LONDON CANCER ALLIANCE

LCA Acute Oncology Clinical Guidelines

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Delivering world class cancer care for London

Contents

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 *Manual for Cancer Services: Acute Oncology – Including Metastatic Spinal Cord Compression Measures* (version 1.0) (2014) stipulates that acute oncology protocols should be available in the chemotherapy and radiotherapy units, A&E departments, acute medical admissions wards and oncology inpatient 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 and revised by representatives from each of these cancer networks and agreed by representatives of all 14 current provider organisations across the LCA. They provide evidence-based clinical information and protocols while allowing sufficient flexibility to reflect good local practice.

They include locally agreed guidance on management of neutropenic sepsis in adults, which is based on the National Institute for Health and Care Excellence (NICE) clinical guideline on neutropenic sepsis (CG151). 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 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 reviewing and revising 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 *Manual for Cancer Services: Acute Oncology – Including Metastatic Spinal Cord Compression Measures* (version 1.0) (2014). This includes major presentations such as metastatic spinal cord compression, which is subject to 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 hyponatraemia, which is a common electrolyte disturbance in cancer patients. The correct diagnosis of the cause of hyponatraemia can be challenging, but is essential for appropriate management.

Section 9 details the common side effects of immunotherapy drugs, a class of agents which are increasingly important in the treatment of cancer. Management of the side effects of immunotherapeutic drugs are often different to those caused by chemotherapy and so, familiarity with the guidelines is important.

Section 10 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.

Section 11 focuses on the management of pleural effusions, which are very common in oncology patients. Appropriate care will greatly improve the patient's symptoms and quality of life.

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 12 provides information on signs and symptoms, assessment and management of MSCC, along with contact telephone numbers for MSCC coordinators within LCA 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 13 describes a number of treatment options.

Section 14 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 15 focuses on the acute management of neutropenic sepsis. While this guidance covers definitions, initial assessment, investigations, treatment and subsequent management, it does not mandate which antibiotics should be used, as all LCA provider trusts should follow local policies that recommend antibiotics based on endemic resistance patterns.

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 16 describes the signs and symptoms, investigations and treatment.

Section 17, 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 18. 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.

Section 19 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.

Given that evidence suggests that a significant proportion of cancer patients presenting to hospital as emergencies have palliative care needs, the final section covers palliative care: referral criteria, service availability and the referral process.

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 Allergic/Hypersensitivity Reactions and Anaphylaxis

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

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 Allergic/Hypersensitivity Reactions

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
- Flu-like symptoms, often with generalised shaking.

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 intra-muscular (IM) injection.
- Corticosteroid: hydrocortisone 100mg by slow IV or IM injection.
- Consider saline nebuliser and/or bronchodilator.

- If symptoms settle:
  - Recommence 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
- Abdominal pain and vomiting
- Collapse and unconsciousness.

1.3.2 Treatment

1. Remove cause, i.e. stop drug/chemotherapy
2. **Call for help**
3. Recline patient and raise legs, administer **high-flow oxygen (5–10 L/min)**.
4. If stridor, wheeze, respiratory distress or shock: **IM epinephrine 0.5ml 1:1000**.

If no improvement after 5 mins:

5. **Repeat IM epinephrine 0.5ml 1:1000**. Several doses may be needed, especially if improvement is transient or the patient deteriorates.

   NOTE: If in doubt, give epinephrine 0.5ml 1:1000.
6. Establish and secure IV access and **start 0.9% sodium chloride (NaCl) IV infusion**.
7. Chlorpheniramine: 20mg IM or slow IV.
8. **Hydrocortisone: 100–300mg slow IV or IM injection**. For patients with a severe or recurrent reaction, and in all patients with asthma.
9. **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 >50x109/L and International Normalized Ratio (INR) <1.4.
- Stop anticoagulants for 24–48 hours pre-procedure.
- Ultrasound evaluation +/- marking of drainage site.

Risks include intestinal injuries, peritonitis, fistulas and significant loss of protein (hypoalbuminaemia) which may lead to metabolic disturbances and eventually cachexia. In the event of haemodynamic compromise secondary to 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')

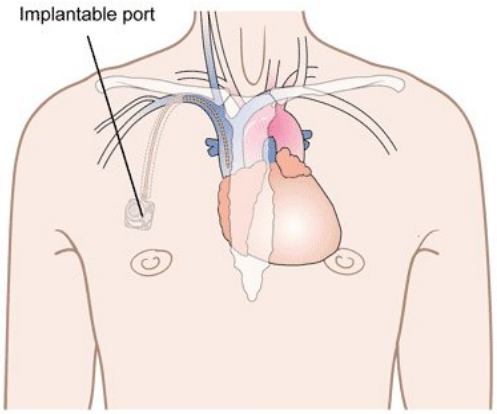


Diagram showing an implantable port
© CancerHelp UK

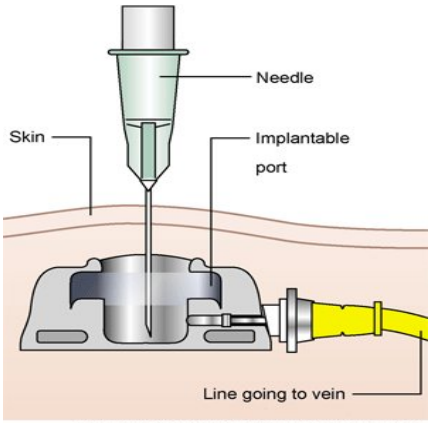


Diagram showing an implantable port under the skin
© CancerHelp UK

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

A port should only be accessed by staff members who are deemed competent to do so in accordance with local policy.

3.1.2 Skin Tunnelled Catheters ('Hickman Lines')

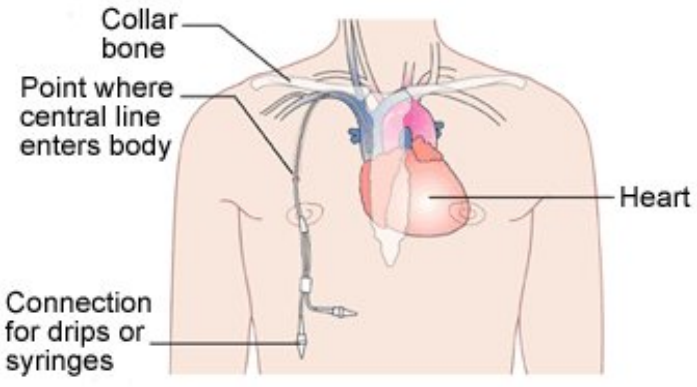
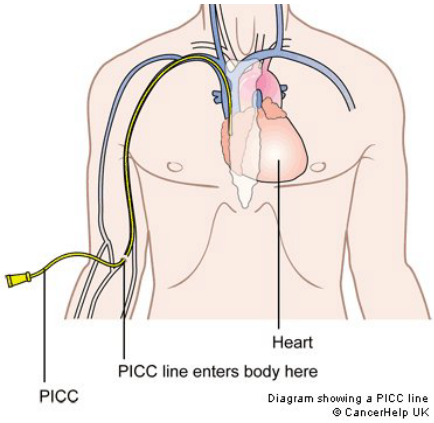


Diagram showing a central line
Copyright © CancerHelp UK

3.1.3 Peripherally Inserted Central Catheters (PICCs)



3.2 Complications Associated With Insertion

3.2.1 Catheter tip malposition

CVAD devices should only be used after correct tip position has been confirmed and documented as suitable for use by the inserting team.

3.2.2 Pneumothorax/Haematoma

Pneumothorax is a potential complication of CVAD insertion where subclavian vein puncture has occurred. All patients should have a chest X-ray (CXR) two hours after implanted port or skin tunnelled catheter insertion. This should be reviewed by a health professional competent to do so 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.

Haematoma formation as a potential complication has a raised risk level in patients with low platelets and/or clotting factor abnormalities (i.e. acute leukaemia and other haematology patients etc.). If haematoma is noted, haematological advice should be sort. If tracheal compression is suspected then urgent surgical opinion should be sought.

3.2.3 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.

3.2.4 Stable Patients with a Significant Pneumothorax (>30% and/or Chronic Respiratory Disease)

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

3.2.5 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 Complications Associated With Ongoing Usage

3.3.1 CVAD Infections

Exit Site Infections

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

Investigations: an exit site swab should be taken, and results of previous swabs reviewed.

Management

- Initial management should follow local Trust guidance for community associated skin and soft tissue infections. At time of guideline compilation this is an 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.

Intra-luminal Infections

Symptoms: rigors, fever and possibly early onset shock, characteristically 15–45 minutes following line flushing.

THIS IS AN ONCOLOGICAL EMERGENCY

For patients in a hospital environment a 2222 call should be implemented

For patients in the community setting a 999 ambulance call should be dispatched

Investigations

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

Management

- **All patients should be managed by the ABCDE approach of immediate life support.**
- 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.

3.3.2 CVAD-associated Thrombosis

Symptoms

- Arm or neck swelling on the side of the CVAD (over-compression by PICC bandaging/dressing should be excluded as a cause of arm swelling).
- 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.

Thrombosis associated Superior Vena Cava Obstruction (SVCO) is rare; however, patients with significant thrombosis extending into central veins should be assessed to exclude as a potential diagnosis (see section 16).

Management

- Start anticoagulation (therapeutic dose low molecular weight heparin (LMWH) is preferred). Local Trust guidelines as to dosing, platelet and renal function parameters should be followed.
- 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.
- All patients commenced on anticoagulation should be followed up and dose adjusted as per local and BNF guidelines.

3.4 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.

3.5 Lymph Fluid Leakage

A rare complication of PICC insertion can be the leakage of lymph fluid from the insertion site. This is due to unintentional puncture of a lymph vessel during insertion. It is recommended that, if leakage persists after 48 hours, then the PICC should be removed and a new PICC re-sited away from the initial site. If leakage persists after device removal then a plastics opinion should be sought.

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 (CG151 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, brand and position of the damage, 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 undergoing treatment for cancer are at risk of developing diarrhoea. This can be caused by chemotherapy, immunotherapy or radiation to the abdomen/pelvis.

Diarrhoea can be a serious and life-threatening complication leading to treatment delays, dose reductions or treatment discontinuation. Mucositis and neutropenia from the chemotherapy also significantly increase complications associated with chemotherapy induced diarrhoea (CID); prompt recognition and appropriate treatment are therefore essential.

4.1 Patients on Clinical Trials

For any patients on a clinical trial, please contact the treating cancer hospital for advice.

4.2 Anti-Cancer Therapy That Can Cause Diarrhoea

4.2.1 Immunotherapy Drugs Causing Diarrhoea

If the patient is on the drugs listed below, please call their treating cancer centre and the acute oncology service **URGENTLY** for advice; please see section 9.2 for general advice on the management of immunotherapy related diarrhoea.

Azetolizumab
Durvalumab
Ipilimumab
Nivolumab
Pembrolizumab
Tremelimumab

For further information on immunotherapy related toxicities, see section 9.

4.2.2 Chemotherapy Drugs Causing Diarrhoea

This is a list of the common chemotherapy drugs that can cause diarrhoea, but is not exhaustive.

Drug	Administration	Action
Afatinib	Oral	Stop medication (see section 4.7)
Capecitabine	Oral	Stop medication (see section 4.7)
Irinotecan	IV	See section 4.9
Erlotinib	Oral	Stop medication (see section 4.7)
Pemetrexed	IV	Ensure patient is taking folic acid 400mcg OD

4.3 Other Causes of Diarrhoea in Patients with Cancer

Bone Marrow Transplantation-related	Conditioning chemotherapy, total-body irradiation, graft-versus-host disease after allogenic bone marrow or peripheral blood stem cell transplants
Drug Adverse Effects	Antibiotics, magnesium-containing antacids, antihypertensives, colchicine, digoxin, iron, lactose, laxatives, methyldopa, metoclopramide, misoprostol, potassium supplements, propanol, theophylline
Concurrent Disease	Diabetes, hyperthyroidism, inflammatory bowel disease (Crohn's disease, diverticulitis, gastroenteritis, HIV/AIDS, ulcerative colitis), obstruction (tumour-related)
Viral Infection	Norwalk virus, rotavirus
Bacterial Infection	*Clostridium difficile (C. diff), Clostridium perfringens, Bacillus cereus, Giardia lamblia, Cryptosporidium, salmonella, Shigella, campylobacter*
Faecal Impaction	Constipation leading to obstruction
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

4.4 Presenting Symptoms

Grade	0	1	2	3	4
Frequency of Stool (Patients with and without Colostomy)	Normal	Increase of <4 stools/day over pre-treatment Or mild increase in ostomy output	Increase of 4–6 stools/day Or moderate increase in ostomy output	Increase of ≥7 stools/day Or severe increase in ostomy output	>10 stools/day
Symptoms	None	None	Moderate cramping, not interfering with normal activity	Severe cramping and incontinence, interfering with daily activities	Grossly bloody and need for parenteral support Life-threatening consequences

4.5 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 (diarrhoeogenics, e.g. bulk agents, softeners, prokinetics).
- Dietary profile (diarrhoea-enhancing foods).

4.6 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.

