Acute Oncology Guidelines
Version 3.0

Network Cancer Leads Group
(Incorporating Network Acute Oncology Group & Network Radiotherapy Group)

Agreed: June 2014

Review Date: October 2016

Review: October 2018
1. Introduction

The National Chemotherapy Action Group (NCAG), guided partly by reports from National Confidential Enquiry in Patient Outcome and Death (NCEPOD) and National Patient Safety Agency (NPSA) and from previous cancer peer review results, has recommended that a more systematic approach should be taken to dealing with cancer-related emergencies. These recommendations have been embodied in the concept of the 'Acute Oncology Service'.

The following is a Merseyside and Cheshire Cancer Network generic guide to the pathways and protocols that should be established in all hospitals with acute oncology services. They should be read in conjunction, and reference to, specific local treatment policies where they exist along with the practitioners clinical judgement.

Key Contact Numbers

<table>
<thead>
<tr>
<th>Area</th>
<th>Phone Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCC Triage - chemotherapy</td>
<td>0151 334 1155 Bleep 5555</td>
</tr>
<tr>
<td>For complications within 6 weeks of receiving chemotherapy in adult cancer patients (&gt;16 years of age)</td>
<td></td>
</tr>
<tr>
<td>CCC Triage - radiotherapy</td>
<td>0151 334 1155 Bleep 4196</td>
</tr>
<tr>
<td>For complications within 6 weeks of receiving radiotherapy in adult cancer patients (&gt;16 years of age)</td>
<td></td>
</tr>
<tr>
<td>St Helens &amp; Knowsley Triage</td>
<td>01744 646170 0151 430 1560 (Whiston)</td>
</tr>
<tr>
<td>(for St H&amp;K chemotherapy patients ONLY)</td>
<td></td>
</tr>
<tr>
<td>Monday to Friday 9am-5pm or</td>
<td></td>
</tr>
<tr>
<td>Out-of-hours and bank holidays</td>
<td></td>
</tr>
<tr>
<td>Walton Cord Compression Co-ordinator</td>
<td>0151 525 3611</td>
</tr>
<tr>
<td>All patients will confirmed/impending Metastatic Spinal Cord Compression (MSCC) on MRI (or where contraindicated)</td>
<td></td>
</tr>
<tr>
<td>Local Trust Acute Oncology</td>
<td></td>
</tr>
<tr>
<td>Direct all enquiries to oncology office</td>
<td></td>
</tr>
<tr>
<td>Monday to Friday 9am-5pm only</td>
<td></td>
</tr>
</tbody>
</table>
2 Complications of Chemotherapy/Radiotherapy

General Principles for the Management of Patients admitted with Chemotherapy/Radiotherapy Toxicities

These are principles only, refer to specific toxicity guidelines for guidance on each toxicity and manage each patient according to their condition, concomitant medication, other medical conditions and the practitioner’s clinical judgement.

- Chemotherapy toxicities can make patients rapidly unwell but are reversible if managed rapidly and appropriately.
- Aggressive management (including HDU/ITU) is appropriate if unstable even in advanced cancer (discuss with the Acute Oncology Team, oncall oncology/haematology team)
- Neutropenia can occur any time after administration of chemotherapy but rarely within a few days or after many weeks (except in transplant patients)
- Review concomitant medications and consider stopping any which may affect their renal function/potential hypotension (for example ACE-inhibitors, diuretics). If the patient is unwell or hypotensive the risks may outweigh the benefits.

If patients are admitted ensure the following are performed:

- STOP ANY ONGOING ORAL ANTICANCER THERAPY
  - Establish intra-venous access (or utilise indwelling lines if appropriately trained to do so). Hydrate if indicated and perform strict fluid balance with daily weights and bloods, particularly if low albumin.
  - Perform NEWS observations as score indicates but twice a day as a minimum following trust NEWS escalation policy if indicated.
  - Daily medical review and daily bloods (watch for neutropenic sepsis/dehydration).
  - Consult Acute Oncology Team and patient’s oncologist if their condition is not improving.
  - Escalate care (for example HDU/ITU) if patient becomes haemodynamically compromised/drowsy/shut down (discuss with specialist team if unsure of appropriateness).
  - Avoid paracetamol/anti-pyretics if neutropenic as they may mask signs of sepsis.
  - If the patient is on a trial, the trials team should be contacted regarding the admission.
  - Inform local specialist team providing cancer treatment as adjustments to the subsequent cycle may be required.
  - All patients admitted with chemotherapy toxicities will need to be reviewed by their oncologist prior to any further treatment as they may need dose delays or adjustment to the next cycle of chemotherapy. The acute oncology/haematology team should annotate the admission into the patient’s oncology/haematology notes and inform the patient’s oncologist/haematologist.
2.1 Nausea/Vomiting
AO Protocol Name: Nausea/Vomiting
AO Type: Type II (Chemo Complication)
Author: JC & SA

Introduction:
Nausea and vomiting are common distressing symptoms in patients with cancer. If not well controlled, they can adversely affect person’s quality of life and lead to deterioration in nutritional intake and performance status with serious consequences on cancer treatment and outcome. This guidance will concentrate on the management of chemotherapy and radiotherapy induced nausea and vomiting.

Common causes of nausea and vomiting in cancer patients:
- Chemotherapy & Radiotherapy
- Anxiety
- Opiate analgesia
- Constipation
- Uraemia
- Hepatic Metastases
- Primary or secondary brain tumours
- Local effects of tumours in the upper GI and intra-abdominal malignancy
- Partial or complete bowel obstruction
- Meningeal metastases
- Hypercalcaemia & Hyponatraemia

Chemotherapy induced nausea and vomiting (CINV):
CINV is thought to occur through a number of mechanisms and involves the action of neurotransmitters both centrally and peripherally. Emesis post chemotherapy can be categorised into
- Acute, occurring within the first 24 hours
- Delayed occurring after 24 hours and usually peaking around 48-72 hours
- Anticipatory. As the incidence and severity of post chemotherapy nausea and vomiting has reduced so has the occurrence of anticipatory nausea and vomiting.

Prevention is the main aim of anti-emetic therapy in the setting of chemotherapy. There are three main groups of drugs used in this setting.

Incidence and severity depends on individual factors, with female gender, younger age, and previous emesis with chemotherapy giving higher risk. Patients with a history of motion sickness are also more susceptible. Alcohol consumption is also predictive, with patients with relatively high tolerance of alcohol being less prone to CINV. Patients with a high pre-treatment expectation of severe nausea are more likely to experience nausea. These risk factors are well established however the most powerful determinant of risk of chemotherapy induced emesis is related to the intrinsic properties of the drug, along with the dose, route and schedule of administration. Current guidelines for antiemetic therapy are based primarily on the properties of the chemotherapy regimen rather than individual factors.
Initial evaluation:
- History, physical examination to identify cause
- FBC, U&Es, Calcium
- If not tolerating oral intake or biochemical dehydration for parenteral hydration and parenteral anti-emetics
- Previous Oncology Correspondence/contact detail

Ongoing management:
Acute oncology team to liaise with patient’s oncologist to ensure anti-emetic regime is reviewed prior to further chemotherapy.

Emetic potential of chemotherapy\textsuperscript{5,6}

<table>
<thead>
<tr>
<th>Emetic Risk</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>High emetic risk</td>
<td></td>
</tr>
<tr>
<td>&gt;90% risk without prophylaxis</td>
<td>Carmustine, Cisplatin, Cyclophosphamide (&gt;1.5g/m\textsuperscript{2}) Dacarbazine, Procarbazine, Streptozocin</td>
</tr>
<tr>
<td>Moderate emetic risk</td>
<td>Bendamustine, Busulfan, Carboplatin, Oral Cyclophosphamide, Cytarabine, Daunorubicin, Doxorubicin/epirubicin Etoside (oral), Ifosfamide, Irinotecan, Melphalan, Methotrexate, &gt;250mg/m\textsuperscript{2} Oxaliplatin, Temozolamide, Vinorelbine (oral)</td>
</tr>
<tr>
<td>Low emetic risk</td>
<td>Capecitabine, Cytarabine (low dose), Docetaxel, Etoposide (IV), Fludarabine (oral), 5-Fluorouracil, Gemcitabine, Ixabepilone Liposomal doxorubicin, Methotrexate &gt;50mg/m\textsuperscript{2}-250mg/m\textsuperscript{2}, Mitomycin, Mitoxantrone, Paclitaxel, Pemetrexed, Topotecan</td>
</tr>
<tr>
<td>Minimal emetic risk</td>
<td>Asparaginase, Bleomycin, Busulfan, Chlorambucil (oral), Fludarabine, Hydroxyurea, Lenalidamide Melphalan (oral low dose), Methotrexate(&lt;50mg/m\textsuperscript{2}), Thalidamide, Vinblastine, Vinorelbine</td>
</tr>
</tbody>
</table>

5HT\textsubscript{3} serotonin receptor antagonists:
The 5HT\textsubscript{3} receptor antagonists act by binding to the 5HT\textsubscript{3} receptors thus blocking the effect of serotonin. This effect is thought to be most marked on peripheral as opposed to central receptors. There are a number of first generation 5HT\textsubscript{3} serotonin receptor antagonists available including ondansetron, granisetron, and dolesetron. When used in appropriate doses these three drugs appear to be equivalent\textsuperscript{7,8}. They also share similar side effect profiles, with constipation, mild headache and transient rises in liver transaminases being some of the more common effects seen.
Corticosteroids:
Corticosteroids have a high therapeutic index in prevention of CINV and are a well established component of preventative anti-emetic regimens based on extensive published evidence. The addition of dexamethasone to a 5HT\textsubscript{3} receptor antagonist prophylaxis reduces the risk both of acute and delayed vomiting by 25-30\%\textsuperscript{11}.

NK\textsubscript{1} receptor antagonists:
NK\textsubscript{1} receptor antagonists, of which aprepitant was the first to gain regulatory approval, work by selectively blocking the binding of substance P at the NK-1 receptor centrally. The addition of aprepitant to a standard combined antiemetic regimen of 5HT\textsubscript{3} and dexamethasone given to patients receiving cisplatin, one of the most highly emetogenic drugs, showed a significant reduction in nausea and vomiting\textsuperscript{12}. A meta-analysis of NK-1 receptor antagonists show that they do not seem to improve acute emesis but do significantly reduce delayed nausea and vomiting\textsuperscript{13}.

For highly emetogenic chemotherapy a combination of aprepitant, dexamethasone and ondansetron is recommended. Antiemetics should start prior to the administration of chemotherapy and then cover the high risk period for delayed emesis over the following three days. Combination chemotherapy regimens are classified according to the drug with the greatest emetic potential.

Radiation induced nausea and vomiting
The risk of nausea and vomiting associated with radiotherapy depends upon which area of the body is being treated as well as the single and total dose, fractionation and irradiated volume. Again patient related factors play a part with younger, female patients again being higher risk features along with level of anxiety and recent experience with chemotherapy\textsuperscript{15}. It is thought that the incidence of radiotherapy induced nausea and vomiting is underestimated by treating health care professionals. Observational studies have shown that around 30-40\% of patients are affected, however only about 15\% of patients are routinely prescribed antiemetics\textsuperscript{15, 16}. Recommendations for preventative anti-emetic therapy are then based on this risk stratification. There is relatively little evidence to support the current guidelines or the defined risk groups. Most evidence that does exist is for the use of 5HT\textsubscript{3} antagonists in the setting of higher risk radiotherapy (total body irradiation or radiotherapy to the upper abdomen)\textsuperscript{15}.

MASCC anti-emetic regimen recommendations\textsuperscript{10}

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Pre-chemotherapy</th>
<th>Post-chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk regimen</td>
<td>5HT\textsubscript{3} serotonin receptor antagonist</td>
<td>Dexamethasone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aprepitant</td>
</tr>
<tr>
<td>Post chemotherapy</td>
<td></td>
<td>Dexamethasone on days 2 and 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aprepitant on days 2 and 3</td>
</tr>
<tr>
<td>Moderate risk regimen-</td>
<td>5HT\textsubscript{3} serotonin receptor antagonist</td>
<td>Dexamethasone</td>
</tr>
<tr>
<td>Doxorubicin/</td>
<td></td>
<td>Aprepitant</td>
</tr>
<tr>
<td>cyclophosphamide (AC) only</td>
<td></td>
<td>Aprepitant on days 2 and 3</td>
</tr>
<tr>
<td>All other moderate risk</td>
<td>5HT\textsubscript{3} serotonin receptor antagonist</td>
<td>Dexamethasone</td>
</tr>
<tr>
<td>regimens</td>
<td></td>
<td>Aprepitant</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dexamethasone OR a 5HT\textsubscript{3} Receptor antagonist days 2 and 3</td>
</tr>
<tr>
<td>Low risk regimens</td>
<td>Dexamethasone OR a 5HT\textsubscript{3} serotonin receptor antagonist</td>
<td>No routine prophylaxis recommended on days 2 and 3</td>
</tr>
<tr>
<td>Minimal risk</td>
<td>No routine pre- or post-chemotherapy antiemetics recommended</td>
<td></td>
</tr>
</tbody>
</table>
References


8. Jordan K, Hinke A. A meta-analysis comparing the efficacy of four 5-HT3-receptor antagonists for acute chemotherapy-induced emesis. Supportive Care in Cancer; 2007; 1115: 1023-1033


15. Aapro MS. How do we manage patients with refractory or breakthrough emesis? Support Cancer Care, 2002; 10: 106-109

Management of Nausea and Vomiting

Caused by Radiotherapy/Systemic Anti-Cancer Treatments

**Risk factors:** Radiotherapy, Chemotherapy (cycle number and day)

**Examination:** Clinical history, examination, MEWS observations and calculate score, ensure any anti-emetics have been taken regularly in adequate doses

**Investigations for all patients:** FBC, U&Es, calcium

**If clinically indicated:** Serum magnesium

**Dietary advice:** Eat small frequent meals, avoid: rich, spicy, greasy foods, alcohol. Sit up to eat meals and away from smells, drink between meals rather than with meals

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**Grade 1**
Able to eat and drink reasonable oral intake, 1 episode of vomiting in 24 hours

- Evidence of dehydration?
  - **NO**
  - **YES**

  - Review anti-emetics ensuring the patient is taking them as prescribed - refer to Classification of Chemotherapy by Emetic Potential, page 7, or Radiotherapy Treatment Algorithms, page 9, if needed

  - Consider administering alternatives (listed below) orally or if indicated, sub-cutaneously

- Reassess patient in 24 hours time

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**Grade 2**
Can eat/drink but intake significant decreased, 2-5 episodes of vomiting in 24 hours

- Take bloods. Review anti-emetics ensuring the patient is taking them as prescribed - refer to Classification of Chemotherapy by Emetic Potential, page 7, or Radiotherapy Treatment Algorithms, page 9, if needed

- Do bloods indicate dehydration?
  - **NO**
  - **YES**

  - Consider administering alternatives (listed below) orally or if indicated, sub-cutaneously

- Reassess patient in 24 hours time

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**Grade 3**
No significant intake, 6-10 episodes of vomiting in 24 hours

- Arrange urgent assessment, take bloods and full review. Consider admission. Review anti-emetics ensuring the patient is taking them as prescribed - refer to Classification of Chemotherapy by Emetic Potential, page 7, or Radiotherapy Treatment Algorithms, page 9, if needed

- Administer alternatives (listed below) orally or if indicated, sub-cutaneously

- If patient is not admitted, reassess patient in 24 hours time

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**Grade 4**
No significant intake, >10 episodes of vomiting in 24 hours

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**Alternatives**
- Cyclizine 50mg 3 times a day is often useful for protracted nausea
- Prochlorperazine 5-10mg oral 3 times a day
- Prochlorperazine suppositories 25mg 3 times a day
- Metoclopramide 10-20mg 4 times a day
- Levomepromazine 6mg at night (this can be increased to 12mg)
Management of

