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INTRODUCTION

Introduction

Acute oncology focuses on the management of patients with complications of their cancer diagnosis and treatment, and the management of patients with an acute new cancer diagnosis. Although patients are often treated in specialist oncology centres, they are more likely to present to their local hospital when acute problems develop.

In 2008, the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report, *Systemic Anti-Cancer Therapy: For better, for worse?*, looked into deaths within 30 days of receiving systemic anti-cancer therapy and identified significant concerns regarding the quality and safety of patient care both at an organisational and a clinical level. Delays in admission, delays in prescribing and administering antibiotics, lack of assessment by senior staff, poor communication between teams, lack of documentation, lack of oncology input and lack of clear policies were just a few of the concerns identified. The ensuing National Chemotherapy Advisory Group report, *Chemotherapy Services in England: Ensuring quality and safety (2010)*, highlighted the need for an acute oncology service (AOS) in every hospital.

The National Cancer Action Team Acute Oncology Measures (2011) stipulate that acute oncology protocols should be available in the chemotherapy and radiotherapy units, A&E departments, acute medical admissions wards and oncology in-patient wards. Although there is significant consensus across the UK about the management of oncology emergencies, no national guidelines are available.

Prior to the establishment of the London Cancer Alliance (LCA), acute oncology within west and south London was organised between three cancer networks – north west, south west and south east. Each developed its own acute oncology clinical guidelines which, although different, covered the same subjects and comprised similar information.

The LCA Acute Oncology Clinical Guidelines have been written by representatives from each of these cancer networks and agreed by representatives of all 17 provider organisations across the LCA. They provide evidence-based clinical information and protocols while allowing sufficient flexibility to reflect good local practice.

They include information from recently published national guidelines, such as the National Institute for Health and Care Excellence (NICE) clinical guideline on neutropenic sepsis (CG15). They also include information on the assessment and management of metastatic spinal cord compression (MSCC) aimed particularly at acute admission through A&E. The LCA is in the process of developing a more comprehensive LCA-wide care pathway for the diagnosis, treatment, rehabilitation and ongoing care of patients with MSCC.

The LCA Acute Oncology Clinical Guidelines are designed to be used by all healthcare professionals in provider organisations across the LCA who are involved in the care of the cancer patient. They have been developed to take into account the wide range of clinical experience of the user and the different clinical settings in which they work. The guidelines are intended to assist in the initial assessment, investigation and management of patients. They are not a substitute for specialist oncology input, and must be used in conjunction with existing protocols, such as local microbiological guidelines. Adoption of the LCA Acute Oncology Clinical Guidelines will allow
widespread implementation of up-to-date and evidence-based management of oncology patients, and will assist in the provision of a consistently high standard of care across the LCA.

All provider organisations are expected to be able to provide the standard of care detailed in these guidelines. For specific areas where it is anticipated that local facilities may not exist (for example out-of-hours magnetic resonance imaging), protocols are given for the transfer to specialist oncology centres. In many other areas of the guidelines there is a limited or absent evidence base to support decision making. In these situations clinical consensus has been used to agree best practice.

I hope these guidelines are helpful. We welcome all feedback and suggestions, and these can be sent to me at the email address below. I would like to thank the LCA Acute Oncology Services Pathway Group for its help in writing this document.

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Executive Summary

The LCA Acute Oncology Clinical Guidelines have been developed to assist in the initial assessment, investigation and management of patients who present with oncology emergencies as set out in Appendix 3 of the National Cancer Peer Review Programme *Manual for Cancer Services: Acute Oncology* (version 1.0). This includes major presentations such as metastatic spinal cord compression, which is subject to recent National Institute for Health and Care Excellence (NICE) clinical guidance, as well as less well publicised conditions such as electrolyte disturbances, gastrointestinal toxicities and the acute management of effusions.

Each topic is covered in a separate section, listed in alphabetical order, with an emphasis on succinct, unambiguous advice and guidance. Each section starts with a brief summary of the condition to allow understanding of its context and importance, followed by the expected clinical presentations. A range of investigations is suggested, with the understanding that these will be tailored to individual cases. In most instances the subsequent management protocols mention generic drugs as opposed to specific brands in order to allow flexibility.

At all times, local guidelines should be adhered to and, where relevant, they should take priority over this document.

Section 1 covers allergy and anaphylaxis, which may occur in the minutes or hours following treatment. It highlights the assessments required prior to treatment, as well as the signs, symptoms and treatments associated with allergies and anaphylaxis.

The management of malignant ascites, most commonly seen in patients with a known diagnosis of ovarian or gastrointestinal cancer is covered in section 2. Early referral of these patients to acute oncology services is encouraged as prolonged inpatient admissions can usually be avoided.

Complications associated with central venous access devices are discussed in section 3, with detailed guidance on dealing with patients with a range of issues that can occur.

Section 4 explains that as many as 50–80% of patients receiving chemotherapy and/or radiotherapy to the abdomen or pelvis are at risk of developing severe diarrhoea. Chemotherapy induced diarrhoea can be a serious and life-threatening complication, and therefore prompt recognition and appropriate treatment are essential.

Extravasation of chemotherapy is the inadvertent administration of vesicant medication or solution into the surrounding tissue instead of into the intended vascular pathway. This can result in damage to nerves, tendons and joints, which can continue for months and, if treatment is delayed, can result in surgical debridement, skin grafting and even amputation. Section 5 describes the signs and symptoms, and immediate and ongoing management, but recognises that local extravasation pathways are also probably in place.

Hypercalcaemia of malignancy is the most common metabolic complication of cancer and occurs in about 10% of patients. It occurs most commonly in patients with advanced disease and is an indicator of poor prognosis. Section 6 highlights the tumours associated with hypercalcaemia, the causes, and the management of this complication.
The subject of section 7 is hypomagnesaemia, which is common but often under-diagnosed, particularly as magnesium does not usually feature in the routine biochemistry test. It can also be secondary to other electrolyte abnormalities, such as hypocalcaemia and hypokalaemia.

Section 8 discusses the signs, symptoms, treatment and management of lymphangitic carcinomatosis, which is the diffuse infiltration of lymphatic channels by tumour, resulting in obstruction and interstitial oedema. Lymphangitic carcinomatosis is associated with a poor prognosis, so prompt recognition and referral to an acute oncology service are essential.

Metastatic spinal cord compression (MSCC) is one of the most serious and devastating complications of malignancy; however, with prompt diagnosis and treatment, many patients can retain good levels of function and independence. Section 9 provides information on signs and symptoms, assessment and management of MSCC, along with contact telephone numbers for MSCC coordinators within LCA provider trusts.

Mucositis is a general term for the erythematous, erosive, inflammatory and ulcerative lesions that occur in the mucosal lining of the mouth, pharynx, oesophagus and entire gastrointestinal tract secondary to cytotoxic treatment. Patients at high risk of mucositis include those receiving high-dose chemotherapy and those receiving radiotherapy, with or without chemotherapy, for head, neck and oral cancers. Section 10 describes a number of treatment options.

Section 11 focuses on the acute management of patients with uncontrolled nausea and vomiting. It does not cover prophylactic anti-emetic use in patients about to receive anti-cancer treatment. The importance of identifying the cause prior to starting regular anti-emetics is stressed, as many anti-cancer therapies have no significant emetic potential, while chemotherapy seldom causes nausea and vomiting more than 1 week after administration.

Section 12 contains a link to current (2012) NICE guidance on the management of neutropenic sepsis. Given the comprehensive nature of this document, and reflecting local policies which recommend antibiotics based on endemic resistance patterns, clinical guidelines for the management of neutropenic sepsis have not been replicated here.

Malignant pericardial effusions occur in up to 20% of cancer patients but are frequently not suspected until clinical signs or symptoms of pericardial tamponade develop. Pericardial effusions occur most commonly in lymphoma, lung, breast and oesophageal cancers, but they can also develop following radiotherapy to the mediastinum and with some chemotherapies. Section 13 describes the signs and symptoms, investigations and treatment.

Section 14, covering radiotherapy induced complications, focuses on acute skin reactions, acute radiation pneumonitis, and acute syndromes caused by radiation induced cerebral or spinal cord oedema. Other radiotherapy induced complications are covered elsewhere in the guidelines. Clinical teams are advised to use the guidelines contained within this section for initial management of symptoms, but to refer to the radiotherapy unit looking after the patient for their advice on further management.

Raised intracranial pressure (ICP) and central nervous system space occupying lesions are covered in section 15. Increased ICP is secondary to obstruction of cerebrospinal fluid flow, cerebral oedema or increased venous pressure. Space occupying lesions are the most common cause of a raised ICP. Secondary metastases from, for example, breast, lung, melanoma and colorectal
cancers are much more common than primary brain tumours. Increased ICP can occur acutely. Without prompt treatment, raised ICP can lead to reduction in cerebral perfusion pressure, cerebral infarction and tonsillar herniation. The section covers assessment and investigations, emergency management and subsequent management.

The final section focuses on superior vena cava obstruction. This is nearly always associated with malignancy, usually lung cancer (80% of cases) but sometimes lymphoma, breast cancer or germ cell tumours. It usually occurs in patients with known cancer, but can be the presenting feature of a new diagnosis. A range of treatments is suggested.

Adoption of the LCA AOS guidelines will allow widespread implementation of up-to-date and evidence-based management of oncology patients, and will assist in the provision of a consistently high standard of care across the LCA.
1 Allergy and Anaphylaxis

If chemotherapy related allergy or anaphylaxis suspected, please refer to Acute Oncology Service.

By kind permission of B Quinn

A hypersensitivity/allergic reaction is an overactive or misdirected immune response that results in local tissue injury or changes throughout the body in response to a foreign body. This reaction may occur shortly after the drug/treatment is commenced or in the hours/days following treatment.

1.1 Assessing for Risk, Early Detection and Prevention

Prior to drug/treatment administration:

- Know the drug’s potential to cause allergic reaction and the patient’s history of allergies and reactions.
- Measure baseline blood pressure, pulse, respiratory rate, oxygen saturation and temperature.
- Inform the patient of possible early signs so they can alert the nurse or doctor immediately.
- Administer any prescribed pre-medication before drugs known to cause hypersensitivity reactions or if the patient has previously reacted to this particular or similar drug/treatment.
- Know where emergency drugs and equipment are located (drugs should only be administered with a doctor or nurse practitioner’s prescription or under Patient Group Directions).

1.2 Hypersensitivity

1.2.1 Signs and Symptoms

- Urticaria (hives)
- Angioedema – tongue, lips, airways
- Hypotension
- Pruritis (itching) – local and generalised
- Flushing/redness, in particular of the face and neck
- Maculopapular rash – on trunk, arms, legs and face
- Nausea and vomiting.

1.2.2 Treatment

- Remove cause, i.e. stop drug/chemotherapy, recline patient.
- Reassure patient and explain plan of care.
- Measure and monitor: blood pressure, pulse, respiratory rate, oxygen saturations and temperature. Administer oxygen if required.
• Antihistamine: chlorphenamine 10mg by slow intravenous (IV) or intramuscular (IM) injection.
• Corticosteroid: hydrocortisone 100mg by slow IV or IM injection.
• Consider saline nebuliser and/or bronchodilator.
• If symptoms settle:
  – Re-commence drug at reduced infusion rate and monitor carefully.
  – Increase infusion rate and continue close observation.
• Discuss with consultant regarding discontinuing drug.

1.3 Anaphylaxis

1.3.1 Signs and Symptoms
• Pruritis – localised and generalised
• Facial flushing leading to generalised erythema
• Angioedema, laryngeal oedema, bronchospasm – tongue, lips, airways
• Hypotension; light-headedness and dizziness
• Sense of impending doom
• Flu-like symptoms, often with generalised shaking
• Collapse and unconsciousness.