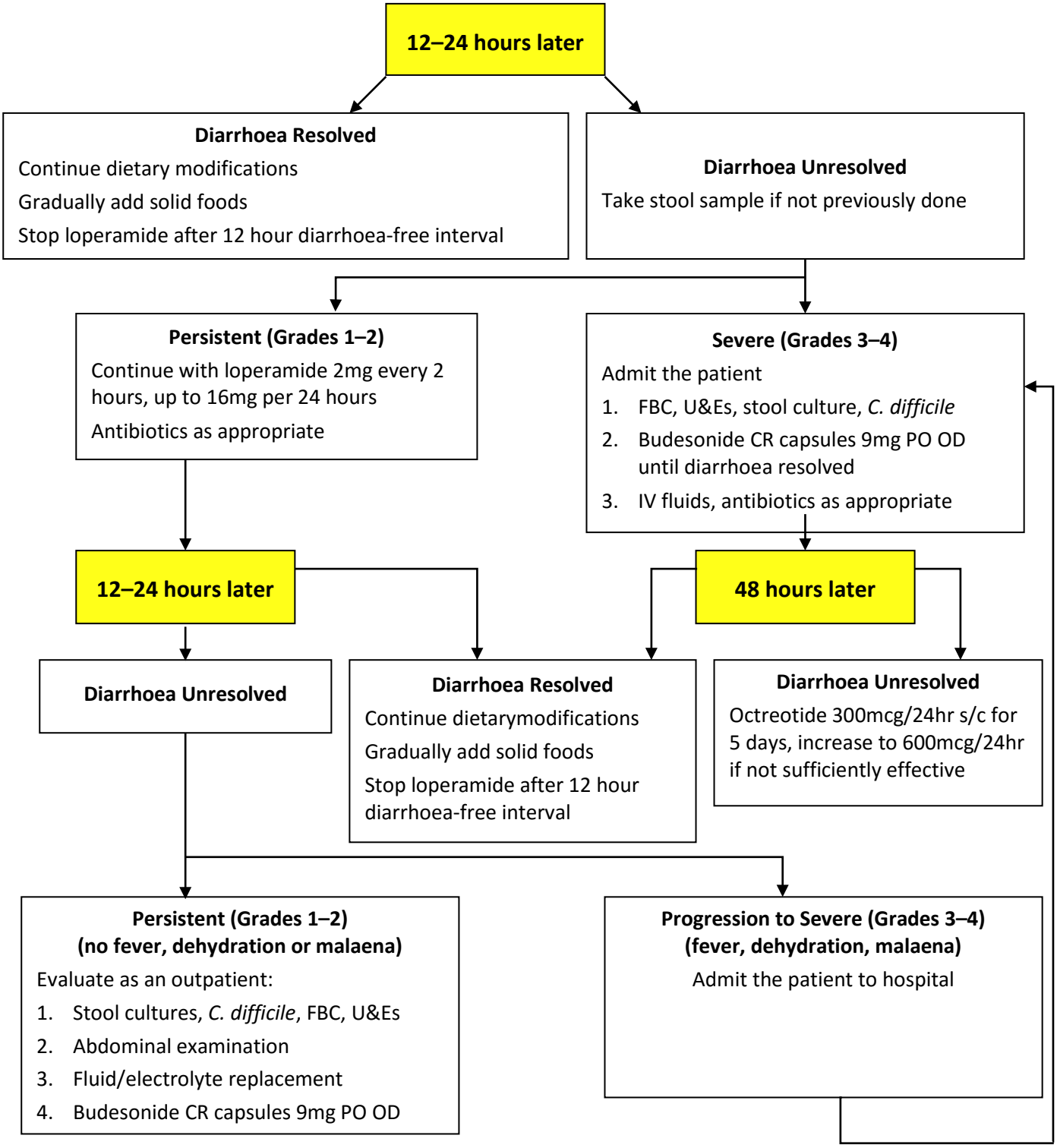
4.7 Initial Management

- Stop oral anti-cancer therapy (capecitabine, afatinib or erlotinib).
- 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).

- Refer to the London Cancer Alliance *Guidance on managing gastro-intestinal consequences of cancer and its treatments* (2016) for further information on ongoing management.

4.8 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 travel 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.
- Reassess after 12 hours and then follow algorithm below.
- For patients on irinotecan-based therapy, see section 4.9.



4.9 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

**If an extravasation injury is suspected,
please refer to Acute Oncology Service.**

Extravasation is the inadvertent administration of 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 with a vesicant, 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 with a small amount of drug. Increased with a larger volume of drug causing extravasation
Others	Change in quality of the infusion or pressure/resistance on the syringe barrel during injection, leaking around the cannula or port needle site

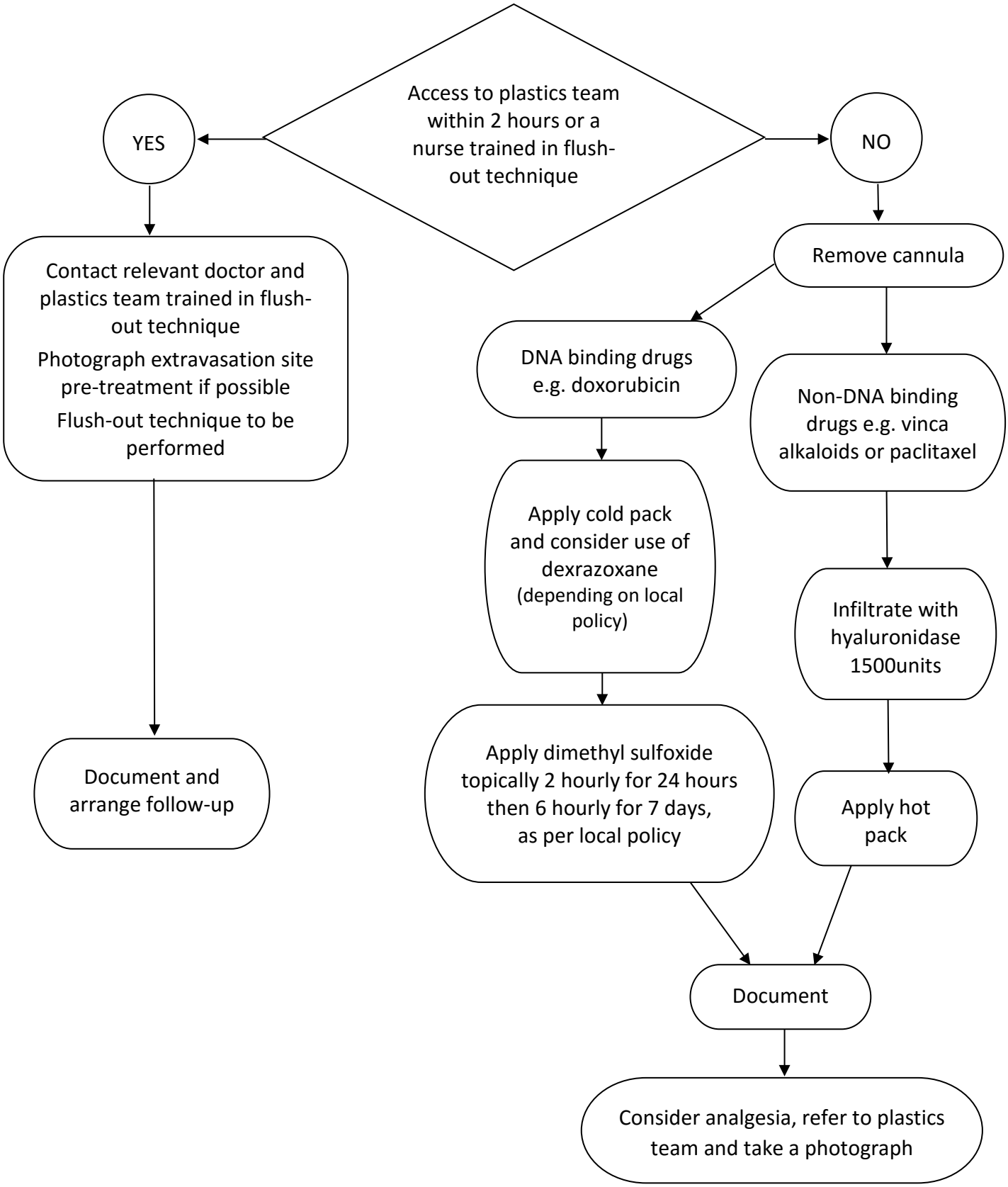
5.2 Immediate Management

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 oxaliplatin)

- Elevate the limb.
- Administer antidote as per local policy and analgesia as required.

5.3 Ongoing Management

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



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 >2.60mmol/L.

6.1 Tumours Associated with Hypercalcaemia

50%	Multiple myeloma
20%	Breast cancer
20%	Lung cancer (usually squamous or adenocarcinoma; seldom small cell)
<10%	Renal cell carcinoma, head and neck cancer, thyroid cancer
Rarely	Prostate, colorectal

6.2 Causes

80%	Tumour production of parathyroid hormone-related peptide (PTHrP)
20%	Lytic bone metastases
<1%	Tumour production of parathyroid hormone (PTH) or vitamin D

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

6.3 Signs and Symptoms

General	Dehydration, polydipsia, polyuria
Gastrointestinal	Anorexia, nausea, vomiting, constipation, weight loss
Neurological	Fatigue, lethargy, confusion, anxiety, seizures, psychosis, coma
Cardiac	Bradycardia, arrhythmias, prolonged PR interval, reduced QT interval

6.4 Investigations

Calcium (Ca^{++}), phosphate (PO_4)	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. May be indicated if PTH low and no apparent malignancy.

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. Treatment with lithium and theophylline toxicity may also be causative factors.

6.5.2 Rehydration

All patients with hypercalcaemia are dehydrated due to polyuria and vomiting, on average 4L in negative balance. Oral rehydration may be all that is needed in mild, asymptomatic cases (Ca^{++} <3.00mmol/L). Asymptomatic or mildly symptomatic hypercalcaemia (3–3.5mmol/L) may respond to oral rehydration. Severe hypercalcaemia (>3.5mmol/L requires urgent treatment. Intravenous rehydration for 24 hours with 0.9% saline, 4–6L. 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 bisphosponate should reflect local Trust policy. Pamidronate is more effective than clodronate. Zoledronic acid normalises calcium in more patients (87–88% c.f. 70%), more rapidly and for longer than pamidronate (32–43 days c.f. 18), 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 treatment of hypercalcaemia but lowers calcium markedly. Increasing numbers of case reports and case series of patients with bisphosphonate refractory hypercalcaemia responding to denosumab. Additionally has the advantage of having no effect on renal function, unlike bisphosphonates (however it is more likely to cause hypocalcaemia, particularly in patients with chronic renal impairment).

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, chronic alcoholism, uncontrolled diabetes mellitus, acute renal failure, diarrhoea or fistulae and be secondary to other electrolyte abnormalities (hyper/hypocalcaemia, hypokalaemia/TPN).

7.1 Definition

Grade	1	2	3	4	5
Serum Magnesium	LLN*– 0.5mmol/L	0.5– 0.4mmol/L	0.4– 0.3mmol/L	<0.3mmol/L	Death

*LLN = lower limit normal

7.2 Clinical Features

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

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, cyclosporine, pentamidine, gentamicin and diuretics, particularly with proton pump inhibitors.

7.4 Investigations

Hypomagnesaemia is frequently accompanied by low calcium and potassium levels so these, along with renal function, must also be checked. If cause unclear, 24 hour urinary Mg^{++}.

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 ($MgSO_4$) in 500ml normal saline over 6–8 hours.

Oral Mg supplementation may be tried but is usually poorly tolerated due to diarrhoea. Preparations such as magnesium glycerophosphate 4–8mmol, up to qds.

7.5.3 Grade 3 or 4

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

5g (20mmol) $MgSO_4$ in 1L normal saline over 8–10 hours.

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

If renal impairment: reduce dose to 2.5g (10mmol) $MgSO_4$ over 24 hours.

If hypocalcaemic

Correct magnesium level until calcium in normal range.

If hypokalaemic

Replace 40mmol potassium chloride (KCl) and 1.25mg (5mmol) $MgSO_4$ 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 $MgSO_4$ IV over 15 minutes (max rate 0.6mmol/minute).
- Followed by infusion of 5g (20mmol) $MgSO_4$ 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 Hyponatraemia

If cancer associated hyponatraemia is suspected, please refer to Acute Oncology Service.

Hyponatraemia is an electrolyte abnormality commonly encountered in oncology practice.

8.1 Definition

Serum sodium level <135 mEq/L

Joint European guidelines classify hyponatraemia in adults as follows:

Grade:	Mild	Moderate	Profound
Serum Sodium	130–134mmol/l	125–129mmol/l	<125mmol/l

8.2 Common Causes

Pulmonary cancer	Small cell carcinoma (11–15%) and mesothelioma
Gastrointestinal cancer	Carcinomas of the duodenum, pancreas and colon
Genitourinary cancer	Adrenocortical carcinoma; carcinomas of cervix, ureter/bladder, and prostate; ovarian tumours
Other cancer	Brain tumours, carcinoid tumours, Ewing sarcoma, leukaemia, lymphoma, nasopharyngeal carcinoma (3%), neuroblastoma (olfactory), and thymoma
Drugs	Adenine arabinoside, cyclophosphamide, ifosfamide, vincristine, vinblastine, (PO2 or FO2) cisplatin, methotrexate. Antidepressants, antipsychotics, NSAIDs, anti-epileptics

8.3 Causes

Iatrogenic	Volume depletion +/- NBM with inappropriate hypotonic fluid
Hypovolaemic (hypotension, tachycardia, dry mucus membranes)	Gastrointestinal loss Renal sodium loss Hypoadrenalism Loop Diuretics +/- ACE-I Thiazide diuretics (elderly may be very sensitive) Cerebral salt wasting (e.g. after subarachnoid) Hypothyroidism

Euvolaemia	SIADH: • Intracranial disease • Bronchogenic carcinoma (small cell) • Other chest disease (hyponatraemia rarely severe) • Other neuro-endocrine malignancies • Drugs: carbamazepine, cyclophosphamide, SSRIs, morphine, monoamine oxidase inhibitors, excess DDVAP, vincristine, cyclophosphamide, cisplatins, pain • Hypothyroidism • Adrenal inufficiency
Hypervolaemia (dependent oedema, ascites)	CCF Advanced liver disease Renal failure

8.4 SIADH

The syndrome of inappropriate antidiuretic hormone (ADH) secretion (SIADH) is defined by the hyponatraemia and hypo-osmolality resulting from inappropriate, continued secretion or action of the hormone despite normal or increased plasma volume, which results in impaired water excretion.