**Nausea & Vomiting**

Caused by Systemic Anti-Cancer Treatment

### Classification of Chemotherapy by Emetic Potential

<table>
<thead>
<tr>
<th>MINIMAL (≤10% frequency of emesis)</th>
<th>LOW (10-30% frequency of emesis)</th>
<th>MODERATE (30-90% frequency of emesis)</th>
<th>HIGH (&gt;90% frequency of emesis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alemtuzumab</td>
<td>Cabazetaxel</td>
<td>Bendamustine</td>
<td>Cisplatin ≥50mg/m²</td>
</tr>
<tr>
<td>Alpha Interferon</td>
<td>Capecitabine</td>
<td>Carboplatin</td>
<td>Cylophosphamide &gt; 1500mg/m²</td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>Docetaxel</td>
<td>Cisplatin &lt;50mg/m²</td>
<td>Dacarbazine</td>
</tr>
<tr>
<td>Bleomycin</td>
<td>Doxorubicin (Liposomal)</td>
<td>Cylophosphamide ≤1500mg/m²</td>
<td>Procabazine (oral)</td>
</tr>
<tr>
<td>Cetuximab</td>
<td>Eribulin</td>
<td>Cylophosphamide (oral)</td>
<td>Streptozocin</td>
</tr>
<tr>
<td>Chlorambucil (oral)</td>
<td>Etoposide (IV)</td>
<td>Dactinomycin</td>
<td>AC (combination defined as either</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>Evorolimus Fludarabine (oral)</td>
<td>Doxorubicin &lt;60mg/m²</td>
<td>Doxorubicin or</td>
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<tr>
<td>Fludarabine Gefitinib</td>
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<tr>
<td>Imatinib (oral)</td>
<td>Fluorouracil</td>
<td>Epirubicin &lt;90mg/m²</td>
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<td>Interferon alpha</td>
<td>Gemcitabine Interferon alpha &gt;5</td>
<td>Etoposide (oral)</td>
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<td>&lt;5 million international</td>
<td>&lt;10 million international</td>
<td>Ifosfamide &lt;10g/m²</td>
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<tr>
<td>units/m²</td>
<td>units/m²</td>
<td>Interferon alpha &gt;10 million</td>
<td></td>
</tr>
<tr>
<td>Ipilimumab</td>
<td>Methotrexate &gt;50mg/m² &lt;250mg/m²</td>
<td>Lomustine</td>
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<td>Lapatinib</td>
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<td>Melphalan &gt;50mg/m²</td>
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<tr>
<td>Melphalan (oral low-dose)</td>
<td>Mitomycin</td>
<td>Methotrexate 250mg/m²</td>
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<td>Methotrexate ≤50mg/m²</td>
<td>Mitoxantrone</td>
<td>Lomustine</td>
<td></td>
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<tr>
<td>Pazopanib</td>
<td>Nilotinib</td>
<td>Melphalan &gt;50mg/m²</td>
<td></td>
</tr>
<tr>
<td>Panitumumab</td>
<td>Paclitaxel</td>
<td>Methotrexate 250mg/m²</td>
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</tr>
<tr>
<td>Rituximab</td>
<td>Paclitaxel-albumin (Abraxane)</td>
<td>Oxaliplatin</td>
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<tr>
<td>Sorafenib</td>
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<tr>
<td>Temsirolimus</td>
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<tr>
<td>Trastuzumab</td>
<td>Pemetrexed</td>
<td>Temozolomide (oral)</td>
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<tr>
<td>Vinblastine</td>
<td>Sunitinib</td>
<td>Vinorelbine (oral)</td>
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<td>Vincristine</td>
<td>Topotecan</td>
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<tr>
<td>Vinorelbine (IV)</td>
<td>Vandetanib</td>
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</tr>
</tbody>
</table>

**What is the chemotherapy regime?**

**MINIMAL (≤10% frequency of emesis)**
- Alemtuzumab
- Alpha Interferon

**LOW (10-30% frequency of emesis)**
- Cabazetaxel
- Capecitabine
- Docetaxel
- Doxorubicin (Liposomal)
- Eribulin
- Etoposide (IV)
- Evorolimus Fludarabine (oral)
- Fluorouracil
- Gemcitabine Interferon alpha >5
- <10 million international units/m²
- Methotrexate >50mg/m² <250mg/m²
- Mitomycin
- Mitoxantrone
- Nilotinib
- Paclitaxel
- Paclitaxel-albumin (Abraxane)
- Pemetrexed
- Sunitinib
- Topotecan
- Vandetanib

**MODERATE (30-90% frequency of emesis)**
- Bendamustine
- Carboplatin
- Cisplatin <50mg/m²
- Cylophosphamide ≤1500mg/m²
- Cylophosphamide (oral)
- Dactinomycin
- Doxorubicin <60mg/m²
- Epirubicin <90mg/m²
- Etoposide (oral)
- Ifosfamide <10g/m²
- Interferon alpha >10 million international units/m²
- Lomustine
- Melphalan >50mg/m²
- Methotrexate 250mg/m²
- Oxaliplatin
- Temozolomide (oral)
- Vinorelbine (oral)

**HIGH (>90% frequency of emesis)**
- Cisplatin ≥50mg/m²
- Cylophosphamide > 1500mg/m²
- Dacarbazine
- Procabazine (oral)
- Streptozocin
- AC (combination defined as either
- Doxorubicin or
Management of

**Nausea and Vomiting**

Caused by Radiotherapy Treatment

**Nausea and Vomiting (Radiotherapy) Treatment Algorithm**

**First line**
Domperidone 10-20mg orally 4 times a day when necessary

**Second line**
Consider **ADDING** Ondansetron 8mg 30minutes orally before radiotherapy treatment as a preventative measure
2.2 Neutropenic Sepsis

AO Protocol Name: Neutropenic Sepsis  
AO Type: Type II (Chemo Complication),  
Author: EM & SA

Definition (NICE cg 151): Neutropenic sepsis (NS) is a potentially fatal complication of anticancer treatment (particularly chemotherapy). Mortality rates ranging between 2% and 21% have been reported in adults. Neutropenic sepsis should be diagnosed in any patient having anticancer treatment whose neutrophil count is $0.5 \times 10^9$ per litre or lower and who has either:

- a temperature higher than 38°C or
- other signs or symptoms consistent with clinically significant sepsis.

NS is an acute medical emergency. Patients require immediate assessment and commencement of antibiotic therapy after taking blood culture (within one hour of arriving to hospital). All patients who are currently or recently been on chemotherapy with fever above 38 should be regarded as having neutropenic sepsis until proven otherwise. Some patients with neutropenic sepsis do not develop fever due to compromised immune reaction or steroid use and high degree of suspicion should be the rule in any unwell patient on chemotherapy. Do not wait for blood count result in order to start initial antibiotic dose (door to needle antibiotic has to be within one hour). Elderly patients are at a higher risk of febrile neutropenia following chemotherapy, with worse morbidity and mortality rates. A & E and medical assessment units should have defined pathways that ensure that patients receiving chemotherapy who present with symptoms suggestive of sepsis are managed with the 60 minute target in mind.

Patient Referral systems:
- Develop neutropenic /chemotherapy alert/pathway with A & E and Medical assessment unit
- Refer to acute oncology service for early input.

Initial evaluation:
- History (including significant microbiology, for example, Clostridium difficile, MRSA or other resistant organism)  
- Physical examination to identify potential source of infection  
- Maintain a high index of suspicion  
- Blood culture, FBC, U&Es, and further investigations as appropriate depending on symptoms  
- Do not routinely offer G-CSF for the prevention or management of uncomplicated neutropenic sepsis unless they are receiving G-CSF as an integral part of the chemotherapy regimen or in order to maintain dose intensity  
- Offer beta lactam monotherapy with piperacillin with tazobactam as initial empiric antibiotic therapy unless there are patient specific or local microbiological contraindications  
- Previous Oncology Correspondence/contact detail  
- All patients with confirmed neutropenic sepsis should have a risk assessment carried out to determine the risk of complications (MASCC index in adult patients). This should be performed as soon as possible and within 24 hours of presentation by a health care professional with competence in managing complications of anticancer treatment.
MASCC scoring index:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burden of illness: no or mild symptoms</td>
<td>5</td>
</tr>
<tr>
<td>Burden of illness: moderate symptoms</td>
<td>3</td>
</tr>
<tr>
<td>Burden of illness: severe symptoms</td>
<td>0</td>
</tr>
<tr>
<td>No hypotension (systolic BP &gt; 90 mmHg)</td>
<td>5</td>
</tr>
<tr>
<td>No chronic obstructive pulmonary disease</td>
<td>4</td>
</tr>
<tr>
<td>Solid tumor/lymphoma with no previous fungal infection</td>
<td>4</td>
</tr>
<tr>
<td>No dehydration</td>
<td>3</td>
</tr>
<tr>
<td>Outpatient status (at onset of fever)</td>
<td>3</td>
</tr>
<tr>
<td>Age &lt; 60 years</td>
<td>2</td>
</tr>
</tbody>
</table>

Scores ≥ 21 are at low risk of complications. Points attributed to the variable ‘burden of illness’ are not cumulative. The maximum theoretical score is therefore 26.

**Ongoing management:**
- Consider initial or step down oral antibiotics in patients with confirmed low risk neutropenic sepsis. Early discharge should take into account the patient’s social and clinical circumstances.
- Daily Acute Oncology review to facilitate step down policies, timely discharge and clinical review by patient’s usual oncologist.
Management of **Neutropenic Sepsis**

Caused by Systemic Anti-Cancer Treatments

Any patient presenting with suspected NS should receive immediate empirical antibiotics **WITHIN 1 HR** of presentation. **DO NOT wait for results of Fbc**

**Signs and symptoms:** Defined as Neutrophils ≤ 0.5 x 10^9/l **AND** pyrexia (over 38.0°C), however, symptoms may be non specific such as diarrhoea, vomiting and confusion despite the absence of fever.

**Risk factors:** Chemotherapy **within 4 weeks** (most commonly day 7-14 post treatment), previous episode of febrile neutropenia.

**Examination:** NEWS observations and calculate score, clinical history and examination including establishing if there **clear** clinical focus of infection for example cellulitis, abscess, central line, pneumonia. Do they have any allergies and if allergic to any antibiotics is it definite, probable or possible allergy? Have they been on any antibiotics in last 7 days? Does the patient have a significant microbiology history, for example, MRSA, Clostridium difficile.

Cycle day and chemotherapy regime to allow consideration of risk

**Investigations all patients:** FBC and differential, U&Es, LFT’s, peripheral venous blood for aerobic and anaerobic cultures and via a CVAD if present, MASCC Prognostic Index ‘score’

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**MASCC Prognostic Index Score**

<table>
<thead>
<tr>
<th>Risk</th>
<th>Score</th>
<th>Weighting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of the patient</td>
<td>≥60yrs = 0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&lt;60yrs = 2</td>
<td>2</td>
</tr>
<tr>
<td>Is the patient dehydrated, requiring IV fluids?</td>
<td>No = 3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Yes = 0</td>
<td>0</td>
</tr>
<tr>
<td>Is the patient hypotensive?</td>
<td>&lt;90 = 0</td>
<td>0</td>
</tr>
<tr>
<td>(systolic BP)</td>
<td>≥ 90 = 5</td>
<td>5</td>
</tr>
<tr>
<td>Does the patient have COPD?</td>
<td>Yes = 0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>No = 4</td>
<td>4</td>
</tr>
<tr>
<td>Does the patient have symptoms related to this febrile neutropenic episode?</td>
<td>No symptoms= 5</td>
<td>Mild = 5</td>
</tr>
<tr>
<td></td>
<td>Moderate = 3</td>
<td>Severe</td>
</tr>
<tr>
<td>Was patient already an in-patient before this episode of febrile neutropenia?</td>
<td>In-patient = 0</td>
<td>Admitted with this episode = 3</td>
</tr>
</tbody>
</table>

**Total Score**

If patients are unwell or any doubt exists manage as **HIGH** risk in the first instance

---

**Less than 17 – HIGH RISK**

**17 or more – LOW RISK**

Refer to local trust guidelines for antibiotics to commence
2.3 Diarrhoea

AO Protocol Name: Diarrhoea
AO Type: Type II (Chemo complication)
Author: EA & SA

Introduction:
Chemotherapy induced diarrhoea is an increase of at least 2-3 stools per day, or diarrhoea at night or an increase in loose, watery stoma output, when compared with normal bowel habit before treatment. Diarrhoea is a common side effect to many chemotherapeutic agents with reported incidence rates of up to 80% (1& 2). Uncontrolled diarrhoea can be severe enough to cause life-threatening complications due to dehydration, volume depletion, electrolyte disturbance, malnutrition, and renal insufficiency. Some chemotherapy drugs like 5-Flourouracil, Capecitabine and Irinotecan cause damage to the gut mucosa with loss of epithelial cells and increase in immature secretory cells and larger amount of fluid output in the small bowel leading to diarrhoea. Patients with DPD enzyme deficiency who have impaired metabolism of 5-Flourouracil (about 3% of the population) can develop extreme diarrhoea which could be fatal, often associated with mucositis and pancytopenia. Many other chemotherapy agents and also targeted therapies such as, Erlotinib, Gefitinib, Sorafenib, Lapatinib and Cetuximab can cause diarrhoea.

Differential diagnosis:
- Viral gastroenteritis
- Clostridium difficile diarrhoea
- Non-chemotherapy drugs: antibiotics, antiacids, Laxatives
- Diet factors
- Anxiety

Evaluation and Management (see appendix 1):
- Detailed medical history including onset, duration and severity of diarrhoea, chemotherapy regimen, significant microbiology for example Clostridium difficile or recent antibiotics to treat infection and dietary history.
- Physical examination including weight and signs of dehydration, abdominal and rectal examination.
- Biochemistry for evidence of dehydration, electrolyte abnormalities & renal dysfunction and Stool culture.
- Full blood count to identify elevated WCC or neutropenia. If neutropenic treat as per neutropenic sepsis protocol.

Initial Management:
- Stop the chemotherapeutic agent or targeted drug
- Fluid replacement
- Isolate patient
- Stool sample for microbial culture
- If neutropenic treat as per neutropenic sepsis protocol
- Loperamide (if no melena, fever, dehydration or recent history of clostridium difficile)

**Ongoing Management:**
Acute oncology team to communicate with the treating oncologist for dose modification.

References:

**Management of Diarrhoea**

**Caused by Capecitabine Chemotherapy**

**Signs and symptoms:** Increased amounts of loose stools, abdominal cramping

**Examination:** Clinical history including if the patient has a significant microbiology history, for example Clostridium difficile or recent antibiotic use. Onset, duration, frequency, odour, colour, consistency of stool. Examination, including: abdominal and rectal examination, fever, neutropenia, abdominal pain/cramps, dizziness, lethargy, do they have an ileostomy or colostomy? Medication profile including use of laxatives, loperamide and/or analgesia. NEWS observations and calculate score.

**Investigations for all patients:** U&Es, FBC, CRP, Stool cultures, consider abdominal x-ray

**If clinically indicated:** Stool sample for clostridium difficile, serum for magnesium

**Dietary advice:** Avoid: high fibre, high fat foods, spices, caffeine, alcohol, fruit juices, Lactose containing products. Drink 9-10 glasses of clear fluids daily, eat small frequent meals.

**Grade 1**
2-3 stools per day over normal pattern

**Grade 2**
4-6 stools per day or nocturnal stools, moderate cramping

**Grade 3**
7-9 stools per day or incontinence or severe cramping

**Grade 4**
>10 stools per day or bloody stool, diarrhoea or need for parental support

For early review in known to have had Clostridium difficile recently

**STOP Capecitabine and consider admission**
If bloods indicate dehydration consider IV fluids and strict fluid balance chart. Commence barrier nursing, Bristol Stool Chart, consider abdominal x-ray, referral to dietician

Are there clinical signs of *Clostridium Difficile*? (watery diarrhoea (5, 6 or 7 on Bristol Stool Chart, maybe green with characteristic smell), nausea, fever, abdominal pain, loss of appetite, no plausible non-infective cause (for example not had laxatives, chemotherapy, radiotherapy)

**Grade 3-4 or persistent grade 1-2**
For review and consider admission

Start Loperamide 4mg and 2mg after each stool max 16mg in 24 hours or Codeine Phosphate 60mg 4 times a day. Consider nutritional support

**Persistent (grade 1-2)**
Add in Codeine Phosphate 60mg 4 times a day

**If diarrhoea unresolved add Octreotide 100-150mcg 3 times a day, for ≥5 days, increased by 50mcg up to 200mcg 3 times a day if needed**

**Review in 24 hours**

Diarrhoea resolved?

**Review in 24 hours**

Diarrhoea unresolved?

**Review in 24 hours**

Diarrhoea resolved

**Review in 24 hours**

Diarrhoea unresolved

Continue dietary advice, stop Loperamide after 12 hours of diarrhoea free interval

If Capecitabine stopped, consult oncology team and consider re-starting Capecitabine

NO

Follow hospital Clostridium Difficile policy

YES

Consult oncology

Acute Oncology Team review in 24 hours
Non-Capecitabine related Diarrhoea

Caused by Radiotherapy/Systemic Anti-Cancer Treatments

**Signs and symptoms:** Increased amounts of loose stools, abdominal cramping

**Examination:** Clinical history including if the patient has a significant microbiology history, for example Clostridium difficile or recent antibiotic use. Onset, duration, frequency, odour, colour, consistency of stool. Examination, including: abdominal and rectal examination, fever, neutropenia, abdominal pain/cramps, dizziness, lethargy, do they have an ileostomy or colostomy? Medication profile including use of laxatives, loperamide and/or analgesia. MEWS observations and calculate score.

**Investigations for all patients:** U&Es, FBC, CRP, Stool cultures, consider abdominal x-ray

**If clinically indicated:** Stool sample for clostridium difficile, serum for magnesium

**Dietary advice:** Avoid: high fibre, high fat foods, spices, caffeine, alcohol, fruit juices, lactose containing products. Drink 9-10 glasses of clear fluids daily, eat small frequent meals.