1.3.2 Treatment
• Remove cause, i.e. stop drug/chemotherapy.
• Recline patient and administer high-flow oxygen (5–10 L/min).
• If stridor, wheeze, respiratory distress or shock: IM epinephrine 0.5ml 1:1000.
• If no improvement after 5 mins:
  • Repeat IM epinephrine 0.5ml 1:1000. Several doses may be needed, especially if improvement is transient or the patient deteriorates.
• Chlorpheniramine: 20mg IM or slow IV.
• Hydrocortisone: 100–300mg slow IV or IM injection. For patients with a severe or recurrent reaction, and in all patients with asthma.
• If not responding rapidly to drug treatment: 0.9% sodium chloride (NaCl) IV infusion.
• Salbutamol nebuliser if bronchospasm is a major feature which has not responded rapidly to other treatment.

NOTE: Beware the possibility of early or late recurrence of symptoms and consider observation for a minimum of 8–24 hours.

Write the name of the agent that caused the reaction prominently in the patient’s notes and drug chart.
2 Ascites (Malignant)

If malignant ascites suspected, please refer to Acute Oncology Service.

Malignant ascites is most commonly seen in patients with a known diagnosis of ovarian or gastrointestinal cancer, but it can occur in any oncology patient. Importantly, ascites may be the presenting feature of a new cancer diagnosis. In this situation correct diagnosis of the malignancy is an important part of the patient management. Please consider early referral of these patients to the Acute Oncology Service (AOS).

2.1 Symptoms

- Abdominal distension, pain, breathlessness, nausea and vomiting.

2.2 Management of Ascites in Patients with Known Cancer

Routine imaging is not required to confirm ascites if it is clinically apparent.

Assess patient suitability for intervention: if too frail for either diuretics or invasive procedures, symptom management with analgesia and anti-emetics should be maximised. Discuss with the palliative care team.

2.3 Paracentesis

If tense ascites or moderate/severe symptoms:

- Check blood pressure (BP), full blood count (FBC), urea and electrolytes (U&E) and clotting. Ensure platelets >50x10^9/L and International Normalized Ratio (INR) <1.4.
- Stop anticoagulants for 24–48 hours pre-procedure.
- Ultrasound evaluation +/- marking of drainage site if concern over diagnosis, suspicion of bowel obstruction or loculation of fluid.

Risks include intestinal injuries, peritonitis, fistulas and significant loss of protein (hypoalbuminaemia) which may lead to metabolic disturbances and eventually cachexia. In order to prevent hypovolaemia it may be necessary to concurrently administer intravenous (IV) fluids when draining large volumes of ascitic fluid.

2.3.1 Contraindications

**Absolute contraindications:** severe and irreversible disorders of coagulation, intestinal obstruction and abdominal sepsis.

**Relative contraindications:** severe portal hypertension with abdominal collateral circulation.

2.3.2 Rate of Drainage

No more than 8000ml should be drained at any one time. Usually, 1–2L can be drained and then the drain should be clamped for a short time (no need to clamp overnight, however). If the patient becomes haemodynamically unstable, the drain should remain clamped until the patient recovers.
2.3.3 Intravenous Fluids

Not routinely required but if dehydrated, renal impairment or symptomatic during paracentesis, consider 0.9% saline, 150ml/L of ascitic fluid drained. Also consider IV fluids if portal hypertension, massive liver metastases, hepatocellular carcinoma +/- cirrhosis.

There is no benefit of colloids (e.g. Gelofusine) over crystalloids.

2.3.4 IV Albumin

No proven role in paracentesis for malignant ascites. However, it should be considered if there is portal hypertension +/- cirrhosis, especially in the setting of large-volume paracentesis (>5L/24 hours). Dose: Albumin 6–8g/L of ascitic fluid drained.

Aim for early discharge. Inform patient’s oncology team about admission and paracentesis.

2.4 PleurX Peritoneal Catheters for Recurrent Ascites

NICE medical technology guidance 9 (March 2012) recommends that “The PleurX peritoneal catheter drainage system should be considered for use in patients with treatment-resistant, recurrent malignant ascites.” It was concluded that PleurX peritoneal drains are effective, have low complication rates and have the potential to improve quality of life by enabling early and frequent treatment of symptoms of ascites in the community.

In keeping with this, where they are available, insertion of PleurX peritoneal catheters should be considered for patients with recurrent ascites.

2.5 Other Management Options

- Spironolactone
- Shunts
- Systemic anti-cancer treatment.

2.6 Management of Patients with a New Presentation of Cancer

- Inform the acute oncology team.
- Full examination, including breast examination in women.
- If investigation is appropriate:
  - Computed tomography (CT) scan chest, abdomen and pelvis.
  - Diagnostic or therapeutic paracentesis. Send large-volume sample for cytology.
  - If ovarian malignancy suspected, send CA125 level.
  - Requesting a whole panel of tumour markers is not appropriate.
- Liaise with relevant specialist multidisciplinary team (MDT), depending on likely tumour site (e.g. gynaecology, gastrointestinal etc.).
3 Central Venous Access Device Complications

If central venous access device complications suspected, please refer to Acute Oncology Service.

Indwelling central venous access devices (CVADs) are required in oncology for the safe infusion of certain chemotherapy schedules and occasionally in patients with poor peripheral access. They are used for chemotherapy, phlebotomy, delivery of blood products and other supportive measures.

The clinical team is advised to seek advice from the acute oncology team during working hours and the acute oncology on-call service out of hours.

3.1 Types of CVAD

3.1.1 Implanted Ports (‘Portacaths’)

Ports should only be accessed with an appropriate non-coring access needle.

A port should only be accessed by staff members who have successful completed a relevant training programme in accordance with local policy.

3.1.2 Skin Tunnelled Catheters (‘Hickman Lines’)

Connections for drips or syringes

Collar bone

Point where central line enters body

Heart

Diagram showing an implantable port

Diagram showing an implantable port under the skin

Diagram showing a central line

Copyright © CancerHelp UK
3.1.3 Peripherally Inserted Central Catheters (PICCs)

3.2 Pneumothorax

Pneumothorax is a potential complication of CVAD insertion. All patients should have a chest X-ray (CXR) two hours after CVAD insertion. This should be seen by a doctor in all cases and the result documented in the notes. If pneumothorax is noted then any chemotherapy treatment should be withheld. Early liaison with the acute medical and/or respiratory team is advised.

3.2.1 Uncompromised Patients (<30% Pneumothorax, No Chronic Respiratory Disease)

- Patients may be observed closely with repeat CXR the following day.
- Providing the repeat CXR is stable and the patient not compromised, then treatment can proceed and the patient advised to observe for further symptoms.
- Out-patient department (OPD) review with repeat CXR should be arranged (~7 days).
- If the pneumothorax has enlarged at 24 hours or the patient has become compromised, then a chest drain should be inserted.

3.2.2 Stable Patients with a Significant Pneumothorax (>30%)

Consider aspiration. If successful, then the patient should have a repeat CXR after 24 hours, before commencing chemotherapy. If unsuccessful, insert chest drain.

3.2.3 Chest Drains

A chest drain should be inserted in the following cases:

- Respiratory compromise (check for tension)
- Large pneumothorax not responded to aspiration
- Significant chronic lung disease
- If small (<30%) pneumothorax has enlarged at 24 hours, or patient is compromised.

If the pneumothorax does not resolve after chest drain insertion, check for leaks around the entry site and tubing. Consider gentle suction and liaise with respiratory team.

Chemotherapy should be delayed until the pneumothorax has resolved and chest drain has been removed.
NOTE: Chest drains should be inserted by radiology under ultrasound guidance or, if not available, on the ward by someone experienced in the procedure.

3.3 CVAD Infections

3.3.1 Exit Site Infections

Symptoms: erythema, pain or discharge around the exit site.

Investigations: a swab should be taken, and results of previous swabs reviewed.

Management

- Empirical 1 week course of flucloxacillin (or clarithromycin if penicillin-allergic).
- If the infection fails to resolve, consider intravenous (IV) antibiotics, according to local microbiological guidelines. Teicoplanin has the advantage of being given on a once daily basis (OD) as an outpatient.
- If the above fails to control the infection it may be necessary to remove the CVAD, but discuss with oncology team first.

3.3.2 Intra-luminal Infections

Symptoms: rigors and fever, characteristically 15–45 minutes following line flushing.

Investigations

- All patients require hospital admission, as septicaemia may ensue.
- Blood cultures should be taken both from the CVAD and peripherally.

Management

- Start IV broad spectrum antibiotics (NOT via the CVAD) according to local microbiological guidelines.
- A significant proportion of infected CVADs may be salvaged in this way if they remain clinically stable.
- If there are no signs of improvement or the patient become compromised, the CVAD should be removed by someone trained to do so. Implanted ports will require surgical or radiological removal.
- Send tip and cuff (skin tunnelled catheter) for microbiological culture if line is removed.
- Neutropenic patients with CVAD infections should have the CVAD removed as a matter of urgency.

3.4 CVAD-associated Thrombosis

Symptoms

- Arm or neck swelling on the side of the CVAD
- Pain (sometimes the only symptom).
**Investigations**

Doppler ultrasound or contrast imaging to confirm the diagnosis.

In most cases the diagnosis should be confirmed before CVAD removal.

**Management**

- Start anticoagulation (therapeutic dose low molecular weight heparin (LMWH) is preferred).
- Confirm thrombosis and remove the CVAD.
- If there is significant swelling, then anticoagulation and removal of the CVAD can be considered before the diagnosis is confirmed. These patients should subsequently undergo imaging investigation.
- The patient should remain on anticoagulation until a new CVAD is inserted (the LMWH is stopped the day prior to CVAD insertion).
- The patient will need to be maintained on LMWH or warfarin throughout the duration of the new CVAD.

**3.5 Pain**

Some patients develop CVAD-associated pain with no evidence of thrombosis. This pain is typically described as an ache occurring over the posterior aspect of the scapula, with the patient often pointing to a point just above or overlying the spine of the scapula.

Doppler studies should be performed to exclude the presence of clot, but in the majority they will be negative. Simple analgesics should be prescribed but if ineffective then CVAD removal may be necessary.

The pain may be due to irritation of the vascular wall by the CVAD tip. Consequently replacement of the CVAD can be considered, as there is a reasonable chance it will not recur when a new CVAD is inserted.

**3.6 Emergency CVAD Removal**

In the event of complications that require CVAD removal (infection, venous thrombosis), this should be discussed first with the oncology team, and carried out by those who have undergone the relevant training and supervision.

NICE clinical guidance on the management of neutropenic sepsis (September 2012) recommends against routine removal of CVADs unless there are patient-specific or microbiological reasons for doing so.

Implanted ports may only be removed surgically, either by the surgical team, plastics team or interventional radiology, depending on local protocols.

**3.7 Damage to Skin Tunnelled Catheters/PICCs**

If a catheter becomes damaged, then depending on the type and brand it may be repaired, e.g. skin tunnelled catheters. Repairs can be carried out by those trained to do so – contact the oncology team. Do not attempt repair unless you are trained to do so.
4 Diarrhoea: Chemotherapy and Radiotherapy Induced

If chemotherapy or radiotherapy induced diarrhoea suspected, please refer to Acute Oncology Service.

Patients receiving chemotherapy or radiotherapy to the abdomen/pelvis are at risk of developing severe diarrhoea, and the prevalence can be as high as 50–80%. It is particularly associated with regimens containing fluoropyrimidines (5-FU, capecitabine) or irinotecan.

Chemotherapy induced diarrhoea (CID) can be a serious and life-threatening complication and can also lead to treatment delays, dose reductions or treatment discontinuation. The mucositis and neutropenia from the chemotherapy treatment can also significantly increase complications associated with CID. Prompt recognition and appropriate treatment are therefore essential.