8.4.1 Diagnostic Criteria for SIADH

- Hyponatraemia with corresponding hypo-osmolality (plasma osmolality <280mosmol/kg
- Urine less than maximally dilute (greater than 100mOsm/kg, generally greater than 400–500mOsm/kg with normal renal function)
- Continued renal excretion of sodium (>40mmol/l)
- Absence of clinical evidence of volume depletion
- Absence of other causes of hyponatraemia
- Correction of hyponatraemia by fluid restriction

8.5 Clinical Features of Hyponatraemia

General	Fatigue, anorexia, nausea, vomiting, muscle cramps, lethargy
Central nervous system	Headache, worsening mental status, weakness, irritability, agitation, confusion, combativeness, delirium, disorientation, hallucinations and poor balance, seizures, coma
Gastrointestinal	Nausea, vomiting

8.6 Investigations

Urea and electrolytes	Renal function frequently deranged.
Blood glucose	High glucose levels can cause hypertonic hyponatraemia as in DKA.
Serum osmolality	Readily differentiates between true hyponatraemia and pseudohyponatraemia (secondary to hyperlipidaemia or hyperproteinaemia) or may be hypertonic hyponatraemia associated with elevated glucose, mannitol, glycine (posturologic or postgynaecologic procedure), sucrose.
Urine osmolality	Helps differentiate between impaired free-water excretion and primary polydipsia. In SIADH, >100mOsm/kg (submaximally dilute) indicates impaired ability of the kidneys to dilute the urine.
Urine sodium	In SIADH the urine sodium >20–40mEq/L. With hypovolaemia <25mEq/L.
TSH, serum cortisol	If hypothyroidism or hypoadrenalism is suspected.
LFTs and lipids	High levels of hyperproteinaemia and hyperlipidaemia can cause pseudohyponatraemia.
CXR	For detection of an underlying pulmonary cause of SIADH.
CT head	To assess underlying etiology in select patients, for detection of cerebral edema secondary to SIADH or to help rule out other potential causes of a change in neurological status.

8.7 Management

Treatment of SIADH and the rapidity of correction of hyponatraemia depend on the following:

8.7.1 Acute symptoms over <48 hours

Where moderate symptoms are noted, treatment options include:

- Aim to raise sodium by 1mmol/L each hour until symptoms resolve or serum sodium >130mmol/L. Do not raise by more than 12mmol/L in first 12 hours.
- Consider giving furosemide to enhance free water loss
- If patient has severe neurological symptoms, consider giving hypertonic (3%) sodium chloride as intravenous infusion at 1–2mL/kg/hour. This treatment requires close monitoring, preferably in Level 1 or High Dependency Unit (HDU) facility.

8.7.2 Chronic symptoms present >48 hours

- Water restriction to 1L/day if volume repleted
- Investigate underlying cause
- Demeclocycline may be useful for patients with SIADH secondary to malignancy. This drug takes 1–2 weeks to have an effect
- Vasopressin-2 receptor antagonists – tolvaptan (titrate starting at 15mg OD to 60mg OD, PO) *Can also be used after demeclocycline, if no improvement.*

Hyponatraemia developing rapidly (within 48 hours) carries a greater risk of permanent neurological sequelae as a result of cerebral oedema unless plasma sodium is corrected.

Patients with chronic hyponatraemia are at risk of **Cerebral Osmotic Demyelination** if correction is excessive or too rapid.

Patients to be treated with a fluid restriction often require education regarding the free water content of foods and an explanation of the need to limit the intake of liquids to a predetermined level.

Consultation with an endocrinologist is valuable in managing patients with symptomatic or refractory hyponatraemia.

9 Immunotherapy Related Toxicities

If immunotherapy related toxicities suspected, please refer patient to the Acute Oncology Service.

Immunotherapy drugs are increasingly being used to treat cancer and have a unique and varied set of autoimmune side effects which, if not recognised and treated promptly, can be fatal.

It is important to appreciate that these side effects, particularly those affecting the endocrine system, can sometimes occur many months after discontinuation of the drugs.

These guidelines cover the initial management of more common immunotherapy related toxicity. However, all patients with suspected or confirmed immunotherapy toxicity should be discussed as soon as possible with the local acute oncology service and, if indicated, with the treating oncology centre.

9.1 Types of Immunotherapy Agents

There are currently three approved immunotherapy monoclonal antibodies: ipilimumab, nivolumab and pembrolizumab. Many others agents are expected to be licensed for use in the near future.

9.2 Diarrhoea

Please also refer to chapter on chemotherapy and radiotherapy associated diarrhoea (section 4), which contains advice on grading (section 4.4), and investigations (section 4.6).

Symptoms suggestive of serious gastrointestinal toxicity include: fever, weakness, abdominal pain, bloating, cramping pain, blood or mucous in diarrhoea, and nocturnal diarrhoea. These patients should be fully investigated and managed with care.

Severity	Signs/Symptoms	Management
Mild	<4 episodes of loose stool WITHOUT abdominal pain, blood, mucus	1. Review diet and increase oral fluids 2. Loperamide 2mg PRN (maximum 16mg/day) 3. Stool cultures (including *C. Difficile*) 4. Patient can be discharged if well, but inform treating oncology centre of events
Moderate	Cramping abdominal pain, blood/mucus or 4–6 episodes of loose stool	1. Admit patient 2. Start immediate IV methyl-prednisolone 1mg/kg/day 3. Stool cultures (including *C. Diff*) 4. Abdominal X-ray 5. Urgent gastroenterology review. Seek flexible sigmoidoscopy where available 6. Discuss with treating oncology centre 7. If clinical deterioration consider treating as

Severity	Signs/Symptoms	Management
		'severe diarrhoea' (see below)
Severe	Diarrhoea with any of the following features: severe electrolyte imbalance, severe abdominal pain or peritonitis, haemodynamic instability, blood/mucus or greater than 6 episodes of diarrhoea per day	1. Admit patient 2. Start immediate IV methyl-prednisolone 1mg/kg/day 3. Stool cultures (including *C. Diff*) 4. Urgent gastroenterology review. Seek flexible sigmoidoscopy where available 5. Urgent CT chest and abdomen to exclude abscess, perforation, megacolon and previous pulmonary TB 6. Discuss with treating oncology team. Patient may require infliximab 5mg/kg if no contraindication (e.g. perforation, sepsis, prior TB), but only after discussion with oncology centre

9.3 Endocrine

A number of endocrine disorders can occur, but thyroid and adrenal abnormalities are the commonest.

Severity	Signs/Symptoms	Management
Moderate	Headache, fatigue or visual disturbance Consider hypophysitis, thyroid failure	1. Pituitary blood profile includes cortisol, ACTH, TFT, prolactin, LH, FSH, testosterone (men), oestrodiol (women) 2. IV methyl-prednisolone 1mg/kg/day 3. Discuss with endocrinologist and treating oncology centre 4. If only abnormality is hypothyroidism: replace thyroxine 5. MRI brain and MRI pituitary fossa (CT brain and pituitary if MRI contra-indicated)
Severe	Collapse Consider primary or secondary adrenal crisis or New onset adult type 1 diabetes mellitus +/- ketoacidosis.	1. Check blood glucose, and ABG and treat with insulin if consistent with DKA 2. If unexplained shock (may be refractory to fluids) treat as adrenal crisis: dexamethasone 10mg IV STAT and further investigations as above 3. Urgent endocrinology review and discuss with treating oncology centre

9.4 Hepatitis

Review medication to exclude other drug associated hepatotoxicity.

Severity	Signs/Symptoms	Management
Mild–moderate	AST or ALT raised but <x5 Upper Limit of Normal (ULN) and/or Bilirubin raised but <x3 ULN	1. Patient can probably be discharged with outpatient monitoring 2. Discuss with treating oncology centre 3. Check HBsAg to exclude HBV reactivation
Severe	AST or ALT raised >x5 ULN and/or Bilirubin raised >x3 ULN	1. Urgent IV methyl-prednisolone 1mg/kg 2. Daily Liver function tests and INR 3. Check viral serology (Hep A, HBsAg, anti-HCV, CMV, EBV) and auto-antibody screen (anti-ANA, SMA, LKMA, AMA, IgG, IgM, IgA) 4. Urgent referral to hepatology team and discuss with treating oncology centre 5. If ALT continues to rise rapidly or fails to improve: 6. Urgent USS of the liver and portal vein to exclude progressive metastatic disease or portal vein thrombus 7. Consider adding in mycophenolate 500mg BD (on advice of hepatology and oncology teams)

9.5 Pneumonitis/Interstitial Lung Disease

Typically presents with shortness of breath, cough, hypoxia or lower grade pyrexia. Plain chest X-ray (CXR) may show lung field changes, but urgent CT pulmonary angiogram is required to define lung toxicity and exclude pulmonary embolism (PE). Any lower respiratory tract infection and/or PE should be treated according to standard protocols (warfarin is not recommended, however).

If pneumonitis is suspected on clinical and radiological basis, treat with corticosteroids (1mg/kg/day of methylprednisolone equivalent), refer for urgent respiratory opinion, and consider atypical pneumonia. Discuss with treating oncology centre.

9.6 Dermatological Complications

Rarely, Stevens-Johnsons syndrome, DRESS syndrome and toxic epidermal necrolysis have been reported. If suspected, seek urgent advice from a dermatologist.

Maculopapular rash is common and the management is described below.

Severity	Signs/Symptoms	Management
Mild–moderate	<50% body surface area	1. Topical emollients with steroids (e.g. Dermovate) and antihistamines for itch. Skin advice including soap-free wash and regular aqueous cream.
Severe	>50% body surface area	1. 1mg/kg/day IV methylprednisolone 2. Contact on-call dermatologist to consider punch biopsy 3. Organise medical photograph

9.7 Neurological Complications

Guillain Barre syndrome, myasthenic syndrome, aseptic meningitis and encephalitis can occur. Less well described neuromuscular syndromes involving respiratory muscle compromise have also been reported.

Any patients who have had immunotherapy and present with neurological symptoms should have an urgent neurology review, and should be discussed with the treating oncology centre.

Corticosteroids (1mg/kg/day of methylprednisolone equivalent) may be indicated.

9.8 Renal Complications

Autoimmune renal disease in the form of nephritic and nephrotic syndromes can occur. Investigate and manage abnormal renal function as per standard procedure, including review of potentially nephrotoxic medications, rehydration if indicated, and renal tract USS if obstruction suspected.

If autoimmune nephritic or nephrotic syndrome possible, seek urgent nephrology advice and consider treat with corticosteroids (1mg/kg/day of methylprednisolone equivalent) if advised. Discuss with treating oncology centre.

9.9 Other Complications

Other rare toxicities include: uveitis, arthritis, myositis, pancreatitis, optic neuritis, rhabdomyolysis, haemolytic anaemia, aplastic anaemia and idiopathic thrombocytopenia purpura (ITP). If suspected, discuss with relevant specialist team, treating oncology centre, and consider treating with corticosteroids (1mg/kg/day of methylprednisolone equivalent) if advised.

10 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.

10.1 Diagnosis

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

10.2 Presentation

10.2.1 Signs and Symptoms

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

10.2.2 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.

10.3 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.

10.4 Management

10.4.1 Hypoxia/Dyspnoea

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

10.4.2 Cough

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

10.4.3 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.

10.4.4 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.

10.4.5 Systemic Anti-cancer Therapies

- Treatment should be specific to underlying tumour if patient fit enough to undergo chemotherapy.

10.5 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.

11 Malignant Pleural Effusion

**If malignant pleural effusion is suspected,
please refer to Acute Oncology Service.**

Malignant pleural effusions can occur with any type of malignancy but lung cancer in men and breast cancer in women are the commonest tumours to metastasise to the pleura (Table 1). Together, they account for 50–65% of all malignant effusions. Malignant effusions imply dissemination of disease and the prognosis is poor with a median survival of 3–12 months. However, not all effusions in patients with known malignancy are necessarily malignant.

Table 1: Causes of malignant pleural effusion

Tumour type	Percentage
Lung	40%
Breast	25%
Lymphoma	10%
Ovarian	5%
Gastric	5%
Malignancy of unknown origin (MUO)	7%

11.1 Symptoms

- **Asymptomatic**
  Incidental finding on physical examination and on chest X-ray (CXR) in up to 25% of cases.
- **Dyspnoea**
  Due to reduced compliance of the chest wall, depression of the diaphragm and reduction in lung volume. This is the commonest presentation.
- **Orthopnoea**
- **Dry cough**
- **Chest pain**
  Due to pleural irritation.

11.2 Signs

Tachypnoea, asymmetric chest expansion, tracheal deviation (away from the effusion), reduced air entry and a dull percussion note located at the site of the effusion.

11.3 Investigations

- **Chest X-ray (CXR).** Small effusions of more than 175ml can be apparent as blunting of the costrophrenic angle and are normally asymptomatic. Larger effusions are associated with opacification of the lower lung fields and apparent elevation of the hemidiaphragm. Massive

pleural effusions are usually symptomatic. They appear as (near) complete opacification of the hemithorax and can be associated with mediastinal shift.