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<th>Grade 3</th>
<th>Grade 4</th>
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<td>&gt;10 stools per day or bloody stool, diarrhoea or need for parental</td>
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</tbody>
</table>

For early review in known to have had Clostridium difficile recently

Loperamide 4mg then 2mg after each stool, max 16mg in 24 hours
Increase oral intake, follow dietary advice

Loperamide 4mg then 2mg after each stool, max 16mg in 24hours
Increase oral intake, follow dietary advice

If bloods indicate dehydration consider IV fluids and strict fluid balance chart. Commence barrier nursing, Bristol Stool Chart, consider abdominal x-ray, referral to dietician

Are there clinical signs of *Clostridium Difficile*? (watery diarrhoea (5, 6 or 7 on Bristol Stool Chart, maybe green with characteristic smell), nausea, fever, abdominal pain, loss of appetite, no plausible non-infective cause (for example not had laxatives, chemotherapy, radiotherapy)

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<th>Persistent (grade 1-2)</th>
<th>Persistent grade 1-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Add Codeine Phosphate 60mg 4 times a day</td>
<td>For review and consider admission</td>
</tr>
</tbody>
</table>

**NO**

Start Loperamide 4mg and 2mg after each stool max 16mg in 24 hours or Codeine Phosphate 60mg 4 times a day. Consider nutritional support

**YES**

Follow hospital Clostridium Difficile policy

Consult oncology

If diarrhoea unresolved add Octreotide 100-150mcg 3 times a day, for ≥5 days, increased by 50mcg up to 200mcg 3 times a day if needed

Review in 24 hours

Diarrhoea resolved?

Diarrhoea unresolved?

Review in 24 hours

Diarrhoea resolved?

Diarrhoea unresolved?

Consult oncology

Acute Oncology Team review in 24 hours

Diarrhoea resolved?

Diarrhoea unresolved?
2.4 Cardiac

AO Protocol Name: Cardiac toxicity
AO Type: Type II
Author: EA & SA

Introduction:
Cardiac toxicity is a serious side effect to many chemotherapy and biological agents used for cancer treatment with significant impact on morbidity and mortality. The risk is higher in patients with existing or previous history of cardiovascular disease. There are concerns that the gain in life expectancy from anticancer drugs could be offset by higher mortality due to cardiovascular toxicity.

Cardiac toxicity can be acute / subacute seen at any time from initiation of therapy up to several weeks after and manifests as arrhythmias (e.g. Paclitaxel), ECG changes and acute coronary syndromes (e.g. 5-FU/capecitabine); or chronic seen within months or years after the completion of chemotherapy typically with anthracyclines that can present as symptomatic or asymptomatic left ventricular dysfunction and heart failure.

Cardiotoxicity ranges from asymptomatic subclinical cardiac damage to irreversible heart failure or death. Anthracyclines, Trastuzumab (Herceptin), Fluopyrimidins (5-FU and Capecitabine), platinum salts and to a lesser degree the new Tyrosin kinas inhibitors among others can all induce toxicity to the heart through various mechanisms (see table below).

Radiotherapy involving cardiac structures can also cause cardiac complications that can manifest as pericardial disease, restrictive cardiomyopathy, accelerated coronary artery disease, and valvular heart disease.

Types of cardiovascular toxicity:
- Arrhythmia
- Acute ischemia or coronary spasm leading to angina or myocardial infarction
- Hypertension
- Pericarditis & myocarditis
- Arterial and venous thromboembolism
- Heart failure
- Cardiac arrest / sudden death

Risk factors: Cumulative dose (particularly anthracyclines)
- Patient age
- Pre-existing cardiac disease
- Concomitant use of cardiotoxic drugs

Patient referral systems:
- Refer urgently to cardiology
- Acute Oncology service for advice

Initial Evaluation:
- History and examination including type of chemotherapy drugs, co-morbidity and pre-existing cardiac condition
- ECG, Echocardiogram and Bloods including Troponin level if appropriate.
- Stop the offending drug
- Patients with acute coronary syndromes and arrhythmias should be treated according to the established local guidelines under supervision of the cardiology team

Cardiotoxicity ranges from asymptomatic subclinical cardiac damage to irreversible heart failure or death. Anthracyclines, Trastuzumab (Herceptin), Fluopyrimidins (5-FU and Capecitabine), platinum salts and to a lesser degree the new Tyrosin kinas inhibitors among others can all induce toxicity to the heart through various mechanisms (see table below).

Radiotherapy involving cardiac structures can also cause cardiac complications that can manifest as pericardial disease, restrictive cardiomyopathy, accelerated coronary artery disease, and valvular heart disease.

Types of cardiovascular toxicity:
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- Heart failure
- Cardiac arrest / sudden death

Risk factors: Cumulative dose (particularly anthracyclines)
- Patient age
- Pre-existing cardiac disease
- Concomitant use of cardiotoxic drugs

Patient referral systems:
- Refer urgently to cardiology
- Acute Oncology service for advice

Initial Evaluation:
- History and examination including type of chemotherapy drugs, co-morbidity and pre-existing cardiac condition
- ECG, Echocardiogram and Bloods including Troponin level if appropriate.
- Stop the offending drug
- Patients with acute coronary syndromes and arrhythmias should be treated according to the established local guidelines under supervision of the cardiology team
- Assess for heart failure

**Ongoing Management:**
- Acute oncology team to communicate with treating oncologist regarding the cardiac event.
- Early review post discharge to discuss further treatment.
- Future options may include the use of an alternative drug (e.g., Raltitrexed), bolus 5FU regimen and/or cardiac prophylaxis (calcium antagonist, aspirin and/or nitrates).
- Management should be coordinated with cardiology advice.
Management of 

**Ongoing Chest Pain**

Caused by Anti-Cancer Treatment

**Signs and symptoms:** Pain in the chest which may extend to left shoulder, arm, jaw, stomach or back, shortness of breath, sweating, nausea or vomiting  

**Risk factors:** Radiotherapy, systemic anti-cancer treatment (particularly 5FU/Capecitabine)  

**Examination:** Clinical history, examination including cardiac evaluation, NEWS observations and calculate score  

**Investigations for all patients:** FBC, U&Es, LFTs, Troponin T (or I), ECG, echocardiogram

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild pain. Not interfering with function</td>
<td>Moderate pain, limiting instrumental ADL’s</td>
<td>Pain at rest, limiting self-care ADL’s</td>
</tr>
</tbody>
</table>

Treat chest pain until proven to be non-cardiac/life threatening

Is this pain cardiac?

**NO**

Other causes of chest pain in oncology patients are pulmonary embolism, indigestion and disease progression. Arrange appropriate investigations

**YES**

STOP IV infusions of 5 Fluorouracil and disconnect  
STOP oral Capecitabine/UFT

These patients are often myelosuppressed and are at risk of neutropenic fever and sepsis. If present, this should be managed according to approved guidelines

Monitor patient and ongoing assessment and management in accordance with local trust guidelines

Inform Acute Oncology team of admission as soon as possible
<table>
<thead>
<tr>
<th>Common chemotherapeutic agents causing cardiovascular complications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anthracyclines (Doxorubicin, Epirubicin etc)</strong></td>
</tr>
<tr>
<td><strong>CHF, arrhythmias</strong></td>
</tr>
<tr>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>CHF, tachyarrhythmias, heart block, haemorrhagic myopericarditis</td>
</tr>
<tr>
<td>Cisplatin</td>
</tr>
<tr>
<td>Arrhythmias, hypertension, heart block, CHF, ischaemia/infarction</td>
</tr>
<tr>
<td>Vinca alkaloids (Vincristine, Vinblastine)</td>
</tr>
<tr>
<td>Ischaemia/infarction</td>
</tr>
<tr>
<td>Taxanes (Pacitaxel, Docetaxel)</td>
</tr>
<tr>
<td>Arrhythmias, hypotension</td>
</tr>
<tr>
<td>5-Fluorouracil, Capecitabine</td>
</tr>
<tr>
<td>Arrhythmias, CHF, ischaemia/infarction</td>
</tr>
<tr>
<td>Methotrexate</td>
</tr>
<tr>
<td>CHF, arrhythmias, infarction</td>
</tr>
<tr>
<td>Etoposide</td>
</tr>
<tr>
<td>Ischaemia/infarction</td>
</tr>
<tr>
<td>Mitomycin</td>
</tr>
<tr>
<td>CHF</td>
</tr>
<tr>
<td>Bleomycin</td>
</tr>
<tr>
<td>Pericarditis, ischaemic heart disease</td>
</tr>
<tr>
<td>Trastuzumab, Lapatinib</td>
</tr>
<tr>
<td>CHF, arrhythmias</td>
</tr>
<tr>
<td>Bevacizumab</td>
</tr>
<tr>
<td>Hypertension, thromboembolism</td>
</tr>
<tr>
<td>Sorafinib, sunitinb</td>
</tr>
<tr>
<td>Hypertension, arrhythmias</td>
</tr>
</tbody>
</table>
2.5 Mucositis
AO Protocol Name: Mucositis
AO Type: Type II (Chemo complication)
Author: M.V & SA

Introduction:
Mucositis is a common complication to chemotherapy which manifests as oral pain, erythema, oedema and ulcers. If severe mucositis can cause difficulty in mouth opening and affect eating, drinking and speaking. Mucositis results from toxicity to the mucosal lining with breakdown and ulceration of the oral mucosa. The severity is variable and can affect the entire alimentary tract with symptoms ranging from mild mouth soreness to severe erosive mucositis accompanied by severe pain and inability to eat or drink.

The cytotoxic drugs most commonly associated with mucositis are 5-Flourouracil/Capceiatbine, Doxorubicin, Bleomycin, Methotrexate, Etoposide, Docetaxel and Cisplatin. It is also a common toxicity of head and neck radiotherapy. Patients with poor oral hygiene and pre-existing dental or periodontal disease are at increased risk for this complication.

Initial Evaluation and Management (see appendix 1):
The diagnosis of oral mucositis is clinical
• History and examination including an assessment of severity- oral examination
• Treatment is supportive and mainly aimed at symptom control
• Oral hygiene and oral care
• Patients unable to eat/drink may need parenteral fluid and nutritional support
• Pain relief- Difflam, topical lidocaine, and mucosal coating agent, Gelclair
• Soluble aspirin, Oramorph or sub cut morphine

Ongoing Management:
Acute oncology team to communicate with the treating oncologist for dose modification of the next cycle if necessary
Management of

**Mucositis/Stomatitis**

Caused by Radiotherapy/Systemic Anti-Cancer Treatments

**Signs and symptoms:** Pain, inflammation of mucosa, ulceration, xerostomia (dry mouth), pyrexia, bleeding, white patches or spots, thick, green or yellow saliva

**Risk factors:** Radiotherapy, systemic anti-cancer treatment

**Examination:** Clinical history, examination, NEWS observations and calculate score

**Investigations for all patients:** FBC, U&Es

**If clinically indicated:** Magnesium, group and save and clotting screen if bleeding, oral swab for cultures and sensitivities, referral to dietician

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Painless ulcers, erythema or mild soreness, able to eat and drink</td>
<td>Painful, erythema, oedema or ulcers but able to eat and drink</td>
<td>Painful, erythema, oedema or ulcers and difficulty with eating and drinking</td>
<td>Mucosa/necrosis and / or requires parenteral or enteral support</td>
</tr>
</tbody>
</table>

**First Line**

- Benzydamine 0.15% oral rinse (Difflam), rinse or gargle, using 15ml every 1½ - 3 hours as required (may dilute with water if stinging occurs)

  **AND** a bland oral rinse:

  - Sodium Chloride 0.9%, rinse mouth 4 times a day and 2 hourly as mouth becomes sore
  - Sodium bicarbonate 1 level teaspoon in 500mls warm water, rinse mouth 4 times a day and 2 hourly as mouth becomes sore
  - Tellodent mouthwash tablets, 1 tablet in 200mls of water – no evidence for benefit but may be used when patients are unable to tolerate other bland oral rinses

**Usually managed as out-patient**

**Usually managed as in-patient**
Management of 

**Mucositis/Stomatitis**

Caused by Radiotherapy/Systemic Anti-Cancer Treatments

---

**Oral Pain Treatment Algorithm**

Does the patient have total dysphagia or intractable nausea?

- **NO**
  - **First Line**
    - Benzydamine 0.15% oral rinse (Difflam), rinse or gargle, using 15ml every 1½ - 3 hours as required (may dilute with water if stinging occurs)
    - Paracetamol soluble tablets, 1g four times a day OR Co-Codamol 8/500mg soluble tablets 1-2 tablets 4 times a day
    - Aspirin soluble gargles, 600mg 4 times a day – Gargle and spit

- **YES**
  - Administer analgesia and anti-emetics if required via the subcutaneous route. Try to avoid IM and IV routes

---

**Second Line**

- Co-Codamol 30/500mg soluble tablets, 1-2 tablets 4 times a day
  - Morphine Sulphate liquid, 5-10mg up to 4 hourly prn, may be rinsed around mouth if tolerated

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**Third Line**

- Morphine Sulphate liquid, titrate dose as required, may be rinsed around mouth if tolerated
  - Antacid and Oxetacaine 10mls 4 times a day (unlicensed product)

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**Fourth Line**

- Oxycodone liquid, 2.5-5mg up to 4 hourly prn – for use in patients unable to tolerate Morphine Sulphate liquid due to stinging

---

If pain is still not controlled consider strong opioids and specialist palliative care advice. Mucositis associated pain is usually transient and regular review of analgesia must take place as symptoms resolve.
2.8 Palmar Plantar Erythema

AO Protocol Name: Palmar Plantar Erythema (Hand-foot syndrome)
AO Type: Type II (Chemotherapy Complication)
Author: SA

Definition:
Palmar plantar erythema (PPE) is a common erythematous skin reaction to several chemotherapy and biological drugs which affects mainly the palms of the hands and soles of feet and occasionally other body areas. PPE can be a dose limiting toxicity. It is most frequently seen with the use of fluoropyrimidines, in particular Capecitabine. It can also occur following treatment with 5-Flourouracil, Pegylated liposomal doxorubicin (Caelyx), Cytarabine, Sunitinib, Sorafenib, Docetaxel and Lapatinib.

Symptoms and signs:
PPE usually starts with tingling and burning sensation in the hands and feet within days to weeks after starting chemotherapy. Drug dose and prolonged exposure increase the likelihood of incidence. Symptoms can progress to erythema, swelling, dryness, flaking, peeling, blisters and pain. Patients’ dexterity and mobility may be impaired. PPE can be severe enough to affect patient’s quality of life during and after chemotherapy due to difficulty in carrying out normal daily activities. It can be particularly severe in patients with Dihydropyrimidine dehydrogenase (DPD) deficiency who are also likely to experience severe gastrointestinal and bone marrow toxicity. Upon discontinuation of the causative agent (temporary or permanent), PPE symptoms will start to improve.

Initial evaluation:
- History & physical examination to ensure no other clinical problems related to toxicity.
- Skin assessment should include colour, integrity, swelling and presence of ulcers, blisters or bleeding.
- Grade PPE according to Common Toxicity Criteria (CTC) grading system
- Identify the causative agent in addition to previous oncology correspondence/contact detail.

Management and referral pathway:
- Management guided by CCC triage service based on CTC grading system (see algorithm below). Patients who phone and describe severe symptoms should be invited for day case review and assessment. Skin swab should be taken in areas of ulceration or suspected infection.
- Out of hours advice from CCC triage regarding interruption or discontinuation of chemotherapy. Patients with grade 2 toxicity should be advised to discontinue oral Capecitabine until symptoms improve to grade 1. Consider hospital admission for patients with grade 3 toxicity.
- Unless the patient has other problems, PPE should not necessitate admission. However patients with severe pain, blisters and desquamation and those with other symptoms like diarrhoea and stomatitis may need urgent admission. DPD deficiency should be suspected in those with early severe reactions (during or post first cycle of Capecitabine or 5FU).
- Skin breakdown and/or ulceration might require dressing to prevent infection
- OPD review with patient usual Oncologists to discuss further management (for example dose reduction or discontinuation)
Prevention:
- Early identification and intervention can prevent further deterioration in symptoms and might help resume the treatment without prolonged delays.
- Stop the culprit drug until symptoms resolve or improve to grade 1.
- Dose adjustment in the remaining cycles may be indicated depending on severity and grade.
- Advise patients to avoid exposure to sources of heat including hot water, sun exposure and also avoid friction and excessive skin pressure.
- Cooling measures like applying ice packs
- Loose well ventilated shoes
- Skin care with creams and emollients
- Pyridoxine (vitamin B6) 50mg tds throughout the treatment course might help.
- Good oral hydration
- Arrange review with patient’s oncologist prior to the next cycle of treatment.

Relevance to acute oncology:
Patients might contact chemotherapy triage service but unlikely to need admission. Therefore acute oncology & acute medical teams may not need to be involved unless the patient required admission.

References:
- http://www.oncolink.org/resources/article.cfm?id=1059
Management of

**Palmar Plantar Erythema [PPE] (Hand and Foot Syndrome)**

**Caused by Systemic Anti-Cancer Treatments**

**Signs and symptoms:** Redness, flaking/peeling skin, swelling, blisters, rash, tingling, pain/tenderness to palms of the hands and soles of the feet.