4.1 Presenting Symptoms

<table>
<thead>
<tr>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
</table>

**Frequency of Stool (Patients with and without Colostomy)**

<table>
<thead>
<tr>
<th>Grade</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Increase of &lt;4 stools/day over pre-treatment</td>
<td>Increase of 4–6 stools/day or moderate increase in ostomy output</td>
<td>Increase of ≥7 stools/day or severe increase in ostomy output</td>
<td>&gt;10 stools/day</td>
<td></td>
</tr>
<tr>
<td>Or mild increase in ostomy output</td>
<td>Or severe increase in ostomy output</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Symptoms**

<table>
<thead>
<tr>
<th>Grade</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>None</td>
<td>Moderate cramping, not interfering with normal activity</td>
<td>Severe cramping and incontinence, interfering with daily activities</td>
<td>Grossly bloody and need for parenteral support</td>
<td>Life-threatening consequences</td>
</tr>
</tbody>
</table>

Life-threatening consequences
### 4.2 Causes of Diarrhoea in Oncology Patients

<table>
<thead>
<tr>
<th>Bone Marrow Transplantation-related</th>
<th>Conditioning chemotherapy, total-body irradiation, graft-versus-host disease after allogenic bone marrow or peripheral blood stem cell transplants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Adverse Effects</td>
<td>Antibiotics, magnesium-containing antacids, antihypertensives, colchicine, digoxin, iron, lactose, laxatives, methyldopa, metoclopramide, misoprostol, potassium supplements, propanol, theophylline</td>
</tr>
<tr>
<td>Concurrent Disease</td>
<td>Diabetes, hyperthyroidism, inflammatory bowel disease (Crohn’s disease, diverticulitis, gastroenteritis, HIV/AIDS, ulcerative colitis), obstruction (tumour-related)</td>
</tr>
<tr>
<td>Viral Infection</td>
<td>Norwalk virus, Rotavirus</td>
</tr>
<tr>
<td>Bacterial Infection</td>
<td><em>Clostridium difficile</em> (<em>C. diff</em>), <em>Clostridium perfringens</em>, <em>Bacillus cereus</em>, <em>Giardia lamblia</em>, <em>Cryptosporidium</em>, <em>Salmonella</em>, <em>Shigella</em>, <em>Campylobacter</em></td>
</tr>
<tr>
<td>Faecal Impaction</td>
<td>Constipation leading to obstruction</td>
</tr>
</tbody>
</table>
| Diet                                | • Alcohol, milk and dairy products  
• Caffeine-containing products  
• High-fibre foods (raw fruits and vegetables, nuts, seeds, whole-grain products, dried legumes)  
• High-fat foods (deep-fat-fried foods, high-fat-containing foods)  
• Lactose intolerance or food allergies  
• Hot and spicy foods  
• Gas-forming foods and beverages (cabbage, cauliflower, dried legumes, melons, carbonated beverages) |
| Psychological Factors               | Stress |

### 4.3 Assessment of Condition

Patients with likely viral gastroenteritis should, in keeping with national advice, avoid coming to hospital and should instead be assessed and managed in the community.

- Onset and duration of diarrhoea: if duration >12 hours, take stool sample.
- Number of stools and stool composition (watery, blood).
- Assess for: pyrexia, neutropenia, abdominal pain, dizziness, weakness.
- Medication profile (diarrhoeogenic, e.g. bulk agents, softeners, prokinetics).
- Dietary profile (diarrhoea-enhancing foods).
4.4 Investigations

- Stool sample if >12 hours symptoms (C. diff, microbiology, ova, cysts, parasites)
- Bloods: full blood count (FBC), urea and electrolytes (U&E), liver function test (LFT), magnesium (Mg++)
- Abdominal X-ray to exclude bowel obstruction or faecal impaction.

4.5 Initial Management

- Stop lactose-containing products (including milk products): lactose intolerance may develop when the mucosa is damaged.
- Avoid spices, high-fibre foods, high-fat foods, caffeine, alcohol, fruit juices.
- Drink 8–10 large glasses of clear fluids/day (water, clear soup, non-fizzy soft drinks).
- Small, frequent meals (bananas, rice, toast, plain pasta).
- Neutropenic patients with diarrhoea Grade ≥3: admit for observation and consider empirical antibiotics (as per local microbiological guidelines).

4.6 Treatment of Chemotherapy Induced Diarrhoea

- Wait for stool culture before starting loperamide in the following situations: hospitalisation within past 6 weeks, antibiotics within past 6 weeks, bloody diarrhoea, recent travelling abroad, history of contact with diarrhoea.
- If indicated: loperamide 4mg followed by 2mg after every loose stool up to 16mg daily.
- Alternative: codeine phosphate 30–60mg QDS.
- Re-assess after 12 hours and then follow algorithm below.
- For patients on irinotecan-based therapy, see section 4.8.
4.7 Specific Recommendation for Patient Receiving Irinotecan:

- **Loperamide** 4mg once after the first liquid stool then 2mg every 2 hours.
- Continue for 12 hours after the last liquid stool (do not continue beyond 48 hours).
- If diarrhoea has not resolved within 24 hours: **ciprofloxacin** 250mg BD PO for 7 days.
- If severe diarrhoea continues beyond 48 hours or is associated with nausea, vomiting or fever, then admit patient to hospital.
5 Extravasation of Chemotherapy

Extravasation is the inadvertent administration of vesicant medication or solution into the surrounding tissue instead of into the intended vascular pathway. Vesicants are drugs with the potential to cause tissue damage and necrosis, and require management.

Once an extravasation has occurred, damage can continue for months and involve nerves, tendons and joints. If treatment is delayed, surgical debridement, skin grafting and even amputation may be the unfortunate consequences.

5.1 Signs and Symptoms

| Pain                          | Severe stinging or burning pain (not always present)  
|                              | Can last from minutes to hours and will eventually subside  
|                              | Occurs during drug administration at the device site and surrounding areas  
| Redness                      | Not always present immediately: more likely to see blanching of the skin as area becomes inflamed, redness will appear around the device site  
| Swelling                     | May occur immediately but may not always be easy to identify straight away  
| Blood Return                 | Inability to obtain blood return (peripheral or central) but blood return may be present throughout  
| Ulceration                   | Unlikely  
| Others                       | Change in quality of the infusion or pressure/resistance on the syringe barrel during injection, leaking around the cannula or port needle site  

5.2 Immediate Management

| Stage 1: Stop infusion/injection Aspirate as much of drug as possible | Helps to lower concentration of drug in area  
| Stage 2: Remove device | No research evidence to support but if access is required to administer antidote this should be via new site  
| Stage 3: Apply cold pack | Some controversy over hot/cold but cooling is considered a better choice – causes vasoconstriction (Exception: vinca alkaloids or taxanes)  

- Elevate the limb.
- Administer antidote where relevant and analgesia as required.
- Apply hydrocortisone cream to reduce local inflammation (BD).
5.3 Ongoing Management

Management will depend on the services available. The chart below can act as a guide.

Access to plastics team within 2 hours or a nurse trained in flush-out technique

YES

Contact relevant doctor and plastics team trained in flush-out technique
Photograph extravasation site pre-treatment if possible
Flush-out technique to be performed

Document

NO

Remove cannula

DNA binding drugs e.g. doxorubicin

Apply cold pack and consider use of dexrazoxane

Apply dimethyl sulfoxide topically 2 hourly for 24 hours then 6 hourly for 7 days

Apply hydrocortisone cream 6 hourly

Document

Consider analgesia, refer to plastics team and take a photograph

Non-DNA binding drugs e.g. vinca alkaloids or paclitaxel

Infiltrate with hyaluronidase 1500units

Apply hot pack

Contact relevant doctor and plastics team trained in flush-out technique

Photograph extravasation site pre-treatment if possible
Flush-out technique to be performed

Document
The use of hot and cold packs may have the following effects:

- Cold packs may localise and neutralise cytotoxic drugs.
- Warm packs may spread or dilute the antidote.

The key is that if a patient presents with blistering, erythema, swelling and/or pain up to 1 week after receiving chemotherapy containing a vesicant, then suspect an extravasation as well as possible local infection and seek advice/refer to plastic surgeons as soon as possible.

5.4 Extravasation from a Central Venous Access Device (CVAD)

Extravasations from a CVAD are more serious as they are often more difficult to detect and a greater amount of drug may extravasate before the patient or nurse is aware of it. It may be due to dislodgement and malposition of the catheter or dislodgement of the port needle. Location of symptoms will depend on where the device is located, e.g. chest or thigh.

5.4.1 Signs and Symptoms

- Pain or burning around the CVAD in the chest, shoulder or neck
- Swelling of the chest wall, shoulder or neck
- Fluid leakage at or around exit site and/or along subcutaneous tunnel.

5.4.2 Management of Extravasation from a CVAD

- Do not remove the CVAD straight away.
- Stop the infusion.
- Aspirate as much of the drug as possible from the device.
- Contact acute oncology and plastic surgeons for further advice.
- Manage the extravasation as for most vesicant drug infused.
- Organise chest X-ray (CXR) to verify tip location and catheter-gram to check if catheter damaged.
- Where appropriate, arrange for removal of the CVAD after discussion with consultant.
6 Hypercalcaemia of Malignancy

If hypercalcaemia of malignancy suspected, please refer to Acute Oncology Service.

Hypercalcaemia of malignancy is the commonest metabolic complication of cancer and occurs in around 10% of patients. It most commonly occurs in patients with advanced disease and is an indicator of poor prognosis (median survival is 3–4 months and 80% die within 1 year).

Definition of hypercalcaemia: corrected serum calcium >2.60 mmol/L.

6.1 Tumours Associated with Hypercalcaemia

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Tumour Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>50%</td>
<td>Multiple myeloma</td>
</tr>
<tr>
<td>20%</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>20%</td>
<td>Lung cancer (usually squamous or adenocarcinoma; seldom small cell)</td>
</tr>
<tr>
<td>&lt;10%</td>
<td>Renal cell carcinoma, head and neck cancer, thyroid cancer</td>
</tr>
<tr>
<td>Rarely</td>
<td>Prostate, colorectal</td>
</tr>
</tbody>
</table>

6.2 Causes

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>80%</td>
<td>Tumour production of parathyroid hormone-related peptide (PTHrP)</td>
</tr>
<tr>
<td>20%</td>
<td>Lytic bone metastases</td>
</tr>
<tr>
<td>&lt;1%</td>
<td>Tumour production of parathyroid hormone (PTH) or vitamin D</td>
</tr>
</tbody>
</table>

Around 20% of patients have no evidence of bone metastases.

6.3 Symptoms

<table>
<thead>
<tr>
<th>Domain</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Dehydration, polydipsia, polyuria, pruritis</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Anorexia, nausea, vomiting, constipation, weight loss</td>
</tr>
<tr>
<td>Neurological</td>
<td>Fatigue, lethargy, confusion, anxiety, seizures, psychosis, coma</td>
</tr>
<tr>
<td>Cardiac</td>
<td>Bradycardia, arrhythmias, prolonged PR interval, reduced QT interval</td>
</tr>
</tbody>
</table>
6.4 Investigations

**Calcium (Ca\(^{++}\)), phosphate (PO4)**  
Do not rely on uncorrected values from arterial blood gases

**Urea and electrolytes (U&E)**  
Renal function frequently deranged and patients are usually dehydrated

**Liver function test (LFT)**  
Alkaline phosphatase (ALP) usually elevated  
(except in myeloma)

**Magnesium (Mg\(^{++}\))**  
Hypomagnesaemia common

**Electrocardiogram (ECG)**

**Serum PTH**  
Unnecessary if known metastatic malignancy  
If malignancy not known, PTH will be normal or low in malignant hypercalcaemia.