- **Computed tomography (CT) scan of the chest**. Not routinely indicated but will assist in further management.

11.4 Management

Malignant pleural effusions that are asymptomatic can be observed, particularly if small. However, most will progress and cause symptoms, requiring drainage.

In symptomatic patients, the aim is to remove pleural fluid by one of several possible methods (Table 2), particularly if the effusion is moderate or large. Further management is influenced by other factors, such as a patient's symptoms, response to previous interventions, performance status, primary tumour type and potential response to systemic therapy and any previous procedures prior to diagnosis.

Table 2: Management of a malignant pleural effusion

Approach	Indication
Observation only	Asymptomatic malignant pleural effusion
Thoracocentesis (pleural aspiration) +/- insertion of an intercostal drain	Emergency management or for prompt symptomatic relief
Long-term indwelling pleural catheter	Recurrent malignant pleural effusion
Chemical pleurodesis via a small bore drain	Recurrent malignant pleural effusion
Surgical pleurodesis: e.g. VATS pleurodesis	Recurrent malignant pleural effusion
Systemic chemotherapy	For chemosensitive tumours

All pleural procedures including aspirations and chest drain insertion should be performed under ultrasound guidance. Consider early referral to the palliative care team in patients with a poor performance status and short life expectancy. Involve the respiratory team in all complex pleural management decisions.

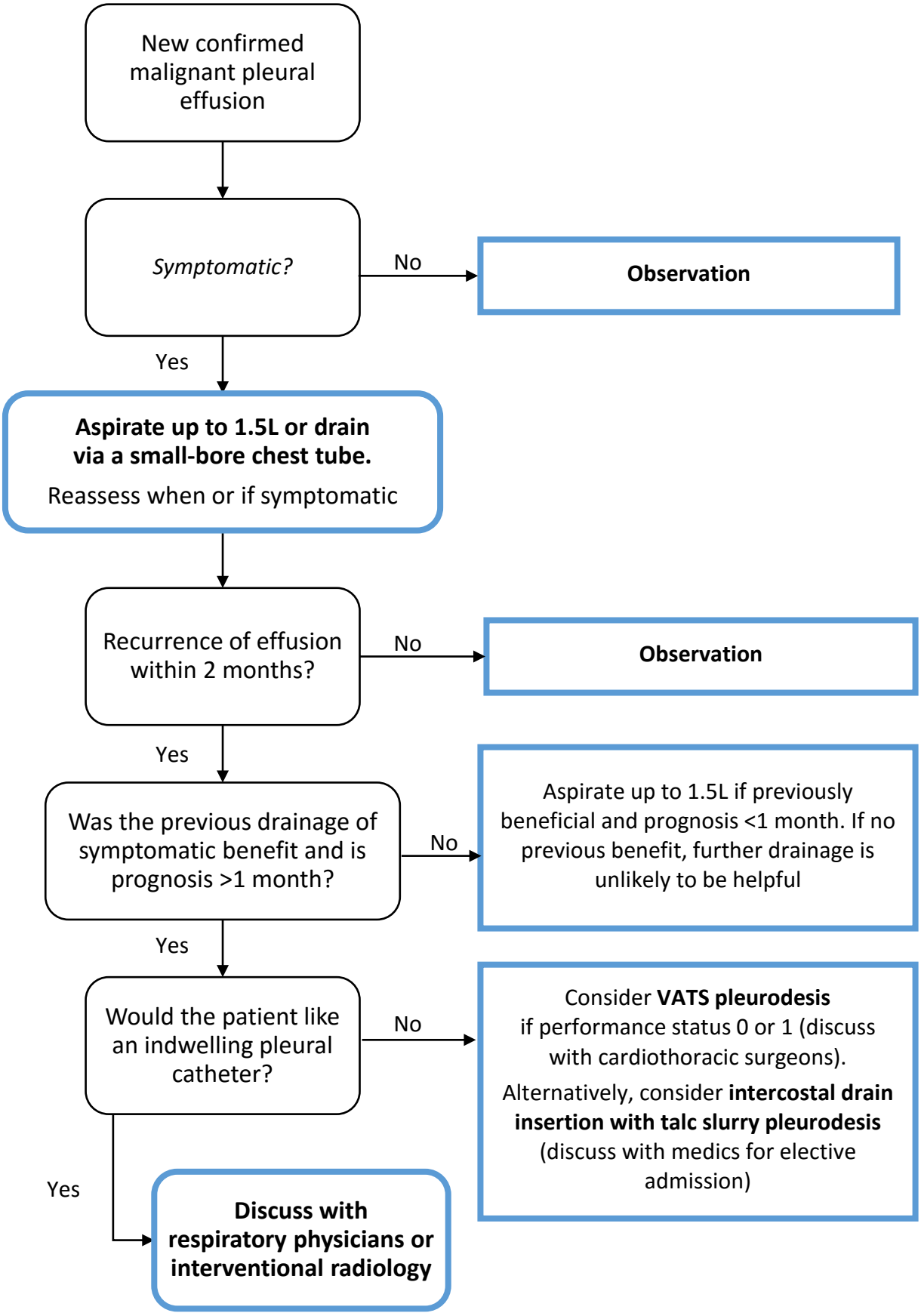
Check blood pressure (BP), full blood count (FBC), urea and electrolytes (U&E) and clotting prior to chest aspiration or drainage. Ensure platelets are >50x109/L and the International Normalized Ratio (INR) <1.5. Stop anticoagulants prior to intervention as per local policies. CXR is recommended post-procedure to exclude an iatrogenic pneumothorax.

A suggested algorithm for the management of malignant pleural effusions is outlined in Figure 1.

11.5 Therapeutic Thoracocentesis

Thoracocentesis is usually reserved for patients *in extremis*. 500–1500ml of pleural fluid can be aspirated in the acute setting to provide symptom relief. Pleural effusions treated by aspiration alone are associated with a high rate of effusion recurrence at one month.

Figure 1. Management algorithm for malignant pleural effusion



11.6 Intercostal Drain (ICD) Insertion

Small-bore chest tubes are widely available and may be inserted with minimal discomfort, making intercostal drain (ICD) insertion preferable to thoracocentesis if >1500ml fluid is suspected.

ICD insertion is an elective procedure in most cases, performed under ultrasound guidance and following local guidelines for insertion. Drainage should be guided by patient symptoms, aiming to drain 1–1.5L every few hours, but titrated to a patient's symptoms. The drain should be removed as early as possible (ideally within 24 hours) to avoid catheter-associated sepsis.

11.7 Long-term Control of a Malignant Pleural Effusion

- **Long-term indwelling pleural catheter** (e.g. PleurX® or Rocket® IPC). The standard management for long-term control of malignant pleural effusions. Spontaneous pleurodesis may result as a consequence of continuous drainage. This is an ambulatory procedure. Patients should be kept under close follow-up to assess for infection and pleurodesis necessitating/allowing for removal of the drain.
- **Chemical pleurodesis with instillation of sclerosant**. Achieves long-term control in >60% of patients. This requires an inpatient stay in order to drain the patient to dryness prior to instillation of the sclerosant (usually talc).
- **Surgical procedures**. Seek respiratory and cardiothoracic advice through the lung MDT for a possible cardiothoracic intervention (e.g. VATS procedure with talc poudrage).
- **Systemic anti-cancer therapy**. Effective for chemosensitive tumours.

11.8 Management of Patients with a New Presentation of Cancer

- Inform the acute oncology service (AOS) and refer to the respiratory team.
- Full examination, including breast examination in women.
- If investigation is appropriate (for undiagnosed unilateral effusions):
  - **Computed tomography (CT) scan**. To include the chest, abdomen and pelvis.
  - **Diagnostic or therapeutic thoracocentesis/ICD insertion**. Send sample for LDH, protein, glucose and MC&S. Malignant effusions are exudative (characterised by a high protein content, low pH and high LDH). Send 60ml fluid for cytology.
  - **Image-guided biopsy**. For a histological diagnosis.
  - If ovarian malignancy suspected, send CA125 level.
  - Requesting a whole panel of serum tumour markers is not routinely indicated.
- Liaise with relevant specialist MDT, depending on likely tumour site (e.g. gynaecology, gastrointestinal, etc.).

12 Metastatic Spinal Cord Compression

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

12.1 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.

12.2 Causes and Presentation

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

Tumour Site	Proportion of Patients Who Develop MSCC
Lung	20–31%
Prostate	18–21%
Breast	13–17%
Haematology	8–10%
Gastrointestinal	5–13%
Kidney	3–12%
Unknown	4–7%
Other	7–14%

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.

12.3 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.

12.4 Assessment

12.4.1 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 12.5.
- 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).
- Consider concurrent referral to the acute oncology service (AOS) team, particularly if surgery may not be an option.

12.4.2 Primary Care Presentation

- Contact MSCC coordinator of nearest MSCC treatment centre.
- Arrange urgent clinical assessment by MSCC team.

12.4.3 Hospital Presentation (Non-MSCC Treatment Centre)

- Arrange urgent investigation as listed in section 12.6.
- Discuss results with local MSCC coordinator.
- If appropriate, transfer patient and imaging to MSCC treatment centre for further assessment and definitive treatment.
- Consider concurrent referral to AOS team, particularly if surgery may not be an option.

12.4.4 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.

12.5 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.

Regional MSCC Treatment Centre	Contact Details
Imperial College Healthcare NHS Trust	In hours: 020 3311 1234 – Bleep 8082 Out of hours: 020 3311 1234 – Bleep 8082
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 6242

Hospital Name	Local MSCC Coordinator Contact Details	Regional MSCC Treatment Centre
Central Middlesex	In hours: 020 3311 1234 – Bleep 8082 Out of hours: 020 3311 1234 – Bleep 8082	Imperial
Charing Cross	In hours: 020 3311 1234 – Bleep 8082 Out of hours: 020 3311 7866 – Bleep 8082	Imperial
Chelsea and Westminster	In hours: 07791 472630 – Bleep 8908 SpR Out of hours: 020 3311 1234 – Bleep 8082	Imperial
Croydon University	In hours: 020 8401 3000 – Bleep 946 or Extension 5726 Out of hours: 020 8672 1255 – Bleep 6242	St George's
Ealing	In hours: 020 3311 1234 – Bleep 8082 Out of hours: 020 3311 1234 – Bleep 8082	Imperial
Epsom	In hours: 01372 735 735 – Bleep 898 Out of hours: 020 8672 1255 – Bleep 6242	St George's
Guy's and St Thomas'	In hours: 020 7188 7188 – Bleep 2069 Out of hours: 020 3299 4207 – Bleep on-call neurosurgical SpR	King's
Hammersmith	In hours: 020 3311 1234 – Bleep 8082 Out of hours: 020 3311 1234 – Bleep 8082	Imperial

Hospital Name	Local MSCC Coordinator Contact Details	Regional MSCC Treatment Centre
Harefield	In hours: 020 3311 1234 – Bleep 8082 Out of hours: 020 3311 1234 – Bleep 8082	Imperial
Hillingdon	In hours: 01895 238282 – Bleep 5175 Out of hours: 020 3311 1234 – Bleep 8082	Imperial
King's College	In hours: 020 3299 5468 Out of hours: 020 3299 4207	King's
Kingston	In hours: via switchboard 020 8546 7711 Blp 086 Out of hours: 020 8672 1255 – Bleep 6242	St George's
Lewisham	In hours: 020 3299 5468 Out of hours: 020 3299 4207	King's
Northwick Park	In hours: 020 8864 3232 – Bleep 003 on-call medical registrar Out of hours: 020 8864 3232 – Bleep 003 on-call medical registrar	Imperial
Queen Elizabeth (Woolwich)	In hours: 020 8836 6000 – Bleep 835 Out of hours: 020 3299 4207 – Bleep on-call neurosurgical SpR	King's
Queen Mary's (Sidcup)	In hours: As for Queen Elizabeth or Princess Royal Out of hours: 020 3299 4207 – Bleep on-call neurosurgical SpR	King's
Princess Royal University (Bromley)	In hours: 01689 863000 – Bleep 340 Out of hours: 020 3299 4207 – Bleep on-call neurosurgical SpR	King's
Royal Brompton	In hours: 020 3311 1234 – Bleep 8082 Out of hours: 020 3311 1234 – Bleep 8082	Imperial
Royal Marsden (Chelsea)	In hours: 020 7352 8171 – Bleep on-call radiotherapy SpR Out of hours: 020 7352 8171 – Bleep 022	St George's
Royal Marsden (Sutton)	In hours: 020 8642 6011 – Bleep on-call radiotherapy SpR Out of hours: 020 8642 6011 – Bleep 022	St George's
St George's	In hours: 020 8672 1255 – Bleep 6027 Out of hours: 020 8672 1255 – Bleep 6242	St George's

Hospital Name	Local MSCC Coordinator Contact Details	Regional MSCC Treatment Centre
St Helier University	In hours: 020 8296 2000 – Bleep 409 Out of hours: 020 8672 1255 – Bleep 6242	St George's
St Mary's	In hours: 020 3311 1234 – Bleep 8082 Out of hours: 020 3311 1234 – Bleep 8082	Imperial
West Middlesex University	In hours: 020 3311 1234 – Bleep 8082 Out of hours: 020 3311 1234 – Bleep 8082	Imperial

12.6 Investigation

Whole spine magnetic resonance imaging (MRI) is the investigation of choice. If an MRI is absolutely contra-indicated, then spinal 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.

12.7 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.