**Risk factors:** Systemic anti-cancer treatments, for example Capecitabine, Sunitinib, 5FU

**Examination:** Clinical history, examination, MEWS observations and calculate score

**Investigations if clinically indicated:** Swab if skin not intact

**Skin care advice:** Rest hands and feet, limit exposure of hands and feet to sources of heat and hot water, avoid exposure to harsh chemicals used in laundry powders and cleaning detergents, wear loose fitting, well ventilated shoes and clothes

---

**Grade 1**
Minimal skin changes or dermatitis, for example erythema, oedema or hyperkeratosis without pain. Not affecting Activities of Daily Living

**Grade 2**
Skin changes, for example peeling, blisters, bleeding, oedema or hyperkeratosis with pain, limiting Instrumental Activities of Daily Living (for example preparing meals, shopping)

**Grade 3**
Severe skin changes, for example peeling, blisters, bleeding, oedema or hyperkeratosis with pain, limiting self care Activities of Daily Living (for example bathing, dressing, feeding themselves)

May be treated as outpatient

If on oral chemotherapy – **CONTINUE** taking
Apply moisturising cream, for example Aveeno or Aqueous cream

If on oral chemotherapy – **STOP** taking
Apply moisturising cream, for example Aveeno or Aqueous cream

If on oral chemotherapy – **STOP** taking
Consider admission and urgent review by patient’s oncologist. Apply moisturising cream, for example Aveeno or Aqueous cream. Do not apply cream to broken skin and apply an appropriate dressing

Review pain, consider commencing analgesia referring to WHO analgesic ladder

For review by patient’s oncologist prior to next cycle as may need a dose reduction, deferral or discontinuation of treatment

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2.9 Extravasation

AO Protocol Name: Extravasaion
AO Type: II
Author: MV & SA

Introduction:

Extravasaion is the accidental leakage of an intravenous fluid or drug into the surrounding subcutaneous tissue. Chemotherapy extravasation is the inadvertent infiltration of chemotherapy into the subcutaneous tissues surrounding the intravenous or intra-arterial administration site. Incidence rates vary but estimated to be between 0.01% and 7% in various publications (ESMO guidelines)

Diagnosis:

Early symptoms: feelings of tingling, burning, discomfort/pain or swelling, and redness at the injection site.

Late symptoms may include blistering, necrosis and ulceration. Chronic pain, contractures and functional loss of the affected limb could follow at a later stage

Signs that frequently raise suspicion of an eventual extravasation are the absence of blood return, resistance on the plunger of the syringe during delivery of a bolus drug, or an interruption to the free flow of an infusion.

If an extravasation is suspected, the cannula should not be removed immediately and general and specific measures should be started as outlined below

Cancer drugs can be grouped into 3 broad categories, based on their potential to cause tissue damage upon extravasation:

- Vesicants: anthracyclines, alkylating agents and vinca alkaloids
- Irritants: 5-Fu, Etoposide, ifosfamide and dacarbazine, platinum drugs and taxanes
- Non-vesicants: like bleomycin, Gemcitabine and methotrexate

Treatment/Early measures (see diagram below):

Discontinue infusion of the chemotherapy drug immediately. Leave the cannula in place

Aspirate as much of the drug as possible from subcutaneous tissue

Elevate the limb

Refer to specific antidote guidance

Extravasation area should be marked clearly

For vesicant drugs consider referral to plastic surgery

Documentation of the event

Arrange review by patient’s oncologist
Management of

Confirmed or Suspected Extravasation

Caused by Systemic Anti-Cancer Treatments

This is a guide to be used in conjunction with the MCCN (2011) Extravasation Policy

Recognition: It is vital an extravasation is diagnosed early and is not misdiagnosed. This can occur when the practitioner fails to differentiate discolouration reactions in the vein, venous shock, flare or phlebitis

Signs and symptoms: Pain, stinging, burning, induration, erythema, venous discoloration, swelling at injection site, no venous blood return (if this is found in isolation, assess for other clinical signs), increased resistance to administration, changes in infusional rate (these may not be noticed if using an infusion pump so close observation is required)

Risk factors: Systemic anti-cancer treatments

Examination: Clinical history and examination

Is systemic cancer treatment currently being infused?

NO

• STOP the infusion or injection – do not remove the access device
• Seek assistance if required
• Disconnect drip and aspirate as much drug as possible, trying also to draw some blood back into the cannula
• Remove cannula with minimal pressure – if central or mixed chemotherapy administration inform consultant with a view to immediate plastic surgeon referral. Extravasations from Portacath needle locking points may be treated as peripheral

YES

• Mark the affected area
• Elevate the limb and encourage movement
• Refer to the specific Antidote Guidance, page 32
• Inform the patient’s oncologist
• For vesicants consider immediate referral to a plastic surgeon
• Provide analgesia according to the WHO analgesic ladder if required
• Measure the area of extravasation, document any treatment and photograph injury if possible
• Provide patient information leaflet with documented measurements of injury – be alert to the possibility of delayed injury
• Patient to contact CCC triage, 0151 334 1155 bleep 5555 if symptoms worsen or persist
• Advise mobility and elevation of affected limb for next 2-3 days.
• Arrange follow-up appointment if needed

Subsequent Steps

• Complete Green Card, trust incident form and any other local documentation as required.
• Send copy of green card to trust and network pharmacist.
• Consider referral to physiotherapist
• Refill extravasation kit – liaise with pharmacy
Management of

Confirmed or Suspected Extravasation

Caused by Systemic Anti-Cancer Treatments

This is a guide to be used in conjunction with the MCCN (2011) Extravasation Policy

**Antedote Guidance**
Determine the type of chemotherapy that has been administered

- **Vinca Alkaloids**
  - Vincristine
  - Vinblastine
  - Vinorelbine
  - **Apply WARM**
  - compression for 24 hours
  - **Hyaluronidase 1500IU** - dilute in 1ml of water for injection. Inject 0.1ml-0.2ml sub-cutaneously at points of the compass around the circumference of the area of extravasation

- **Bendamustine**
  - **Apply COLD**
  - compression for 30 minutes in every 2 hours for 24 hours. Place dry gauze between skin and
  - **No evidence for any specific antidote** - Topical hydrocortisone 1% cream may be applied if there are signs of erythema. Apply sparingly to the affected area 4 times a day while symptoms persist

- **Anthracyclines**
  - Daunorubicin
  - Doxorubicin
  - Epirubicin
  - Idarubicin
  - Mitoxantrone
  - Mitomycin C
  - **Apply COLD**
  - compression for 30 minutes in every 2 hours in 24 hours. Place dry gauze between skin and
  - **Topical Dimethyl Sulfoxide (DMSO) 50%** - Apply using a cotton bud every 2 hours for 24 hours to the extravasation site. Avoid contact with good skin. For the next 7 days apply every 6 hours alternating with topical hydrocortisone 1% cream every 6 hours so a preparation is applied every 3 hours. Do not use an occlusive cover. If blistering occurs discontinue DMSO and seek advice from Acute Oncology Team or local trust IV and Intervventional Procedure nurse CNS. If further advice needed phone CCC IV and Intervential Procedures CNS 0151 334 1155 bleep 4095 (Monday – Friday 9am – 5pm)

- **Oxaliplatin**
  - Cisplatin or Carboplati
  - **Hot or cold compression is NOT required. However, if symptoms warrant apply intermittent WARM compress**

- **All other cytotoxic drugs**
  - **Hot or cold compression is NOT required. However, if symptoms warrant apply intermittent COLD compress**

  **No specific antidote needed** - Topical hydrocortisone 1% cream may be applied if there are signs of erythema. Apply sparingly to the affected area 4 times a day while symptoms persist.
2.10 **Acute hypersensitivity reactions**

**AO Protocol Name:** Acute hypersensitivity reactions  
**AO Type:** Type II (Chemo Complication),  
**Author:** SA

**Definition:**  
The European Academy of Allergology and Clinical Immunology proposed the following definition:  
*Anaphylaxis is a severe, life-threatening, generalised or systemic hypersensitivity reaction.*  
This is characterized by rapidly developing life-threatening airway and/or breathing and/or circulation problems usually associated with skin and mucosal changes.

**Introduction:**  
Anaphylaxis is an uncommon reaction to systemic chemotherapy which requires an immediate intervention and treatment. It can be triggered by various substances but most commonly food, drugs and venoms. It is estimated that 75.5 cases per 100,000 or 1 in 1,333 of the population experience anaphylaxis at some point in their lives. Case fatality ratio reported as 1%/ in most population based studies.

**Diagnosis:**  
Sudden reaction developing within minutes of exposure to certain chemotherapy or biological drug with rapidly progressing symptoms including life threatening breathing/airway and or circulation problems associated with skin/ mucosal changes and possible gastrointestinal symptoms. Other symptoms include rhinitis, conjunctivitis, abdominal pain, vomiting, diarrhoea, and a sense of impending doom. The most likely cause of anaphylactic reactions within a cytotoxic chemotherapy service is the administration of intravenous drugs, especially cytotoxic drugs, antibiotics, contrast media, blood, and blood products.

**Treatment:**  
Treatment of an anaphylactic reaction should be based on general life support Principles (see diagrams below):  
- Use the Airway, Breathing, Circulation, Disability, Exposure (ABCDE) approach to recognise and treat problems.  
- Call for help early, arrest team may be needed followed by admission for observation  
- Treat the greatest threat to life first.  
- Initial treatments should not be delayed by the lack of a complete history or definite diagnosis.  
  - Stop the drug immediately  
  - If hypotensive lie patient flat  
  - Adrenalin IM 0.5 mg (0.5 ml of 1:1000)  
  - Oxygen 10-15 l/min via non-rebreathing mask  
  - IV Fluids  
  - Anti-histamine: Chlorphenamine 10mg IM or IV  
  - Steroids: Hydrocortisone 200mg IM or IV  
  - bronchodilator
References:
Resuscitation council (UK) 2008
NICE guidance CG 134 -2012
Management of

**Acute Hypersensitivity Reactions**

Caused by Systemic Anti-Cancer Treatments

**Signs and symptoms:** Angio-oedema, urticaria, dyspnoea, hypotension, laryngeal oedema, rhinitis, conjunctivitis, abdominal pain, vomiting, diarrhoea, sense of impending doom, flushed or pale skin, cardiovascular collapse

**Risk factors:** Administration of drugs, especially cytotoxic agents, blood and blood products, contrast media, anaesthetics, insect stings and certain foods

**Examination:** Clinical history, examination, NEWS observations and calculate score

**Investigations if clinically indicated:** FBC, U&Es, LFTs

---

**This treatment flow chart covers both anaphylactic and hypersensitivity reactions**

---

### Mild
Urticarial rash, pruritis, rhinitis

Chlorpheniramine 10mg slow IV push and hydrocortisone 200mg IV

Observe the patient

### Moderate
Tachycardia, dyspnoea, wheeze, malaise, flush, nausea, vomiting, anxiety, agitation

Chlorpheniramine 10mg slow IV push, hydrocortisone 200mg IV, an inhaled bronchodilator eg Salbutamol, Oxygen 10-15 litres per minutes

Monitor vital signs

### Severe
Angio-oedema, laryngeal oedema, hoarseness, urticaria, dyspnoea, hypotension, rhinitis, conjunctivitis, abdominal pain, cold & clammy, sense of impending doom

Remove the trigger to the reaction if possible

Assess the patient: **Airway, Breathing, Circulation, Disability, Exposure**

---

Look for acute onset of illness and any life threatening problems

<table>
<thead>
<tr>
<th>Airway</th>
<th>Swelling, hoarseness, stridor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathing</td>
<td>Rapid breathing, wheeze, fatigue, cyanosis, oxygen saturations &lt;92%, confusion</td>
</tr>
<tr>
<td>Circulation</td>
<td>Pale, clammy, low blood pressure, faintness, drowsy/coma</td>
</tr>
</tbody>
</table>

---

Call for help

---

Follow Anaphylaxis Algorithm for Adults and Children (below)
Management of

**Acute Hypersensitivity Reactions**

Caused by Systemic Anti-Cancer Treatments

This treatment flow chart covers both anaphylactic and hypersensitivity reactions

**Anaphylaxis Algorithm for Adults and Children**

- Establish airway. Administer oxygen 10-15litres/min via non re-breathable mask
- Monitor vital signs – BP, TPR, oxygen saturations
- Administer adrenaline (IM unless experienced with IV adrenaline) doses of 1:1000 adrenaline (repeat after 5 minutes if no improvement)
  - **Age** | **Adrenaline**
  - Adult | 500 micrograms IM (0.5ml)
  - Child more than 12 years | 500 micrograms IM (0.5ml)
  - Child 6-12 years | 300 micrograms IM (0.3ml)
  - Child less than 6 years | 150 micrograms IM (0.15ml)
  - Titrate: adults 50micrograms; children 1 microgram/kg
- Perform IV fluid challenge
  - **Age** | **IV fluids**
  - Adult | 500 – 1000ml
  - Child | Crystalloid 20ml/kg
  - Stop IV colloid if this might be the cause of anaphylaxis
- Administer chlorphenamine AND hydrocortisone (IM or slow IV)
  - **Age** | **Chlorphenamine** | **Hydrocortisone**
  - Adult or child more than 12 years | 10mg | 200mg
  - Child 6-12 years | 5mg | 100mg
  - Child 6 months – 6 years | 2.5mg | 50mg
  - Child less than 6 months | 250micrograms/kg | 25mg
- Perform ECG and monitor vital signs
- Inform patient’s oncologist
2.11 Hypomagnesaemia

AO Protocol Name: Hypomagnesaemia
AO Type: Type II (Chemo Complication)
Author: SA

Introduction:
Hypomagnesaemia is probably more common in cancer than non-cancer patients due to chemotherapy induced renal and GI loss in addition to reduced oral intake secondary to various factors. Hypomagnesaemia can cause potentially fatal complications like cardiac arrhythmia, coronary artery spasm and sudden death. Symptoms include muscle cramps, generalized weakness, anorexia, tremor, agitation, confusion, depression and psychosis. Magnesium replacement should be instituted as per hospital guidelines.

Main causes:
- Cisplatin & Carboplatin
- EGFR inhibitors like Cetuximab, panitutumab
- Cyclosporin

Grades of Hypomagnesaemia:

<table>
<thead>
<tr>
<th>Grade</th>
<th>0.5 mmol/L-LLN (lower limit of normal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>0.4-0.5 mmol/L</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0.3-0.4 mmol/L</td>
</tr>
<tr>
<td>Grade 4</td>
<td>&lt;0.3 mmol/L</td>
</tr>
</tbody>
</table>

Patient Referral systems:
Magnesium should be replaced as indicated and acute oncology team informed so that review by patient's oncologist can be arranged if necessary.

Initial evaluation:
Check Magnesium in patients who present with symptoms suggestive of hypomagnesaemia and those who previously had hypomagnesaemia and who are due to have further platinum chemotherapy. Consider urgent replacement if Magnesium<0.4 and/or cardiac history.

Ongoing management:
Patients with Grade 1&2 can be managed with oral Mg replacement
Grade 3&4 hypomagesaemia requires intravenous replacement of Mg

A review with patient's usual oncologist should be arranged.
Management of

Hypomagnesaemia

Caused by Systemic Anti-Cancer Treatments

Signs and symptoms: Muscle cramps, numbness/tingling, palpitations, swollen ankles, shortness of breath

Risk factors: Systemic cancer treatment

Examination: Clinical history, examination, NEWS observations and calculate score

Investigations for all patients: FBC, U&Es, Magnesium

Urgent replacement: If Magnesium <0.4 and cardiac history (IHD, AF, AVF).

- Give magnesium 40mmol and re-assess symptoms
- Review by Acute Oncology Team
- Re-check magnesium if symptoms persist or if clinically indicated

- Check serum magnesium 5-7 days post infusion or earlier if
Radiation Pneumonitis

AO protocol Name: Radiation Pneumonitis
AO Type: Type II (radiotherapy complication)
Author: SA & ACM

Introduction:
Radiation pneumonitis (RP) is a serious complication to thoracic irradiation particularly following treatment of lung, oesophageal, breast and some haematological malignancies. Radiation-induced lung injury results from the combination of direct cytotoxicity on normal lung tissue and the development of fibrosis triggered by radiation-induced cellular signal transduction. Incidence varies depending on volume of lung irradiation, total dose, fractionation and concurrent use of chemotherapy.

Radiation pneumonitis usually occurs within 6 months of treatment with peak incidence at 1-3 months. However radiation fibrosis develops 6 months to 2 years following radiotherapy.

Symptoms of radiation pneumonitis tend to be insidious at the start and develop 4 to 12 weeks post radiation and include dyspnoea, dry cough, and malaise. Patients can also develop low grade fever, fatigue and weight loss. CXR typically shows perihilar infiltrates and parenchymal opacities that conform to the radiation port. CT is more sensitive with typical findings of ground glass opacities, patchy consolidation, pleural reactions and fibrosis.

Oral corticosteroids are the main treatment modality often with good clinical response but occasionally symptoms can take up to 2-3 months to resolve after completion of radiotherapy. See management algorithm below.

Differential diagnosis:
- Pulmonary embolism
- Chest infection/pneumonia
- Cancer progression
- Cardiac causes

Patient Referral systems:
Referral to acute oncology team so that review by patient’s clinical oncologist can be arranged.