**Serum PTHrP**  
Not routinely tested. Requires special processing and advance warning to lab.

6.5 Management

If this is new presentation of malignancy, please contact the AOS.

6.5.1 Review All Medications

Stop thiazide diuretics, calcium, vitamin A, vitamin D supplements.

6.5.2 Rehydration

All patients with hypercalcaemia are dehydrated due to polyuria and vomiting, on average 4L in negative balance. Rehydration may be all that is needed in mild, asymptomatic cases (Ca\(^{++}\) <3.00mmol/L). Slower rehydration rates may be needed if there are other co-morbidities.

Rehydration may provoke hypokalaemia and hypomagnesaemia, so check U&E and Mg\(^{++}\) daily and replace as necessary. Consider catheterisation if patient does not pass urine for 4 hours.

6.5.3 Bisphosphonates

Bisphosphonates inhibit osteoclast function. They should not be given until the patient is rehydrated and has a good urine output.

Bisphosphonates will usually begin to reduce Ca\(^{++}\) within 48 hours and will usually normalise it within 5 days. If the Ca\(^{++}\) level is not falling, do not repeat the dose until at least day 5. If Ca\(^{++}\) has not normalised by day 5 then a repeat dose of bisphosphonate can be given at the next dose level up.

Pamidronate is the most common bisphosphonate used but choice of bisphosphonate should reflect local Trust policy. Pamidronate is more effective than clodronate. Zoledronic acid normalises calcium in more patients, more rapidly and for longer than pamidronate, and it is a quicker infusion.
6.5.4 Refractory Hypercalcaemia

Refractory hypercalcaemia is associated with a poor prognosis, and referral to special palliative care team should be considered. The following treatments may have a role.

- **Bisphosphonates**
  Repeat bisphosphonate infusion (if not tried already).
  If initially treated with pamidronate, consider zoledronic acid.

- **Corticosteroids**
  Inhibit gut Ca\(^{++}\) absorption and osteoclastic bone resorption.
  Benefit largely confined to myeloma, lymphoma, leukaemia.
  If indicated: prednisolone 40–100 mg/day.

- **Calcitonin**
  Reduces osteoclastic bone resorption and increase calciuresis.
  Effective in 30% of refractory cases; rapid onset of action (<4 hours).
  However, effects are short lived and daily S/C injections are required.

- **Denosumab**
  Anti-RANKL monoclonal antibody used to treat bone metastases.
  Not licensed for hypercalcaemia but lowers calcium markedly.
  May be available on named patient basis.
7 Hypomagnesaemia

If chemotherapy associated hypomagnesaemia is suspected, please refer to Acute Oncology Service.

Hypomagnesaemia is an under-diagnosed problem, particularly as magnesium (Mg) does not usually feature in the routine biochemistry test. However, it is common in oncology patients receiving treatment as it can be caused by a number of chemotherapies.

It can also be caused by malabsorption, malnutrition, diarrhoea or fistulae and be secondary to other electrolyte abnormalities (hypocalcaemia, hypokalaemia).

7.1 Definition

<table>
<thead>
<tr>
<th>Grade</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serum Magnesium</strong></td>
<td>LLN*–0.5 mmol/L</td>
<td>0.5–0.4 mmol/L</td>
<td>0.4–0.3 mmol/L</td>
<td>&lt;0.3 mmol/L</td>
<td>Death</td>
</tr>
</tbody>
</table>

*LLN = lower limit normal

7.2 Clinical Features

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>Ventricular arrhythmias</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supraventricular arrhythmias</td>
<td>Enhancement of digoxin toxicity</td>
</tr>
<tr>
<td>ECG Changes</td>
<td>ST-segment depression</td>
<td>Reduction in overall voltage</td>
</tr>
<tr>
<td></td>
<td>Altered T waves</td>
<td>PR interval, widened QRS complexes</td>
</tr>
<tr>
<td>Neuromuscular</td>
<td>Tetany</td>
<td>Muscle fasciculation</td>
</tr>
<tr>
<td></td>
<td>Muscle cramps</td>
<td>Carpopedal spasm</td>
</tr>
<tr>
<td></td>
<td>Convulsion</td>
<td>Weakness</td>
</tr>
<tr>
<td>Neurological</td>
<td>Confusion</td>
<td>Ataxia</td>
</tr>
<tr>
<td></td>
<td>Psychosis</td>
<td>Spasticity</td>
</tr>
<tr>
<td></td>
<td>Depression</td>
<td>Tremor</td>
</tr>
<tr>
<td></td>
<td>Agitation</td>
<td>Delirium</td>
</tr>
<tr>
<td>Other</td>
<td>Nausea/vomiting</td>
<td>Diarrhoea</td>
</tr>
</tbody>
</table>

7.3 Oncology Drugs and Hypomagnesaemia

These include cisplatin (commonest cause), interleukin-2, cyclosporine, tacrolimus, pegylated liposomal doxorubicin, carboplatin, cetuximab and panitumumab.

A number of other support drugs commonly used in cancer patients can cause or contribute to hypomagnesaemia, such as amphotericin B, pentamidine, gentamicin and diuretics.
7.4 **Investigations**

Hypomagnesaemia is frequently accompanied by low calcium and potassium levels so these, along with renal function, must also be checked.

7.5 **Management**

7.5.1 **Grade 1**

No replacement strategy is necessary. Patients usually asymptomatic.

7.5.2 **Grade 2**

5g (20mmol) magnesium sulphate (MgSO₄) in 500ml normal saline over 6–8 hours.

Oral Mg supplementation may be tried but is usually poorly tolerated due to diarrhoea.

7.5.3 **Grade 3 or 4**

Risk of cardiac arrhythmia so consider cardiac monitor in severe cases.

5g (20mmol) MgSO₄ in 1L normal saline over 8–10 hours.

Repeat for up to 3–5 days until serum magnesium normal.

If renal impairment: reduce dose to 2.5g (10mmol) MgSO₄ over 24 hours.

**If hypocalcaemic**

Correct magnesium level until calcium in normal range.

**If hypokalaemic**

Replace 40mmol potassium chloride (KCl) and 1.25mg (5mmol) MgSO₄ in 500ml normal saline over 6 hours and repeat for up to 24 hours, checking potassium and Mg levels regularly.

7.6 **EMERGENCY**

Severe hypomagnesaemia with cardiac arrhythmias (e.g. ventricular tachycardia):

- 2g MgSO₄ IV over 5–7 minutes.
- Followed by infusion of 5g (20mmol) MgSO₄ in 1 normal saline for 3–5 days (see above).
- Rapid IV Mg therapy can cause hypocalcaemia, hypotension: this should only be undertaken in an emergency, with adequate acute medical support.
- Patients must be on a cardiac monitor and have regular assessment of all electrolytes.
8 Lymphangitic Carcinomatosis

If lymphangitic carcinomatosis suspected, please refer to Acute Oncology Service.

Lymphangitic carcinomatosis is the diffuse infiltration of lymphatic channels by tumour, resulting in obstruction and interstitial oedema.

The lung is a common site of metastatic disease from many tumour types, and approximately 6–8% of lung metastasis presents as lymphangitis.

The most common underlying tumour types are breast (33%), lung and gastrointestinal cancers.

8.1 Diagnosis

Chest radiography and high-resolution computed tomography (HRCT) of the chest are usually diagnostic in suspicious clinical context.

8.2 Presentation

8.2.1 Signs and Symptoms

- Dyspnoea out of proportion to physical findings
- Unproductive cough or haemoptysis
- Chest pain
- Fevers, tachycardia
- Fine crepitations.

8.2.2 Radiological Changes

- Chest X-ray
  Reticular or reticulonodular shadowing, septal lines, peribronchial cuffing.
  Normal in 50% of those with histologically proven disease.
- HRCT
  Interlobular septal thickening, thickening of fissures, peribronchovascular thickening.
  Mediastinal lymphadenopathy or pleural effusion in approximately 50% of cases.

8.3 Histological

In the absence of a known malignancy and if clinically appropriate, referral to the respiratory multidisciplinary team (MDT) for consideration of biopsy is essential and should be done before starting steroids.
8.4 Management

8.4.1 Hypoxia/Dyspnoea
- Oxygen therapy
- Oral morphine solution 2.5mg 4 hourly
- Lorazepam 0.5mg 4–6 hourly S/L.

8.4.2 Cough
- Simple linctus TDS
- Codeine linctus 15mg/5ml 5–10ml 6–8 hourly
- Oral morphine solution 2.5mg 4 hourly.

8.4.3 Secretions
- Nebulised 0.9% sodium chloride 2.5–5ml if trying to clear
- Glycopyrrolate 0.2–0.4mg S/C 2–4 hourly if trying to dry secretions
- Seek input from palliative care team.

8.4.4 Corticosteroids
- May give some improvement: dexamethasone 8mg BD (morning and lunchtime) or prednisolone
- One week trial: if no improvement, stop; if improvement, titrate to lowest effective dose.

8.4.5 Systemic Anti-cancer Therapies
- Treatment should be specific to underlying tumour if patient fit enough to undergo chemotherapy.

8.5 Prognosis
- Poor, but dependent on underlying tumour type
- Approximate 50% 3-month survival
- Determine patient preferences for future care as appropriate in view of poor prognosis.
9 Metastatic Spinal Cord Compression

The guidelines should be read in conjunction with NICE guidance on the management of metastatic spinal cord compression (2008).

9.1 Introduction

Metastatic spinal cord compression (MSCC) is the compression of the spinal cord, or cauda equina, by direct pressure and/or vertebral collapse as a result of metastatic spread that may cause neurological deficit and paralysis. MSCC is one of the most serious and devastating complications of malignancy; however, with prompt diagnosis and treatment many patients can retain good levels of function and independence. On the other hand, unnecessary delays in diagnosis and treatment impact on patients’ quality of life and prognosis.

The incidence is poorly documented in the UK but in comparable populations 2.5% of patients with advanced cancer will develop MSCC.

9.2 Causes and Presentation

MSCC can occur in virtually all types of malignancy, but myeloma, lung, prostate and breast cancer are the most common.

<table>
<thead>
<tr>
<th>Tumour Site</th>
<th>Proportion of Patients Who Develop MSCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>20–31%</td>
</tr>
<tr>
<td>Prostate</td>
<td>18–21%</td>
</tr>
<tr>
<td>Breast</td>
<td>13–17%</td>
</tr>
<tr>
<td>Haematology</td>
<td>8–10%</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>5–13%</td>
</tr>
<tr>
<td>Kidney</td>
<td>3–12%</td>
</tr>
<tr>
<td>Unknown</td>
<td>4–7%</td>
</tr>
<tr>
<td>Other</td>
<td>7–14%</td>
</tr>
</tbody>
</table>

The majority of MSCC cases occur in patients with a pre-existing cancer diagnosis; however, in around 20% of patients it is their first cancer presentation.

9.3 Signs and Symptoms

- Pain in the middle (thoracic) or upper (cervical) spine
- Progressive lower (lumbar) spinal pain
- Severe unremitting lower spinal pain
- Spinal pain aggravated by straining (for example at stool, or when coughing or sneezing)
- Localised spinal tenderness
• Nocturnal spinal pain preventing sleep
• Radicular pain
• Any limb weakness or difficulty in walking
• Sensory loss, or bladder or bowel dysfunction
• Neurological signs of spinal cord or cauda equina compression.

A patient with a cancer diagnosis and confirmed vertebral metastases is at high risk of developing MSCC. It is important that the patient is educated about the risks of developing MSCC, how to identify these symptoms, what to do and who to contact.