12.7.1 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 FBC, U&E, clotting, group and save.
- Consider pre-operative investigations such as CXR and ECG.
- If referral from another hospital, please ensure prompt availability of imaging via image exchange portal (IEP)/CD/picture archiving and communication system (PACS).

12.7.2 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.

12.7.3 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.

12.7.4 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.

12.7.5 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.
- Manual handling risk assessment, wheelchair assessment where needed.

12.7.6 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.

12.8 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.

13 Mucositis

If uncontrolled mucositis or concurrent neutropenic sepsis is suspected, refer urgently to local Acute Oncology Service.

Mucositis is the acute inflammatory response of the upper aero-digestive tract in response to cancer treatment. It presents as soreness of the mouth with erythema and may progress to painful ulceration which can become confluent and dramatically affect the patient's ability to eat and drink.

A degree of mucositis is inevitable for patients receiving radical dose (chemo) radiotherapy to head and neck tumours. Mucositis often develops following high-dose chemotherapy such as for leukaemia or lymphoma, after 5-FU or methotrexate-based treatment, and is recognised with most cytotoxic agents.

Radical radiotherapy for head and neck cancer **should not be delayed** for mucositis without discussion with the patient's treating clinical oncologist.

13.1 Assessment

The severity of mucositis is usually graded using the World Health Organization (WHO) scale or the National Cancer Institute common toxicity criteria (v4.0 listed).

Grade	WHO Scale	NCI – CTC
1	Soreness +/- erythema, no ulceration.	Mild symptoms, no intervention required
2	Erythema, ulcers. Patient can swallow solid diet.	Moderate pain, modified diet required
3	Ulcers, extensive erythema. Patient cannot swallow solid diet.	Severe pain, interferes with oral intake
4	Oral mucositis to the extent that alimentation is not possible.	Life-threatening consequences, requires urgent intervention

13.2 Management of Mucositis

13.2.1 Mouth Care

- Ensure good oral hygiene – brush teeth qds with baby soft toothbrush and fluoride-based toothpaste; careful dental flossing if platelet count >50.
- Regular non-alcoholic mouthwashes (see below for recommendations) at least qds, increasing up to every 90 minutes.
- Dentures should be regularly cleaned and soaked nightly; if too irritant they may be removed but caution necessary to ensure adequate enteral intake.
- Referral to dietitian is required if eating and drinking are affected.
- Avoid smoking and alcohol.

13.2.2 Topical Treatments

Standard

- Sodium chloride 0.9% solution: can also be prepared at home as 1 teaspoon of salt in one glass of tepid water and used as mouthwash as above.

Alternatives

- Sodium bicarbonate: 1 teaspoon added to a glass of saline solution, or to water alone, as mouthwash
- Soda water: 10ml as mouthwash.

Analgesics

- Benzydamine 0.15% oral solution (Difflam): 10ml rinsed around the mouth and spat out. Repeat every 1½ to 3 hours as required. If it causes stinging, dilute 50:50 with water and use 10ml of this solution.
- Oxetacaine with antacid: especially for mucositis caused by radiotherapy to larynx and hypopharynx
- Sucralfate: 5ml used as a mouthwash and then swallowed qds. Owing to its coating action, sucralfate must be used last in the oral care medication sequence as it will block the effect of any topical agent. The sucralfate coat may mask mucosal infections so there should be close monitoring for oral infections. To be used in caution in patients taking enteral feeds.
- Consider Mugard or Gelclair if insufficient relief from above (discuss with local head and neck team).

Avoid

- Chlorhexidine (Corsodyl); alcohol-containing liquids; cocaine mouthwash.

Analgesia

- Ensure adequate systemic relief as per WHO pain ladder (consider laxatives if opiates used):
  - Soluble paracetamol 1g qds
  - Soluble cocodamol 30/500x2 qds
  - Oramorph 2.5–5mg every 4 hours and as required, rapidly titrated to effective dose; take advice from pain specialists if insufficient

13.2.3 Specific Symptoms

Thick oral secretions/mucus

- 3% hydrogen peroxide mouthwash 20ml qds
- Nebulised 0.9% sodium chloride 10ml 1–4 hourly
- Carbocisteine 750mg tds

Haemorrhagic mucositis

- 500mg tranexamic acid injection added to 5ml sterile water and used as mouthwash qds (not to swallow)

Dry mouth

Encourage oral hydration where possible. The following may provide relief:

- Sucking crushed ice or frozen tonic water
- Saliva replacements – AS Saliva Orthana; Glandosane spray; Biotene Oralbalance gel

Dry lips

- Yellow paraffin or lidocaine ointment 5%

Mouth ulcers

- Lidocaine 5% ointment; or lidocaine 10% spray (Xylocaine); or choline salycilate (Bonjela)
- Sodium hyaluronate: 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.
- Hydrocortisone lozenges or Triamcinolone oral paste if severe

Oropharyngeal infection

May underlie rapidly worsening mucositis or delayed recovery after radiotherapy. Take local microbiological advice and consider:

Fungal – fluconazole 100mg OD for 7 days

Viral – topical aciclovir 5% for local infection in low-risk patients; 800mg PO x5/day or IV infusion 10mg/kg tds.

14 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 cause 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 situations.

14.1 Grading Nausea and Vomiting CTCAE 4.03

	Nausea	Vomiting
Grade 1	Loss of appetite without alteration in eating habits	1–2 episodes (separated by 5 minutes) in 24 hours
Grade 2	Oral intake decreased without significant weight loss, dehydration or malnutrition	3–5 episodes (separated by 5 minutes) in 24 hours
Grade 3	Inadequate oral caloric or fluid intake; tube feeding, total parenteral nutrition (TPN) or hospitalisation indicated	≥ 6 episodes (separated by 5 minutes) in 24 hours; tube feeding, TPN or hospitalisation indicated
Grade 4	–	Life-threatening consequences; urgent intervention indicated
Grade 5	–	Death

14.2 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-emetic 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

Drug	D_2 antagonist	H_1 antagonist	ACh antagonist	$5HT_2$ antagonist	$5HT_3$ antagonist	$5HT_4$ antagonist	NK1 inhibitor
Metoclopramide	++					++ (agonist)	
Domperidone	++						
Cyclizine		++	++				
Hyoscine			+++				
Haloperidol	+++						
Levomepromazine	++	+++	++	+++			
Aprepitant/ Fosaprepitant							+++
Ondansetron					+++		
Granisetron					+++		
Palonosetron					+++++++		

Table adapted from Twycross R and Wilcock A (eds) (2007) *Palliative Care Formulary* 3rd Edn. Nottingham: Palliativedrugs.com Limited (modified).

- 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 (risk of oculogyric crisis with metoclopramide).

14.3 Causes of Nausea and Vomiting in Oncology Patients

Cause	Treatment Options
Anxiety/anticipatory nausea	Lorazepam Antidepressants in longer term: seek advice from patient's GP or from oncology team
Bowel obstruction	Levomepromazine or haloperidol or cyclizine
Chemotherapy	See section 14.4
Constipation	Treat cause
Delayed gastric emptying	Metoclopramide

Cause	Treatment Options
Drugs* (non-chemotherapy)	Stop drug if possible Haloperidol or levomepromazine
Gastric irritation	Treat cause (e.g. proton pump inhibitor) Metoclopramide if needed
Hypercalcaemia	Treat cause (see section 6) Haloperidol or levomepromazine
Renal failure	Haloperidol or levomepromazine
Metabolic causes (e.g. hyperglycaemia, hyponatraemia)	Haloperidol or levomepromazine
Raised intracranial pressure (e.g. brain metastases)	Treat cause (see section 18) Dexamethasone and cyclizine

*Common culprits include antibiotics, antidepressants, NSAIDs and opiates.

14.4 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. Commonly resolves within 24 hours.
- **Delayed:** from 24 hours after chemotherapy. Seldom persists beyond 1 week.
- **Anticipatory:** occurs prior to any chemotherapy administration and is a learned response to previous chemotherapy, typically after a past 'negative' experience.

In addition, CINV can be classified as:

- **Breakthrough:** development of nausea and vomiting despite standard prophylactic anti-emetic therapy, which requires treatment with an additional pharmacological agent ('rescue' anti-emetics).
- **Refractory:** emesis that occurs during subsequent treatment cycles despite standard and rescue anti-emetic therapy.

14.5 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.

	Anti-emetic	Comments
Step 1	**REGULAR** Domperidone or Metoclopramide or Cyclizine +/- Dexamethasone 4–8mg BD (if platinum chemo) **AND** PRN Anti-emetic (see comments)	• Do not use domperidone and metoclopramide together • Consider IV and PR routes • Options for PRN anti-emetics: – PRN Haloperidol 0.5–2mg 4 hourly PO or 0.5–1mg 4 hourly SC or – PRN Levomepromazine 6.25mg 4 hourly PO or 3.125–6.25mg 4 hourly SC or – PRN Ondansetron 8mg BD IV/PO (if 1–3 days post chemo)
Step 2	Add regular dose of the PRN anti-emetic from Step 1	• Consider PRN Lorazepam 0.5–1mg 6 hourly PO if element of anticipatory nausea suspected.
Step 3	Escalate doses if applicable, providing no toxicity observed	• Obtain palliative care review • Consider syringe driver for S/C administration of anti-emetics, especially in cases with impaired absorbance, e.g. bowel obstruction.

14.6 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 site treated, e.g. upper abdominal irradiation = moderately emetogenic.
- 5HT3 antagonists are particularly effective in radiation-induced nausea and vomiting.
- Refer to recommendations above for treatment of breakthrough nausea and vomiting.

14.7 Emetogenic potential of individual intravenous drugs

Minimal Emesis (<10% Incidence)	Alemtuzumab Asparaginase Bevacizumab Bleomycin Bortezomib Cetuximab Cladribine Cytarabine <100mg/m^2 Decitabine Denileukin difditox Dexrazoxane Fludarabine	Interferon alpha <5 million IU/m^2 Ipilimumab Methotrexate <50mg/m^2 Nelarabine Nivolumab Obinutuzumab Ofatumumab Panitumumab Pegaspargase Peginterferon Pembrolizumab	Pertuzumab Ramucirimumab Rituximab Ciltuximab Temsirolimus Trastuzumab Valrubicin Vinblastine Vincristine (+ liposomal formulation) Vinorelbine
Low Emesis (10–30%)	Ado-Trastuzumab Emtasine Amifostine <300mg/m^2 Aldesleukin <12 million IU/m^2 Belinostat Brentuximab Vedotin Cabazitaxel Cytarabine 100–200mg/m^2 Docetaxel	Doxorubicin (liposomal) Eribulin Etoposide 5FU Floxuridine Gemcitabine Interferon alpha 5–10 million IU/m^2 Ixabepilone Methotrexate 50–250mg/m^2	Mitomycin Mitoxantrone Paclitaxel Paclitaxel-albumin Pemetrexed Pentostatin Thiotepa Topotecan Ziv-aflibercept
Moderate Emesis (30–90% Incidence)	Aldesleukin >12–15 million IU/m^2 Amifostine >300mg/m^2 Arsenic trioxide Azacytidine Bendamustine Busulphan Carboplatin Carmustine <250mg/m^2 Clofarabine	Cyclophosphamide <1500mg/m^2 Cyatarbine >200mg/m^2 Actinomycin D Daunorubicin Doxorubicin <60mg/m^2 Epirubicin <90mg/m^2 Idarubicin Ifosfamide <2g/m^2/dose	Interferon alpha >10 million IU/m^2 Irinotecan Melphalan Methotrexate >250mg/m^2 Oxaliplatin Temozolomide
High Emesis (>90% Incidence)	Doxorubicin/Epirubicin + Cyclophosphamide Carmustine >250mg/m^2 Cisplatin Cyclophosphamide >1500mg/m^2	Dacarbazine Doxorubicin >60 mg/m^2 Epirubucin >90 mg/m^2 Ifosfamide >2mg/m^2/dose	Mechlorethamine Streptozocin

14.8 Emetogenic potential of individual oral drugs

Minimal to Low	Afatinib Axitinib Bosutinib Busulphan <4mg/day Cabozantinib Capecitabine Chlorambucil Cyclophosphamide <100 mg/m^2/day Dasatinib Dabrafenib Erlotinib Everolimus Fludarabine Gefitinib Hydroxyurea Ibrutinib Imatinib Lapatinib Lenalidomide Melphalan	Mercaptopurine Methotrexate Nilotinib Palpociclib Pazopanib Pomalidomide Regorafenib Ruxolitinib Sorafenib Sunitinib Temozolomide <75 mg/m^2/day Thalidomide Diguanine Topotecan Trametinib Tretinoin Vandetanib Vemurafenib Vorinostat
Moderate to High	Altretamine Busulphan >4mg/day Ceritinib Crizotinib Cyclophosphamide >100 mg/m^2/day Estramustine Etoposide Lomustine (single day)	Mitotane Olaparib Panobinostat Procarbazine Temozolomide >75 mg/m^2/day Vismodegib

Sources:

Hesketh PJ et al. (1997). Proposal for classifying the acute emetogenicity of cancer chemotherapy. *Journal of Clinical Oncology* 15(1):103–9.

Grunberg SM et al. (2011). Evaluation of new antiemetic agents and definition of antineoplastic agent emetogenicity – state of the art. *Supportive Care in Cancer* (19 Suppl)1:S43–7.