Ongoing management:
A review with the patient usual oncologist should be arranged
See diagram below
Management of **Radiation Pneumonitis**

**Caused by Radiotherapy Treatment**

**Signs and symptoms:** Mild hypoxia, fine crepitations – wide spread if drug induced, localised if following focal radiation, low grade fever, development of acute or sub-acute dyspnoea, new or worsening cough

**Risk factors:** Radiotherapy, low performance status, co-morbidity lung disease, smoking history, low pulmonary function tests. The risk is increased in patients who have undergone biopsy only compared to those who undergo complete surgical resection.

**Examination:** History and physical examination including assessment of performance status and history of previous effusions and management, MEWS observations and calculate score.

**Investigations for all patients:** Chest x-ray and comparison with previous imaging, FBC, U&Es, LFTs, CT and CTPA to exclude pulmonary embolism and cancer progression

**If clinically indicated:** Admit under a Respiratory Physician, if appropriate

---

Has pulmonary embolism, cancer progression or infection been excluded?

- **NO**
  - Perform chest x-ray, CT and CTPA to exclude them
  - Review by Acute Oncology Team and Respiratory Physician

- **YES**
  - **Grade 1** Mild symptoms
    - Dry cough, dyspnoea on exertion
    - Can be managed at home.
    - Arrange review by patient’s oncologist as an out-patient
  - **Grade 2** Persistent cough requiring a narcotic, dyspnoea with minimal effort but not at rest
    - Usually managed at home.
    - Consider Dexamethasone 4mg once or twice daily if symptoms persist. Arrange review by patient’s oncologist as an out-
  - **Grade 3** Severe cough, chest x-ray shows evidence of acute pneumonitis, requiring intermittent oxygen
    - ADMIT
    - Commence high dose oral/IV steroids, consider Dexamethasone 6mg twice a day. Review by the acute oncology team within 24 hours and thereafter daily. For review by patient’s oncologist
  - **Grade 4** Severe respiratory insufficiency, requiring continuous oxygen or assisted ventilation

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NWCSCN Acute Oncology Guidelines 2016.doc
Cerebral oedema due to cranial irradiation

AO Protocol Name: Cerebral Oedema
AO Type: Type II
Author: ACM & SA

Introduction:

Brain radiotherapy used to treat primary and metastatic brain tumours can result in cerebral oedema; a transient and reversible brain reaction during or shortly after cranial irradiation. The mechanism is likely due to disruption of blood brain barrier secondary to apoptosis of endothelial cells. Corticosteroids can lessen the radiation-induced blood-brain-barrier disruptions and improve the symptoms.

Patients with recognized significant pre-treatment cerebral oedema should begin oral or parenteral corticosteroids (for example dexamethasone 8 to 16 mg daily) prior to initiating radiation. Maintaining the dose for the first two weeks of radiotherapy can prevent clinical deterioration due to transiently worsened peritumoral oedema. However, a short-term increase in corticosteroid dose may be warranted if symptoms are severe.

Symptoms:

- Headache
- Visual disturbance
- Dizziness
- Nausea & vomiting
- Lack of concentration / Confusion
- Seizures

Management:

- Steroids (dexamethasone 4-8 mg bd)
- Antiemetics
- Hospitalisation for severe symptoms such as confusion and seizures

Patient Referral systems:

Referral to acute oncology team so that review by patient’s clinical oncologist can be arranged if cranial irradiation is complete.
Management of  

**Cerebral Oedema**

Caused by Malignant Disease or Anti-Cancer Treatments

**Signs and symptoms:** Headaches (typically worse on waking and lying flat), nausea/vomiting, seizure – focal or generalised, reduced conscious level, papilloedema, focal neurology, cushing triad (a late sign comprising raised systolic BP, widened pulse pressure, bradycardia and abnormal respiratory pattern), ocular palsies

**Risk factors:** Malignant disease or cancer treatments

**Examination:** History and physical examination, NEWS observations and calculate score, previous oncology correspondence/contact details (regarding timing of radiotherapy).

**Investigations for all patients:** FBC, U&Es, LFTs, CT or MRI brain with IV contrast to check for:- new tumour; treatment induced oedema; haemorrhage; infection

---

CT or MR brain with IV contrast confirms intracranial malignancy with raised intracranial pressure

Is the patient on Dexamethasone?

- **NO**
  - Start Dexamethasone 8mg twice a day (at 8am and 12noon) IV or orally

- **YES**
  - Increase Dexamethasone to a maximum of 12mg twice a day (at 8am and 12noon)

Ensure patient is on a Proton Pump Inhibitor (PPI)

Inform Acute Oncology Team and ensure review by patient’s oncologist and consider referral to palliative care for symptom control

Has the patient had a seizure?

- **YES**
  - Consider starting an anti-convulsant, usually phenytoin

- **NO**

Is surgery an option?

- **YES**
  - Contact neurosurgical registrar

- **NO**

Continue with treatment and review by Acute Oncology Team. Ensure follow-up by patient’s oncologist
3. **New Cancers**

**AO Protocol Name:** CUP  
**AO Type:** Type 1 (New Cancer)  
**Author:** EM & SA

**Introduction:**  
Metastatic cancer with no evidence of an anatomical primary site at the time of diagnosis despite appropriate investigations. More than 10,000 patients are diagnosed with CUP every year in the UK (3-5% of all cancers) and CUP is the 4th most common cause of cancer death. (See NICE cg 104 for full guidance)

**Presentation:**  
Majority of CUP patients present as emergency (57%) compared with 23% of other cancers. It affects older age group with 45% aged 80 or over. Due to tendency to metastasize early, most patients with CUP have disseminated malignancy at the time of diagnosis. Symptoms vary according to the affected body organ. Majority of patients are unfit for investigations or treatment due to poor performance status.

**Investigations:**  
Refer the patient to local acute oncology team before proceeding for further investigations, a member to the team will review inpatients within a working day. Acute oncology team will refer the patient for discussion at the network CUP MDT.

Patient’s fitness is the most important factor in deciding whether to pursue further investigations. Unfit patients with poor performance status (3 & 4) should not be investigated given that they are not going to be suitable for further treatment and referral to palliative care team should take priority in this group to guide symptom management.

In line with NICE guidance, Investigations to find the primary should only be carried out if:

- The patient is fit for treatment should the primary be found
- The results are likely to affect treatment decision
- The patient understands why the investigations are being performed and the potential risks and benefits of investigation and treatment
- The patient is prepared to accept the eventual treatment

Consider the following investigations for fit patients:

- Always start with a thorough history and physical examination
- Blood count, electrolytes, kidney and liver functions
- CXR & CT chest, abdomen and pelvis
- Myeloma screen in lytic bone lesions
- Mammography if breast cancer suspected
- Symptom directed endoscopy
- Biopsy

**Tumour markers:**  
Tumour markers are not usually helpful during the diagnosis of CUP except for:
- AFP and hCG in patients with presentations compatible with germ-cell tumours
- AFP in patients with presentations compatible with hepatocellular cancer.
- PSA in men with presentations compatible with prostate cancer.
- CA125 in women with presentations compatible with ovarian cancer.

Carefully interpret the results because of limited test specificity.

References:
NICE clinical guideline 104, July 2010
NCIN.org.uk
Management of

**Malignancy of Uncertain Origin (MUO) - Generic**

Caused by Malignant Disease

- Urgent referral to local CUP MDT and Acute Oncology Team
- For review by local CUP team or Acute Oncology Team and following to be performed:
  - Organise appropriate investigations
  - Ensure symptom control
  - Inform the patient
  - Commence early discharge planning
  - Consider referral to palliative care team for patients who are symptomatic or performance status 3-4

"Provisional CUP"
- Joint management with specialist CUP MDT

Primary identified
- Refer through to site specific oncologist/MDT

Non-malignant
- Refer on
3.1 Diagnosis and Management of malignancy of uncertain origin (MUO) - Brain

**Unknown primary pathway-Brain**

**AO Protocol name:** CUP-Brain  
**AO Type:** Type I  
**Author:** EM

**Introduction:**
Treatment of brain metastases can improve survival and reduce neurological symptoms. Significant delays to treatment by extended periods of investigation will limit the effectiveness of any further palliative surgery or radiotherapy. The aim of this document is to provide a framework for a rapid assessment and appropriate referral for treatment in Merseyside and Cheshire.

The patient’s presentation, premorbid state, comorbidities, and performance score on full dose dexamethasone (8mg bd with PPI cover) as well as imaging results will determine their suitability for treatment. Patients with a poor performance score are often unlikely to benefit from aggressive surgical intervention. The exception is those patients who have a life threatening tumour (large lesion with mass effect, tumour producing hydrocephalus, metastatic spinal cord compression etc). Surgery can provide a diagnosis as well as treatment.

It is imperative that these patients are investigated and treated rapidly and not lost in multiple MDTs of various specialties for weeks before any investigations or treatment starts.

<table>
<thead>
<tr>
<th>RPA Class</th>
<th>Clinical Features</th>
<th>Median Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>KP ≥ 70, Controlled primary Site, Age ≤ 65, No extracranial metastatic disease</td>
<td>7 months</td>
</tr>
<tr>
<td>II</td>
<td>Neither Class I nor III</td>
<td>4 months</td>
</tr>
<tr>
<td>III</td>
<td>KP &lt; 70</td>
<td>2.3 months</td>
</tr>
</tbody>
</table>
Unknown primary pathway

Imaging evidence of probable malignant brain tumour

Fit for treatment? Early referral to Acute Oncology (inpatients) (Consider advanced age, significant comorbidity, poor performance unlikely to be improved with treatment, and if patient wants to be treated)

YES  NO

Full history and general examination
MRI Brain (WCFT protocol)
CT chest/abdo/pelvis staging (If imaging suggestive of metastasis)
FBC, U+E, LFT. Tumour markers/ myeloma screen only if relevant.
Start planning discharge
Dexamethasone 8mg BD with PPI cover.
If large lesion and/ or significant effects on patient, please do not wait for staging before asking advice from WCFT
The completed staging should take no more than 72 hours

Cerebral lesion with unknown primary

Refer to WCFT. Either On call registrar for advice, or faxed referral form to named consultant neurosurgeon.

Urgent outpatient (within 7 days) or inpatient assessment .If outpatient, can patient go home with support before appointment?

Neuroscience MDT discussion (Thursday PM)

Treatment Outcome
Surgery, biopsy, radiotherapy, SRS, chemotherapy, palliative care
MDT will feedback who responsible for RXT or referral to Oncology if required. 0151 529 5713
CancerServices@thewaltoncentre.nhs.uk
If the patient has been discussed with Neurosurgery On Call and they have suggested more tests, these should be complete as soon as possible. Delay in full staging will cause delay in MDT listing and the patient may then have to wait for a further week if deadline for MDT is missed. Patients will not be listed until WCFT are informed of completion of staging scans etc.

It is important to pass on as much information regarding the patient’s current condition and performance to enable MDT to make an appropriate treatment decision. It is also important to provide information regarding the patients consultant and the where abouts of the patient as the MDT need to know who the MDT outcome is to be feedback to. WCFT require patient contact details as they will be arranging follow up appointments as appropriate.

Please note; SRS may be considered if patient’s prognosis is more than 6 months, the patient has 4 metastases or less and they are less than 30mm with otherwise stable disease.

Acute Oncology Teams can contact the CNS Brain Tumour team at WCFT on Bleep 5391 at the Walton Centre or send information by email to CancerService@thewaltoncentre.nhs.uk
3.3 Cancer Relapse

AO Protocol Name: Cancer Relapse (generic)
AO Type: Type III (Cancer Complication)
Author: EM (St H&K AO)

Introduction:
Approximately, 50% of emergency admissions occur in known cancer patients. 50% of these are linked to disease progression/relapse and 50% due to unrelated complications (PE, infection etc). AO teams can improve communication, provide prognostic information and guide appropriate inpatient management. 20% of patients have a prolonged inpatient stay and AO assessment and audit can facilitate discharge strategies with PCT and DN liaison.

Patient Referral systems:
Develop a electronic alert system for all cancer patients
Ensure pathways are in place to support referral to appropriate site specific cancer teams and/or acute oncology within 24 hours of admission

Education:
Rolling programme of education aimed at key departments and junior doctors

Time to response:
Clinical review and/or telephone advice within 24 hours working time (medical and/or nursing)

Initial evaluation:
- Patient/family understanding and expectations
- PS, clinical diagnosis, prognosis
- Ensure Previous Oncology Correspondence/contact detail made available in case notes

Ongoing management:
- Determined by likely diagnosis and prognosis
- Information/support and symptom control with consideration of early PCT input
- Define the named key worker
- Cancel unnecessary investigations
- Start discharge planning
- Inform treating oncologist and/or site specific team as appropriate

Specialist referral:
- Establish links with existing clinical team and/or MDT for information and review
- Consider development of early discharge team for complex cases (DN, PCT)
Management of

**Cancer Relapse**

Caused by Malignant Disease

Review patient’s performance status, clinical history and perform any necessary investigations

Review patient’s prognosis and cancel any unnecessary investigations

Consider referral to Palliative Care Team

Start discharge planning

Is the case complex?

**YES**

Consider development of early discharge team including DN and PCT

**NO**

Establish links with existing clinical team and / or MDT referral for information and review

3.4 Cancer and Diabetes

**AO protocol name:** Cancer and diabetes  
**AO type:** Type III  
**Author:** SA & ACM

**Introduction**

Cancer and diabetes are both common diseases. They share some common risk factors like obesity, aging, diet and less physical activity in addition to alcohol and smoking. They increasingly occur in the same individual. Possible mechanisms of association include Hyperinsulinemia, hyperglycemia and inflammation. Cancer patients with diabetes may have increased tumour cell proliferation and metastases in a physiologic environment of hyperinsulinemia and hyperglycemia.

There is evidence that cancer patients who have preexisting diabetes are at increased risk for long-term, all-cause mortality compared with those without diabetes (1). Meta-analysis of 23 studies showed that diabetes was associated with an increased mortality HR of 1.41 (95%
confidence interval [CI], 1.28-1.55) compared with normoglycemic individuals across all cancer types.

Patients with pre-existing diabetes may have poorer response to cancer treatment along with increased infection risk and intra-operative mortality. Furthermore, the diagnosis and treatment of cancer may distract both the patient and the health care team from appropriate management of glycaemia, blood pressure, and lipids, proven to reduce morbidity and mortality in diabetic adults. Although results are not consistent, a multidisciplinary approach that includes a diabetes-management team for the treatment of cancer patients with diabetes may be important for improving long-term outcomes and decreasing mortality.1,2,3

**Diabetic Ketoacidosis (DKA)**

DKA is a serious potentially life threatening complication of diabetes particularly type 1 with mortality rates of 2-5%. Precipitating factors include infection and poor adherence to diabetes medications. Main symptoms are thirst, urinary frequency, dehydration, weakness, nausea/vomiting, abdominal pain, ketotic smell and decreased conscious level/confusion or coma.

Initial investigations include blood glucose level (> 11 mmol/L), Blood gases (PH<7.3), potassium level, urinalysis (ketones+++), FBC, U/Es, ECG, CXR, lactate and blood culture. Clearly these patients are better managed under Diabetes / Endocrinology or medical team, this guidance is for initial management mainly at CCC until patient is transferred safely to APH. See algorithm below
Blood Glucose monitoring and insulin adjustment

a) At 1 hour

If blood glucose has not fallen by 3-5mmol increase insulin infusion rate by 50-100%

b) Insulin rate adjustment if necessary after 1 hour

<table>
<thead>
<tr>
<th>Blood Glucose</th>
<th>Rate of Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5mmol/L</td>
<td>Decrease by 0.5-1 unit/hour to a minimum of 0.5-1 units/hour</td>
</tr>
<tr>
<td>5-12 mmol/h</td>
<td>Continue at current rate</td>
</tr>
<tr>
<td>&gt;12mmol/L and not falling</td>
<td>Increase by 0.5-1 unit/hour</td>
</tr>
</tbody>
</table>

Hourly capillary blood glucose (plus ketones if available)
Venous pH, bicarbonate and K+ at 60 mins, 120mins then 2 hourly (use ABG analyser)
4 hourly U+Es (laboratory)
Continue I.V. insulin venous pH > 7.3 and or bicarbonate > 18mmol/L and Ketones <0.6mmol/L

Potassium replacement table

<table>
<thead>
<tr>
<th>Potassium level</th>
<th>Potassium replacement of infusion solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;5.5 mmol/L</td>
<td>Nil</td>
</tr>
<tr>
<td>3.5-5.5 mmol/L</td>
<td>20 mmol</td>
</tr>
<tr>
<td>&lt;3.5</td>
<td>40 mmol</td>
</tr>
</tbody>
</table>

References


4. Royal Liverpool Hospital – DKA guidelines

4. Cancer Complications

4.1 Hypercalcaemia

AO Protocol Name: Hypercalcaemia  
AO Type: Type I & III (New Cancers and Cancer Complication)  
Author: EM & SA

Introduction:
Hypercalcaemia is a common metabolic disorder in patients with advanced cancer particularly those with bone metastases. It is usually associated with poor prognosis and short survival in the range of weeks to months in some patients. 10-20% of patients develop hypercalcaemia during the course of their disease (1). Any malignancy could cause hypercalcaemia, but it is most commonly seen in patients with breast, lung, kidney, prostate cancers and multiple myeloma.