9.4 Assessment

9.4.1 Urgency of Assessment
• MSCC coordinators are contactable 24 hours a day for rapid access to the MSCC pathway, all urgent referrals and review of patients with suspected MSCC.
• A list of local MSCC coordinators and regional MSCC treatment centres is in section 1.5.
• If there is a neurological deficit, the patient must immediately be discussed with the local MSCC coordinator and managed as an emergency.
• If an oncology patient has any of the symptoms above, this should still be discussed urgently with the local MSCC coordinator.
• Assessment and investigation must not be delayed due to lack of local out-of-hours services. If these are not available, contact the local MSCC coordinator to arrange urgent transfer to your regional MSCC treatment centre (the patient will be transferred back if there is no MSCC).

9.4.2 Primary Care Presentation
• Contact MSCC coordinator of nearest MSCC treatment centre.
• Arrange urgent clinical assessment by MSCC team.

9.4.3 Hospital Presentation (Non-MSCC Treatment Centre)
• Arrange urgent investigation as listed in section 1.6.
• Discuss results with local MSCC coordinator.
• If appropriate, transfer patient and imaging to MSCC treatment centre for further assessment and definitive treatment.

9.4.4 Spinal Stability
• Patients with severe pain suggestive of spinal instability, or any neurological signs or symptoms suggestive of MSCC, should be nursed flat with neutral spine alignment (including ‘log rolling’ and use of a slipper bed pan) until bony and neurological stability are ensured.
• Assume the spine unstable until clearly documented in the medical notes.
• Full neurological assessment including PR examination.
• Respiratory assessment and treat as appropriate.
• Nurse patient with spine in neutral alignment.
• For cervical lesions, ensure immobilisation with hard collar.

9.5 Contact Details for MSCC Services Within the LCA

All trusts have a local MSCC coordinator who should be the first point of contact for patients with suspected or proven MSCC. There are also regional MSCC treatment centres within the LCA.

<table>
<thead>
<tr>
<th>Regional MSCC Treatment Centre</th>
<th>Contact Details</th>
</tr>
</thead>
</table>
| Imperial College Healthcare NHS Trust | In hours: 020 3311 7866  
Out of hours: 020 3311 7866 |
| King’s College Hospital NHS Foundation Trust | In hours: 020 3299 5468  
Out of hours: 020 3299 4207 |
| St George’s Healthcare NHS Trust | In hours: 020 8672 1255 – Bleep 6027  
Out of hours: 020 8672 1255 – Bleep 6027 |
<table>
<thead>
<tr>
<th>Hospital Name</th>
<th>Local MSCC Coordinator Contact Details</th>
<th>Regional MSCC Treatment Centre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Middlesex</td>
<td>In hours: 020 3311 7866</td>
<td>Imperial</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 3311 7866</td>
<td></td>
</tr>
<tr>
<td>Charing Cross</td>
<td>In hours: 020 3311 7866</td>
<td>Imperial</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 3311 7866</td>
<td></td>
</tr>
<tr>
<td>Chelsea and Westminster</td>
<td>In hours: 07791 472630 – Bleep 8908 SpR</td>
<td>Imperial</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 3311 7866</td>
<td></td>
</tr>
<tr>
<td>Croydon University</td>
<td>In hours: 020 8401 3000 – Bleep 946 or Extension 5726</td>
<td>St George’s</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 8672 1255 – Bleep 6027</td>
<td></td>
</tr>
<tr>
<td>Ealing</td>
<td>In hours: 020 3311 7866</td>
<td>Imperial</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 3311 7866</td>
<td></td>
</tr>
<tr>
<td>Epsom</td>
<td>In hours: 01372 735 735 – Bleep 898</td>
<td>St George’s</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 8672 1255 – Bleep 6027</td>
<td></td>
</tr>
<tr>
<td>Guy’s and St Thomas’</td>
<td>In hours: 020 7188 7188 – Bleep 2069</td>
<td>King’s</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 3299 4207 – Bleep on-call neurosurgical SpR</td>
<td></td>
</tr>
<tr>
<td>Hammersmith</td>
<td>In hours: 020 3311 7866</td>
<td>Imperial</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 3311 7866</td>
<td></td>
</tr>
<tr>
<td>Harefield</td>
<td>In hours: 020 3311 7866</td>
<td>Imperial</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 3311 7866</td>
<td></td>
</tr>
<tr>
<td>Hillingdon</td>
<td>In hours: 01895 238282 – Bleep 5175</td>
<td>Imperial</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 3311 7866</td>
<td></td>
</tr>
<tr>
<td>King’s College</td>
<td>In hours: 020 3299 5468</td>
<td>King’s</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 3299 4207</td>
<td></td>
</tr>
<tr>
<td>Kingston</td>
<td>In hours: 07528 977590</td>
<td>St George’s</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 8672 1255 – Bleep 6027</td>
<td></td>
</tr>
<tr>
<td>Lewisham</td>
<td>In hours: 020 3299 5468</td>
<td>King’s</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 3299 4207</td>
<td></td>
</tr>
<tr>
<td>Northwick Park</td>
<td>In hours: 020 8864 3232 – Bleep 003 on-call medical registrar</td>
<td>Imperial</td>
</tr>
<tr>
<td></td>
<td>Out of hours: 020 8864 3232 – Bleep 003 on-call medical registrar</td>
<td></td>
</tr>
<tr>
<td>Hospital Name</td>
<td>Local MSCC Coordinator Contact Details</td>
<td>Regional MSCC Treatment Centre</td>
</tr>
<tr>
<td>---------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>--------------------------------</td>
</tr>
<tr>
<td>Queen Elizabeth (Woolwich)</td>
<td>In hours: 020 8836 6000 – Bleep 835 Out of hours: 020 3299 4207 – Bleep on-call neurosurgical SpR</td>
<td>King’s</td>
</tr>
<tr>
<td>Queen Mary’s (Sidcup)</td>
<td>In hours: As for Queen Elizabeth or Princess Royal Out of hours: 020 3299 4207 – Bleep on-call neurosurgical SpR</td>
<td>King’s</td>
</tr>
<tr>
<td>Princess Royal University (Bromley)</td>
<td>In hours: 01689 863000 – Bleep 340 Out of hours: 020 3299 4207 – Bleep on-call neurosurgical SpR</td>
<td>King’s</td>
</tr>
<tr>
<td>Royal Brompton</td>
<td>In hours: 020 3311 7866 Out of hours: 020 3311 7866</td>
<td>St George’s</td>
</tr>
<tr>
<td>Royal Marsden (Chelsea)</td>
<td>In hours: 020 7352 8171 – Bleep on-call radiotherapy SpR Out of hours: 020 7352 8171 – Bleep 022</td>
<td>St George’s</td>
</tr>
<tr>
<td>Royal Marsden (Sutton)</td>
<td>In hours: 020 8642 6011 – Bleep on-call radiotherapy SpR Out of hours: 020 8642 6011 – Bleep 022</td>
<td>St George’s</td>
</tr>
<tr>
<td>St George’s</td>
<td>In hours: 020 8672 1255 – Bleep 6027 Out of hours: 020 8672 1255 – Bleep 6027</td>
<td>St George’s</td>
</tr>
<tr>
<td>St Helier University</td>
<td>In hours: 020 8296 2000 – Bleep 409 Out of hours: 020 8672 1255 – Bleep 6027</td>
<td>St George’s</td>
</tr>
<tr>
<td>St Mary’s</td>
<td>In hours: 020 3311 7866 Out of hours: 020 3311 7866</td>
<td>Imperial</td>
</tr>
<tr>
<td>West Middlesex University</td>
<td>In hours: 020 3311 7866 Out of hours: 020 3311 7866</td>
<td>Imperial</td>
</tr>
</tbody>
</table>
9.6 Investigation

Whole spine magnetic resonance imaging (MRI) is the investigation of choice. If an MRI is absolutely contra-indicated, then spinal computed tomography (CT) is an alternative; however, it is inferior in this setting.

- Imaging must be performed within 24 hours of presentation for any patient with spinal pain suggestive of spinal metastases and with neurological signs or symptoms suggestive of MSCC.
- Imaging must be performed more urgently if there is clear neurological deficit or deterioration.
- In these situations, if out-of-hours MRI is not available, then investigations must not be delayed. Instead, the patient should be transferred to the relevant regional MSCC treatment centre.
- For patients with pain suggestive of spinal metastases but no neurological signs or symptoms, imaging should be performed as an outpatient within 1 week of presentation.
- Consider up-to-date CT of brain, chest, abdomen and pelvis as this assists surgical planning with regard to bone strength, structural integrity and ensuring that surgery is used appropriately.

9.7 Management of MSCC

- Dexamethasone 16mg PO or intravenous (IV) stat.
- Follow with dexamethasone 8mg BD (IV or PO) with proton pump inhibitor cover.
- Analgesia as described in the World Health Organization (WHO) three-step analgesia ladder.
- All patients with radiologically confirmed MSCC must be discussed urgently with a consultant clinical oncologist, consultant neuro- or spinal surgeon and, where possible, the treating oncology consultant prior to definitive treatment decisions.
- Decisions regarding the role of surgery or radiotherapy should be made bearing in mind the cancer diagnosis, characteristics of the MSCC, functional level of the patient (neurological and performance status), overall disease status and likely prognosis.
- It may be appropriate to manage patients with MSCC palliatively, without surgery or radiotherapy; however, this decision should be made by a consultant oncologist, neurosurgeon or palliative medicine physician, usually following joint discussion.

9.7.1 Neurosurgical Management in Regional MSCC Treatment Centres

- Discuss referral with neurosurgical spinal team in hours (Monday–Friday, 08.00–17.00) or on-call neurosurgical SpR out of hours.
- Bloods for full blood count (FBC), urea and electrolytes (U&E), clotting, group and save.
- Consider pre-operative investigations such as chest X-ray and electrocardiogram (ECG).
- If referral from another hospital, please ensure prompt availability of imaging via image exchange portal (IEP)/CD/picture archiving and communication system (PACS).
9.7.2 Radiotherapy Management

- Confirm dexamethasone and proton pump inhibitor administration.
- Review the clinical situation, radiology with the imaging team and surgical opinion with the neurosurgical team before decision on definitive treatment.
- If the patient is not previously known to have cancer and if neurosurgical decompression is not planned, then a biopsy of the mass should be obtained urgently.
- Radiotherapy can be started in advance of a biopsy result being available if the clinical and radiological diagnoses are consistent with a malignant process and the clinical indication for treatment is urgent.
- Radiotherapy treatment plan should be delivered in line with the local trust radiotherapy protocols.
- Radiotherapy can be given post-operatively (usually 2 weeks) and once the wound has healed. Cases should be considered on an individual basis.

9.7.3 Chemotherapy Sensitive Tumours

- Some patients with MSCC may have a chemotherapy sensitive tumour and primary treatment with chemotherapy, rather than surgery or radiotherapy, should be considered.
- This particularly applies to proven or likely gestational trophoblastic disease, germ cell tumours, small cell lung cancer, lymphoma, leukaemia or myeloma.
- In these cases the on-call medical oncologist or haematology specialist should be contacted.

9.7.4 New Diagnosis of Malignancy

- Patients without a pre-existing diagnosis of malignancy should be considered for diagnostic biopsy if spinal surgery is not indicated.
- Treatment of MSCC should not be delayed if biopsy result is not available.

9.7.5 Spine Stability after Definitive Treatment

- Please refer to NICE guidance on the management of MSCC.
- Ensure referral to physiotherapist within 24 hours of admission.
- Consider spinal brace.
- Gentle mobilisation under instruction when pain well controlled.
- Encourage gradual sitting from supine to 45 degrees; once tolerated, progress to 60–90 degrees as able. Monitor neurology and pain during this process.
9.7.6  Further Management

- Please refer to NICE guidance on the management of MSCC.
- Venous thromboembolism prophylaxis as per local guidelines.
- Ensure appropriate bowel management.
- Catheterisation if bladder function affected.
- Liaise with acute pain service and/or palliative care to optimise symptom control.
- Refer to occupational therapist within 48 hours of admission.
- Ensure that protocol is in place for weaning off dexamethasone.

