NICaN

Acute Oncology

Clinical Guidelines

January 2022

Document Title	**NICaN Acute Oncology Clinical Guidelines**
Document Date	Originally developed 2015 Current version 2021/22
Document Purpose	This guidance has been produced to support the diagnosis and treatment of acute oncological complications. Treatment decisions for individual patients require the weighing of a multiplicity of factors, which cannot all be accounted for in a clinical guideline. The Clinical Guidelines provide a description of the range of treatment options available for a clinical scenario.
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2021/22 Review	Dr Judith Carser, Consultant Medical Oncologist, BHSCT Dr Lois Mulholland, Consultant Clinical Oncologist, SEHSCT With input from various colleagues & sources referenced throughout e.g. Hypercalcaemia of malignancy by Dr Catherine Doherty, Palliative Care Reviewed by: NICaN AOS Clinical Reference Group 28th January 2022
2024 Review	Reviewed by NICaN AOS CRG on 20 September 2024 - - Chemotherapy Extravasation – Drug Specific Management procedures included - Hypomagnesaemia included - General advice on Radiation Skin reactions removed 4 March 2025 – Update to SACT Hypersensitivity Management principals and hyperlink to SACT guidelines. Up to date version available on NICaN Space - Eolas Medical

Contents

Introduction

The introduction of Acute Oncology Services in Northern Ireland follows recommendations by the National Chemotherapy Advisory Group, guided by reports from National Confidential Enquiry into Patient Outcome and Death (NCEPOD) and the National Patient Safety Agency requiring a more systematic approach to acute care for patients with cancer. The structure and function of the service is described in the Manual for Cancer Services and Acute Oncology is subject to the National Cancer Peer Review programme. Acute Oncology Services (AOS) provide a single point of hospital contact for advice/support and bring together expertise from many disciplines including oncology, palliative care, haematology, acute and emergency medicine, surgery, radiology, microbiology and pathology amongst others.

In Northern Ireland, patients with acute cancer-related complications may present in a number of ways and to different healthcare settings. Whilst some patients are treated in the Northern Ireland Cancer Centres in Belfast City Hospital (NICC) and North West Cancer Centre (NWCC) at Altnagelvin Area Hospital, others may present to any acute trust throughout Northern Ireland, including but not limited to the Cancer Units at Craigavon Area Hospital, Antrim Area Hospital and the Ulster Hospital. These guidelines reflect the best evidence-based practice and provide advice regarding the initial support for patients requiring acute cancer-related care, whether that is due to the cancer itself or the treatment for it. The guidelines are not exhaustive and allow for local flexibility where good practice already exists.

The Acute Oncology Clinical Guidelines are intended to be used by all members of the healthcare team as a regional document to provide standardisation to guide best practice. They are not a substitute for specialist oncology input and patients should be referred to the local AOS or designated oncology teams for ongoing advice and management. These guidelines are designed to be used in conjunction with existing local protocols e.g. antibiotic guidelines.

Many patients referred to the AOS will have advanced disease or other symptom control requirements and early referral to the hospital and community specialist palliative care teams is encouraged.

Network Configuration of Services

The Northern Ireland Cancer Centre on the Belfast City Hospital site currently provides radiotherapy services, as well as complex systemic therapy for rarer cancers, or those who require inpatient treatment. The Belfast City Hospital also acts as the local cancer unit for the Belfast Trust area, providing day case chemotherapy for all cancers. The North West Cancer Centre on the Altnagelvin Hospital site opened in 2016 and provides radiotherapy services for patients in the North West of the province as well as cross-border services to Donegal in the Republic of Ireland. The NWCC also provides inpatient oncology services and treatment as well as day case systemic anti-cancer therapy services to the local population of the Western Trust area.

Each of the remaining Trust areas has a designated cancer unit providing day case systemic therapy and outpatient services for the more common cancers such as colorectal, breast, prostate and lung cancers. Craigavon Area Hospital (Southern Trust), Antrim Area Hospital (Northern Trust), Ulster Hospital (South Eastern Trust) are currently supported by a mix of resident and visiting oncologists as well as acute oncology Clinical Nurse Specialists. Whilst it is recognised that cancer patients may present to any acute Trust within Northern Ireland, acute oncology services are currently based in Craigavon, Antrim, Altnagelvin, Ulster and Royal Victoria Hospitals. Each local AOS can provide some liaison services to all acute hospitals within each Trust area, however there will be no designated acute oncology beds.

The role and scope of the AOS in each trust will differ depending upon the local provision of oncology services and each AOS integrates, develops and lead on acute oncology pathways that already exist within each trust with liaison to the NICC or NWCC when necessary. The AOS acts as a single focal point for advice and support for all acute admissions which fulfil the referral criteria. The AOS is a liaison service and does not provide acute oncology inpatient beds beyond the cancer centres in Belfast and Altnagelvin.

Urgent out-of-hours advice may be sought from the registrar or consultant on call via respective arrangements in the NICC and NWCC.

Referral Guidelines

Patients should be referred to the local Acute Oncology Service meeting any of the following criteria and can be referred by any member of the healthcare team. Patients should be referred as early as possible and usually within 24 hours of admission:

1. Patients who are receiving or who received any anti-cancer therapy (including radiotherapy or systemic therapy) within the last 6 weeks and who are admitted with potential complications from treatment. AOS will also provide support and advice regarding patients receiving immunotherapy up to 12 months after cessation of treatment

2. Patients with complications from a previously diagnosed cancer whether they have received recent treatment or not.

3. Patients with a previously undiagnosed cancer who are found to have a confirmed or suspected malignancy for which there is no obvious primary site after a preliminary set of investigations.

Systemic anti-cancer therapy complications	Radiotherapy complications	Disease-related complications
Neutropenic sepsis	Acute skin reactions	Brain metastases
Uncontrolled nausea and vomiting	Uncontrolled nausea and vomiting	Malignant spinal cord compression
Uncontrolled diarrhoea	Uncontrolled diarrhoea	Ascites
Uncontrolled mucositis	Uncontrolled mucositis	Pleural or pericardial effusions
Acute hypersensitivity reactions	Acute radiation pneumonitis	Hypercalcaemia of malignancy
CVAD complications	Acute radiation neurotoxicity	Hyponatraemia
Extravasation injuries		Lymphangitis carcinomatosis
Electrolyte disturbances e.g. hypomagnesaemia		Malignant bowel obstruction
Uncontrolled skin toxicity		Superior vena cava obstruction
		Venous thromboembolism

Contact Directory

Patients are advised to contact the oncology helpline for the unit where they are receiving treatment. They should contact the helpline if they are within 6 weeks of receiving chemotherapy or 12 months of receiving immunotherapy.

There is an on-call oncology registrar based in the cancer centre available 24/7 through the BCH switchboard for **urgent** enquiries. There is a similar process in North West Cancer centre. Contact details below.

For non-emergency enquiries it is best to contact the hospital specific acute oncology team or clinical team through the relevant consultant's secretary.