Bone metastases with osteoclast activity and bone resorption is responsible for the majority of hypercalcaemia cases, the remaining are due to humoral hypercalcaemia through the secretion of parathyroid hormone related peptide (PTRHrP) in patients with or without bone metastases. It is important to remember that hypercalcaemia in some cancer patients may not necessarily be due to the underlying cancer and it is important to rule out primary hyperparathyroidism by checking parathyroid hormone level in some patients.

Symptoms:
- Nausea & vomiting
- Dehydration
- Abdominal pain and constipation
- Poor appetite and anorexia
- Fatigue and lethargy
- Polydipsia and polyuria
- Headache
- Confusion and depression
- Can be asymptomatic

Initial evaluation:
- Clinical presentation (symptomatic or routine blood test?)
- Underlying malignancy
- Previous Oncology Correspondence/contact detail should be made available in case notes

Ongoing management:
- Oral hydration in mild hypercalcaemia (<3 mmol/l)
- Intravenous N Saline to correct dehydration
- Intravenous Bisphosphonate (Pamidronate or Zolodronate)
- Response to bisphosphonate can take 2-7 days
- Consider early discharge unless symptomatic. Clinically well patients can receive outpatient bisphosphonates
- Information & support to patient and carer
- Inform oncologist in charge of the patient overall management.
- Start discharge planning

References:
Management of

**Hypercalcaemia**

**Caused by Malignant Disease**

**Signs and symptoms:** Fatigue, weakness, constipation, nausea, vomiting, polyuria, polydipsia, cardiac arrhythmias, delirium, drowsiness and coma. The severity of symptoms correlates more closely with the rate of increase in calcium rather than the actual level.

**Risk factors:** Malignant disease

**Examination:** Clinical history, examination, NEWS observations and calculate score

**Investigations for all patients:** FBC, U&Es, calcium, albumin

**Normal range:** Normal serum corrected calcium is 2.2-2.6mmol/l. Decision to treat should be based on patient symptomology rather than absolute calcium level

---

Is the serum corrected calcium >2.6mmol/l AND patient symptomatic?

- **NO**
  - Monitor patient symptoms

- **YES**
  - **Re-hydrate with 1-3 litres of 0.9% sodium chloride IV.**
    - The volume and rate of fluid replacement should be adjusted in each patient according to their age, severity of hypercalcaemia, degree of dehydration and ability of the cardiovascular system to tolerate rehydration
    - Drugs which reduce renal blood flow or renal calcium excretion should be **discontinued/avoided** where appropriate (for example non-steroidal anti-inflammatory agents and thiazide diuretics)

  - **Treat with IV Bisphosphonate - Zoledronic Acid IV,** dilute in 100mls of sodium chloride 0.9% or 100mls of dextrose 5% and infuse over 15-30 minutes. Monitor renal function and prescribe dose according to creatinine clearance:

    | Creatinine clearance (ml/min) | Dose |
    |-------------------------------|------|
    | >60                          | 4mg  |
    | 50-60                        | 3.5mg|
    | 40-49                        | 3.3mg|
    | 30-39                        | 3mg  |
    | <30                          | no treatment |

  - If creatinine clearance is <30ml/min Ibandronic acid 50mg weekly orally may be considered

  - Inform patient’s oncologist and check corrected calcium levels **5-7days** post bisphosphonate infusion

  - Refer to Hypercalcaemia Follow-Up Treatment Algorithm, page 50
Management of

Hypercalcaemia

Caused by Malignant Disease

Hypercalcaemia Follow-up Treatment Algorithm

Are the corrected calcium levels >3.0mmol/l OR symptoms persist?

NO

Corrected calcium levels to be rechecked every 3-4 weeks or when symptoms occur

YES

Is it 7 days post initial infusion?

NO

Wait at least 7 days from initial infusion to allow maximal response to the initial dose

YES

Consider a further infusion of bisphosphonates and recheck bloods 5-7 days post infusion. Options include:
- The same dose of bisphosphonates
- An increased dose
- Change to an alternative Bisphosphonate

Is the patient experiencing subsequent episodes of symptomatic hypercalcaemia?

NO

Corrected calcium levels to be rechecked every 3-4 weeks or when symptoms occur

YES

Consider a further infusion of bisphosphonates and recheck bloods 5-7 days post infusion. Depending on how close the recurrence is to the original episode options include:
- The same dose of bisphosphonates
- An increased dose
- Change to an alternative Bisphosphonate

Is the patient experiencing subsequent episodes of symptomatic hypercalcaemia?

NO

YES

Seek advice from the Acute Oncology Team and patient’s oncologist
4.2 Venous Thromboembolism

AO Protocol Name: Venous Thromboembolism (VTE)
AO Type: Type II, and III (Complication of cancer and cancer treatment)
Author: SA

Introduction:
Patients with cancer are at high risk of venous thromboembolism (VTE) due to hypercoagulable state associated with malignancy. The clinical spectrum of VTE ranges from asymptomatic incidental finding on CT imaging to life threatening/fatal pulmonary embolism. Malignancy is associated with a fourfold increased risk of VTE and patients on chemotherapy have a sevenfold increase in the risk of VTE. Hospitalised cancer patients are even at higher risk of VTE.

Recurrent VTE is more common in cancer patients and confers worse prognosis. Patients with advanced cancer are particularly at high risk of VTE with a significant impact on morbidity and mortality. There is evidence that old age, obesity, previous history of VTE and pre-chemotherapy thrombocytosis & leukocytosis increase the risk of VTE in patients receiving chemotherapy. Although VTE is common with malignancy (up to 10% of patients), it is worth noting that the majority of cancer patients do not develop VTE.

Thrombosis may represent the presenting symptom (pancreatic cancer) or complicate a known cancer. The risk of VTE is greatest in the first few months after malignancy diagnosis and can persist for many years after first episode. Increasingly, asymptomatic PE is diagnosed on routine CT imaging and follow up. Conventional treatment should apply, however patients should be stabilised on low molecular weight heparin (LMWH) until full oncological history and prognosis is established. AO team should work in collaboration with Haematology and Radiology to allow the development of common patient pathways.

Symptoms & Signs:
Low index of suspicion is justified in cancer patients.

DVT: recent onset of unilateral leg swelling, pain or tenderness
  Remember, upper limb DVT is not uncommon in patients with central catheters like PICC line

PE: breathlessness, chest pain, collapse, haemoptysis, hypotension, tachycardia, tachypnoea with or without hypoxia.

Commence therapeutic dose LMWH while waiting for scan results unless there is contraindication like thrombocytopenia or active bleeding.

Initial evaluation:
- Clinical assessment and symptoms
- Wells score
- FBC, U/Es & LFTs and D-dimer
- Patient/family understanding and expectations
- Previous oncology correspondence/contact detail should be made available in case notes.

Investigations:
Doppler Ultrasound is the investigation of choice for suspected DVT. Repeat scan within a week may be needed when initial scan negative with persistent symptoms.

CTPA is the standard investigation for suspected PE.

Management:
• Commence low molecular weight heparin on suspicion and inform acute oncology team
• Thrombolysis (streptokinase/urpkinase) might be indicated in patients undergoing adjuvant therapy or treatment with curative intent, this needs discussion between senior clinicians.
• Withhold oral anticoagulation until clarity concerning prognosis and relative contraindications (for example chemotherapy, history of bleeding)
• Consider outpatient management for asymptomatic PE
• Patient information and support
• Inform oncologist in charge of the patient
• Start discharge planning

Patient Referral systems:
Develop radiology alert for unsuspected VTE. Make sure the local radiology department has a system in place to contact the relevant clinician as soon as DVT or PE confirmed particularly in outpatient setting.

Specialist referral:
Establish links with haematology, radiology, MAU and A&E
Arrange OP review by the oncologist in charge.

References:

5-Epidemiology of cancer-associated venous thrombosis.
Timp JF, Braekkan SK, Versteeg HH, Cannegieter SC
Management of

**Venous Thromboembolism**

Caused by Malignant Disease

**Signs and symptoms:** DVT - swelling, pain, redness and warmth. PE – dyspnoea, pleuritic chest pain, retrosternal chest pain, cough, haemoptysis, dizziness and syncope

**Risk factors:** Malignant disease with or without chemotherapy

**Examination:** Clinical history, examination, NEWS observations and calculate score

**Investigations for all patients:** Wells score

**Investigations if clinically indicated:** Proximal leg vein ultrasound scan, D-dimer if the scan cannot be carried out within 4 hours of request or if the result of this is negative, CTPA if suspected PE

---

Positive venous thromboembolism (VTE)

Discuss with the patient’s consultant

**Pharmacological Management**

This will depend on the severity of the episode of VTE and the patient’s oncology plan.

- **Commence low molecular weight heparin**, taking into account co-morbidities and contraindications

- **Withhold oral anti-coagulation** until clarity concerning prognosis and relative contraindications (for example chemotherapy, history of bleeding)

Consider treatment according to local policy as an out-patient if the patient has an asymptomatic PE

For patients with a proximal DVT **AND** an ankle pressure greater than 23mmHg

**Mechanical Management**

Offer below knee graduation compression stockings to be worn to the affected leg or legs **one week after** diagnosis or when swelling is reduced sufficiently and if there are **no** contraindications. Follow local policy regarding ongoing use.
4.3 Spinal Cord Compression

Please refer to MCCN full guidelines and NICE cg 75

AO protocol: Metastatic Spinal Cord Compression (MSCC)
AO Type: Type III (Cancer complication) and Type I (new cancer)
Author: SA &ST

Introduction:

Nice guidance (cg 75) defines MSCC as spinal cord or cauda equina compression by direct pressure and or induction of vertebral collapse or instability by metastatic spread or direct extension of malignancy that threatens or causes neurological disability.

MSCC is estimated to occur in 5-10% of cancer patients and usually associated with poor prognosis, worse quality of life and short survival. Misdiagnosis and late presentation could lead to irreversible paraplegia and bladder/bowel dysfunction therefor urgent evaluation, investigation and treatment are paramount in order to optimize patients’ outcome. Most common cancers to cause MSCC are breast, prostate, lung and myeloma. MSCC could be the presenting symptom of new cancer with estimated 23% of MSCC cases occur in patients who are not known to have cancer in the past.

Symptoms/signs on presentation:

- Pain in the middle (thoracic), lower (lumbar) or upper (cervical) spine
- Severe unremitting spinal pain
- Spinal pain aggravated by straining e.g. at stool, or when coughing or sneezing
- Nocturnal spinal pain preventing sleep.
- Sensory loss/disturbance like numbness, pins & needles sensation or paraesthesia
- Localised spinal tenderness
- Limb weakness, mobility deterioration and sphincter disturbance occur at later stage.

Initial management (NICE cg 75):

Contact the MSCC coordinator urgently (within 24 hours) to discuss the care of patients with cancer and any symptoms suggestive of spinal metastases (as listed above)

- Perform MRI of the whole spine as soon as possible in patients with suspected MSCC, unless there is a specific contraindication.
- Patients with severe mechanical pain suggestive of spinal instability, or any neurological symptoms or signs suggestive of MSCC, should be nursed flat with neutral spine alignment
- Corticosteroids (see treatment below)
- Start definitive treatment, if appropriate, before any further neurological deterioration and ideally within 24 hours of the confirmed diagnosis of MSCC.

Discharge planning and ongoing care, including rehabilitation for patients with MSCC, should start on admission and be led by a named individual from within the responsible clinical team.
Treatment:

- Analgesia
- Corticosteroids: dexamethasone 8mg bd should be initiated when MSCC is suspected with PPI cover.
- Surgery: spinal decompression should be considered for fit patients particularly those with single site metastatic lesion or contiguous vertebral lesions
- Radiotherapy: should be initiated as soon as possible if spinal surgery is not indicated
- Systemic Anti-cancer therapy for tumours sensitive to chemotherapy
- Bisphosphonate
- Refer patients who have potential to regain mobility to physiotherapy and occupational therapy for rehabilitation
- Palliative Care: for pain, symptomatic and emotional support.
- Discharge planning: Significant number of patients may not be fit enough for active treatment and admission to the hospice for end of life care under specialist palliative care team would be the appropriate management.

References:

NICE clinical guidance 75
MCCN MSCC clinical guidelines & pathway
West of Scotland Guidelines for Malignant Spinal Cord Compression/Oct 2013 71
Care pathway for patients where MSCC is suspected

**Urgent senior clinical assessment within 2 hours of contact – history, neurological examination, fitness to treat**

- **Fit to treat**
  - Patient has cancer* + Progressive spinal pain (no neurological symptoms or signs; no neuropathic pain features)
  - Escalating spinal pain with neurological signs e.g. weakness, sensory loss, bowel/bladder disturbance.
  - Standard - MRI and treatment within 24 hours

- **Unfit**
  - Inform the referring clinician urgently. Contact specialist palliative care/acute oncology for further management of symptoms. Do not discharge until a full care package/placement is in place.

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**Contact oncologist/ specialist palliative care consultant/ site specific team/ cancer clinician who has seen the patient most recently**

Choose clinician actively managing the patient, (or the clinician who has most recently seen the patient if not under active management).

Make same day contact with responsible consultant or covering colleague.

Flag letter ‘SUSPECTED MSCC’ Do not just send referral/ fax a letter- may cause delay.

Agree who will organise and be responsible for MRI

Standard – investigation and treatment concluded within 1 week

**If the patient develops neurological symptoms in the meantime, arrange urgent admission for MRI and flag as ‘suspected spinal cord compression’**.

If the patient does not have symptoms of neurology, but evidence of MSCC is seen

**Triage as ‘suspected malignant spinal cord compression’ - assess within 2 hours of presentation. Inform senior medical staff of suspected diagnosis.**

Document and time full history and physical examination, including a neurological examination.

Organise MRI urgently – do not waste time doing bone scans nor allow plain film x ray to delay MRI. Identify who will receive the MRI report and give their details to the MRI department. (Contact the Walton Centre for advice where MRI is contraindicated).

Advise patient to remain flat until MRI if possible. Fit TED stockings. Do not start low molecular weight heparin until discussed with MSCC Coordinator.

Assess pain control and prescribe analgesics. Specialist palliative care can advise if required. If patient can’t lie flat due to pain, complete MRI compatibility/ request form and consider sedation if indicated, to prevent delays

Give dexamethasone 16mg daily orally or subcutaneously (unless you have a strong suspicion of lymphoma) and consider proton pump inhibitor for gastric protection.

Starve patient.

Communicate ‘suspected MSCC’ if handing over to another team.
Where patient has no cancer diagnosis, progressive spinal pain only (no neurological signs) manage and refer urgently for urgent spinal assessment as per regional spinal assessment protocols.

MRI negative for MSCC

MRI positive for MSCC/ cauda equina/ impending MSCC

* Ring MSCC Clinical coordinator immediately – The Walton Centre - 0151 525 3611
  * Start referral form – fax to 0151 529 6626; don’t delay contact if you don’t have all the details; arrange to share scans electronically.
  * Responsibility of referrer to confirm referral has been received.
  * Telephone triage with MSCC Coordinator - clinical history; presenting symptoms; tumour type; extent of disease; co-morbidity; previous treatments. Discussion will include initial management advice, including moving and handling; drug treatment.

**Clinical decision**
  * A senior spinal surgeon will review the case and discuss the patient with a Consultant Oncologist and Consultant Radiologist if appropriate.
  * Response to referrer will usually be within 2 hours – If the patient requires radiotherapy then the referrer will be asked to discuss the case with Clatterbridge Cancer Centre - 0151 334 1155 (on-call clinical oncologist).
  * Information will be passed from Walton to CCC via a secure fax.
  * Referrer to send blood, calcium, haemoglobin results; scans; notes; describe moving and handling advice given to patient, and organise transport (stretcher ambulance)

Local management of ongoing symptoms

Surgical assessment at the Walton Centre
Radiotherapy at Clatterbridge
Supportive/palliative care
Management of

**Corticosteroids**

Administered for Metastatic Spinal Cord Compression (MSCC)

**Management of Corticosteroids Treatment Algorithm**

Is the patient to be referred for surgical assessment?

- **NO**
- **YES**

**YES**

Discuss the use of corticosteroids with the MSCC Co-ordinator on 0151 525 3611

Unless contra-indicated (including significant suspicion of lymphoma) administer a loading dose of Dexamethasone 16mg followed by Dexamethasone 8mg twice a day

Ensure a proton pump inhibitor is prescribed as a gastric protector and monitor blood glucose levels in all patients receiving corticosteroids

Has the patient had surgery, at the start of radiotherapy or for supportive/palliative care?

- **NO**
- **YES**

**YES**

Reduce the dose of daily Dexamethasone gradually over 5-7 days

Has the patient’s neurological function deteriorated at any time?

- **NO**
- **YES**

**NO**

Continue reducing dose of Dexamethasone gradually over 5-7 days and stop

**YES**

Dexamethasone dose to be reviewed and increased temporarily
4.4 Superior Vena Cava Obstruction

AO protocol Name: Superior Vena Cava Obstruction
AO Type: Type I (new cancer) & Type III (cancer complication)
Author: ST & SA

Introduction:
SVCO is partial or complete obstruction of the blood flow through the superior vena cava (SVC) by neoplastic invasion, thrombosis or external pressure. It is rarely considered an acute emergency now. More than 80% of cases are secondary to malignancy particularly lung cancer and lymphoma. SVCO develops in 5-10% of right sided intra-thoracic malignant lesions, more commonly at initial presentation. SVC normally drains the venous blood from the head, neck, arms and upper chest.