9.8  Rehabilitation and Discharge Planning

- Please refer to NICE guidance on the management of MSCC.
- Early referral to appropriate allied health professionals (including speech and language therapists for swallow assessment as required).
- Liaise with physiotherapy, occupational therapy, social services and palliative medicine to develop discharge plan.
- Review steroid dose and, in liaison with neurosurgical or clinical oncology team, plan reduction after treatment.
- If the patient has been transferred to a regional MSCC treatment centre, facilitate timely transfer back to referring hospital following completion of surgical or oncology treatment.
10 Mucositis

If uncontrolled mucositis suspected, please refer to Acute Oncology Service.

Adapted from management protocol by B Quinn

Mucositis is a general term for the erythematous, erosive, inflammatory and ulcerative lesions that occur in the mucosal lining of the mouth, pharynx, oesophagus and entire gastrointestinal tract secondary to cytotoxic treatment.

Patients at especial risk of mucositis include those receiving high-dose chemotherapy (e.g. for leukaemia or lymphoma) and those receiving radiotherapy, with/without chemotherapy, for head, neck and oral cancers.

10.1 Assessment

Check if patient is neutropenic. If evidence of neutropenic sepsis, treat according to guidelines in section 12.

<table>
<thead>
<tr>
<th>WHO Grade Oral Mucositis</th>
<th>Clinical Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Soreness +/- erythema, no ulceration.</td>
</tr>
<tr>
<td>2</td>
<td>Erythema, ulcers. Patient can swallow solid diet.</td>
</tr>
<tr>
<td>3</td>
<td>Ulcers, extensive erythema. Patient cannot swallow solid diet.</td>
</tr>
<tr>
<td>4</td>
<td>Oral mucositis to the extent that alimentation is not possible.</td>
</tr>
</tbody>
</table>

10.2 Management of Grade 1 or 2 Mucositis

Check to see if the patient has evidence of oral infection and if so ensure an anti-infective agent is prescribed (see section 10.5).

10.2.1 Mouth Care

- Ensure good oral hygiene.
- Stop any mouthwashes containing alcohol.
- Consider increasing the number of saline rinses to hourly if required.
- Remove dentures if they are irritating.
- Referral to dietician is required if eating and drinking are affected.
10.2.2 Topical Treatment Options

- Soluble paracetamol: two tablets dissolved in water and used as a mouthwash. Use with caution as it may mask fever and these patients may be neutropenic.
- Benzydamine 0.15% oral solution: 10ml rinsed around the mouth and spat out. Repeat between every 1.5 and 3 hours as required. If it causes stinging, dilute 10ml benzydamine with 10ml water prior to administration and use 10ml of the solution.
- Sucralfate: 5ml to be used as a mouthwash and then swallowed QDS. Owing to its coating action, sucralfate must be used last in the oral care medication sequence, otherwise it will block the effect of any topical agent. The sucralfate coat may mask mucosal infections, therefore there should be close monitoring of infections in the mouth. To be used in caution in patients taking enteral feeds.

10.3 Management of Grade 3 or 4 Mucositis

As for Grades 1 and 2, plus:

10.3.1 Topical Treatments

Sodium hyaluronate topical for mouth ulcers: the contents of one sachet should be rinsed around the mouth to form a protective layer over the sore areas, applied 1 hour before eating.

10.3.2 Analgesia

- Immediate-release strong opioid (e.g. liquid morphine sulphate) to alleviate pain. Ensure that intravenous (IV) hydration is prescribed, as oral intake may be reduced. Consult dietician.
- Systemic analgesia: if unresponsive to measures above. Consider syringe driver or patient-controlled analgesia. Ensure that laxative medications are prescribed.

10.4 Specific Symptoms

10.4.1 Dry Lips

Patients undergoing chemotherapy can experience dry lips. Petroleum jelly, yellow/white soft paraffin or normal lip salve can be used to moisten lips. Some of these products are contraindicated if the patient is receiving radiotherapy to the head and neck region, as they may act as another layer of skin and affect the depth of treatment.

If on oxygen therapy, apply a water-soluble lubricant.

10.4.2 Dry Mouth

Encourage oral hydration where possible. Where patients are on oxygen treatment, early intervention to prevent dry mouth should help. The following may provide relief:

- Chewing tinned pineapple chunks (may cause irritation if there is mouth ulceration)
- Sucking crushed ice or frozen tonic water
- Artificial saliva
- Sugar-free chewing gum (stimulates saliva production).
10.4.3 Bleeding from the Mouth
Add 500mg tranexamic acid injection to 5ml sterile water and use as a mouthwash. Rinse 4 hourly. Swallowing is permitted if a systemic effect is required.

10.5 Anti-infective Treatments
Despite prophylaxis, patients may still present with a viral or fungal infection of the mouth. Swabs should take from the mouth for both fungal and viral infections. Consult with the acute oncology team. Treatment options include:

10.5.1 Neutropenic Sepsis
All patients who are neutropenic and have signs of infection should be treated according to the neutropenic sepsis guidelines in section 12.

10.5.2 Fungal
Refer to local microbiological guidelines.

10.5.3 Viral
Consider topical aciclovir 5% for local infection in low-risk patients. Increase the dose of aciclovir to 800mg orally five times a day or IV infusion 10mg/kg TDS.
11 Nausea and Vomiting

If nausea and vomiting suspected, please consider referral to Acute Oncology Service.

These guidelines are for the acute management of patients with uncontrolled nausea and vomiting. They are not guidelines for prophylactic anti-emetic use in patients about to receive anti-cancer treatment.

Do not assume that nausea and vomiting are chemotherapy related. Many chemotherapies have no significant emetic potential, while chemotherapy will seldom causes nausea and vomiting more than 1 week after administration.

Therefore identify the cause before starting regular anti-emetics. Reflecting their mechanism of action, certain anti-emetics are indicated in specific situation.

11.1 Grading Nausea and Vomiting

<table>
<thead>
<tr>
<th>Grade</th>
<th>Nausea</th>
<th>Vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Loss of appetite without alteration in eating habits</td>
<td>1 episode in 24 hours</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Oral intake decreased without significant weight loss, dehydration or malnutrition; intravenous (IV) fluids indicated &lt;24 hours</td>
<td>2–5 episodes in 24 hours; IV fluids indicated &lt;24 hours</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Inadequate oral calorific or fluid intake; IV fluids, tube feeding or total parenteral nutrition (TPN) indicated &gt;24 hours</td>
<td>≥6 episodes in 24 hours; IV fluids or TPN indicated &gt;24 hours</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Life-threatening consequences</td>
<td>Life-threatening consequences</td>
</tr>
</tbody>
</table>

11.2 General Guidance on Anti-emetic Use

- Anti-emetics are best given regularly, not PRN.
- Ensure that courses are completed.
- Consider whether there is a failure to absorb oral medication. If so, change the route of anti-emetics administration.
- Choice of anti-emetics should take into consideration cause of symptoms and drug mechanism of action (see table below).
**Action of anti-emetics on main receptor sites**

<table>
<thead>
<tr>
<th>Drug</th>
<th>D₂ antagonist</th>
<th>H₁ antagonist</th>
<th>ACh antagonist</th>
<th>5HT₂ antagonist</th>
<th>5HT₃ antagonist</th>
<th>5HT₄ antagonist</th>
<th>NK₁ inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoclopramide</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Domperidone</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclizine</td>
<td>++</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyoscine</td>
<td></td>
<td></td>
<td>++</td>
<td></td>
<td></td>
<td></td>
<td>+++</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>+++</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aprepitant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+++</td>
</tr>
<tr>
<td>Ondansetron</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Granisetron</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
</tbody>
</table>


- Cyclizine blocks the prokinetic effects of domperidone/metoclopramide so they should not be used together.
- Drugs acting on the same receptor (e.g. domperidone and metoclopramide) should not be used together.
- For patients <20 years old the dose of metoclopramide should be 10mg, or consider using domperidone.

### 11.3 Causes of Nausea and Vomiting in Oncology Patients

<table>
<thead>
<tr>
<th>Cause</th>
<th>Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>Lorazepam&lt;br&gt;Antidepressants in longer term: seek advice from patient’s GP or from oncology team</td>
</tr>
<tr>
<td>Bowel obstruction</td>
<td>Levomepromazine or haloperidol or cyclizine</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>See section 11.5</td>
</tr>
<tr>
<td>Constipation</td>
<td>Treat cause</td>
</tr>
<tr>
<td>Delayed gastric emptying</td>
<td>Metoclopramide</td>
</tr>
<tr>
<td>Drugs* (non-chemotherapy)</td>
<td>Stop drug if possible&lt;br&gt;Haloperidol or levomepromazine</td>
</tr>
<tr>
<td>Gastric irritation</td>
<td>Treat cause (e.g. proton pump inhibitor)&lt;br&gt;Metoclopramide if needed</td>
</tr>
<tr>
<td>Hypercalcaemia</td>
<td>Treat cause (see section 6)&lt;br&gt;Haloperidol or levomepromazine</td>
</tr>
<tr>
<td>Renal failure</td>
<td>Haloperidol or levomepromazine</td>
</tr>
<tr>
<td>Metabolic causes</td>
<td>Haloperidol or levomepromazine</td>
</tr>
<tr>
<td>Raised intracranial pressure</td>
<td>Treat cause (see section 15)&lt;br&gt;Dexamethasone and cyclizine</td>
</tr>
</tbody>
</table>

*Common culprits include antibiotics, antidepressants, NSAIDs and opiates.
11.4 Chemotherapy and Emesis

Chemotherapy induced nausea and vomiting (CINV) is one of the commonest side effects of chemotherapy; however, persistent nausea and vomiting are now fairly rare with the use of the modern anti-emetic drugs. CINV is often grouped into three phases:

- **Acute**: within 24 hours of receiving chemotherapy.
- **Delayed**: from 24 hours after chemotherapy. Seldom persists beyond 1 week.
- **Anticipatory**: occurs prior to any chemotherapy and is a learned response to previous treatments.

In addition, CINV can be classified as:

- **Breakthrough**: development of symptoms (nausea and vomiting), despite standard anti-emetic therapy, which require treatment with an additional pharmacological agent.
- **Refractory**: patients who have failed on both standard and rescue medication.

Breakthrough nausea and vomiting refers to symptoms despite regular anti-emetics and requiring additional agents. Dexamethasone should be given prophylactically, not as a treatment for CINV.