Belfast Trust	
24 hour Oncology helpline telephone advice service for patients	Oncology patients: **02895045555** Haematology patients: **02895040666**
Oncology registrar on call for **urgent** enquiries	Available through BCH switchboard **07788283794**
Belfast City Hospital Switchboard	**028 90329241**
RVH ED Triage Front of House	**028 96150631 or 02896150621**
Mater Hospital ED reception	Available through main switchboard **028 90741211**
Radiotherapy department	**028 95040457** On-treatment review clinic Out of hours please contact: **028 90329241** (BCH switchboard) - Clinical oncology registrar on-call
Radiotherapy nurses	**028 90329241** **Ext: 40477/48068**
Acute Oncology Clinical Nurse Specialists	**07885238128**
Northern Ireland Clinical trials unit (9am – 5pm)	**028 96152652**
Northern Trust	
24 hour Chemotherapy helpline telephone advice service for patients	**028 94424201** *(8.30am - 5pm)* **028 94424473** *(out of hours including bank holidays, AMU1, Acute Medical Unit/A6/C7 Antrim Area Hospital)*
Laurel House chemotherapy unit reception	**028 94424201** *(8.30am- 5pm)*
Antrim ED reception	**028 94426262**
Acute Oncology Clinical Nurse Specialists	**07584580876**
Southern Trust	
24 hour Chemotherapy helpline telephone advice service for patients	**028 37 562821** *(9am – 5pm)* **028 37 562509** *(Out of hours including bank holidays)*
Mandeville chemotherapy unit reception	**028 37 562462**
Craigavon ED reception	**028 37 560931 / 028 37 561750**
Acute Oncology Clinical Nurse Specialists	**028 37 560756 / 028 37 560757** **BLEEP 1782**

South Eastern Trust	
24 hour Chemotherapy helpline telephone advice service for patients	**07713082649**
MacDermott chemotherapy unit reception	**028 90561437**
Ulster Hospital ED reception	**028 90564875**
Acute Oncology Clinical Nurse Specialists	02890550407 / 07885447618
Western Trust	
24 hour NW Cancer Centre Triage helpline telephone advice service for patients	**02871 611289**
North West Cancer Centre reception	**02871 611320**
Altnagelvin ED reception	Available through main switchboard **028 71345171** The 'phone first' number to ring is **0300 020 6000**
SWAH ED reception	Available through main switchboard **028 66382000** The 'phone first' number to ring is **0300 020 6000**
Radiotherapy Dept.	**02871 345171 ext. 212209** 24/7 On-Call Oncology Consultant via **02871 345 171** (Altnagelvin Switchboard)
Radiotherapy Nurses	**02871 345171 ext. 212229**
Acute Oncology Clinical Nurse Specialists	**02871 611320 (reception)** **Bleep Number : 8250**
All contact details correct at Sept21	

Ascites

- Associated with a wide variety of cancers, most commonly ovarian and gastrointestinal.
- Often the presenting feature of a new cancer diagnosis.

Symptoms and signs

Symptoms: Pain, anorexia, early satiety, indigestion, nausea and vomiting, altered bowel motility, dyspnoea and reduced mobility.

Signs: Abdominal distension, shifting dullness and fluid thrill.

Investigations

Cytology	If new cancer presentation a good volume of ascitic fluid should be sent for cytology.
CT chest, abdomen, pelvis	If appropriate also consider CT imaging. Then liaise with relevant specialist multidisciplinary meeting depending on likely tumour site.

Initial Management

Refer to local Acute Oncology

Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

Paracentesis (either single aspiration or Bonanno catheter) will provide immediate relief from symptomatic ascites.

Indications – Tense ascites or moderate/severe symptoms and patient fit enough.

Contraindications – severe and irreversible coagulation disorders, intestinal obstruction and abdominal sepsis.
In patients with advanced cancer cachexia, particularly if there is liver failure (significant hypoalbuminaemia of <25g/L), paracentesis may precipitate a rapid deterioration in their clinical condition and risk should be weighed carefully against possible symptomatic benefit.

Risks – Visceral injury, peritonitis, bleeding, hypotension and protein loss leading to metabolic disturbances.

Pre Procedure – Bloods - Clinical assessment is necessary to decide if blood tests are required or if anticoagulants need stopped. Consider in 'at risk' patients i.e. patients with known liver or renal disease, recent chemotherapy, on treatment dose anticoagulants or extensive bruising around venepuncture sites. Corrective steps should be taken if appropriate. Consider platelet transfusion if platelets <50 x 10^9 /L. Consider delaying procedure if neutropenic.

LMWH and DOACs are usually withheld 24 hours pre-procedure, with anti-platelet agents (excluding aspirin) held for up to 7 days pre-procedure, taking into account the individual risk-benefit for each patient.
Point-of-Care-Ultrasound should be used real-time to identify the site and guide the procedure where skill and equipment is available. Radiology departmental ultrasound evaluation and marking may be available as an alternative. It is only by rare exception that paracentesis should be considered without either. Written informed consent should be obtained and a set of observations (NEWs) checked pre procedure.

Rate of drainage – Usually no more than 6000ml should be drained at one time.
Drainage should be tailored to clinical situation. Normally left on free drainage so long as patient remains well and blood pressure maintained. It is not necessary to clamp drains to control drainage rate. If patient becomes haemodynamically unstable then clamp until blood pressure recovers. In patients with advanced cachexia or liver failure removing large volumes of fluid can lead to a rapid deterioration and drainage should be more controlled.

Intravenous fluids not normally required but consider 0.9% normal saline if the patient is dehydrated, has renal impairment, symptomatic during paracentesis, portal hypertension secondary to massive liver metastases or hepatocellular carcinoma +/- cirrhosis.

No proven role for albumin in malignant ascites. May be considered if portal hypertension +/- cirrhosis or SAAG>11g/L, especially in the setting of large volume paracentesis (>5L/24hrs). (100mls of 20% albumin for every 2L fluid removed)

Most patients have drain removed within 24 hours. Symptomatic benefit is most marked after first few litres removed. Drains left in indefinitely continue to drain as ascites reaccumulates.

If symptomatic benefit, arrange repeat paracentesis as required.

Consideration should be given to a long term PleurX peritoneal catheter.
This is often an attractive option for patients not receiving anti-cancer treatment.
Normally discussed with patients oncologist taking into consideration prognosis and planned anti-cancer treatment.

Subsequent Management Options

1. **Systemic Anti-Cancer Treatment** is useful if underlying malignancy likely to respond and the patient fit enough for treatment.
2. **Diuretics** may be effective in some patients especially if massive liver metastases causing portal hypertension (serum/albumin gradient >11g/L).
   U&E and electrolytes need checked at baseline and monitored.
   - Spironolactone (e.g. starting 100-200mg/day, increased by 100mg every 3-7 days, normal maintenance dose 300mg/day).
   - If no response after 2 weeks and renal function satisfactory, consider addition of furosemide (starting 40mg/day). Response may take up to 4 weeks to be evident. Discontinue if not tolerated or not benefiting.
3. **Peritoneovenous shunts** are rarely used as high complication rate often outweighs benefits.

Prognosis

Ascites is indicative of disseminated disease and generally associated with a poor prognosis. However optimally treated Stage III ovarian cancer presenting with ascites can result for example in a 30-40% 5 year survival. It is therefore important patients are assessed for suitability for investigation and treatment.

Reference

Therapeutic paracentesis in the management of malignant ascites, NI Cancer Centre and Bridgewater suite – BHSCT hub version 1, June 2017. Dr P Wilkinson et al - accessed December 2020

Brain Metastases

- These account for the vast majority of all intracranial tumours.
- The most common tumour types to metastasise are lung, breast, kidney, cancer of unknown primary, melanoma and colon.

Symptoms and signs

Symptoms can vary depending on the level and rate of change in pressure caused by the metastases. Classical features include

- Headache (worse on wakening and exacerbated by a change in posture, sneezing, coughing or straining).
- Nausea and vomiting
- Confusion / changing mood or personality
- Focal neurological deficit
- Impaired consciousness
- Seizures

Investigations

Bloods	FBP, Coagulation, blood culture (if infection suspected).
CT brain	Good for demonstration of acute haemorrhage, oedema, mass effect and hydrocephalus
CT after intravenous contrast	Will detect most metastases.
MRI brain	May demonstrate metastases not visualised on CT, particularly in the posterior fossa. Also useful for further characterisation of suspected abnormalities seen on CT: discuss with local Radiologist
CT chest/abdomen/pelvis	If first presentation of cancer to look for primary site and extent of extracranial disease.
Stereotactic biopsy	Discuss with neurosurgery – may be considered in new cancer presentation with no systemic disease to biopsy.