Notes on individual anti-emetics

$5HT_3$ Antagonist	Patients may complain of constipation and headaches. Patients need to be advised accordingly, e.g. movicol to relieve constipation and paracetamol to relieve headache. If severe, consider an alternative anti-emetic. Long-acting $5HT_3$ antagonists are available and may be used if locally approved, i.e. palonosetron stat pre-chemotherapy dosing.
Aprepitant	Aprepitant is an NK-1 receptor antagonist which has been shown to inhibit emesis induced by cytotoxic chemotherapeutic agents, such as cisplatin, via central actions. In addition, studies show that aprepitant augments the anti-emetic activity of the $5HT_3$ receptor antagonists and dexamethasone, and inhibits both the acute and delayed process of cisplatin-induced emesis. When given in combination 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.
Cyclizine	Cyclizine may cause antimuscarinic side effects such as dryness of the mouth and drowsiness. Children and the elderly are more susceptible to these effects. Pre-existing cardiac failure decompensation = rare.
Dexamethasone	Corticosteroids can cause sleep disturbances, hyperactivity, psychiatric manifestations 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. They can be particularly effective when managing platinum-related acute CINV. Minimise use in view of the high risk of avascular necrosis in the long term with chronic exposure.
Domperidone	Domperidone should not be used when stimulation of the gastric motility could be harmful, e.g. gastrointestinal haemorrhage, mechanical obstruction or perforation (similar caution applies to metoclopramide). Do not exceed 30mg/day. MHRA warning: Domperidone is now contra-indicated in people: with conditions where cardiac conduction is, or could be, impaired; with underlying cardiac diseases such as congestive heart failure; receiving other medications known to prolong QT interval or potent CYP3A4 inhibitors.
Levomepromazine	Avoid in patients with liver dysfunction. Inhibits cytochrome P-450. Common side effects are somnolence, asthenia, dry mouth,

	hypotension, photosensitivity and skin reactions.
Lorazepam	Can cause drowsiness and may affect performance of skilled tasks (driving).
Metoclopramide	Can rarely cause agitation or the development of extra-pyramidal symptoms particularly in the young female patients (oculogyric crisis: antidote= procyclidine). 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.

15 Neutropenic Sepsis

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

15.1 Introduction

Suspected or proven infection in a neutropenic patient is a **MEDICAL EMERGENCY** and is an indication for immediate assessment and prompt treatment with intravenous (IV) antibiotics **WITHIN 1 HOUR OF PRESENTATION** to anywhere within the hospital.

Patients who are neutropenic following anti-cancer treatment may initially appear well. However, infections may progress within hours to shock or death, especially when due to gram-negative bacilli.

This guideline exists to provide assistance to admitting clinicians when faced with a case of suspected infection and neutropenia in both solid tumour oncology and haemato-oncology.

If there is clinical suspicion of neutropenic sepsis in existing inpatients, they should be treated within 1 hour of clinical onset, as defined by baseline observations, Early Warning Score (EWS) or clinical suspicion.

15.2 Definitions

15.2.1 Neutropenic Sepsis

Neutropenic sepsis can be diagnosed in patients who present with a neutrophil count of $\leq 1.0 \times 10^9$/L and/or a fever.

NB fever may not be present in some infected neutropenic patients. Infection should be suspected in any patient who is feeling generally unwell following chemotherapy. If in doubt, give antibiotics and seek specialist advice from the Acute Oncology Service (AOS).

15.2.2 Neutropenia

Neutropenia can be diagnosed in patients who present with a neutrophil count of $<0.5 \times 10^9$/L or a count of $<1.0 \times 10^9$/L with a predicted decrease to $<0.5 \times 10^9$/L.

NB a patient with a neutrophil count of $<1.0 \times 10^9$/L and evidence of infection should be treated using this guideline.

Neutropenia is usually secondary to chemotherapy. It may occur with radiotherapy if large amounts of bone marrow are irradiated, or may be part of a pancytopenia.

15.2.3 Fever

Fever is a single oral temperature of $\geq 38^{o}$C.

Diagnose neutropenic sepsis in patients having anti-cancer treatment whose neutrophil count is $\leq 1.0 \times 10^9$/L and who have either a temperature $\geq 38^{o}$C, a temperature of $\geq 37.5^{o}$C on two occasions recorded 1 hour apart, or other signs or symptoms consistent with clinically significant sepsis.

NB fever may not be present in some infected neutropenic patients. Infection should be suspected in any patient who is feeling generally unwell following chemotherapy. If in doubt, give antibiotics and seek specialist advice from the AOS.

15.2.4 Healthcare Professionals with Competence in Managing Complications of Anti-cancer Treatment

These healthcare professionals include oncology consultants, haematology consultants, oncology specialist registrars (SpRs), haematology SpRs, acute oncology clinical nurse specialists (CNSs) and clinical site practitioners.

15.3 Initial Assessment

- Baseline observations and EWS.
- Establish whether the patient has any known drug allergies, in particular to penicillin or other antibiotics.
- A side room is preferable, but not essential, for management. Do not wait to treat patients if a side room is unavailable.
- If EWS is high:
  - This suggests **severe sepsis**.
  - Start fluid resuscitation immediately.
  - Inform Critical Care/HDU/Intensive Therapy Unit (ITU), if needed; a diagnosis of cancer need not preclude a patient being assessed for HDU/ITU.
- Take all necessary blood tests (see section 15.4).
- Empirically prescribe and ensure immediate administration of appropriate IV antibiotics (see section 15.5).
  - Do not wait for results of the blood tests before giving antibiotics.
  - Antibiotics should be given within **60 minutes of arrival**.*
- Complete other investigations once antibiotics have been given.
- Contact the AOS, or on-call oncology team, for all oncology patients; or the relevant haematology team for haematology patients.
- If high EWS, consider administration of granulocyte-colony stimulating factor (G-CSF) (see section 15.7.4).
- If found not to be neutropenic, treat according to Trust adult sepsis guidelines.

15.4 Investigations

- Urgent full blood count.
- Venous blood cultures: take peripheral cultures and cultures from all lumens of central venous access device (CVAD), if present. Ensure adherence to Trust policy for taking blood culture by using blood culture packs as recommended.
- Renal profile, clotting profile, liver function tests (including albumin), calcium, magnesium, C-reactive protein (CRP), lactate, and group and save all (send as urgent).

* Or of a new neutropenic sepsis episode in an inpatient.

- **NB CRP levels do not correlate with the presence or absence of sepsis and therefore CRP levels should not be used as criteria to determine whether a patient should or should not be treated for neutropenic sepsis.**
- If clinically indicated: urinalysis, midstream specimen of urine, chest X-ray, swabs (throat, CVAD site if present, and any other focal lesions as appropriate), sputum and stool culture.

15.5 Treatment

15.5.1 IV Antibiotics

First Line	Penicillin Allergic/Alternative
As per Trust guidance	*As per Trust guidance*
If suspected central venous catheter infection **or** suspected methicillin-resistant *Staphylococcus aureus* (MRSA) infection • *As per Trust guidance* If suspected atypical pneumonia • *As per Trust guidance*	
If, after administration of first antibiotic treatment, the patient is found not to be neutropenic, treat according to Trust adult sepsis guidance.	

15.5.2 Assessing the Patient's Risk of Septic Complications

A healthcare professional with competence in managing complications of anti-cancer treatment should assess the patient's risk of septic complications, arising from neutropenic sepsis, within 24 hours of presentation, using a recognised scoring system such as the Multinational Association of Supportive Care in Cancer (MASCC) risk index. These healthcare professionals include oncology consultants, haematology consultants, oncology specialist registrars, haematology registrars and acute oncology nurse specialists.

15.6 MASCC Risk Index Scoring System

		Yes	No	Score
Does the patient have a solid tumour or lymphoma (except Burkitt's)?		4	0	
Is the patient dehydrated or requiring IV fluids?		0	3	
Is the systolic blood pressure <90mmHg?		0	5	
How sick is the patient now?	No or mild symptoms	5	0	
	Moderate symptoms	3	0	
	Severe symptoms	0	0	
Is the patient <60 years old?		2	0	
Does the patient have chronic obstructive pulmonary disease?		0	4	
Did the patient develop febrile neutropenia while an inpatient?		0	3	
Total MASCC score				

NB points attributed to the variable 'burden of illness' are not cumulative. The maximum theoretical score is therefore 26. Patients with a MASCC score of >21 are considered to be at low risk of septic complications. Patients with a MASCC score of <21 are considered to be at high risk of septic complications.

15.6.1 Patients at Low Risk of Septic Complications (MASCC Score of >21)

For patients with confirmed neutropenic sepsis but a low risk of developing septic complications, outpatient antibiotic therapy may be considered, where established treatment protocols exist, and after discussion with the acute oncology team. This should also take into account the patient's social and clinical circumstances, discussing with them the need to return to hospital promptly if a problem develops.

15.6.2 Patients at High Risk of Septic Complications (MASCC Score of <21)

Patients with confirmed neutropenic sepsis and a high risk of developing septic complications should be reviewed by a member of the acute oncology team daily to review the patient's clinical status. The patient's risk of septic complications should be assessed daily using the MASCC score.

15.7 Subsequent Management

15.7.1 Duration of Empiric Antibiotic Treatment

- Do not switch initial empiric antibiotics in patients with unresponsive fever unless there is clinical deterioration or a microbiological indication.
- If causative organism is identified at any stage, change antibiotics according to microbiological advice. However, cultures are often negative.
- If no response at 48 hours, review antibiotics with microbiologist advice. Discontinue empiric antibiotic therapy in patients whose neutropenic sepsis has responded to treatment, irrespective of neutrophil count.

15.7.2 Switching to Oral Antibiotics

Consider switching from IV to oral antibiotic therapy after 24–48 hours of treatment in patients (including haematology patients) whose risk of developing septic complications has been reassessed as low (with the aid of the MASCC risk index) by a healthcare professional with competence in managing complications of anti-cancer treatment[†], regardless of the absolute neutrophil count.

15.7.3 Discharging Policy

Consider discharge for patients who have been converted to oral antibiotics, taking into account the patient's social and clinical circumstances. These patients need clear follow-up arrangements in place, either with the local acute oncology team or the appropriate treating oncologist.

15.7.4 G-CSF

- Advice should be sought regarding the use of G-CSF. For oncology patients, contact the AOS; for haematology patients, contact the relevant haematology consultant.
- G-CSF can be considered if the patient is septic or at high risk of complications (e.g. profound neutropenia $<0.5 \times 10^9$/L), pneumonia, hypotension multi-organ dysfunction or invasive fungal infection.
- G-CSF should be stopped once the neutrophil count is $>1.0 \times 10^9$/L and is stable and rising.

15.7.5 CVAD (e.g. Hickman Lines, Peripherally Inserted Central Catheter Lines or Portacaths)

- Use the Trust blood culture packs in order to minimise contamination.
- Blood cultures should be taken from all lumens of the line (do not discard the first aliquot of blood from venous catheters – this is suitable for microbiological culture). Ensure accurate and correct labelling of all samples.
- Blood cultures should also be taken peripherally at the same time as the cultures from the central lines.

[†] Haematology consultant, haematology CNS, haematology SpR, chemotherapy CNS, oncology consultant, oncology CNS, oncology SpR, clinical site practitioner or other healthcare professional who has been deemed competent by the Trust acute oncology lead.

- Assess the line site and swab as indicated.
- Clinical judgement needs to be used when considering use of the line based on:
  - likelihood of the line being the focus of infection
  - alternative access with priority being given to the need for IV antibiotics.
- Empirical removal of the CVAD is not necessary if the patient is clinically stable.

16 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).

16.1 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.

16.2 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.

16.3 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 reaccumulation of fluid and subsequent tamponade, and for the anticipated survival of the patient.

17 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.

17.1 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.

Grade	Skin Changes
0	No visible changes
1	Faint or dull erythema; dry desquamation
2a	Tender or bright erythema without dry desquamation
2b	Patchy moist desquamation; moderate oedema
3	Confluent moist oedema; pitting oedema

17.1.1 Treatment

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

*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.

17.2 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.

17.2.1 Signs

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

17.2.2 Symptoms

Classically develop 4 weeks–3 months after radiation, and persist for up to 7 months. They include:

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

17.2.3 Assessment

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

Source: Common Terminology Criteria for Adverse Events 4.0 CTCAE (2009)

17.2.4 Investigations

- **Chest X-ray (CXR)**
  Commonest finding is patchy opacification within the radiation field, 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.

17.2.5 Differential Diagnosis

- Infection
- Recurrence of disease
- Lymphangitic carcinomatosis.

17.2.6 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.

17.3 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 signs and symptoms depend on the area of radiation.

17.3.1 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.

17.3.2 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.

17.4 Radiotherapy Induced Nausea and Vomiting

Please refer to management of nausea and vomiting in section 14.5.

17.5 Radiotherapy Induced Diarrhoea

Please refer to management of diarrhoea in section 4.7.

17.6 Radiotherapy Associated Mucositis

Please refer to management of mucositis in section 13.

18 Raised Intracranial Pressure/Central Nervous System Space Occupying Lesions

If raised intracranial pressure or space occupying lesions suspected, please refer to Acute Oncology Service.

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 most common cause of 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%

18.1 Assessment

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

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

18.1.1 Symptoms

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

18.1.2 Signs

- Papilloedema
- Decrease in conscious level
- Focal neurology
- Late signs related to herniation (rare except if haemorrhage), e.g. respiratory irregularity, pupillary dilatation, extension to pain

18.1.3 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:
  - Mass effect and midline shift
  - Cerebral oedema
  - Hydrocephalus
  - Acute haemorrhage.

If new malignant diagnosis suspected, investigate according to local Carcinoma Unknown Primary guidelines. Refer to the AOS at time of referral to neurosurgery.