11.5 Management of Uncontrolled CINV

- Establish which anti-emetic regimen has been prescribed by the oncology team.
- Ensure that patient has been taking these anti-emetics correctly and regularly (see tables below).
- Investigate cause of nausea and vomiting (see above) and treat any non-chemotherapy related causes.
- If confirmed breakthrough CINV, select the appropriate additional anti-emetics as detailed below, starting at Level 1 and working upwards.
- If patient has persistent vomiting, is dehydrated or is unable to tolerate oral fluids, start IV rehydration and arrange admission.
- Delayed nausea and vomiting can occur with cisplatin chemotherapy. Ensure good rehydration and consider dexamethasone 4mg BD PO/IV as this can be particularly effective.
<table>
<thead>
<tr>
<th>Level</th>
<th>Anti-Emetic</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Level 1| Domperidone or Metoclopramide | • Do not use domperidone and metoclopramide together  
• Can use IV metoclopramide or domperidone PR |
| Level 2| Levomepromazine or Cyclizine or Prochlorperazine | • Levomepromazine dose = 6.25mg BD PO  
• Prochlorperazine can be given as suppository (25mg PR) if needed  
• These agents replace metoclopramide/domperidone |
| Level 3| Ondansetron or Lorazepam or Levomepromazine or Haloperidol | • Ondansetron is only effective in acute CINV. Only use a short course (max 3 days)  
• Lorazepam is especially helpful for anticipatory nausea and vomiting Can be given 1mg PO, IV or S/L  
• Consider S/C levomepromazine infusion  
• Haloperidol is oral (1–2mg QDS) or IV (1–3mg TDS) |

### 11.6 Radiation Induced Nausea and Vomiting

- As for CINV, the goal of anti-emetic therapy is to prevent nausea and vomiting.
- The risk of radiation induced emesis varies with the treatment administered.
- Refer to section 11.5 (above) for treatment of breakthrough nausea and vomiting.
## 11.7 Emetogenic Potential of Individual Drugs

<table>
<thead>
<tr>
<th>Low Emetosis (&lt;30% Incidence)</th>
<th>Alemtuzumab</th>
<th>Lenolidamide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asparaginase</td>
<td>Liposomal daunorubicin</td>
<td></td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>Liposomal doxorubicin</td>
<td></td>
</tr>
<tr>
<td>Bleomycin</td>
<td>Melphalan oral</td>
<td></td>
</tr>
<tr>
<td>Bortezomib</td>
<td>Mercaptopurine</td>
<td></td>
</tr>
<tr>
<td>Busulfan &lt;10mg/m²</td>
<td>Methotrexate &lt;250mg/m²</td>
<td></td>
</tr>
<tr>
<td>Cetuximab</td>
<td>Nelarabine</td>
<td></td>
</tr>
<tr>
<td>Capecitabine</td>
<td>Nilotinib</td>
<td></td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>Pemetrexed</td>
<td></td>
</tr>
<tr>
<td>Cladribine</td>
<td>Pentostatin</td>
<td></td>
</tr>
<tr>
<td>Dasatinib</td>
<td>Rituximab</td>
<td></td>
</tr>
<tr>
<td>Erlotinib</td>
<td>Sorafenib</td>
<td></td>
</tr>
<tr>
<td>Etoposide ≤120mg/m²</td>
<td>Thalidomide</td>
<td></td>
</tr>
<tr>
<td>Fludarabine</td>
<td>Thiguanine</td>
<td></td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>Trastuzumab</td>
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</tr>
<tr>
<td>Gefitinib</td>
<td>Vinblastine</td>
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</tr>
<tr>
<td>Gemtuzumab</td>
<td>Vincristine</td>
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</tr>
<tr>
<td>Hydroxycarbamide</td>
<td>Vindesine</td>
<td></td>
</tr>
<tr>
<td>Imatinib</td>
<td>Vinorelbine IV</td>
<td></td>
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<tr>
<td>Lapatinib</td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderate Emetosis (30%–60% Incidence)</th>
<th>Arsenic</th>
<th>Mitomycin C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carmustine &lt;100mg/m²</td>
<td>Mitoxantrone</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide &lt;750mg/m²</td>
<td>Paclitaxel</td>
<td></td>
</tr>
<tr>
<td>Cytarabine &lt;900mg/m²</td>
<td>Procarbazine</td>
<td></td>
</tr>
<tr>
<td>Daunorubicin &lt;50mg/m²</td>
<td>Temozolomide</td>
<td></td>
</tr>
<tr>
<td>Doxorubicin &lt;60mg/m²</td>
<td>Raltitrexed</td>
<td></td>
</tr>
<tr>
<td>Etoposide &gt;120mg/m²</td>
<td>Trabectedin</td>
<td></td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>Topotecan PO/IV</td>
<td></td>
</tr>
<tr>
<td>Methotrexate &gt;250mg/m² – &lt;1000mg/m²</td>
<td>Vinorelbine PO</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>High Emetosis (60%–90% Incidence)</th>
<th>Altretamine</th>
<th>Docetaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amsacrine</td>
<td>Doxorubicin &gt;60mg/m²</td>
<td></td>
</tr>
<tr>
<td>5 Azacitadine</td>
<td>Epirubicin</td>
<td></td>
</tr>
<tr>
<td>Carboplatin</td>
<td>Estramustine</td>
<td></td>
</tr>
<tr>
<td>Clofarabine</td>
<td>Idarubicin</td>
<td></td>
</tr>
<tr>
<td>Carmustine &gt;100mg/m² – &lt;250mg/m²</td>
<td>Ifosfamide &lt;3g/m²</td>
<td></td>
</tr>
<tr>
<td>Cisplatin &lt;60mg/m²</td>
<td>Irinotecan</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide &gt;750mg/m² – &lt;1500mg/m²</td>
<td>Lomustine</td>
<td></td>
</tr>
<tr>
<td>Cytarabine &gt;900mg/m²</td>
<td>Melphalan IV &gt;100mg/m²</td>
<td></td>
</tr>
<tr>
<td>Dactinomycin</td>
<td>Methotrexate &gt;1000mg/m²</td>
<td></td>
</tr>
<tr>
<td>Daunorubicin &gt;50mg/m²</td>
<td>Oxaliplatin</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Very High Emetosis (&gt;90% Incidence)</th>
<th>Busulfan high doses</th>
<th>Dacarbazine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carmustine &gt;250mg/m²</td>
<td>Ifosfamide &gt;3mg/m²</td>
<td></td>
</tr>
<tr>
<td>Cisplatin &gt;60mg/m²</td>
<td>Streptozocin</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide &gt;1500mg/m²</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
11.8 Notes on Individual Anti-emetics

<table>
<thead>
<tr>
<th>5HT₃ Antagonist</th>
<th>Patients may complain of constipation and headaches. Patients need to be advised accordingly, e.g. lactulose to relieve constipation and paracetamol to relieve headache. If severe, consider an alternative anti-emetic. Long acting 5HT₃ antagonists are available and may be used if locally approved.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aprepitant</td>
<td>Aprepitant is an NK-1 receptor antagonist which has been shown to inhibit emesis induced by cyclotoxic chemotherapeutic agents, such as cisplatin, via central actions. In addition, studies show that aprepitant augments the antiemetic activity of the 5HT₃ receptor antagonist and dexamethasone and inhibits both the acute and delayed process of cisplatin-induced emesis. When given in combinations with corticosteroids, the SPC suggests: reduce oral dexamethasone dose by 50%, reduce methylprednisolone IV dose by 25% and oral dose by 50%. NB for practical reasons it is not necessary to halve post chemotherapy dexamethasone doses as confirmed in the aprepitant trial data. Common side effects include headaches, hiccups and fatigue.</td>
</tr>
<tr>
<td>Cyclizine</td>
<td>Cyclizine may cause antimuscarinic side effects such as dryness of the mouth and drowsiness. Children and the elderly are more susceptible to these effects.</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Corticosteroids can cause sleep disturbances, hyperactivity and excessive appetite. They also produce glucose intolerance; use with care in patients with diabetes mellitus. Patients may experience perineal discomfort if the drug is given by IV bolus. This can be avoided by administration via IV infusion.</td>
</tr>
<tr>
<td>Domperidone</td>
<td>Domperidone should not be used when stimulation of the gastric motility could be harmful, e.g. gastro-intestinal haemorrhage, mechanical obstruction or perforation.</td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>Avoid in patients with liver dysfunction. Inhibits cytochrome P-450. Common side effects are somnolence, asthenia, dry mouth, hypotension, photosensitivity and skin reactions.</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Can cause drowsiness and may affect performance of skilled tasks (driving).</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Can rarely cause agitation or the development of extra-pyramidal symptoms particularly in the young female patients. These can occur up to 24 hours after a dose and may vary from facial grimacing and dystonic movements to odd feelings in the mouth, restlessness, somnolence and irritability. Bowel transit time may be reduced and some patients experience diarrhoea.</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>Prochlorperazine should be avoided in patients with liver or renal dysfunction, Parkinson’s disease, hypothyroidism, cardiac failure, phaeochromocytoma, myasthenia gravis and prostatic hypertrophy. A mild leukopenia occurs in up to 30% of patients on prolonged high dosage. May cause drowsiness.</td>
</tr>
</tbody>
</table>
12 Neutropenic Sepsis

If neutropenic sepsis suspected, please refer to Acute Oncology Service.

Please refer to NICE clinical guidance on the management of neutropenic sepsis (Sept 2012):

www.nice.org.uk/nicemedia/live/13905/60866/60866.pdf
13 Pericardial Effusion (Malignant)

If malignant pericardial effusion suspected, please refer to Acute Oncology Service.

Malignant pericardial effusions occur in up to 20% of cancer patients but are frequently not suspected until clinical signs or symptoms of pericardial tamponade develop. Pericardial effusions occur most commonly in lymphoma, lung, breast and oesophageal cancers. They can also develop following radiotherapy to the mediastinum and with some chemotherapies (e.g. doxorubicin, bulsulfan, cytarabine).

13.1 Signs and Symptoms

The majority of pericardial effusions are asymptomatic. When present, symptoms include dyspnoea and fatigue. Pericardial tamponade results from increasing fluid accumulation in the pericardium, leading to elevated pressure, reduced stroke volume and cardiac output, and haemodynamic compromise, resulting in death if not treated.

Generally haemodynamic compromise occurs when the normal amount of pericardial fluid (15–50ml) increases rapidly to >200ml or more, then slowly accumulates up to 1L.

13.2 Investigations

- **Chest X-ray (CXR):** widening of the cardiac silhouette if >250 ml fluid. CXR cannot assess degree of cardiac compromise.
- **Electrocardiogram (ECG):** bradycardia and diminished QRS amplitude in all leads. Very rarely: electrical alternans pattern.
- **Echocardiography:** gold-standard investigation. Can demonstrate the presence and volume of pericardial effusions as well as associated pericardial masses and inflammation, and can also determine right and left ventricular function and the possibility of right ventricular or atrial diastolic collapse.

13.3 Treatment

There are little randomised data as to the optimal management of a pericardial effusion and current treatment should be aimed at symptom relief with minimal impact on quality of life. If intervention is being considered, patient must be discussed with the local cardiology and/or cardiothoracic surgical team.

Elective treatment options include percutaneous pericardiocentesis, pericardial sclerosis, subxiphoid pericardial window, pericardiectomy, or pericardotomy by thoracotomy or video-assisted thoracoscopy.

Catheter drainage is recommended for large effusions to prevent rapid re-accumulation of fluid and subsequent tamponade, and for the anticipated survival of the patient.
14 Radiotherapy Induced Complications

If radiotherapy induced complications suspected, please refer to Acute Oncology Service.

Patients who are currently receiving or who have recently undergone radiotherapy are at risk of a number of complications. Guidelines on the initial management are detailed below but please also liaise with the radiotherapy unit looking after the patient for their advice on further management.

14.1 Acute Skin Reactions

The skin is affected by nearly all radiotherapy treatments. The degree of skin reaction depends on several factors, including type of radiation, dose, treatment schedule, area of treatment and co-existing skin conditions. Please liaise with the relevant radiotherapy team at the first opportunity.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Skin Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No visible changes</td>
</tr>
<tr>
<td>1</td>
<td>Faint or dull erythema; dry desquamation</td>
</tr>
<tr>
<td>2a</td>
<td>Tender or bright erythema without dry desquamation</td>
</tr>
<tr>
<td>2b</td>
<td>Patchy moist desquamation; moderate oedema</td>
</tr>
<tr>
<td>3</td>
<td>Confluent moist oedema; pitting oedema</td>
</tr>
</tbody>
</table>

14.1.1 Treatment

<table>
<thead>
<tr>
<th>Skin Reaction</th>
<th>Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Aqueous cream BD</td>
<td>To prevent itching and maintain moisture</td>
</tr>
<tr>
<td>1</td>
<td>Aqueous cream PRN</td>
<td>To moisturise and soothe</td>
</tr>
<tr>
<td>2a</td>
<td>Aqueous cream BD, Hydrocortisone 1% sparingly</td>
<td>To moisturise and soothe</td>
</tr>
<tr>
<td></td>
<td>Use hydrogel, hydrocolloid or alignate dressing*</td>
<td>To reduce itching</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do not use adhesive tape to hold in place</td>
</tr>
<tr>
<td>2b</td>
<td>Stop applying aqueous cream</td>
<td>To prevent trauma</td>
</tr>
<tr>
<td></td>
<td>Use hydrogel, hydrocolloid or alignate dressing*</td>
<td>Do not use adhesive tape to hold in place</td>
</tr>
<tr>
<td></td>
<td>Swab area</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Use hydrogel, hydrocolloid or alignate dressing*</td>
<td>Do not use adhesive tape to hold in place</td>
</tr>
<tr>
<td></td>
<td>Swab area</td>
<td></td>
</tr>
</tbody>
</table>

*Use of dressings should be discussed with the tissue viability nurse at the first opportunity.