Initial Management

Refer to Local Acute Oncology Team or referral to neurosurgical team if clinically indicated

Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

1. **Corticosteroids to improve neurological symptoms**.

- Dexamethasone 8mg BD IV/PO (am and lunchtime) with PPI cover if significant symptoms or mass effect.
- Lower doses may be sufficient if only mild symptoms (e.g. 2-4mg BD). Steroids are not required in asymptomatic patients.
- Oral dexamethasone preferred unless highly symptomatic/unable to swallow.
- Dexamethasone can be slowly tapered down to lowest dose required to control symptoms. If patient is for radiotherapy steroids should start to be reduced after completing radiotherapy, which may initially worsen oedema.
- If evidence of hydrocephalus senior discussion with neurosurgery if felt appropriate for consideration of surgical intervention or use of mannitol.

2. **Supportive measures with analgesia and antiemetics.**

3. **Commence anti-convulsants if seizures.**
   - Acute treatment of seizures as per standard practice.
   - Prophylactic use of anti-convulsants in the absence of seizures is not indicated.
   - Long term regular anti-convulsants are recommended after the ***first*** seizure in patients with a space occupying lesion.
   - Discuss with neurology team about best choice of agent. Keppra (Levetiracetam) is commonly prescribed as a first line agent.

4. **Studies demonstrate anticoagulation (LMWH) can be used safely in patients with brain metastases for venous thromboembolism prophylaxis and treatment**.
   - Even in patients with melanoma with haemorrhagic brain metastases, anticoagulation has not been shown to significantly increase the risk of intracranial haemorrhage.

5. **Advise the patient they must not drive and should inform the DVA for further driving advice.**

6. **Consider referral to Physiotherapy and OT as patients may present with cognitive or functional changes which may impact on safety.**

Subsequent Management

Options depend on number, size and location of brain metastases, performance status, co-morbidities, whether systemic disease is controlled and an assessment of prognosis.

Solitary or a small number of brain metastases may be considered for surgical excision or stereotactic radiotherapy. These cases will be discussed at the neurosurgical MDM and should be discussed directly with one of the core members of the MDM.

Whole brain radiotherapy may be indicated for multiple brain metastases from a known primary in patients well enough to receive treatment. It may offer temporary tumour control, modest improvement in survival and allow a reduction in steroids without deterioration in symptoms. Careful consideration is required however as to whether radiotherapy will benefit the patient and referral to palliative care should also be considered.

Some SACT agents can be effective against brain metastases and may be an early choice, especially in asymptomatic patients and/or sensitive primary tumours

Reference

Lin X, DeAngelis L. Treatment of brain metastases, Journal of Clinical Oncology. 2015. Oct 20; 33(30); 3475-84

Central Venous Access Device Complications

- Indwelling CVADs are commonly used in oncology patients.
- Provides reliable venous access for patients requiring a wide range of therapies including chemotherapy, phlebotomy, blood product transfusions and other supportive measures.
- The most commonly used CVADs are:
- Peripherally Inserted Central Catheters (PICCs)
- Tunnelled Catheters (‘Hickman lines’)
- Implantable Ports (‘Portacaths’)

Management

Refer to local Acute Oncology Service or infusional services for advice.

Infection

- Exit site infections usually respond to oral antibiotics alone, tunnel infections require treatment with parenteral antibiotics. For suspected exit site infections (erythema, pain or discharge around the exit site) a swab should be taken and results of previous swabs reviewed. If the infection fails to resolve IV antibiotics may be required.
- A fever/rigor related in time to access of a central line (characteristically 15-45 minutes post flushing) should be treated as a catheter related bacteraemia unless an alternative source of infection is obvious clinically.
- Treatment requires appropriate cultures and a decision as to whether the catheter requires immediate removal, or whether a period of observation with appropriate treatment is required.
- Paired blood cultures i.e. both central and peripheral are important in considering whether a bacteraemia is catheter related. The source of the blood must be clearly labelled on each blood culture bottle.
- A diagnosis of catheter related bacteraemia is highly probable when culture samples obtained from the catheter become positive at least 2 hours earlier than those from blood cultures. Microbiology will advise.
- A laboratory confirmed catheter related bacteraemia is indicated by the identification of the same organism from blood cultures and line tip culture.
- **Removal of long term lines must be discussed with senior clinician.** A significant proportion of CVADs will not require removal if the patient remains clinically stable. Removal should always be considered urgently in neutropenic patients with CVAD infections.
- Refer to local trust guidelines for empirical antibiotic prescribing in adults for management of CVAD infections. IV antibiotics **should not** be administered via the CVAD if CVAD infection suspected unless no other means of venous access.

Occlusion

- Inability to infuse through catheter or to withdraw 2ml of blood despite standard procedures. Causes include catheter malposition or device failure, intra-luminal clotting or precipitate, fibrin sleeve, external compression or venous thrombosis. PICCs and tunnelled catheters are flushed once weekly and implantable ports once

monthly when not in use. All are flushed before/between/after drug administration and immediately following blood sampling.

- Always ensure there is no delay in flushing following completion of IV infusions
- CVADs should be flushed using a pulsatile (push-pause) method, completing procedure using a positive pressure technique

If occlusion occurs;

Check catheter for extrinsic compression e.g. kinking, clamps and assess if occlusion related to postural changes. Check history of recent infusions and care of catheter.

- Assess for signs of arm oedema, redness, pain and signs of SVC obstruction.
- Repeated aspiration by gentle pressure and suction action using 10mls 0.9% sodium chloride may be of benefit.
- PA chest x-ray for verification of tip position.
- If tip position satisfactory Urokinase administration will be required
- If problems persist a linogram will be required which can demonstrate a fibrin sheath if present. Treatment with urokinase can be effective.

Thrombosis

- If patient symptomatic: shoulder, jaw pain, oedema, cyanosis, SVCO, catheter occlusion, a Doppler ultrasound or venogram should be performed to confirm thrombosis.
- Treatment is based on severity
- Recommended treatment in patients without future access needs is removal
- All patients should be treated with LMWH
- If the catheter is to be salvaged and functioning, continue with treatment for the duration of the catheter required, provided symptoms settle

The duration of anticoagulation is in discussion with the patient's consultant – see section entitled venous thromboembolism

Migration

- Migration can be seen as lengthening or shortening of the catheter on measurement

- The ideal tip position for CVADs is the lower third of the superior vena cava or near its junction with the right atrium. If in doubt discuss with a radiologist/ infusional services/acute oncology team
- If a catheter migrates internally or externally by 2cm or more, reassess catheter tip position by PA chest x-ray.
- Do not administer any solutions via the catheter until X ray is reported
- There may be exceptional circumstances depending on the patient's condition, prognosis and venous access where a migrated PICC may be acceptable to the treating Consultant but it must be documented in writing.
- If catheter malpositioned it should be discussed immediately with infusional services/interventional radiology/ acute oncology team.

Reference

Adapted from McParlan, D, Infusional Services Co-ordinator, Infusional Services Team, Benson, G., Regional haemophilia Centre Director. Central Venous Access Device Guidelines - (excluding non-tunnelled catheters) (BHSCT, 2017).