18.2 Management

Raised ICP in primary or metastatic disease may be associated with poor prognosis and the decision to escalate treatment to critical care or neurosurgical intervention should be made in conjunction with senior medical and/or oncology staff. Decisions regarding definitive treatment of brain metastases should be made by a specialist neurology multidisciplinary team (MDT) via the local neurosurgical unit and in conjunction with the site-specific local MDT and treating oncologist.

If in doubt, please liaise with the AOS for advice and details regarding how to contact your local neurosurgical unit.

18.2.1 Emergency Management

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

Keep nil by mouth.

18.2.2 Steroids

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

18.2.3 Other Measures

- Rehydration: aim for euvolaemia.
- Management of pain and agitation as appropriate.
- Anti-emetics: consider cyclizine 50mg tds IV.
- Head of bed elevation: elevating the bed to 30° improves jugular venous outflow and lowers ICP in patients who are hypovolaemic; this may be associated with a fall in blood pressure and an overall fall in cerebral perfusion pressure.
- Analgesia and sedation: consider opiates and midazolam in conjunction with advice from palliative care/critical care teams.
- 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.

18.2.4 Subsequent Management

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

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

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 a parallel referral to the specialist palliative care team is advised.

19 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.

19.1 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%).

19.2 Symptoms

These usually present as worsening over the preceding few days.

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

19.3 Investigations

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

- Observations, including oxygen saturations
- CXR
- Bloods: FBC, U&E, 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 CT chest

- If lymphoma is suspected from radiology, send HIV, Hep B/C. Contact acute oncology or haematology for review according to local protocols.

19.4 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.

19.4.1 Symptomatic Relief

- Sit the patient up, prescribe oxygen, prescribe analgesia (if needed), support arms.
- If dyspnoeic: 5mg of morphine sulphate 10mg/5ml oral solution 4 hourly is usually effective.

19.4.2 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.

19.4.3 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.

Following stent insertion, short-term anticoagulation is considered mandatory. The stent is highly thrombogenic in the first month post insertion until neoendothelium covers the endovascular surfaces. There is no consensus on anticoagulant regimens. Short-term treatment with complete heparinisation for 4–7 days has been recommended if no contraindication. This may be followed by different anticoagulation approaches; oral antiplatelet agents and coumarins have been cited previously. Local advice should be sought.

19.4.4 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.

19.4.5 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.

19.4.6 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.

20 Palliative Care

20.1 General

Around a third of cancer patients, presenting to hospital as an emergency have incurable cancer (McPhail et al. 2013, and Chauhan et al., 2015).

Patients presenting as new cancer diagnoses through the Emergency Department have a poor one-year survival (RCP AOS toolkit 2013).

It is therefore important to consider whether:

- There is a chance the patient may die during the current admission
- The patient may be within the last year of their life. (Ask yourself "Would I be surprised to hear that the patient died within the next year?")
- The patient has been offered an opportunity to discuss wishes for care (advance care plan) and if these have been shared, for instance on Coordinate My Care (CMC)
- The patient (and/or their carers) has need of referral to specialist palliative care (SPC) professional, to address their physical, psychological, social or emotional needs.

20.2 Referral

Guidance from the LCA Palliative Care Group, regarding referral to SPC services within south and west London, suggests the following:

1. The patient has active, progressive advanced disease, a limited prognosis, and the focus of care is on quality of life, for example:

- Potentially fatal conditions where treatment has changed from curative to palliative intent, e.g. cancer, multiple co-morbidities where curative treatment is no longer possible
- Complex symptom control issues during treatment
- Treatment available to prolong life but prognosis is uncertain, e.g. advanced chronic obstructive pulmonary disease, advanced heart failure
- Palliative treatment from the outset with no cure available, e.g. motor neurone disease, multiple systems atrophy, advanced dementia.

2. The patient has unresolved complex needs that cannot be met by the team responsible for the patient's care. These needs may be physical, psychological, social and/or spiritual. Examples may include complicated symptoms, difficult family situations, or ethical issues, regarding treatment decisions.
3. Patient consent for referral (where the patient has capacity for this consent).

If in any doubt, please contact the SPC team available in all LCA Trusts.

Referral can be made by an appropriate healthcare professional, who is in contact with the patient.

Patients who may benefit from SPC services should be identified, the referral discussed with the patient and carers and then referral made as soon as possible.

The SPC team within each Trust is available for advice about symptom management.

It is also important to consider whether, if it has not been done already, referral should be made to the relevant community SPC service for ongoing support of the patient at home, following diagnosis in the outpatient department or hospital discharge.

Again, the hospital SPC team can advise.

20.3 Service Availability

All hospital trusts across the LCA have a palliative care team, accessible via the trust switchboard. Not all trusts provide a 7-day face-to-face service, but all do have access for health professionals to 24/7 palliative care telephone advice.

There are 11 hospice units covering south and west London and beyond, all but one of which have inpatient beds. Contact details to discuss referral are available on the referral form. Not all hospices can admit patients 24/7.

Most community palliative care services are provided by the hospices, though some are provided by specific hospital trusts – again contact details are available on the referral form. Urgent referrals should be discussed with the team to determine ability to respond as requested.

20.4 Referral Process

Referral can be made

- by phone (for some hospital inpatient units only)
- in writing (via the referral form opposite)
- or by email (via the electronic referral form available towards the bottom of the page at: www.londoncanceralliance.nhs.uk/information-for-healthcare-professionals/forms-and-guidelines/lca-forms,-protocols-and-guidance/).

20.5 Management

LCA SPC teams have adopted the nationally available Palliative Care Adult Network Guidelines available at: http://book.pallcare.info/

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Ascites (Malignant)	Jillian Noble	Consultant Medical Oncologist	Croydon University Hospital/Royal Marsden NHS Foundation Trust
	Susannah Stanway	Consultant Medical Oncologist	
Central Venous Access Device Complications	Michael Flynn	Chemotherapy Nurse Consultant	Guy's and St Thomas' NHS Foundation Trust (both sites)
Diarrhoea: Chemotherapy and Radiotherapy Induced	Jaishree Bhosle	Consultant Medical Oncologist	Royal Marsden Hospital Sutton
Extravasation of Chemotherapy	Rebecca Johl	Lead Chemotherapy Nurse	Imperial College Healthcare Trust
Hypercalcaemia of Malignancy	Fiona Castell	AOS Consultant	King's College Hospital NHS Foundation Trust
Hypomagnesaemia	Sheea Parkinson	Acute Oncology Cancer Nurse Specialist	Princess Royal University Hospital, King's College Hospital NHS Foundation Trust
	Kitrick Perry	Locum Consultant Clinical Oncologist for Colorectal Cancer and Acute Oncology	
Hyponatraemia	Nadia Yousaf	Locum Consultant Medical Oncologist (AOS/Lung)	Royal Marsden NHS Foundation Trust
	Preetha Aravind	Clinical Oncology Fellow	King's College Hospital NHS Foundation Trust
Immunotherapy Related Toxicities	Tom Newsom-Davis	LCA AOS Pathway Chair and Consultant Medical Oncologist	Chelsea & Westminster Hospital NHS Foundation Trust
	Nadia Yousaf	Locum Consultant Medical Oncologist (AOS/Lung)	Royal Marsden NHS Foundation Trust
Lymphangitic Carcinomatosis	Nadia Yousaf	Locum Consultant Medical Oncologist (AOS/Lung)	Royal Marsden NHS Foundation Trust
	Alicia Okines	Locum Consultant Medical Oncologist (Breast/AOS)	Royal Marsden NHS Foundation Trust

Malignant Pleural Effusion	Michael Gonzales	Locum Consultant in Medical Oncology	Imperial College Healthcare Trust
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	Lena Karapanagiotou	Consultant Medical Oncologist	
Nausea and Vomiting	Tom Newsom-Davis	LCA AOS Pathway Chair and Consultant Medical Oncologist	Chelsea & Westminster Hospital NHS Foundation Trust
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Neutropenic Sepsis	Tom Newsom-Davis	LCA AOS Pathway Chair and Consultant Medical Oncologist	Chelsea & Westminster Hospital NHS Foundation Trust
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Appendix 1: Specialist Palliative Care (SPC) Community and SPC Inpatient Unit Referral Form

Specialist Palliative Care Community Teams & Inpatient Units across South & West London

Greenwich & Bexley Community Hospice Bostall Hill, Abbey Wood **SE2 0GB** Assessment Coordination Team Tel: 020 8320 5837 **Email:** gbch.referrals@nhs.net	**Lewisham Macmillan Community Team:** Lewisham High Street **SE13 6LH** Tel: 020 8333 3017 Fax: 020 8333 3270 **Email:** LG.UHLPalliativeCareTeam@nhs.net	**St Christopher's Hospice** Lawrie Park Rd, London **SE26 6DZ** Home care: Tel: 020 8776 5656 Fax: 020 87765798 Admissions: Tel. 020 87684582 Fax: 02086595051 St Christopher's Bromley Tel: 01689 825755 Fax: 01689 892999 **Email:** stc.referral@nhs.net
Guy's & St Thomas' Community Team: Guy's Hospital, Great Maze Pond **SE1 9RT** Tel: 020 71884754 Fax: 020 71884748 **Email:** gst-tr.gstt-palliativecare@nhs.net	**Meadow House Hospice** Southall **UB1 3HW** Tel: 020 89675179 Fax 020 89675756 **Email:** referralsmeadowhouse@nhs.net	**St John's Hospice** Grove End Road, St John's Wood **NW8 9NH** Tel:020 78064040 Fax: 020 78064041 **Email: TBC**
Harlington Hospice St Peter's Way, Harlington **UB3 5AB** Tel: 020 87590453 Fax: 020 87590600 **Email: TBC**	**Michael Sobell House** Northwood, Middlesex **HA6 2RN** Tel:01923 844531 Fax: 01923 844565 **Email:** msh.enh-tr@nhs.net	**St Luke's Hospice** Kenton Road, Harrow **HA3 0YG** Tel: 020 83828000 Fax: 020 83828080 **Community Team** Fax: 020 83828092 **Email: TBC**
Harrow Community Team Kenton Road, Harrow **HA3 0YG** Tel: 020 83828084 Fax: 020 83828085 **Email: TBC**	**Pembridge Palliative Care Centre** Exmoor Street, **W10 6DZ** Tel: 020 8962 4410 Inpatient Fax: 020 89624422 Community Services Fax: 020 89624413 **Email:** CLCHT.PembridgeUnit@nhs.net	**St Raphael's Hospice** London Road, North Cheam **SM3 9DX** Tel: 020 80997777 Fax: 020 8099 1724 **Email: TBC**
Hillingdon Community Team Pield Heath Road, Uxbridge **UB8 3NN** Tel:01895 279412 Fax: 01895 279452 **Email:** thh-tr.pallcare@nhs.net	**Princess Alice Hospice** West End Lane, Esher **KT10 8NA** Tel: 01372 461804 Fax: 01372 470937 **Email:** clinicaladminpah@nhs.net	**Trinity Hospice** Clapham Common **SW4 0RN** Tel: 020 7787 1000 Ref & Admissions Nurse: 020 77871065 Fax: 020 7787 1067 **Email:** WACCG.TrinityHospicereferrals@nhs.net

For further information and advice on these services, please visit the Hospice UK service directory at: http://www.hospiceuk.org/about-hospice-care/find-a-hospice and enter the postcode provided above.

Every LCA hospital has a Specialist Palliative Care team;
if your patient is a *hospital inpatient,* please contact the team, via the relevant hospital switchboard.

FAX MESSAGE	
From:	**To:**
Fax No:	**Date:**
No. of pages (incl. cover sheet):	
Additional information	
Confidentiality: The content of this fax and attached documents are confidential and intended for the use of the addressee designated above. If you are not the addressee, you are hereby notified that you may not disclose, reproduce or otherwise disseminate or make use of this information for yourself or any third party. If you have received this in error, please notify us on the telephone number given above.	
PLEASE SEND COPIES OF RECENT CLINICAL CORRESPONDENCE WITH THIS FORM – including recent clinic letters, blood tests and most recent imaging **NB. INSUFFICIENT INFORMATION MAY DELAY PATIENT ASSESSMENT**	

PATIENT NAME …….. **NHS No:**……

Essential Patient Details		
Surname	Male / Female Age:	Patient consent to pall care involvement? Yes ☐ No ☐ Best interest decision ☐
First Name	DoB	Is GP aware of referral? Yes ☐ No ☐
Address		
Postcode	Marital Status	Ethnicity
Tel	Mob	
NHS number	**Hospital No.**	

Primary diagnosis(es)

Communication	Other barriers to communication / registered disabilities:
Fluent in English? Yes ☐ No ☐ (If 'no' proceed with remaining questions)	
First Language, if not English:	
Would interpreter be helpful to patient and Palliative Care staff? Yes ☐ No ☐	

Next of Kin/Patient Representatives	**District Nurse** Yes ☐ No ☐	**General Practitioner**
Name	Name	Name
Address	Based at	Address
	Telephone	
Telephone	Fax	
Relationship to patient		Postcode
Main Carer (if different from above) Name	**Social Services** Yes ☐ No ☐ Name	Telephone
Telephone	Based at	Fax/email
Relationship to patient	Tel Fax	
	Continuing care assessment completed: Yes ☐ No ☐ **Continuing care funding agreed:** Yes ☐ No ☐	CCG:

