reduce the risk of either graft rejection (host-versus-graft disease) or graft-versus-host disease.

Following conditioning, bone marrow or peripheral blood stem cells are infused into the blood. This is followed by a period of myelosuppression (7-25 days), following which engraftment occurs. Typically neutrophil engraftment (neutrophils >1 x 10^9/L for 3 days) is followed by platelet engraftment (platelets >50 x 10^9/L) and later red cell engraftment. The return of lymphocyte numbers and function takes many months. These observations explain the classical variation in susceptibility to different infections in the post-transplant phase.

Patients with malignancy may be critically ill from their disease or therapy and are prone to infection.

Major sources of infection include

- Central Venous Catheter
- GI Tract and perineum: especially typhlitis (inflammation of caecum), colitis, mucositis
- Lung: including oropharynx and sinuses

Screening patients requiring advanced cardio-respiratory support

a) Exclude non-infectious cause (Usually by a combination of clinical examination, CT scan and pulmonary function tests including transfer factor) Pneumonitis can occur secondary to chemotherapy (e.g.: bleomycin, cyclophosphamide, methotrexate, bleomycin, G-CSF, rituximab) and radiotherapy.
Risk factors for developing chemotherapy induced lung injury include

- increasing age
- administration of high concentration of oxygen
- underlying lung pathology
- concomitant administration of drugs with known pulmonary toxicity
- history of radiation
- asbestos exposure

b) Infectious agents include

Bacterial	Common: S. Pneumonia, H. influenza Opportunistic: S. Aureus, P. Aeruginosa, Enterobacter, E Coli, Klebsiella, Acinetobaceter Uncommon: Legionella, Chlamydia, Mycoplasma
Fungal	Candida, Aspergillus, Mucor
Viral	CMV, VZV, HSV, EBV, RSV and Adenovirus
Protozoa	Pneumocystis, Toxoplasma

Investigations

a) Microbiology

Chest: Nasopharyngeal secretions or sputum. Broncho-alveolar lavage is most sensitive (to be performed at the earliest opportunity if there are no contraindications)

Tests on BAL fluid	Container	If Urgent
Gram stain, PCP stain, Culture and Sensitivity, Acid fast bacilli (AFB) Viral PCR	Universal sterile container (White top) All tests require to be specifically marked	Call the Lab at 31344

PS: AFB is not usually sent as part of routine screening

Blood: Peripheral stab and separate samples from central line and arterial, if present, for culture and sensitivity.

Tests on Blood	Container
Full blood count	Lavender topped vacutainer tube (EDTA)
Urea, creatinine, electrolytes, C-reactive protein	Gold topped vacutainer tube (SST II)

Liver function tests	Gold topped vacutainer tube (SST II)
Coagulation	Light blue topped vacutainer tube (sodium citrate)
Group & Save	Pink topped vacutainer tube (K_2EDTA)
Culture and Sensitivity, Gram stain, Fungal stain	Blood culture bottle
Viral PCR including EBV, CMV, VZV, HSV, RSV and Adenovirus	Lavender topped vacutainer tube (EDTA) (Blood **AND** sputum samples need to be sent for viral PCR)
Mycoplasma	Gold topped vacutainer tube (SST II)

Urine: MSU if possible. Catheter sample, from sample port if catheterized.

Tests on urine	Container
Dipstick (for MSU)	Near patient testing
Culture and sensitivity	Universal sterile container (White top)
Legionella antigen	Universal sterile container (White top)

Others: Catheter (Venous or arterial cannula) tip to be sent for culture in the universal container (White topped), if suspected as source of infection. Wounds, if any, to be swabbed using transwab. Add throat / mouth swabs if indicated.

b) Radiology

Chest X-ray- Routine
CT scan, Chest Ultrasound/ Echocardiogram- subsequent investigations, if and as indicated.

c) 12 lead ECG

Management

a) Administer oxygen. Consider non-invasive ventilatory support (CPAP, BIPAP) as indicated. Discuss appropriateness of invasive ventilation with consultant on-call and parent team.
b) Administer antibiotics- Discuss with microbiology. Refer to trust antibiotics guidelines (2)
c) Cardiovascular support. Consider phenylephrine infusion via peripheral access, if indicated, till central venous access established. Use noradrenaline as first line vasopressor.
d) Ensure appropriate hydration. Catheterise urinary bladder. Monitor urine output.
e) Platelet transfusion to maintain count > $10x10^9$/L. In case of sepsis or other haemostatic abnormality, aim > $20x10^9$/L. If actively bleeding, aim > $50x10^9$/L (3). Other blood component transfusion as per usual protocol.