Diarrhoea (treatment related)

- SACT and radiotherapy induced diarrhoea is common. It requires prompt and effective management to prevent escalating severity. It can be life threatening, particularly if the patient is neutropenic.
- Anti-cancer drugs most frequently associated are fluropyrimidines (fluorouracil, 5-FU, capecitabine), irinotecan, tyrosine-kinase inhibitors (e.g. gefitinib, sunitinib) and small molecule monoclonal antibodies (e.g. cetuximab) and immunotherapy (e.g. Ipilimumab and Pembrolizumab).
- Radiation induced diarrhoea is generally an acute side effect from pelvic/abdominal radiotherapy, although there is the possibility of persistent or chronic gastro-intestinal symptoms. It is more common and severe if patients are receiving concurrent chemoradiotherapy.
- Other causes of diarrhoea which need assessed for include:
  - Infective episodes including *Clostridium Difficile*
  - Medications (e.g. antibiotics, laxatives, oral electrolyte replacements, metoclopramide, proton pump inhibitors, NSAIDs)
  - Constipation with overflow

- Sub-acute obstruction e.g. colonic tumour in situ, post-surgical adhesions
- Malabsorption in biliary and pancreatic malignancies
- Hypersecretion of 5HIAA in carcinoid tumours
- Other co-morbidities e.g. hyperthyroidism, inflammatory bowel disease.

Symptoms and signs

Symptoms: Assess previous normal bowel function, onset and duration of diarrhoea, number of stools and stool composition. Important questions include presence of nocturnal diarrhoea, steatorrhoea or urgency of defecation/faecal incontinence.
Check for fever, abdominal pain, symptoms of dehydration and weakness as well as a detailed medication and dietary history (high fibre, high lactose diets can contribute). Check for problems outside the GI tract e.g. chest/urinary sepsis, recent travel, infectious contacts and other treatment related side effects e.g. nausea/vomiting, mouth ulceration, red hands or feet.

Signs: Check for fever, dehydration, abdominal distension/tenderness, abnormal/absent bowel sounds, peri-anal/rectal or peristomal abnormalities.

Grading of Diarrhoea NCI CTCv5.0

	Grade 1	Grade 2	Grade 3	Grade 4
Frequency of Stool	Increase of <4 stools/day over baseline; mild increase in stoma output compared to baseline	Increase of 4-6 stools/day over baseline; moderate increase in stoma output compared to baseline; limiting instrumental ADL	Increase of ≥ 7 stools/day over baseline; hospitalization indicated; severe increase in stoma output compared to baseline; limiting self-care ADL	Life threatening consequences; urgent intervention indicated.

Investigations

Bloods	FBP, U&E, Bone profile, LFTS, CRP
Stool O+S	Urgent stool samples should be sent ASAP **but results are not needed prior to starting anti-diarrhoeals.**
Abdominal x-ray	To exclude bowel obstruction or faecal impaction.
Other investigations as indicated. Examples include • CT abdomen if signs of peritonism (guarding, rebound tenderness) to assess for small/large bowel involvement, neutropenic enterocolitis (typhlitis) or complications e.g. perforation, abscess. • Endoscopy and biopsy after discussion with gastroenterology. Colonoscopy relatively contraindicated if suggestion of neutropenic enterocolitis due to risk of perforation.	

- Additional investigations as advised by gastroenterology e.g. for pancreatic insufficiency (faecal elastase), bile acid malabsorption or small bowel bacterial overgrowth.

General Management Principles

Interrupt any systemic anti-cancer therapy including oral drugs until discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

- All patients should be informed if they develop any diarrhoea to start self-medicating with loperamide, with the exception of patients receiving immunotherapy – please see separate immunotherapy guidelines available on NICaN SACT Sharepoint.
- If there is no improvement after 12 hours or Grade 3 or above diarrhoea urgent clinical assessment is required.
- Patients who are well hydrated, not vomiting and otherwise well can normally be managed at home.
- If there are any concerning features patients need admitted to hospital e.g. dehydrated, vomiting, increasing fatigue/weakness, neutropenia, fever, gastrointestinal bleeding, abdominal cramps not relieved by loperamide or previous admissions for diarrhoea.

Initial management

- **Fluid resuscitation** is crucial. Increase oral fluids and ensure adequate IV fluids if required. Careful assessment of fluid balance essential.
- **Electrolyte replacement** needs careful attention.
- **Stool chart** should be commenced**.**
- **Medication review** for any contributing drugs.
- **Dietary Advice** - Small, frequent meals as tolerated, avoiding spicy, high fibre, or high fat foods as well as raw vegetables, caffeine and carbonated drinks.

  Some patients with severe diarrhoea may try limiting milk and milk products temporarily to see if this improves symptoms, as the bowel may become temporarily lactose intolerant. Referral to a dietician should be considered.

Anti-diarrhoeals

Do NOT wait for stool cultures prior to commencing antidiarrhoeals.

Do NOT stop antidiarrhoeals even if sepsis suspected. The probability of infection in patients receiving chemotherapy with diarrhoea is low although *Clostridium.Difficile* should be excluded quickly. The patient's diarrhoea needs actively treated with antidiarrhoeals alongside any suspected infection.

- **Loperamide** is first line treatment e.g. 4mg PO stat dose followed by 2mg after each loose stool or every 2 hours to a maximum 16mg daily. Loperamide is normally continued for 12 hours after resolution of diarrhoea.
- **Codeine phosphate** can be tried as an alternative or adjunct to loperamide e.g. 30-60mg, maximum 4 times daily. (Can cause dose limiting nausea and sedation).
- **Octreotide**, a somatostatin analogue, is recommended for Grade 1-2 diarrhoea which is persisting despite loperamide or first line in Grade 3-4 diarrhoea.

  It is normally delivered via a syringe driver e.g. Starting dose of 300micrograms/24hrs, titrating up in 300mcg increments to 1500mcgs every 24 hours if required.

  It can normally be discontinued 24 hours after resolution of diarrhoea.

Summary treatment algorithms can be found at the end of this chapter.

Special Considerations

For patients with **Irinotecan** associated diarrhoea please see appendix at the end of this chapter for treatment algorithm.

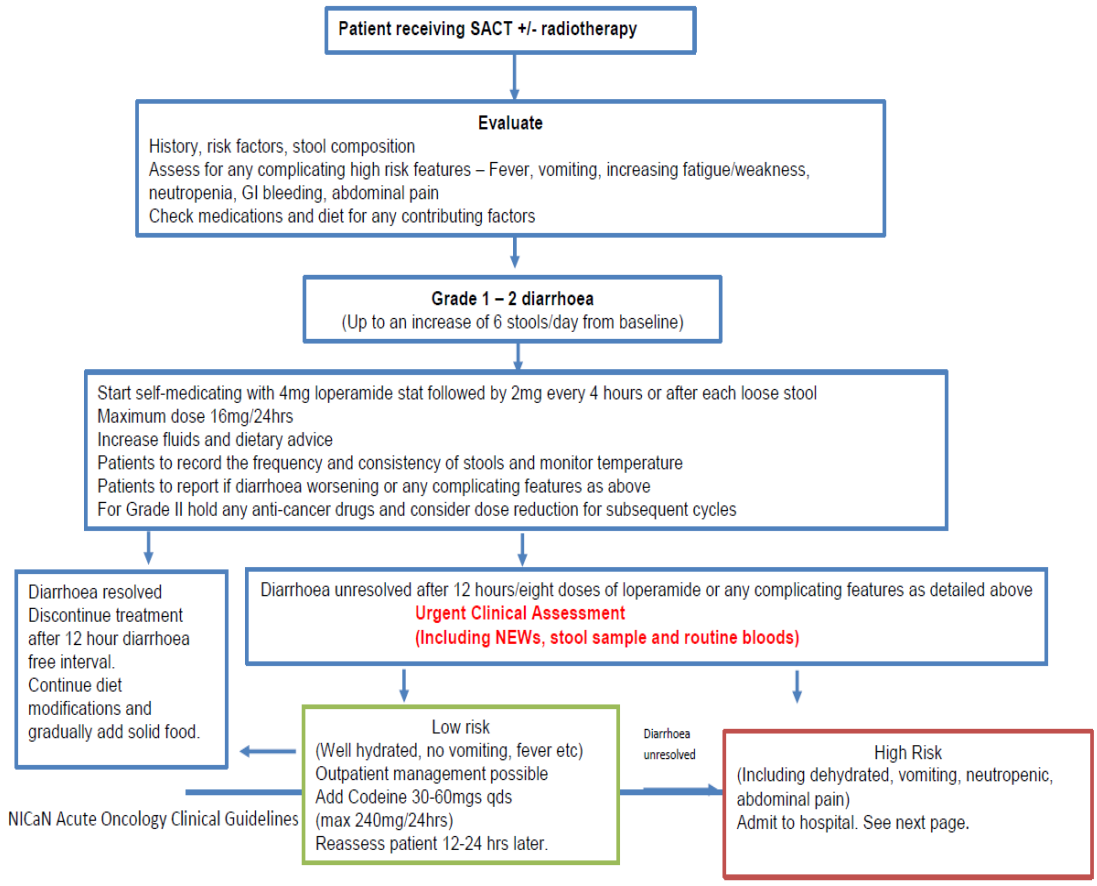
Ipilimumab, Pembrolizumab and Nivolumab are examples of immunotherapies being increasingly used across a range of sites including advanced melanoma, lung and genitourinary cancers. Patients can develop severe diarrhoea secondary to an immune mediated colitis. It is essential the patient's own oncology team is involved from the earliest opportunity –high dose steroids (PO/IV) may be required. Please refer to regional immunotherapy guidelines available on NICaN SACT SharePoint For patients on continuous **5FU** or **Capecitabine** therapy, *treatment should be interrupted for Grade II or above diarrhoea*. Note that severe diarrhoea (and mucositis) early in