Reason for Referral	**Service requested**	**The patient is currently**
Pain/symptom control ..... ☐	Home assessment and support ..... ☐	At Home ..... ☐
Emotional/psychological support ..... ☐	Hospital assessment ..... ☐	In Hospital (see over) ..... ☐
Social/financial ..... ☐	Day Care ..... ☐	Other e.g. Nursing Home ..... ☐
Assessment for hospice admission ..... ☐	Outpatient service ..... ☐	Please specify.....
Carer support ..... ☐	Admission (circle) ..... ☐	
Other reason (*please give details below*) ☐	Respite / symptom control / terminal care	Does patient live alone? Yes ☐ No ☐
.....	Hospice at Home..... ☐	

Any access issues (e.g. key safe):	
MRSA Status Positive ☐ Negative ☐ Not known ☐	**Any other communicable infection:** .....
Special device in situ? Yes ☐ No ☐ If yes, give details (e.g. trache / PEG / ICD / NIPPV):	
Referrer's Name: (please print)	**Contact number:** **Bleep no:**
Hospital/Surgery:	*This information required on both pages if faxing*

IS REFERRAL URGENT (assess within 2 working days)? Yes ☐ No ☐

IF URGENT, PLEASE PHONE US FOR IMMEDIATE ADVICE

In-Patient details	**Patient Name:**
Hospital	NHS No:
Ward Direct Ward Ext.	Telephone
Key worker	Date of discharge (if known)
Consultant	Is Palliative Care team involved? Yes ☐ No ☐

Brief History of diagnosis(es) and Key treatments		
Date	Progression of disease and investigations/treatment	Consultant and hospital

Current palliative care problems	
1.	4.
2.	5.
3.	6.
Patient Mobility:	**Bariatric Nursing required?** Yes ☐ No ☐
Any other comments/information (including preferences expressed about care or other psychosocial or spiritual issues)	
Referrer's expectation of current treatment (please circle) symptom control / life prolonging / curative	
Prognosis: In your opinion, is the patient **Stable?** Yes ☐ No ☐ **Unstable?** Yes ☐ No ☐ **Deteriorating?** Yes ☐ No ☐ **Dying?** Yes ☐ No ☐ Is death anticipated within: Months ☐ Weeks ☐ Days ☐	
Patient on Coordinate My Care? Yes ☐ No ☐ Unknown ☐ If not please give reason…… **On the GSF register?** Yes ☐ No ☐ Unknown ☐ **DNACPR in place?** Yes ☐ No ☐	

Past Medical and Psychiatric History	**Current Medication**	
		Known Drug Sensitivities/Allergies: Yes ☐ No ☐
		Details:
Insight: Has patient been told diagnosis? Yes ☐ No ☐ **Is the carer aware of patient's diagnosis?** Yes ☐ No ☐ **Does patient discuss the illness freely?** Yes ☐ No ☐		

Please ensure patients are aware information will be held on computer according to the Data Protection Act.

Referrer's signature:	**Name:** (please print)
Job title:	**Contact number:** **Bleep no:**
Surgery or Hospital:	**Date:**

References

Adrogué HJ and Madias NE (2000). Hyponatremia. *New England Journal of Medicine* 342:1581–1589.

Allan L et al. (2009). Suspected malignant cord compression – improving time to diagnosis via a 'hotline': a prospective audit. *British Journal of Cancer* 100(12):1867–72.

Bartter FC and Schwartz WB (1967). The syndrome of inappropriate secretion of antidiuretic hormone. *American Journal of Medicine* 42:790–806.

Beck SL (2004). 'Mucositis'. In Henke-Yarbro C, Hansen-Frogge M and Goodman M (eds) *Cancer Symptom Management* 3rd Edn. Sudbury: Jones & Bartlett Learning, pp 276–92.

Bone RC et al. (1992). The phases of the syndrome form a continuum of severity with increased risk of morbidity and mortality. *Chest* 101:1644–55.

Bruce DM, Heys SD and Eremin O (1996). Lymphangitis carcinomatos: a literature review. *Journal of the Royal College of Surgeons of Edinburgh* 41(1):7–13.

Cancer Therapy Evaluation Program (2009). *Common Terminology Criteria for Adverse Events*, Version 4.0. Bethesda, Md: National Cancer Institute, Division of Cancer Treatment and Diagnosis.

Castillo JJ, Vincent M and Justice E (2012). Diagnosis and management of hyponatremia in cancer patients. *The Oncologist* 17(6)756–765.

Chauhan, N, Ridge M, Parker, M and Pritchard-Jones, K (2015). *Survival of cancer presenting through A&E affected by age, cancer and treatment intent. Findings from the London Cancer A&E Audit.* NCRI Cancer Conference Abstracts A158. Available at: http://abstracts.ncri.org.uk/abstract/survival-of-cancer-presenting-through-ae-affected-by-age-cancer-and-treatment-intent-findings-from-the-london-cancer-ae-audit-2/ [Date accessed 11/12/15]

Cheng KK et al. (2001). Evaluation of an oral care protocol intervention in the prevention of chemotherapy-induced oral mucositis in paediatric cancer patients. *European Journal of Cancer* 37(16):2056–63.

Cooley C (2002). Oral health: basic or essential care. *Cancer Nursing Practice* 1(3):33–9.

Davies A and Finlay I (eds) (2005). *Oral Care in Advanced Disease*. Oxford: Oxford University Press.

De Naurois J et al. (2010). Management of febrile neutropenia: ESMO Clinical Practice Guidelines. *Annals of Oncology* 21(S5): v252–6.

Dellinger RP et al. (2008). Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock. *Critical Care Medicine* 36(1): 296–327.

Dixon MB and Lien YH (2008). Tolvaptan and its potential in the treatment of hyponatremia. *Therapeutics and Clinical Risk Management* 4(6):1149–55.

Eilers J (2004). Nursing interventions and supportive care for the prevention and treatment of oral mucositis associated with cancer treatment. *Oncology Nursing Forum* 31(4 Suppl):13–23.

Grunberg SM, Warr D, Gralla, RJ, Rapoport BL, Hesketh PJ,Jordan K & Espersen BT. (2011). Evaluation of new antiemetic agents and definition of antineoplastic agent emetogenicity-- – state of the art. *Supportive Care in Cancer*. March; 19, Supplement 1: S43-–7.

Herrstedt J and Roila F on behalf of the European Society for Medical Oncology Guidelines Working Group (2009). Chemotherapy-induced nausea and vomiting: ESMO Clinical Recommendations for prophylaxis. *Annals of Oncology* 20(4 Suppl):156–8.

Hesketh PJ et al. (2003). The oral neurokinin-1 antagonist aprepitant for the prevention of chemotherapy-induced nausea and vomiting: a multinational, randomized, double-blind, placebo-controlled trial in patients receiving high-dose cisplatin – The Aprepitant Protocol 052 Study Group. *Journal of Clinical Oncology* 21(22):4112–19.

Jordan K et al. (2007). Guidelines for anti-emetic treatment of chemotherapy-induced nausea and vomiting: past, present, and future recommendations. *The Oncologist* 12(9):1143–50.

Keefe DM et al. (2007). Updated clinical practice guidelines for the prevention and treatment of mucositis. *Cancer* 109(5):820–31.

Klastersky J, Paesmans M, Rubenstein EB, Boyer M, Elting L, Feld R, Gallagher J, Herrstedt J, ,Rapoport B, Rolston K, Talcott J. (2002)The Multinational Association for Supportive Care in Cancer risk index: A multinational scoring system for identifying low-risk febrile neutropenic cancer patients. *Journal of Clinical Oncology* 18(16): 3038-51.

Klastersky J et al. (2006). Outpatient oral antibiotics for febrile neutropenic cancer patients using a score predictive for complications. *Journal of Clinical Oncology* 24(4): 129–34.

Kris MG et al. (2006). American Society of Clinical Oncology guideline for antiemetics in oncology: Update 2006. *Journal of Clinical Oncology* 24:2932–47.

Levack P et al., Scottish Cord Compression Study Group (2002). Don't wait for a sensory level – listen to the symptoms: a prospective audit of the delays in diagnosis of malignant cord compression. *Journal of Clinical Oncology (Royal College of Radiologists)* 14(6):472–80.

Loblaw DA et al. (2003). A population-based study of malignant spinal cord compression in Ontario. *Journal of Clinical Oncology (Royal College of Radiologists)* 15(4):211–7.

London Cancer Alliance (2016) *Guidance on managing gastro-intestinal consequences of cancer and its treatments.* London. LCA. Available at: http://www.londoncanceralliance.nhs.uk/media/121451/lca-guidance-gi-consequences-of-cancer-jan-2016-v2.pdf [Date accessed 25/02/2016]

McPhail S, Elliss-Brookes L, Shelton J, Ives A, Greenslade M, Vernon S, Morris EJA, Richards M (2013). Emergency presentation of cancer and short-term mortality. *British Journal of Cancer* 109:2027–2034.

National Peer Review Programme (2014). *Manual for Cancer Services: Acute Oncology – Including Metastatic Spinal Cord Compression Measures* (version 1.0). London: NHS.

NIH National Cancer Institute (2009) *Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0.* NIH.

NIH National Cancer Institute (2009) *Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03.* NIH.

National Institute for Health and Clinical Excellence (NICE) clinical guidelines 75 (2008). *Metastatic spinal cord compression: Diagnosis and management of adults at risk of and with metastatic spinal cord compression*. London: NICE.

National Institute for Health and Clinical Excellence (NICE) clinical guidelines 151 (2012). *Neutropenic sepsis: Prevention and management of neutropenic sepsis in cancer patients.* London: NICE.

National Institute for Health and Clinical Excellence (NICE) medical technology guidance (March 2012). *The PleurX peritoneal catheter drainage system for vacuum-assisted drainage of treatment-resistant, recurrent malignant ascites.* Available at: https://www.nice.org.uk/guidance/mtg9/resources

Navari RM (2009). Pharmacological management of chemotherapy-induced nausea and vomiting: focus on recent developments. *Drugs* 69(5):515–33.

Papas AS et al. (2003). A prospective, randomized trial for the prevention of mucositis in patients undergoing hematopoietic stem cell transplantation. *Bone Marrow Transplant* 31:705–12.

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

Poli-Bigelli S et al. (2003). Addition of the neurokinin-1 receptor antagonist aprepitant to standard antiemetic therapy improves control of chemotherapy-induced nausea and vomiting. Results from a randomised, double-blind, placebo-controlled trial in Latin America. *Cancer* 97(12):3090–98.

Quinn B (2011). Personal hygiene: oral care. In Dougherty L and Lister S (eds) *The Royal Marsden Hospital Manual of Clinical Nursing Procedures* 8th Edn. Oxford: Wiley-Blackwell, pp 647–59.

Quinn B et al. (2008). Guidelines for the assessment of oral mucositis in adult chemotherapy, radiotherapy and haematopoietic stem cell transplant patients. *European Journal of Cancer* 44(1):61–72.

Raftopoulos H (2007). Diagnosis and management of hyponatremia in cancer patients. *Supportive Care in Cancer* 15:1341–1347.

Roila F et al. (2006). Prevention of chemotherapy- and radiotherapy-induced emesis: results of the 2004 Perugia International Antiemetic Consensus Conference. *Annals of Oncology* 17(1):20–28.

Rowell NP and Gleeson FV (2002). Steroids, radiotherapy, chemotherapy and stents for superior vena caval obstruction in carcinoma of the bronchus: a systematic review. *Clinical Oncology* 14(5):338–51.

Royal College of Physicians (2013). *Acute care toolkit 7: Acute oncology on the acute medical unit.* London. Royal College of Physicians. Available at: https://www.rcplondon.ac.uk/guidelines-policy/acute-care-toolkit-7-acute-oncology-acute-medical-unit [Date accessed 11/12/15]

Royal United Hospital Bath NHS Trust (2005). Prevention and Treatment of Stomatitis & Mucositis in patient receiving chemotherapy. Accessed online via:

http://spotidoc.com/doc/70059/prevention-and-treatment-of-stomatitis-mucositis-in-patient [Date accessed 26/02/16]

Rubenstein EB et al. (2004). Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. *Cancer* 100(9 Suppl):2026–46.

Salahudeen AK, Ali N, George M, Lahoti A and Palla S. (2014). Tolvaptan in hospitalized cancer patients with hyponatremia: A double-blind, randomized, placebo-controlled clinical trial on efficacy and safety. *Cancer* 20(5):744–751.

Schmoll HJ et al. (2006). Comparison of an aprepitant regimen with a multiple-day ondansetron regimen, both with dexamethasone, for antiemetic efficacy in high-dose cisplatin treatment. *Annals of Oncology* 17(6):1000–06.

Scott-Brown M, Spence RAJ and Johnston P (eds) (2007). *Emergencies in Oncology*. Oxford: Oxford University Press.

Sonis ST (2004). The pathobiology of mucositis. *Nature Reviews Cancer* 4(4):277–84.

Spasovski G, Vanholder R, Allolio B et al (2014). Clinical practice guideline on diagnosis and treatment of hyponatraemia. *European Journal of Endocrinology* 170:G1–G47.

Talcott JA et al. (2011). Safety of early discharge for low-risk patients with febrile neutropenia: a multicenter randomized controlled trial. *Journal of Clinical Oncology* 29(30):3977–83.

Twycross R and Wilcock A (eds) (2011). *Palliative Care Formulary* 4th Edn. Nottingham: Palliativedrugs.com Limited. Available online at: www.palliativedrugs.com (subscription required).

Wilson E et al. (2002). Radiological stenting provides effective palliation in malignant central venous obstruction. *Clinical Oncology* 14(3):228–32.

Zhang K and Huang Y (2006). [Clinical features and diagnosis of pulmonary lymphangitic carcinomatosis]. [Article in Chinese] *Ai Zheng* 25(9):1127–30.

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