Symptoms and signs:
- Breathlessness & Cough
- Swelling and venous distention in face, neck, upper chest and arms
- Plethora & cyanosis
- Altered mental state
- Hoarse voice
- Symptoms are worse by bending forward or lying flat

Diagnosis:
- Clinical
- CXR
- CT
- Occasionally MRI or Venography might be indicated

Patient Referral systems:
- Refer to respiratory physicians and acute oncology. Inform patient’s oncologist if known malignancy.

Management:
- Elevate the head of the bed or put patient in upright position if possible
- Oxygen
- Sterids
- Diuretics
- Stent
- Biopsy for undiagnosed malignancy
- Thrombolysis or anticoagulation should be considered in cases of thrombosis
- Radiotherapy or systemic anti-cancer therapy or both following histological diagnosis of the underlying primary and MDT discussion
- Information & support to patient and carer
Management of

**Superior Vena Cava Obstruction (SVCO)**

Caused by Malignant Disease

**Signs and symptoms:** Breathlessness, plethora, facial/conjunctival oedema, cyanosis, distension of collateral vessels in neck, dyspnoea, facial/arm swelling, cough, chest pain, dysphagia, stridor

All signs and symptoms are exacerbated by bending forward or lying down. Treatment will usually be palliative and therefore symptom control is foremost in the management of SVCO

**Risk factors:** Malignant disease

**Examination:** History, physical examination, NEWS observations and calculate score, performance status.

**Investigations for all patients:** Chest x-ray, CT thorax, biopsy for histological diagnosis

**If clinically indicated:** FBC, U&Es, LFTs

---

**Decision Tree: Management of SVCO**

**Does the patient have a confirmed SVCO?**

**NO**

- Arrange urgent biopsy and consider stenting (chest physician/radiologist)
- Inform Acute Oncology Team

**YES**

- Contact relevant clinician (eg chest physician, oncologist, haematologist)
- Inform Acute Oncology Team

**SCLC/Lymphoma**

- Dexamethasone 6mg twice a day
- Chemotherapy
- Palliative radiotherapy

**NSCLC**

- Dexamethasone 6mg twice a day
- Stent
- Palliative radiotherapy

**Unknown malignancy**

- Dexamethasone 6mg twice a day
- Stent
- Palliative radiotherapy

Ensure follow-up with relevant patient’s oncologist
4.5 Hyponatraemia

AO Protocol Name: SIADH/hyponatraemia
AO Type: Type II (Chemo Complication), Type III (Cancer Complication)  Author: RWG

Introduction:
Hyponatraemia is the most commonly observed electrolyte abnormality and is associated with excess in-hospital mortality. Hyponatraemia is usually a consequence of water excess because of a failure in renal water excretion rather than a sodium deficit. In cancer patients, this can occur as a result of ectopic ADH (anti-diuretic hormone) production from the cancer or as a side effect of drug therapy. Hyponatraemia in the context of euvolaemia is usually caused by excess ADH secretion (e.g. ectopic secretion) or by enhancing the sensitivity of the renal tubules to the effects of physiologically released ADH (e.g. cyclophosphamide, NSAIDs). Hyponatraemia can also cause hyponatraemia through the action of baroreceptors stimulating appropriate ADH release. Some hypervolaemic states such as cardiac failure, renal failure, nephrotic syndrome and liver cirrhosis can cause hyponatraemia due to impaired clearance of water relative to sodium. Careful assessment of the patient’s fluid balance, serum/plasma osmolalities and renal sodium excretion are therefore key to elucidating the cause of hyponatraemia and implementing appropriate management.

Common causes of hyponatraemia in cancer patients:

<table>
<thead>
<tr>
<th>Euvolaemic</th>
<th>Hypovolaemic</th>
<th>Hypervolaemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ectopic ADH production</td>
<td>Vomiting</td>
<td>Cardiac failure</td>
</tr>
<tr>
<td>Drugs</td>
<td>Acute renal failure</td>
<td>Chronic renal failure</td>
</tr>
<tr>
<td>Cisplatin*</td>
<td>Salt wasting states</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>CNS metastases</td>
<td></td>
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<tr>
<td>Vinca alkaloids</td>
<td>Meningitis</td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>Cisplatin*</td>
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<td>Strenuous physical exercise</td>
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<tr>
<td>Demyelinating conditions</td>
<td></td>
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<tr>
<td>Nausea &amp; Pain</td>
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*Cisplatin can cause inappropriate ADH release in addition to causing a salt wasting state. Differentiation of these two states is essential to implement appropriate management

Implications of hyponatraemia
Hyponatraemia has long been recognized as associated with excess mortality in hospital inpatients and a range of malignancies. Furthermore, patients with chronic hyponatraemia are affected by impaired quality of life and suffer from a range of neurocognitive symptoms. Acute or severe hyponatraemia can be life threatening and requires urgent management.
Approach to Investigation and Diagnosis of Hyponatraemia

Initial Approach
Management of hyponatraemia is very dependent on its aetiology. The flowchart describes the initial investigations required to accurately identify the cause of hyponatraemia. Management is aimed at addressing the underlying cause but severe (Na⁺ <125mmol/l) or symptomatic hyponatraemia may require urgent treatment to increase the serum sodium.

Management of confirmed SIADH

Diagnostics are essential!
Serum: U&E, PO₄³⁻, uric acid, glucose, TSH, cortisol, osmolality
Urine: Na⁺, K⁺, osmolality

Serum osmolality <280 mOsm/kg

Urine osmolality >100 mOsm/kg
Inappropriate Antidiuresis

Urine osmolality <100 mOsm/kg
Appropriate renal dilution – excessive water intake?

Assess Volume Status

Hypovolaemia
Physical exam
Cr and uric acid high
Urine Na <10mmol/l when due to dehydration
Urine Na >20mmol/l when due to renal salt wasting

Euvolaemia
Physical exam
Cr and uric acid low
Urine Na >30mmol/l

Hypervolaemia
Physical exam
Cr and uric acid low
Urine Na <10mmol/l

Euvolaemic Hyponatraemia
Treat as SIADH
Stop any medications contributing
Review cortisol and TFT

Pseudohyponatraemia
Check cholesterol/lipids/glucose
Exogenous compounds? e.g. mannitol

Serum osmolality >280 mOsm/kg

Urine osmolality <100 mOsm/kg

Urine osmolality >100 mOsm/kg

Serum: U&E, PO₄³⁻, uric acid, glucose, TSH, cortisol, osmolality
Urine: Na⁺, K⁺, osmolality

Initial Approach
Management of hyponatraemia is very dependent on its aetiology. The flowchart describes the initial investigations required to accurately identify the cause of hyponatraemia. Management is aimed at addressing the underlying cause but severe (Na⁺ <125mmol/l) or symptomatic hyponatraemia may require urgent treatment to increase the serum sodium.

Management of confirmed SIADH
Patients presenting with depressed level of consciousness, coma or seizures should be considered for management in an intensive care environment. Such patients should be considered for the use of hypertonic (3%) saline. Other patients can be managed by fluid restriction and/or medications to correct sodium homeostasis.

**Fluid Restriction**
Aim to correct sodium by no more than 12mmol/l per 24 hours. A faster rise may cause irreversible central pontine myelinolysis, particularly in patients with chronic hyponatraemia.

**Drug Therapy:**
Demeclocycline is a tetracycline antibiotic that causes nephrogenic diabetes insipidus. It is unlicensed for treatment of SIADH. The dose used is 150-300mg qds. It has an effect in around 60% of patients, can cause reversible renal dysfunction and photosensitive skin rashes.

Tolvaptan is an oral V2 receptor antagonist and directly blocks the effect of ADH on its receptor. It promotes a rapid aquareysis and therefore patients are encouraged to drink adequate amounts of water. Dose is 15mg a day and it is recommended that patients are admitted overnight in hospital for the first dose to avoid too rapid a rise in sodium. Over correction or too rapid correction is rare and usually only seen when there is co-existing hypovolaemia. It is therefore important to ensure that patients are well hydrated. If too rapid correction of Na occurs (>12mmol/l per 24 hours or >18mmol/l in 48 hours) then give 5% dextrose intravenously. Tolvaptan is only recommended for short term (<4 weeks) treatment of SIADH induced hyponatraemia. Side effects are thirst, dehydration, hyperglycaemia and hepatotoxicity.
4.6 Acute Kidney Injury

AO protocol name: Acute Kidney Injury
AO type: type II & III
Author: Abdallah (COCH)

Introduction:
Acute kidney injury (AKI) is rapid impairment of renal function resulting in fluid and electrolyte disturbance, elevation in serum urea and creatinine and failure to excrete certain metabolic waste products normally excreted by the kidney.
AKI is common among cancer patients particularly the older ones, often due to a combination of factors which could be as a complication of the underlying cancer or secondary to the use of nephrotoxic drugs. One study showed that over 20% of cancer patients may experience AKI during the first year after diagnosis with higher incidence and worse prognosis among critically ill cancer patients due to its association with multi organ dysfunction in this setting. AKI may preclude cancer patients from receiving optimal anticancer drugs and is associated with high morbidity and mortality compared with non-cancer patients.

Types of AKI:
Pre renal: dehydration/hypovolemia due to diarrhoea, vomiting and sepsis
Renal: mainly due to nephrotoxic drugs including chemotherapy, bisphosphonate and NSAIDs. Tumour lysis syndrome and myeloma can cause intrinsic renal failure also.
Post renal: urinary tract obstruction due to cancer infiltration by tumours like prostate, bladder uterus and cervix.

Presentation:
Post chemotherapy nausea, vomiting, diarrhoea, mucositis and reduced oral intake leading to dehydration and volume depletion.
Nephrotoxicity post chemotherapy without dehydration
Sepsis
Oligouria due to renal tract obstruction
Tumour lysis syndrome should be suspected in rapidly proliferating cancers like haematological malignancies particularly after initiation of cytotoxic chemotherapy
Symptoms of uraemia include lethargy, general malaise, anorexia, nausea & vomiting, and muscle cramps. AKI could be asymptomatic.
Incidental finding on routine blood test

Anticancer drugs at high risk of nephrotoxicity:
- Cisplatin
- Mitomycin
- Methotrexate
- Ifosfamide
- Gemcitabine
- Streptozotocin
- Bisphosphonate
Evaluation & Investigations:
Cancer patients with AKI require detailed history including drug history, pre-existing renal function and careful clinical assessment of volume status in order to identify possible causes and reversibility.

- Serial blood tests including U&Es, estimated GFR, calcium, phosphate, magnesium and FBC
- Urinalysis
- ECG
- Infection screen if sepsis suspected
- Renal tract US
- Non- contrast CT

Management:
- Involve renal physicians in managing AKI particularly in severe cases and in patients with good prognosis malignancy.
- Patients with life threatening complications of AKI like hyperkalemia, metabolic acidosis or volume depletion should be admitted and treated immediately.
- Hyperkalemia requires immediate treatment with calcium chloride, intravenous insulin and glucose. Hypocalcemia is also common mainly due to increase in serum phosphate level.
- Patients with volume depletion should be commenced on IV fluids like normal saline as soon as possible
- Urinary catheterisation for patients with urinary retention. Urology referral may be required.
- Renal dialysis reserved for patients with hyperkalemia or rapidly rising potassium, metabolic acidosis and volume overload not responding to medical therapy.

References:
1-Incidence of acute kidney injury in cancer patients: A population-based cohort study in Denmark. J Clin Oncol 27:15s, 2009 (suppl; abstr 9570)
Management of

**Acute Kidney Injury**

**Signs and symptoms:** Oliguria, raised serum urea and creatinine

**Risk factors:** Dehydration, anti-cancer systemic treatments, nephrotoxic drugs (for example cisplatin, NSAIDS, aminoglycosides), ureteric obstruction from a pelvic tumour

**Examination:** Clinical history, examination, MEWS observations and calculate score

**Investigations for all patients:** U&Es, urinalysis

**Investigations if clinically indicated:** Renal tract USS within 24 hours (if renal tract obstruction is suspected)

Acute Kidney Injury is defined as:-
- Serum creatinine rises by ≥ 26µmol/L within 48 hours OR
- Serum creatinine rises ≥1.5 fold from the reference value, which is known or presumed to have occurred within one week OR
- Urine output is <0.5ml/kg/hr for > 6 consecutive hours

Is medical intervention appropriate? (maybe inappropriate if patient is terminally ill with advanced cancer)

- **No**
  - Consider referral to palliative care team

- **Yes**
  - Commence immediate medical management, for example:
    - IV fluids for hypovolaemia
    - treat hyperkalaemia
    - stop nephrotoxic drugs
    - urgent USS to exclude obstruction
    - treat any underlying sepsis

Refer to oncall urologist if obstruction present: nephrostomy or utereric stent?

Refer to Acute Oncology Team if first presentation of cancer or opinion needed, for example appropriateness of ureteric stents or dialysis

Is medical management effective?

- **No**
  - Early referral to renal physicians as may need dialysis

- **Yes**
  - Continue

Early Palliative Care Team involvement if required

Inform patient’s oncologist
4.7 Pleural Effusion

AO Protocol Name: Pleural effusion
AO Type: Type I (New Cancer), Type III (Cancer Complication)
Author: ACM (NCT AO)

Introduction:
Pleural effusion may be due to known malignancy or be a presentation of MUO. It is rarely an acute emergency and in the absence of critical signs, an attempt at a histological diagnosis should be made before treatment (chest drain/pleurodesis). Aspiration can provide rapid relief and also cytological confirmation of malignancy.

Patient Referral systems (define alerts, referral pathway etc):
- Develop MUO alert with radiology:
- Refer to acute oncologist. Inform patient’s oncologist if known malignancy.
- Involve respiratory physicians and consider referral to Liverpool Heart and Chest hospital

Education:
Develop rolling programme of education aimed at key departments and junior doctors

Time to response:
Acute oncology review within 24 working hours (medical and/or nursing)

Initial evaluation:
- Patient/family understanding and expectations
- PS, assess clinical signs. Organise imaging.
- Previous Oncology Correspondence/contact detail

Ongoing management:
- Information/support and symptom control with consideration of early PCT involvement
- Focussed investigation according to PS, pattern and prognosis: CXR, staging CT scan
- Consider pleurodesis once diagnosis confirmed
- Start discharge planning

Specialist referral:
- Urgent referral to appropriate MDT for histological diagnosis
- Refer to acute oncologist or arrange review by patient’s own oncologist (if relapse)
Management of

**Malignant Pleural Effusion**

**Caused by Malignant Disease**

**Signs and symptoms:** Dyspnoea, chest pain, cough

**Risk factors:** Malignant disease

**Examination:** History, physical examination, MEWS observations and calculate score, assessment of performance status, life expectancy and history of previous effusions and management and outcomes

**Investigations for all patients:** Chest x-ray and comparison with previous imaging

**If clinically indicated:** FBC, U&Es, clotting

---

- **Confirmed malignant pleural effusion**
  - Is it a recurrence or are they symptomatic?
    - **NO**
      - Observe
    - **YES**
      - Seek specialist opinion from a member of the thoracic malignancy team and Acute Oncology Team

**Drainage**

- Use intercostal tube – small bore (10-14F)
- Preferably under ultrasound guidance
- Drain up to 1.5 litres each session according to tolerance and symptoms

- **Perform chest x-ray**
  - Is there complete lung re-expansion?
    - **NO**
    - **YES**
      - **Perform Chemical pleurodesis**

**Consider:**

- Thoracoscopy
- Long term indwelling catheter
- Pleuroperitoneal shunt

**Recurrence of effusion?**

- **NO**
- **YES**
  - **Ongoing management. Ensure follow-up with relevant primary oncologist**

**Consider**

- Repeated pleurodesis
- Thoracoscopy
- Long term indwelling catheter
- Pleuroperitoneal shunt
4.8 Pericardial Effusion

AO Protocol Name: Pericardial effusion
AO Type: Type I (New Cancer), Type III (Cancer Complication)
Author: M. Varey (RLUH AO)

Introduction:
Pericardial effusion may be due to known malignancy or be a presentation of MUO. It can be an acute emergency and with critical signs, urgent drainage is necessary.

Patient Referral systems (define alerts, referral pathway etc):
- Refer to acute oncologist. Inform patient’s oncologist if known malignancy.