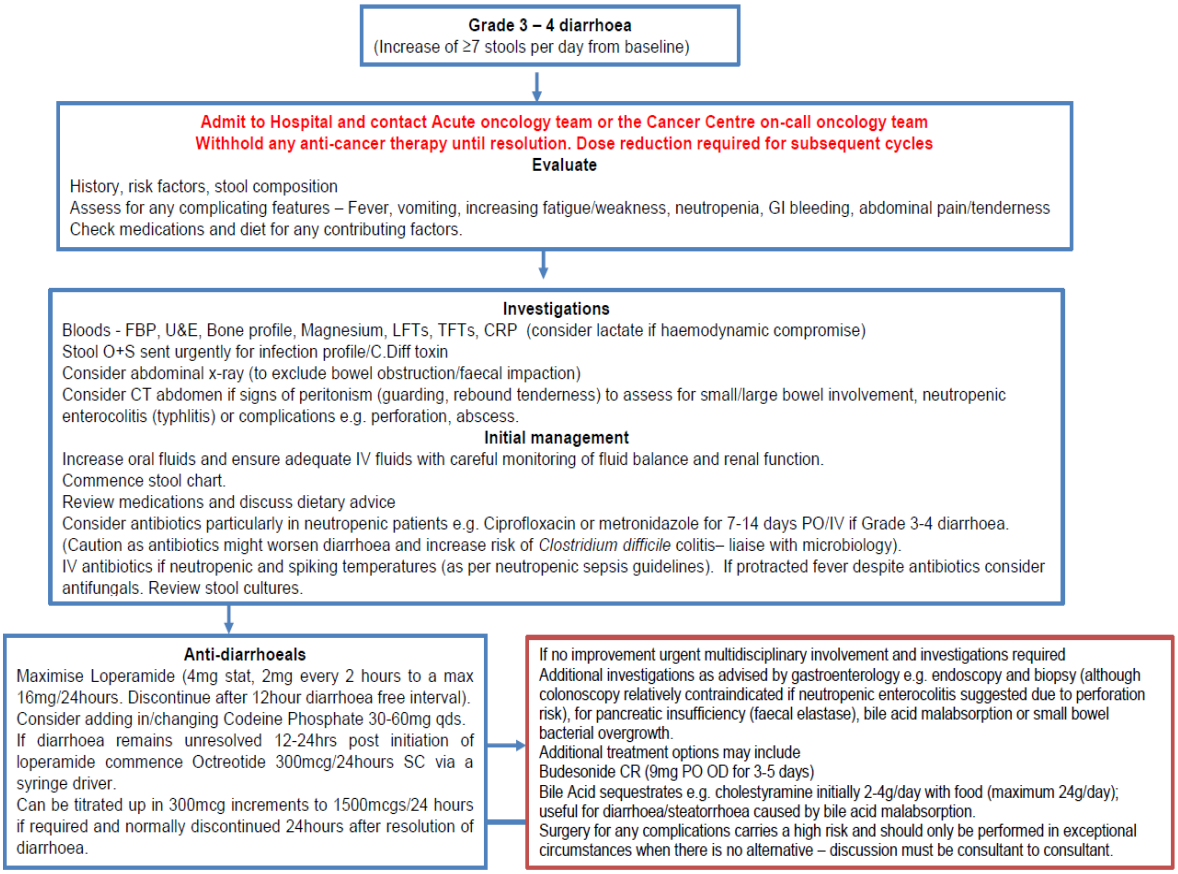
the first cycle can be due to DPD enzyme deficiency, in which case severe neutropenia can quickly follow.

References

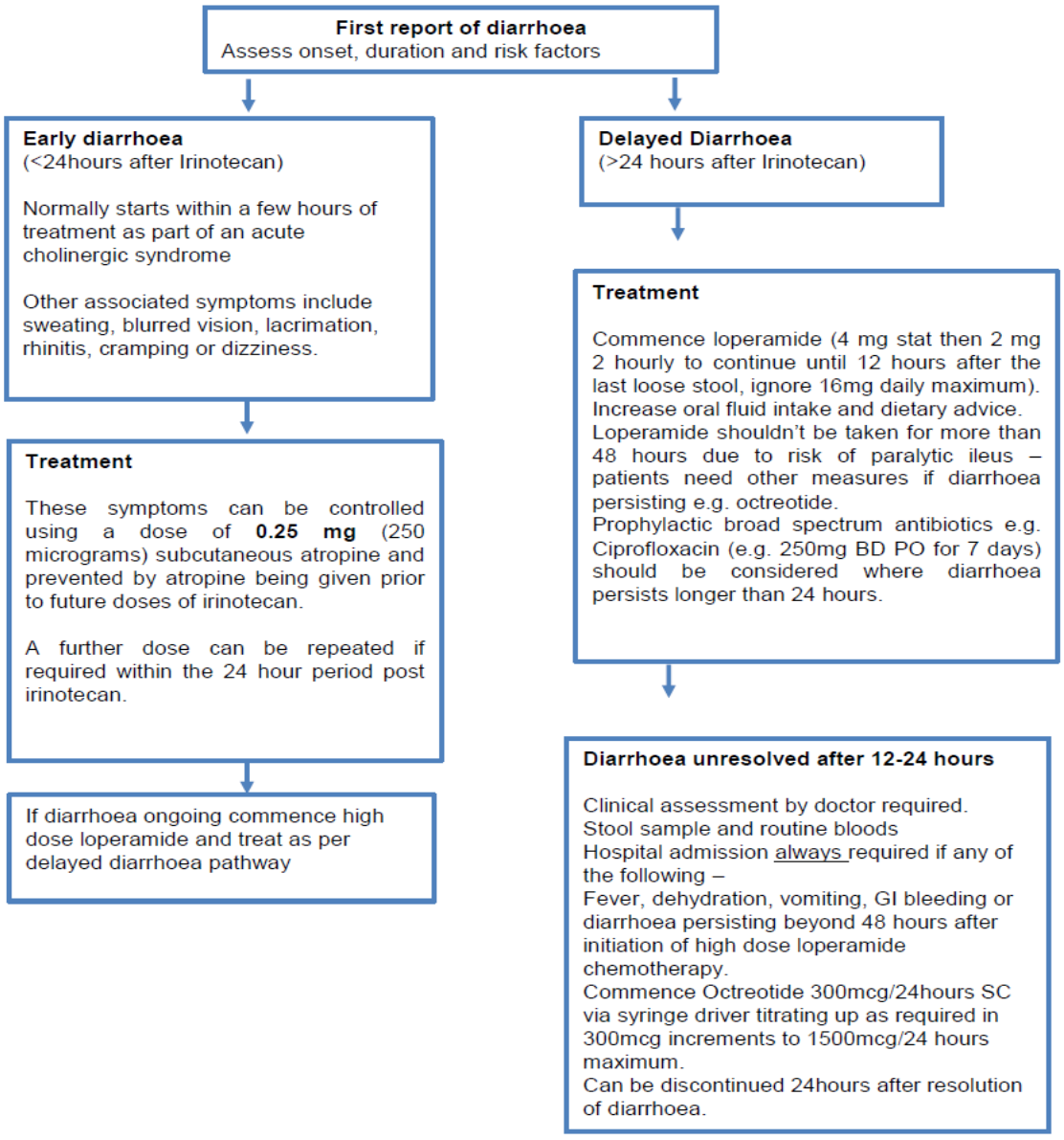
- *Andreyev J et al. Guidance on the management of diarrhoea during cancer chemotherapy. Lancet Oncology 2014; 15: e447-60.*
- *Benson et al. Recommended Guidelines for the Treatment of Cancer Treatment Induced Diarrhoea. JCO 2004; 22(14): 2918-2926.*