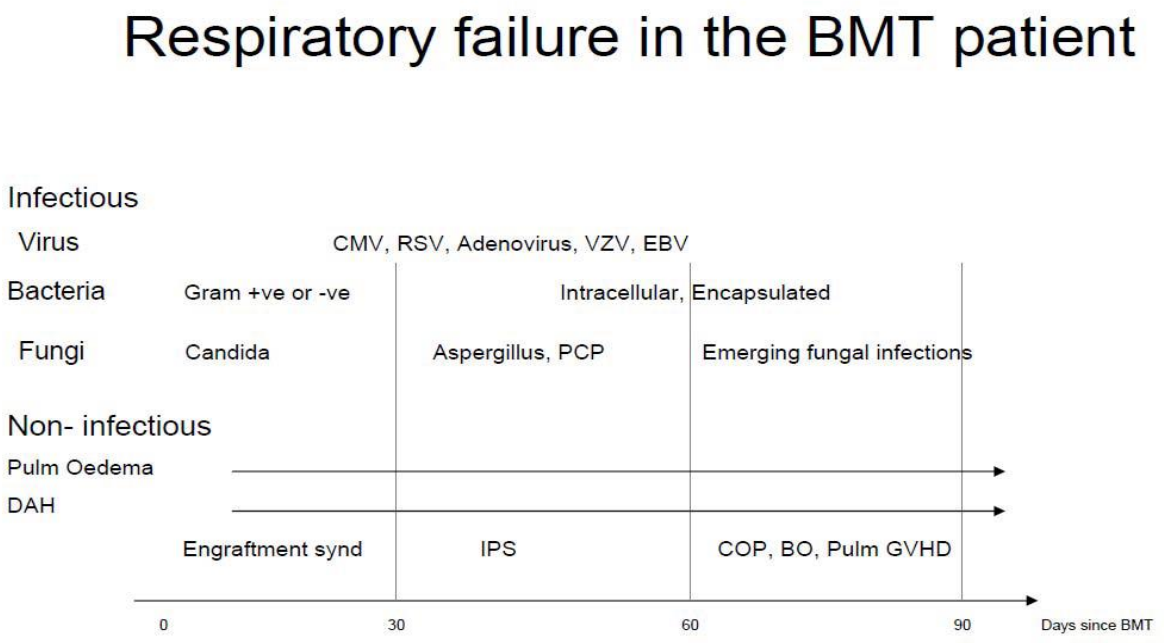
f) Insert nasogastric or orogastric tube, as appropriate, and start feeding if intubated and ventilated otherwise, maintain hydration using intravenous crystalloids.
g) Continue general nursing care.

Reference

1. Oxford Handbook of Clinical Haematology. 3rd edition. Oxford University Press.
2. Trust guidelines on antibiotic use
3. Trust guidelines for the use of platelet transfusions

Appendix 1

Time frame for the usual cause of respiratory failure in BMT patients.



Idiopathic pneumonia syndrome (IPS)

- Occurs in fewer than 10% of HSCT patients, but has a high (75%) case fatality rate
- Most common in allogenic transplants with GVHD.
- Occurs at median 21 days post HSCT.
- If ventilated, unlikely to survive to hospital discharge

Diffuse Alveolar Haemorrhage (DAH)

- A rare complication (<5%) of HSCT, but with a high (>70%) mortality rate.
- Although is non-infectious, some consider DAH to be a variant of Infection related alveolar haemorrhage (IAH), with infection being missed in DAH cases.
- Most have low platelets, but DAH is not prevented with platelet transfusion.
- Onset 11-19 days median, usually within 30 days of HSCT.

Bronchiolitis obliterans organising pneumonia (BOOP, also known as COP-Chronic Organising pneumonia)

- Clinically like pneumonia, but with negative microbiology and no response to antibiotics
- Relatively common complication (5-30% depending on definition).
- 80% present 6 months or more post transplant.
- Rare after autologous HSCT, more common if GVHD (almost unknown if no GVHD)

Appendix 2

Indications for use of specific blood products

- CMV negative
    - Post transplant patients
- Irradiated
    - Hodgkin's disease
    - Patients who received purine analogue (fludarabine, clofarabine, cladrabine, deoxycoformicin)
    - Patients who received Campath
    - All allograft recipients, unless specified.
    - All autograft recipients until 3 months post transplant