Analgesia prescribed should be as defined in the World Health Organization (WHO) analgesia ladder.
14.2 Acute Radiation Pneumonitis

- **Radiation pneumonitis** is an acute phase injury that occurs within 6 months of treatment.
- **Lung fibrosis** is the resulting chronic injury and develops after 1 year.

All patients with suspected radiation pneumonitis should be discussed with their own clinical oncology team.

14.2.1 Signs

Usually unremarkable, but sometimes pleural friction rub. Haemoptysis is not typical and more likely suggests a different pathology.

14.2.2 Symptoms

Classically develop 2–3 months after radiation, and persist for up to 7 months. They include:

- Shortness of breath
- Dry cough
- Low-grade fever.

14.2.3 Assessment

<table>
<thead>
<tr>
<th>Grade</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Asymptomatic: clinical or diagnostic observations only; intervention not indicated</td>
</tr>
<tr>
<td>2</td>
<td>Symptomatic: medical intervention indicated; limiting instrumental activities of daily living (ADL)</td>
</tr>
<tr>
<td>3</td>
<td>Severe symptoms: limiting self-care ADL; oxygen indicated</td>
</tr>
<tr>
<td>4</td>
<td>Life-threatening respiratory compromise: urgent intervention indicated (e.g. tracheostomy or intubation)</td>
</tr>
<tr>
<td>5</td>
<td>Death</td>
</tr>
</tbody>
</table>

Source: Common Terminology Criteria for Adverse Events 4.0

14.2.4 Investigations

- **Chest X-ray (CXR)**
  Commonest finding is patchy opacification peaking 12 months after treatment. Later changes include fibrosis, volume loss and pleural thickening.

- **Computed tomography (CT)**
  Not routinely indicated but can be considered if pulmonary embolism (PE) in differential diagnosis. Findings include ground glass changes, consolidation and volume loss.

- **Arterial blood gases**
- **Spirometry**
• Other
White cell count (WCC)/neutrophils should be normal in radiation pneumonitis. Consider bronchoscopy if condition worsening.

14.2.5 Differential Diagnosis
• Infection
• Recurrence of disease
• Lymphangitic carcinomatosis.

14.2.6 Management
• Exclude other pathology: infectious pneumonitis, PE, tumour recurrence.
• If likely radiation pneumonitis: prednisolone 30–40mg for 1–2 weeks followed by a slow taper.
• Some patients will require long-term low-dose prednisolone.
• Ensure appropriate oncology or respiratory follow-up.
• Severe pneumonitis may require oxygen and hospitalisation. Liaise with respiratory team.

14.3 Acute Syndromes Caused by Radiation Induced Cerebral or Spinal Cord Oedema
Oedema of the brain and spinal cord can occur as an early (days) or late (months) effect of radiation. Most patients will receive prophylactic steroids while receiving radiotherapy; however, they are still at risk of developing treatment associated oedema. The symptoms and signs depend on the area of radiation.

14.3.1 Investigations
Full imaging of the affected area is not necessary if this has recently been done as part of their radiotherapy treatment and if signs and symptoms are consistent with radiation induced oedema. Repeat CT of head or magnetic resonance imaging (MRI) of spine is reasonable if a different pathology (e.g. haemorrhage) is suspected.

14.3.2 Treatment
• Start steroids, or increase dose if already prescribed. Dexamethasone 4–8mg BD PO/IV is usually initially required. Increasing dexamethasone beyond 16mg/day is unlikely to produce additional benefit.
• Add proton pump inhibitor and consider prophylactic fluconazole and co-trimoxazole in patient likely to be on extended courses of high-dose steroids.
• For patients not responding to dexamethasone, mannitol can be considered, but this should be discussed first with the oncology consultant in charge.

14.4 Radiotherapy Induced Nausea and Vomiting
Please refer to management of nausea and vomiting in section 11.6.
14.5 Radiotherapy Induced Diarrhoea
Please refer to management of diarrhoea in section 4.6.

14.6 Radiotherapy Associated Mucositis
Please refer to management of mucositis in section 10.
15 Raised Intracranial Pressure/Central Nervous System (CNS) Space Occupying Lesions

Increased intracranial pressure (ICP) is secondary to obstruction of cerebrospinal fluid (CSF) flow, cerebral oedema or increased venous pressure. Space occupying lesions (SOL) are the commonest cause of a raised ICP. Secondary metastases from breast, lung, melanoma and colorectal cancers etc are much more common than primary brain tumours.

Raised ICP can occur acutely. Without prompt treatment, it can lead to reduction in cerebral perfusion pressure, cerebral infarction and tonsillar herniation.

The most common tumour types to metastasise are:
- Lung 50%
- Breast 15–20%
- Unknown primary 10–15%
- Melanoma 10%
- Colon 5%

15.1 Assessment

Patients present in several different ways depending on the site of the lesion.

Physical assessment (including breasts in women), neurological examination and Glasgow Coma Scale (GCS) assessment.

15.1.1 Symptoms
- Headache
- Vomiting
- Confusion
- Neck stiffness
- Speech disturbance
- Seizures
- Nausea
- Diplopia
- Fever
- Visual symptoms
- Limb symptoms.

15.2 Investigations
- Full blood count (FBC), urea and electrolytes (U&E), liver function test (LFT), blood sugar, calcium (Ca++)
- Chest X-ray (CXR)
- Urgent computed tomography (CT): SOL are clearly seen on CT imaging. Radiological signs suggestive of imminent neurological compromise include:
If new malignant diagnosis suspected, investigate according to local Carcinoma Unknown Primary guidelines. Refer to the AOS at time of referral to neurosurgery.

15.3 Management

15.3.1 Emergency Management

If GCS ≤ 12: contact critical care team for urgent review, as per local guidelines.
Keep nil by mouth.

15.3.2 Steroids

Dexamethasone 8mg BD IV/PO (8am and 12 noon). Consider adding proton pump inhibitor.

15.3.3 Other Measures

- Rehydration: aim for euvoalaemia.
- Anti-emetics: consider cyclizine 50mg TDS IV.
- Anti-convulsants: start anti-convulsants if seizures. Prophylactic use of anti-convulsants in the absence of seizures is not indicated. Discuss with neurology team for advice about best choice of agent.
- Mannitol: this is sometimes used for those with persistently and/or severely elevated ICP. Advice from the neurosurgical and/or critical care team should be sought.

15.3.4 Subsequent Management

An urgent neurosurgical referral should be made in the following situations.

1. **CT demonstrates hydrocephalus**: de-bulking surgery may reduce the risk of cerebral infarction and tonsillar herniation.
2. **Solitary or oligometastatic lesions**: consider for surgical excision.
3. **Need for histological diagnosis** in patient with a new presentation of cancer, or in whom a different cancer diagnosis is now suspected.

If in doubt please liaise with the AOS for advice on how to contact your local neurosurgical unit.

Stereotactic radiosurgery is indicated if there are solitary or oligometastatic lesions (but patient should be considered for neurosurgery as well). Whole brain radiotherapy (WBRT) may be indicated for multiple brain metastases from a known primary in patients well enough to receive treatment. Careful consideration as to whether WBRT will benefit the patient is needed, however, and referral to the specialist palliative care team is advised.

Decisions regarding definitive treatment of brain metastases should be made by the multidisciplinary team (MDT).
16 Superior Vena Cava Obstruction

If superior vena cava obstruction suspected, please refer to Acute Oncology Service.

Superior vena cava obstruction (SVCO) is nearly always associated with malignancy, usually lung cancer (80% of cases) but sometimes lymphoma, breast cancer or germ cell tumours. It occurs most commonly in patients with known cancer, but can be the presenting feature of a new diagnosis.

16.1 Signs

Although the signs of SVCO are characteristic, they are often absent and so an index of suspicion is needed based on tumour type and symptoms.

- Thoracic vein distension (65%)
- Neck vein distension (55%)
- Tachypnoea
- Facial/conjunctival oedema (55%)
- Central/peripheral cyanosis (15%)
- Arm oedema (10%)
- Plethora (15%)
- Vocal cord paresis (3%).

16.2 Symptoms

These usually present as worsening over the preceding few days.

- Dyspnoea
- Head fullness/headache
- Cough
- Dysphagia
- Neck and facial swelling
- Trunk and arm swelling.

16.3 Investigations

In the absence of a known malignancy, biopsy is preferable prior to starting steroids.

- Observations, including oxygen saturations
- Chest X-ray (CXR)
- Bloods: full blood count (FBC), urea and electrolytes (U&E), liver function test (LFT), clotting (in case interventional procedure required)
- If new diagnosis: consider human chorionic gonadotropin (HCG), alpha-fetoprotein (AFP), lactate dehydrogenase (LDH) but discuss with acute oncology team first
- Urgent computerised tomography (CT) chest.

16.4 Management

There is little evidence that unrelieved SVCO is life threatening except in the presence of cerebral dysfunction, decreased cardiac output or upper airways obstruction.
16.4.1 Symptomatic Relief

- Sit the patient up, prescribe oxygen, prescribe analgesia (if needed), support arms.
- If dyspnoea: 5mg oramorph 4 hourly is usually effective.

16.4.2 Steroids

If this is the first presentation of a suspected malignancy: hold off steroids as they may compromise interpretation of subsequent biopsies. Discuss with acute oncology team.

If the patient already has a diagnosis of a malignancy: dexamethasone 8mg BD PO/IV (8am and 12 noon).

If the patient has respiratory compromise: treatment should be started urgently. Prescribe proton pump inhibitor if needed.

16.4.3 Stent Insertion

Percutaneous placement of self-expanding endoprostheses gives rapid symptomatic relief in >95% of patients. Discuss the case with the interventional radiology +/- the cardiothoracic team.

Stents are recognised to give best symptomatic benefit and rapid restoration of the normal pattern of flow, although they are used less frequently in potentially curable cancer such as lymphoma.

16.4.4 Chemotherapy

Urgent chemotherapy is an alternative to stenting for patients with curable chemo-sensitive cancers such as lymphoma and germ cell tumours, and is an addition to stenting for other cancers such as small cell lung cancer.

16.4.5 Radiotherapy

This may be recommended depending on the underlying histological subtype, particularly if the occlusion is not amenable to stent placement. Radiotherapy schedules depend on the volume of disease and the performance status of the patient.

16.4.6 Anticoagulants and Antifibrinolytics

There is a high incidence of thrombus with intravascular stents and therefore prophylactic anticoagulation or antiplatelet therapy can be considered, depending on local guidelines and individual patient factors.

Full anticoagulation should be given, where appropriate, for those with evidence of thrombus.
References


Patient.co.uk. Accessed online via: [www.patient.co.uk/health/Mouth-Care.htm](http://www.patient.co.uk/health/Mouth-Care.htm) [Date accessed 28/06/2013]