Treatment algorithm for management of treatment induced diarrhoea.




Grade 3 – 4 diarrhoea
(Increase of ≥7 stools per day from baseline)
Admit to Hospital and contact Acute oncology team or the Cancer Centre on-call oncology team
Withhold any anti-cancer therapy until resolution. Dose reduction required for subsequent cycles
Evaluate
History, risk factors, stool composition
Assess for any complicating features – Fever, vomiting, increasing fatigue/weakness, neutropenia, GI bleeding, abdominal pain/tenderness
Check medications and diet for any contributing factors.
Investigations
Bloods - FBP, U&E, Bone profile, Magnesium, LFTs, TFTs, CRP (consider lactate if haemodynamic compromise)
Stool O+S sent urgently for infection profile/C.Diff toxin
Consider abdominal x-ray (to exclude bowel obstruction/faecal impaction)
Consider CT abdomen if signs of peritonism (guarding, rebound tenderness) to assess for small/large bowel involvement, neutropenic enterocolitis (typhlitis) or complications e.g. perforation, abscess.
Initial management
Increase oral fluids and ensure adequate IV fluids with careful monitoring of fluid balance and renal function.
Commence stool chart.
Review medications and discuss dietary advice
Consider antibiotics particularly in neutropenic patients e.g. Ciprofloxacin or metronidazole for 7-14 days PO/IV if Grade 3-4 diarrhoea.
(Caution as antibiotics might worsen diarrhoea and increase risk of Clostridium difficile colitis– liaise with microbiology).
IV antibiotics if neutropenic and spiking temperatures (as per neutropenic sepsis guidelines). If protracted fever despite antibiotics consider antifungals. Review stool cultures.
Anti-diarrhoeals
Maximise Loperamide (4mg stat, 2mg every 2 hours to a max 16mg/24hours. Discontinue after 12hour diarrhoea free interval).
Consider adding in/changing Codeine Phosphate 30-60mg qds.
If diarrhoea remains unresolved 12-24hrs post initiation of loperamide commence Octreotide 300mcg/24hours SC via a syringe driver.
Can be titrated up in 300mcg increments to 1500mcgs/24 hours if required and normally discontinued 24hours after resolution of diarrhoea.
If no improvement urgent multidisciplinary involvement and investigations required
Additional investigations as advised by gastroenterology e.g. endoscopy and biopsy (although colonoscopy relatively contraindicated if neutropenic enterocolitis suggested due to perforation risk), for pancreatic insufficiency (faecal elastase), bile acid malabsorption or small bowel bacterial overgrowth.
Additional treatment options may include
Budesonide CR (9mg PO OD for 3-5 days)
Bile Acid sequestrates e.g. cholestyramine initially 2-4g/day with food (maximum 24g/day); useful for diarrhoea/steatorrhoea caused by bile acid malabsorption.
Surgery for any complications carries a high risk and should only be performed in exceptional circumstances when there is no alternative – discussion must be consultant to consultant.

Treatment algorithm for management of Irinotecan chemotherapy induced diarrhoea.



Chemotherapy Extravasation

While extravasation is possible with IV injection of any SACT agent it is only considered problematic with those compounds, which are vesicants, exfoliants or irritants.

Vesicants: Capable of causing pain, inflammation and blistering of local skin, underlying flesh and structures, leading to tissue death and necrosis.

Exfoliants: Capable of causing inflammation and skin shedding, but less likely to cause tissue death.

Irritants: Capable of inflammation and irritation, rarely proceeding to breakdown of tissue.

Inflammatory agents: Capable of mild to moderate inflammation and flare in local tissue.

Neutral: Do not cause inflammation or damage.

Check SACT Extravasation Extant List on NICaN SACT SharePoint however this list is not exhaustive. There are other drugs for which the risk of extravasation injury is unknown. For investigational medicinal products used in clinical trials information may be available from the trial sponsor or clinical trials pharmacist.

Extravasation Management – Peripheral Site

- Stop SACT and any other infusions being administered via affected cannula.
- Do not remove cannula initially.
- Ensure personal protective equipment is being worn.
- Mark the area affected with a pen and ensure exact measurements of affected area are recorded in patient's notes.
- Attach a 10ml syringe and attempt to withdrawal residual drug and if possible some blood back.
- Identify the drug and apply any drug specific treatment – refer to NICaN Extravasation Policy flowchart within NICaN Policy: Management of Systemic Anti-Cancer Therapy (SACT) Extravasation (see NICaN SACT CMG SharePoint site.)
- Remove the cannula
- If no specific management recommended apply 1% hydrocortisone cream to affected area.
- Avoid applying pressure as this will increase the area of extravasation.

- **Follow up**: Provide analgesia if required. Ask patient to keep arm elevated for 48 hours and report any changes or deterioration (written information to be provided to patient also). If a vesicant, exfoliant or irritant drug involved should be reviewed after 24 hours and at appropriate intervals until resolution. If a vesicant injury has occurred medical team must be aware and will decide if admission required.

Documentation: Document incident in patient's medical/nursing notes; consider photographing the area for notes. If a patient extravasates, an IR1 must be completed and the treatment must be documented in the patient's notes/ on RISOH.

Extravasation Management – Central Venous Access devices

The incidence is lower but the severity may be greater due to later detection. Extravasation may occur if a patient complains of changes in sensation, pain, burning or swelling at any point along the catheter pathway or in the ipsilateral chest, or if a change in IV flow rate occurs.

Extravasation in the tunnelled subcutaneous section is treated in the same way as other extravasation injuries above. A diagnosis is most readily made if 10mL of sodium chloride 0.9% is injected rapidly down the line. This usually raises a bleb at the point of damage/leakage allowing targeted treatment.

Extravasation in the deep implanted area is rare but far more serious. If suspected, the patient requires admission for analgesia, antibiotics and assessment. Local debridement may be necessary with plastics input.