Education:
Develop rolling programme of education aimed at key departments and junior doctors

Time to response:
Acute oncology review within 24 working hours (medical and/or nursing)

Initial evaluation:
- Refer to cardiologist regarding possible drainage; ask for fluid to be sent for cytology
- Patient/family understanding and expectations
- PS, assess clinical signs. Organise imaging.
- Previous Oncology Correspondence/contact detail

Ongoing management:
- Information/support and symptom control with consideration of early PCT involvement
- Focussed investigation according to PS, pattern and prognosis
- Start discharge planning

Specialist referral:
- Cardiologist/ Liverpool Heart and Chest hospital
- Arrange review by patient’s own oncologist (if relapse)
Management of

**Malignant Pericardial Effusion**

Caused by Malignant Disease

**Signs and symptoms:** Chest pain, lightheadedness, palpitations, cough, dyspnoea, fatigue

**Risk factors:** Malignant disease

**Examination:** History, physical examination, assess clinical signs and performance status, TPR, BP, oxygen saturations

**Investigations for all patients:** Echocardiography, ECG, chest x-ray

**If clinically indicated:** Drainage fluid for cytology, pericardiocentesis

---

**Confirmed malignant pericardial effusion**

Refer to cardiologist regarding possible drainage. Ask for fluid to be sent for cytology

Consider referral to Palliative Care Team

Focus investigation according to performance status, pattern and prognosis
4.9 Lymphangitis Carcinomatosis

AO Protocol Name: Lymphangitis Carcinomatosis
AO Type: III
Author: AC & SA

Introduction:

Lymphangitic carcinomatosis (LC) is a metastatic lung disease characterized by diffuse infiltration and obstruction of pulmonary parenchymal lymphatic channels by metastatic cancer cells. Various neoplasms can cause lymphangitic carcinomatosis, but 80% are due to adenocarcinomas. The most common primary sites are breast, lung, colon, and stomach, although it could be caused by any metastatic neoplasm. LC constitutes 6-8% of pulmonary metastatic disease and usually indicates poor prognosis and short survival.

Presenting Symptoms:

- Breathlessness
- Dry cough
- Haemoptysis

Investigations:

Patients who are known to have cancer
- CXR: coarse bronchovascular markings
- High Resolution CT (HRCT): diffuse interstitial thickening

Patients who are not known to have cancer previously need staging CT and referral to the appropriate MDT.

Ongoing Management:

Information and support to patient and carer

Inform patient’s usual oncologist, if not known refer to appropriate MDT

Corticosteroids for symptomatic relief

Systemic therapy of the underlying cancer if felt appropriate by patient’s oncologist

References:

Management of

**Lymphangitis Carcinomatosis**

Caused by Malignant Disease

**Signs and symptoms:** Dyspnoea, dry cough

**Risk factors:** Malignant disease

**Examination:** History, physical examination, TPR, BP, oxygen saturations

**Investigations for all patients:** Chest x-ray and comparison with previous imaging, sputum culture to exclude concomitant infection

**If clinically indicated:** FBC, U&Es

---

**Are there typical chest x-ray features of lymphangitis carcinomatosis with other reversible causes excluded (for example, infection, effusion)?**

- **NO**
  - Exclude reversible causes

- **YES**
  - Does the patient have known malignancy?
    - **NO**
    - Follow-up review with patient’s oncologist
    - CT of chest/abdomen/pelvis
    - Consider a mammogram
    - Refer to relevant MDT and Acute Oncology team

    - **YES**
      - *Obtain latest correspondence from CCC*
      - *Oxygen*
      - *Dexamethasone, consider 4mg twice a day (with breakfast and lunch)*
      - *Oramorph, consider 5mg/2.5ml for dyspnoea*
      - *Consider referral to palliative care team for support*
      - *Review by Acute Oncology team within 24 hours*
4.10 Abdominal Ascites

AO Protocol Name: Abdominal Ascites
AO Type: Type I (New Cancer), Type III (Cancer Complication)
Author: HNW & SA

Introduction:

Ascites is the accumulation of free fluid within the abdominal cavity. This can be secondary to benign or malignant process with malignancy responsible for about 10% of cases. Malignant ascites is a sign of peritoneal carcinomatosis and generally indicates poor prognosis with average survival of 4 months, however when it is caused by ovarian cancer, survival tends to be longer between 6-12 months. Most common malignancies to cause ascites are ovarian, colon, stomach, pancreas, endometrial and breast cancers. The pathophysiology is multifactorial, however it is postulated that ascites formation is most likely due to a combination of altered vascular permeability and obstructed lymphatic drainage.

Symptoms:

- Abdominal bloating and swelling
- Anorexia
- Nausea
- Early satiety
- Dyspnea
- Fatigue
- Peripheral oedema

Initial evaluation

Patients who are not known to have malignancy need a diagnostic paracentesis for cytology. Laparoscopic tissue biopsy may be needed for fit patients if cytology not diagnostic. Patients who are known to have intra-abdominal malignancy don't require further investigations unless there is suspicion of other causes or contributing factors.

- FBC, U/Es & LFTs
- Coagulation screen prior to paracentesis
- If infection suspected ascetic fluid sample should be sent for analysis and culture
- CT staging
- Tumour markers have poor sensitivity and specificity, however Ca-125 & CEA should be checked if ovarian or gastrointestinal cancer suspected

Management:

Relieving patient symptoms and improving quality of life is the first aim of managing ascites.

- Paracentesis is considered the best way of achieving immediate relief from tense ascites, this would be safer to perform under ultrasound guidance. Approximately 93% of patients show relief of nausea, vomiting, dyspnea and/or abdominal discomfort. Paracentesis of up to 5L of ascites can be safely carried out with minimal risk of hypotension and renal failure. Larger volume paracentesis may require clamping after every 4-5 L to allow time for the haemodynamic system to adjust.
- Diuretics: diuretics are useful in about 43-44% of cases. Spironolactone at a starting dose of 100mg per day (less may be needed in elderly, frail patients). Ensure monitoring
of renal function and titrate up, every 3 days, to 400mg maximum per day. It can take 3 to 4 days to work.

- The PleurX® peritoneal catheter and drainage system has been approved by NICE for use in patients with recurrent malignant ascites. The device consists of a silicone peritoneal catheter that is permanently placed inside the abdominal cavity with a cuff that is placed subcutaneously with a safety valve on the abdominal wall of the patient. A vacuum bottle can be intermittently attached to the port to enable drainage of ascitic fluid by the patient or their carer in the community and reduce hospitalisation.
- Peritoneo-venous shunts have been used effectively in patients with expected longer median survival (months rather than weeks).
- Octreotide may be useful in chylous ascites, at a dose of 200 to 600 micrograms/24 hours, via continuous subcutaneous infusion.
- Cytotoxic therapy. Treatment of the underlying malignancy with chemotherapy, surgery or biological agents can be helpful in reducing risk of recurrent ascites, especially in breast or ovarian cancers.
- Please see diagram below

References:
Management of *Abdominal Ascites* Caused by Malignant Disease

**Signs and symptoms:** Abdominal bloating/swelling, pain, nausea, vomiting, anorexia, fatigue, peripheral oedema, heartburn, dyspnoea, weight loss

**Risk factors:** Malignant disease

**Examination:** History, physical examination, TPR, BP, oxygen saturations

**Investigations for all patients:** FBC, U&Es

**If clinically indicated:** Clotting screen if the patient is bleeding, has liver metastases, is jaundiced or is on anticoagulant therapy. Ultrasound prior to paracentesis if there is diagnostic uncertainty or suspected loculation of fluid. Computerised tomography and/or magnetic resonance imaging

Management should be aimed at maximising patient comfort and quality of life

---

**Diuretic Therapy**

- Check U&Es before and throughout diuretic therapy
- **Spironolactone** 100-400mg is first choice
- Consider lower dose for elderly patients and titrate according to individual response
- It may take 3-5 days to get a response
- The dose should be increased every 3-7 days in 50mg-100mg increments to a maximum of 400mg a day
- If there is no improvement - **ADD Frusemide** 40mg-80mg daily

---

**If the patient is resistant to diuretics or for control of acute symptoms**

**Therapeutic Paracentesis**

- Check FBC, U&Es and clotting screen if indicated and weigh the patient
- Empty the bladder. Analgesia should be available before, during and after procedure
- Perform paracentesis and drain fluid as quickly as is comfortable for the patient, limited only by their clinical condition. Clamping of the drain is often not required. Perform strict fluid balance
- Remove the drain when no longer in use and weigh the patient
- May be necessary to repeat paracentesis for ongoing symptom control
- **Contra-indications:** disseminated intravascular coagulation and clinical evidence of fibrinolysis. Relative contraindication includes severe bowel distension and previous extensive abdominal/pelvic surgery

---

**Consider ambulatory drainage or Peritoneovenous shunts**

To be considered if recurrent ascites is the main clinical problem and prognosis is measured in months rather than weeks. This may limit the need for diuretics and paracentesis

---

**Octreotide**

Useful in chylous ascites. The dose is 200-600 micrograms via a continuous subcutaneous infusion over 24 hours

---

**Cytotoxic Therapy**

May be of benefit of the primary disease is known to be responsive to cytoxics
5.1 Central Venous Access Devises (CVAD)

Management of

**Exit site Inflammation/Phlebitis**

Caused by Central Venous Access Devises (CVAD)

**Signs and Symptoms:** Pyrexia, vein hard on palpation, swelling at and above exit site, change in colour or tenderness at exit site of CVAD, exudate at exit site, raised WCC and CRP

**Examination:** Clinical history, examination, temperature

**Investigations:** FBC, CRP, venous blood for aerobic and anaerobic cultures peripherally to be taken and first and then immediately via CVAD

**If Clinically Indicated:** CVAD exit site culture swabs

---

**Signs and symptoms suggestive of exit site inflammation/phlebitis**

- Apply alternate hot/cold compress to the affected area
- Cleanse the area using a 2% Chlorhexidine and 70% alcohol applicator (Chlorprep) and re-dress the device using a skin fixing device and moisture permeable dressing to prevent movement and enable observation in case of mechanical phlebitis
- Ensure daily observation

---

**Have the symptoms resolved?**

- **NO**
  - Monitor for signs of infection and swab the exit site if exudate present
  - Discuss with Medical Microbiologist
  - Assess the need for CVAD and consider re-siting
  - Seek advice from Acute Oncology Team or local trust IV and Interventional Procedure CNS. If further advice needed phone CCC IV and Interventional Procedures CNS 0151 334 1155 bleep 4095 (Monday to Friday 9am – 5pm)

- **YES**
  - Proceed with caution as long as there are no other complications or pain
Management of

**Systemic Infection**

Caused by Central Venous Access Devises (CVAD)

**Signs and symptoms:** Fever and chills without other apparent reason, malaise, nausea and vomiting, low grade pyrexia, unresponsive to broad spectrum antibiotics, headache, raised WCC and CRP, maybe discharge from exit site or no evidence of sepsis at catheter site

**Examination:** Clinical history, examination, temperature

**Investigations:** FBC, CRP, venous blood for aerobic and anaerobic cultures peripherally and via CVAD

**If Clinically Indicated:** CVAD exit site culture swabs, wound swabs, sputum and urine cultures

---

**Signs and symptoms suggestive of systematic infection**

- Monitor site daily
- Continue to use strict asepsis and needle free system
- Take peripheral venous blood cultures and from CVAD
- Treat with IV antibiotics or combination of oral and IV’s as indicated in local policy or by Medical Microbiologist
- CVAD may be used to administer IV antibiotics

---

**Have the symptoms resolved?**

- **NO**
  - Swab catheter site, any wound, sputum and urinalysis
  - Line lock if clinically well to salvage line
  - Discuss with Medical Microbiologist
  - Assess the need for CVAD and patient’s immune system
  - Seek advice from Acute Oncology Team or local trust IV and Interventional Procedure CNS. If further advice needed phone CCC IV and Interventional Procedures CNS 0151 334 1155 bleep 4095 (Monday to Friday 9am – 5pm)

- **YES**
  - Proceed with caution as long as there are no other complications or pain
Management of Persistent Withdrawal Occlusions (PWO)

Of Central Venous Access Devise (CVAD)
(fluids can be infused freely by gravity but blood cannot be withdrawn)

Blood return is absent
- Check the line for position, kinking, unclamp any clamps, massage length of catheter
- Blood return is obtained?
  - NO
  - YES

Flush CVAD with 0.9% sodium chloride in 10ml/20ml syringe using a push-pull motion. Check for flashback of blood
- Are you able to flush CVAD?
  - NO
  - YES
- Can you withdraw blood?
  - NO
  - YES

Is the patient to receive highly irritant-vesicant drugs or chemotherapy?
- NO
- YES

Proceed with caution as long as there are no other complications or pain

The following steps should initially be done on admission or prior to drug administration and documented in nursing care plan so that all staff are aware that patency has been verified.

**Step 1**
- Administer a 250ml normal saline “challenge” (unless serum sodium ≤120mmol/l) via an infusion pump over 15 minutes to test for patency – the infusion will probably not resolve the lack of blood return (unless the patient has a high sodium or fluid restricted go to step 2).

If there have been no problems, therapy can be administered as normal. If the patient experiences ANY discomfort or there is any unexplained problems then stop and seek medical advice. If may be necessary to verify tip local by chest x-ray **OR** **Step 2**
- Infuse Urokinase 10000iu in 3.5mls, using the push lock method over a 30 minute period. Withdraw the urokinase and assess the catheter again. Repeat as necessary. If blood return is still absent, it may be necessary to verify tip location by chest x-ray.
- Seek advice from Acute Oncology Team or local trust IV and Interventional Procedure CNS.

**Push Lock Method**
Reconstitute Urokinase 10,000iu in 3.5ml / 0.9% sodium chloride for each lumen
- Lock each lumen with 2.5ml 0 mins
- Push 0.5ml solution/lumen 10 mins
- Push 0.5ml solution/lumen 20 mins
- Aspirate lumen 30 mins
Management of Blocked and Occluded Central Venous Access Devices (CVAD)

Unable to flush with 0.9% sodium chloride → Check the line for position, kinking, unclamp clamps, massage length of catheter → Ask the patient to cough, take deep breaths, change position – stand up or lie down with the foot of the bed tipped up.

Are you able to flush the CVAD?
- NO
- YES

Attach a 3 way tap to end of the catheter, add an empty 10ml syringe to 1 port and to the 2nd port a 10ml syringe with Urokinase 10,000 units/2ml

Can you withdraw blood?
- NO
- YES

Refer to Persistent Withdrawal Occlusions Treatment Algorithm page 74

Use CVAD as usual

Attempt to unblock the catheter using a negative pressure

When Urokinase has been draw into catheter clamp and leave for 1-2 minutes

Attach empty syringe and attempt to aspirate clots

Is blood obtained?
- NO
- YES

Instil a 2nd Urokinase dose and leave for a longer period (for example overnight)

Is blood obtained?
- NO
- YES

Withdraw a minimum of 10mls and discard. Flush the catheter with 10ml sodium chloride using pulsating flush and then with hepsal

If occlusion cannot be removed the catheter is no longer patent. It may be necessary to remove the catheter if a single lumen or multi-lumen to refrain from using the blocked lumen. This should be discussed with the interventional radiologist in x-ray to determine if catheter can be salvaged.
### 6.0 Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AO</td>
<td>Acute Oncology</td>
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<tr>
<td>BP</td>
<td>Blood pressure</td>
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<td>BSC</td>
<td>Best Supportive Care</td>
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<tr>
<td>CCC</td>
<td>Clatterbridge Cancer Centre</td>
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<tr>
<td>CHF</td>
<td>Congestive Heart Failure</td>
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<td>CRP</td>
<td>C-reactive protein</td>
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<td>CUP</td>
<td>Carcinoma of Unknown Primary</td>
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<tr>
<td>CVAD</td>
<td>Central Venous Access Device</td>
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<tr>
<td>CXR</td>
<td>Chest x-ray</td>
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<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
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<td>FBC</td>
<td>Full blood count</td>
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<td>IM</td>
<td>Intramuscular</td>
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<tr>
<td>IV</td>
<td>Intravenous</td>
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<tr>
<td>LC</td>
<td>Lymphangitis Carcinomatosis</td>
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<tr>
<td>LFTs</td>
<td>Liver function tests</td>
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<tr>
<td>MASCC</td>
<td>Multinational Association of Supportive Care in Cancer</td>
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<tr>
<td>MCCN</td>
<td>Merseyside and Cheshire Cancer Network</td>
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<tr>
<td>MEWS</td>
<td>Modified Early Warning Score</td>
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<tr>
<td>MDT</td>
<td>Multi-Disciplinary Team</td>
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<td>MSCC</td>
<td>Metastatic Spinal Cord Compression</td>
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<tr>
<td>MUO</td>
<td>Malignancy of Unknown Origin</td>
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<tr>
<td>NBM</td>
<td>Nil by mouth</td>
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<tr>
<td>NCAG</td>
<td>National Chemotherapy Advisory Group</td>
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<td>NCEPOD</td>
<td>National Confidential Enquiry into Patient Outcome and Death</td>
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<td>NPSA</td>
<td>National Patient Safety Agency</td>
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<td>NSCLC</td>
<td>Non small cell lung cancer</td>
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<td>Palliative Care Team</td>
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<td>Proton Pump Inhibitor</td>
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<td>Performance Status</td>
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<td>Palmar Plantar Erythema</td>
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<td>Radiotherapy</td>
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<td>Radiation Therapy Oncology Group</td>
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<td>Stereotactic Radiosurgery</td>
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<tr>
<td>SVC</td>
<td>Superior Vena Cava</td>
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<tr>
<td>SVCO</td>
<td>Superior Vena Cava Obstruction</td>
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<tr>
<td>TPR</td>
<td>Temperature, pulse, respiration rate</td>
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<tr>
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<td>Urea and electrolytes</td>
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<td>White cell count</td>
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<td>World Health Organisation</td>
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