Reference:

McGrady M. Management of Systemic Anti-Cancer Therapy Extravasation – NICaN guidelines (February 2020)

Drug Specific Management Procedures

Refer to the - NICaN AOS SharePoint - Drug Specific Management Procedures

Hypercalcaemia of Malignancy

Hypercalcaemia of malignancy occurs in around 10% of patients. It most commonly occurs in patients with advanced disease and is an indicator of poor prognosis with median survivals of 3–4 months. Tumours most often associated with hypercalcaemia include myeloma, breast, lung (usually squamous or adenocarcinoma) with renal, thyroid, head &neck and prostate cancers accounting for the remainder.

Causes: in 80% of cases hypercalcaemia is a paraneoplatic effect of ectopic tumour production of PTHrP (parathyroid hormone related peptide). In around 20% of cases it is due to calcium release from bone metastases.

Signs and symptoms

General – fatigue, dehydration, thirst, polyuria, anorexia, nausea, constipation

Neurological – confusion, anxiety, seizures, coma, psychosis

Cardiac – bradycardia, arrhythmia, prolonged PR interval, prolonged QT

Investigations

Serum calcium corrected for albumin	**Definition**: **corrected serum Calcium > 2.6 mmol/L** <3.0mmol/L – mild, may be asymptomatic 3.0-3.5mmol/L – moderate, requires treatment >3.5mmol/L – severe, urgent treatment
U&E	Frequently deranged with clinical dehydration, hypomagnesaemia
PTH	Not routinely required in cases of known metastatic cancer in which hypercalcaemia is a recognised feature. PTH will be normal or low in malignant hypercalcaemia
Bone scan	Not routinely required unless patient has symptomatic bony pain and there is a clinical suspicion of bone metastases
ECG	May see changes in severe hypercalcaemia

Management

Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

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Management of Hypercalcaemia of Solid Malignancy in Adults

The severity of symptoms correlates more closely with the **rate** of calcium increase rather than the actual level

Normal Range Corrected Calcium: 2.2- 2.6 mmol/l

Decision to treat should be based on patient symptomology rather than absolute calcium level [1]

Consider: The patient's symptoms, Life expectancy, Presence of other disorders, Renal and cardiac function

Clinical features

General: dehydration, weakness and fatigue

Neurological: fatigue, lethargy and confusion

GI: anorexia, vomiting, pain

Cardiac: shortened QT, prolonged PR, arrhythmias

Renal: polydipsia, polyuria

Hypercalcaemia is a poor prognostic indicator – mortality can be 50% within 30 days diagnosis [2-4]

This guidance recommends therapy should be initiated for symptomatic patients and/or those who have serum corrected calcium >3.0mmol/l

<3.0mmol/l
Often asymptomatic and may not need urgent correction

3.0-3.5mmol/l
May be well tolerated if has risen slowly, may be more symptomatic and prompt treatment as below is usually indicated

>3.5mmol/l
Requires urgent correction due to risk of dysrhythmia and coma

Decision to treat

- Rehydration with Sodium Chloride 0.9% IV
- Adjust rate and quantity in each patient according to age, severity of hypercalcaemia, degree of dehydration and ability of cardiovascular and renal system to tolerate

Decision not to treat

- Drugs which reduce renal blood flow or renal calcium excretion should be discontinued / avoided where appropriate (for example non-steroidal anti-inflammatory agents and thiazide diuretics)
- Encourage mobility and oral fluid intake.

Treat with IV Bisphosphonate - Zoledronic Acid IV [3,4], dilute in 100mls of sodium chloride 0.9% or 100mls of glucose 5% and infuse over 15-30 minutes. Monitor renal function and check serum creatinine prior to initiation. Consider specialist advice if creatinine clearance (NOT eGFR) < 30ml/min

Serum Creatinine and CrCl	Dose
< 400microgram/L AND CrCl >30ml/min	4mg
> 400microgram/L OR CrCl <30ml/min	See below

If serum creatinine >400microgram/L, or creatinine clearance (NOT eGFR) <30ml / min consider:

- Ibandronic acid [7] – lower initial dose recommended in severe renal impairment

Creatinine Clearance (CrCl) ml/min	Ibandronic Acid [7] Dose (in 500mls Sodium Chloride 0.9% /2hrs)
< 30ml/min	2mg

- Denosumab [8-12] (unlicensed indication) Can be considered in cases of renal impairment or persistent hypercalcaemia. Specialist Advice should be sought

- Calcitonin may be used in the first 24 to 48 hours following bisphosphonate administration to transiently reverse severe symptomatic hypercalcaemia while awaiting the therapeutic effect of bisphosphonate therapy [6]

- Clinical utility limited by transient effect, side effects and tachyphylaxis

Dose: 4-8 international units / kg intramuscularly / subcutaneously every 12 hours

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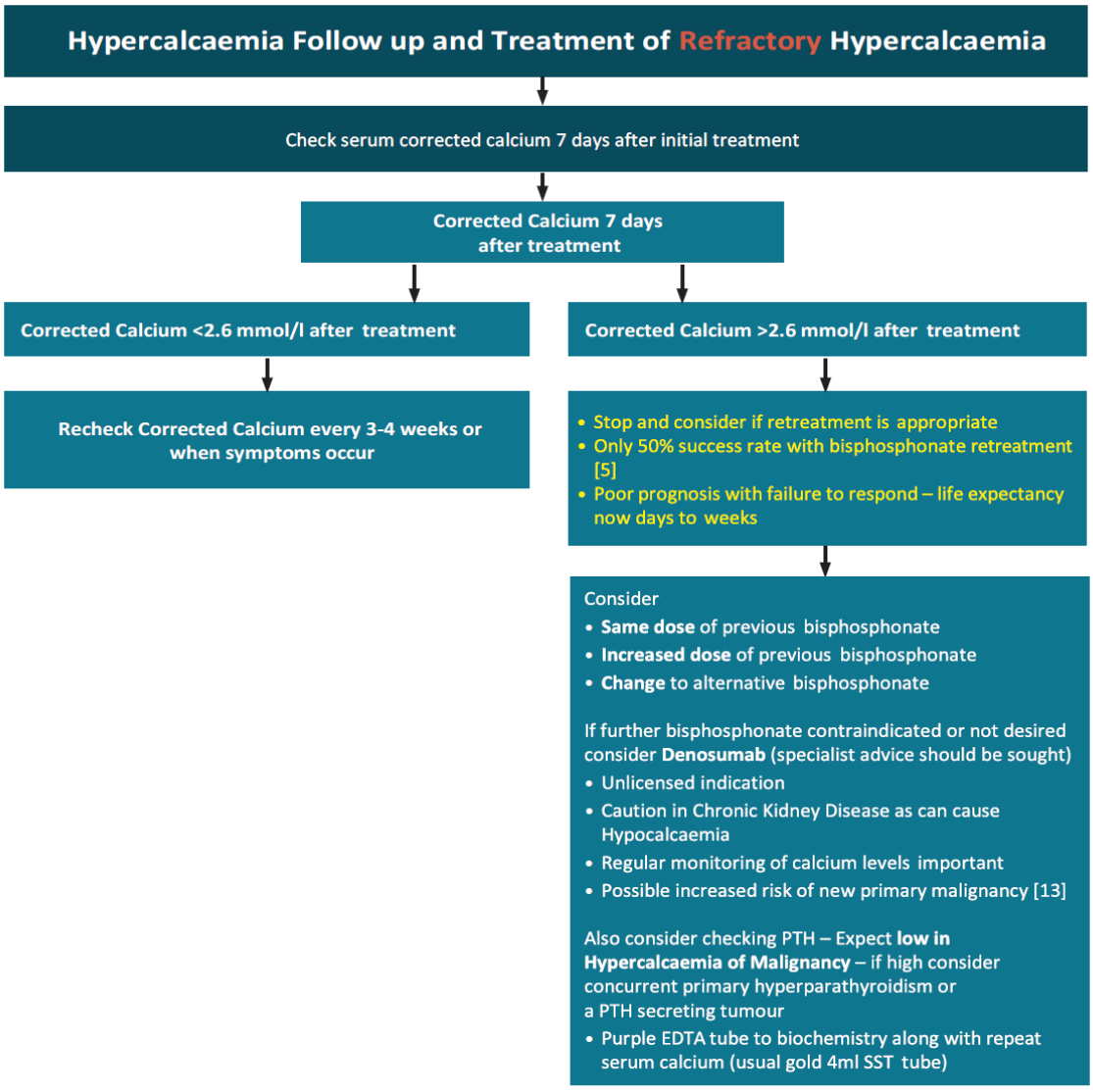
Management of Hypercalcaemia of Malignancy (HOM)
Refractory to initial treatment



produced by Dr Catherine Doherty (ST6 Palliative Medicine) and Chris Black Specialist Palliative Pharmacist

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13. Medicines and Healthcare products Regulatory Agency. Denosumab (Xgeva) for advanced malignancies involving bone: study data show new primary malignancies reported more frequently compared to zoledronate. Jun 2018 [internet publication].

Please contact Specialist Palliative Care Team for further advice if required.

References

Northern Ireland Palliative Care Regional Guidelines 2019

Hypomagnesaemia

- Common causes in oncology patients: drugs, systemic anti-cancer treatment e.g. platinum chemotherapy, diuretic therapy, total parenteral nutrition with inadequate magnesium, gastrointestinal losses, poor nutrition or malabsorption.
- Whilst serum levels usually rise quickly with therapy, intracellular stores take longer to replete – it is advisable if normal renal function to continue magnesium repletion for at least 1-2 days after serum magnesium concentration normalizes.
- Apparent hypomagnesaemia will complicate hypoalbuminaemic states –there is no reliable calculation to correct for albumin levels but caution advised when interpreting magnesium levels in severely hypoalbuminaemic states (serum albumin <25 g/l).
- Plasma magnesium concentrations are regulated solely by renal excretion. IV doses in particular can result in hypermagnesaemia when GFR is severely impaired (eGFR<30ml/min) and close post infusion magnesium monitoring is warranted.

Symptoms and signs

Symptoms are often non-specific and unrecognised.

Muscle weakness, cramps, carpopedal spasm or seizures may accompany hypomagnesaemia with or without hypocalcaemia. Mental changes and cerebellar signs may be associated with more severe magnesium depletion.

Investigations

Bloods	Renal function, magnesium and other electrolytes including potassium, phosphate, calcium, albumin.
ECG	Prolonged PR interval widened QRS and prolonged QT possible with severe magnesium depletion.

Management

Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

Correct calcium and potassium abnormalities.

Mild	0.5-0.7 mmol/l	Oral magnesium is poorly absorbed and larger doses are poorly tolerated due to GI side effects. Prophylactic low dose PO therapy may be indicated in at risk subjects. A total of 20-24 mmol magnesium daily in divided doses is recommended. Oral magnesium products include- **Magnesium aspartate** 6.5 g sachets (10 mmol Mg2+ per sachet) - one sachet BD. Magnesium glycerophosphate tablets (4 mmol Mg2+ per tablet) – two tablets TID. This is an unlicensed preparation and should only be used for patients unable to tolerate magnesium aspartate sachets. Should be given with or after food to minimise risk of diarrohea If intolerant of PO treatment and patient is symptomatic, consider IV infusion of 2g (8 mmol) magnesium (4 ml magnesium sulphate 50% injection) in 100ml sodium chloride 0.9% over 1 hour. If eGFR 15-30 ml/min, administer over 4 hours. If eGFR<15ml/minute, administer over 6 hours.
Moderate	0.3-0.5 mmol/l Normal renal function	**IV infusion** of between 2-5g (8-20mmol) magnesium (4-10ml magnesium sulphate 50% injection), depending on serum magnesium level, in 100mls sodium chloride 0.9% over **1 hour**, if renal function normal. Consider rechecking serum magnesium in 24 hours and repeat treatment if required or earlier if patient symptomatic.
	0.3-0.5 mmol/l eGFR <30ml/min	2g (8mmol) magnesium (4ml magnesium sulphate 50% injection) in 100mls sodium chloride 0.9% over **4 hours (eGFR 15-30ml/min) or over 6 hours (eGFR <15ml/min)**. Recheck 4 hours after infusion to exclude accumulation of magnesium.
Severe	<0.3 mmol/l Normal renal function	Intravenous infusion of 7g (28mmol) magnesium (14ml magnesium sulphate 50% injection) in 250ml sodium chloride 0.9% over **2 hours**. Recheck serum magnesium in 24 hours and repeat treatment if required or earlier if symptomatic. Symptomatic patients e.g. tetany, arrhythmias or seizures should have continuous cardiac monitoring.
	<0.3 mmol/l eGFR <30ml/min	2-4 g (8-16 mmol) magnesium (4-8 ml of magnesium sulphate 50% injection) in 100ml sodium chloride 0.9% over **4 -12 hours (eGFR <30ml/min) and 6-12 hours (eGFR <15ml/min)**. Recheck serum magnesium 4 hours after infusion to exclude accumulation of magnesium.

- Side effect due to hypermagnesaemia are very unlikely with magnesium replacement doses in patients with normal renal function but could include flushing, thirst, nausea and vomiting, depression of reflexes, drowsiness, hypotension, bradycardia, cardiac arrhythmias, respiratory depression and coma. In very rare circumstances hypocalcaemia may occur. Patients should be observed and monitored for these if renal failure present.
- In the exceptional circumstance of severe symptomatic hypermagnesaemia (e.g. accidental overdose) seek senior clinical advice and give 10 ml calcium gluconate 10% (2.25 mmol calcium) over 10 minutes and repeat as required.

Reference

Adapted from T Trinick, Treatment of Hypomagnesaemia in adults, SEHSCT.

Hyponatremia

- Normal plasma sodium is 135-145mmol/L.
- Symptomatic hyponatremia is usually associated with a plasma sodium <125mmol/L. Symptoms are related to the severity and rapidity of the fall in plasma sodium.
- Common causes in oncology patients include medications (diuretics, PPIs, opioids, NSAIDS, certain anti-cancer drugs, anti-depressants and anti-epileptics) and gastrointestinal losses. Other causes include renal failure, cirrhosis, congestive cardiac failure, Addison's disease and hypothyroidism.
- Syndrome of Inappropriate Anti-Diuretic Hormone secretion (SIADH) is a diagnosis of exclusion often over diagnosed in patients with cancer. It does occur more commonly in patients with small cell lung cancer and head and neck cancers.

Criteria for diagnosis of SIADH include:

- Hyponatremia
- Euvolemic
- Low plasma osmolality (<270mOsm/kg) with inappropriately high urine osmolality (>100mOsm/kg)
- Continued urinary sodium excretion >20mmol/L
- Normal renal, adrenal and thyroid function

Symptoms and signs

Symptoms: Often asymptomatic. If unwell, symptoms tend to be neurological and include malaise, nausea and vomiting, weakness, ataxia, headache, confusion, seizures and coma.

Signs: An accurate assessment of volume status is important.
Hypovolemia – decreased skin turgor, tachycardia, postural hypotension, oliguria.
Hypervolemia – raised JVP, peripheral oedema, pulmonary oedema, ascites.

Investigations

Bloods	U&E, plasma osmolality. LFTs, glucose, thyroid function. Cortisol +/- short synacthen test if adrenal failure suspected.
Urine	Urinary sodium and urine osmolality.
Chest x-ray	?pulmonary pathology causing SIADH if no other clear cause

Management

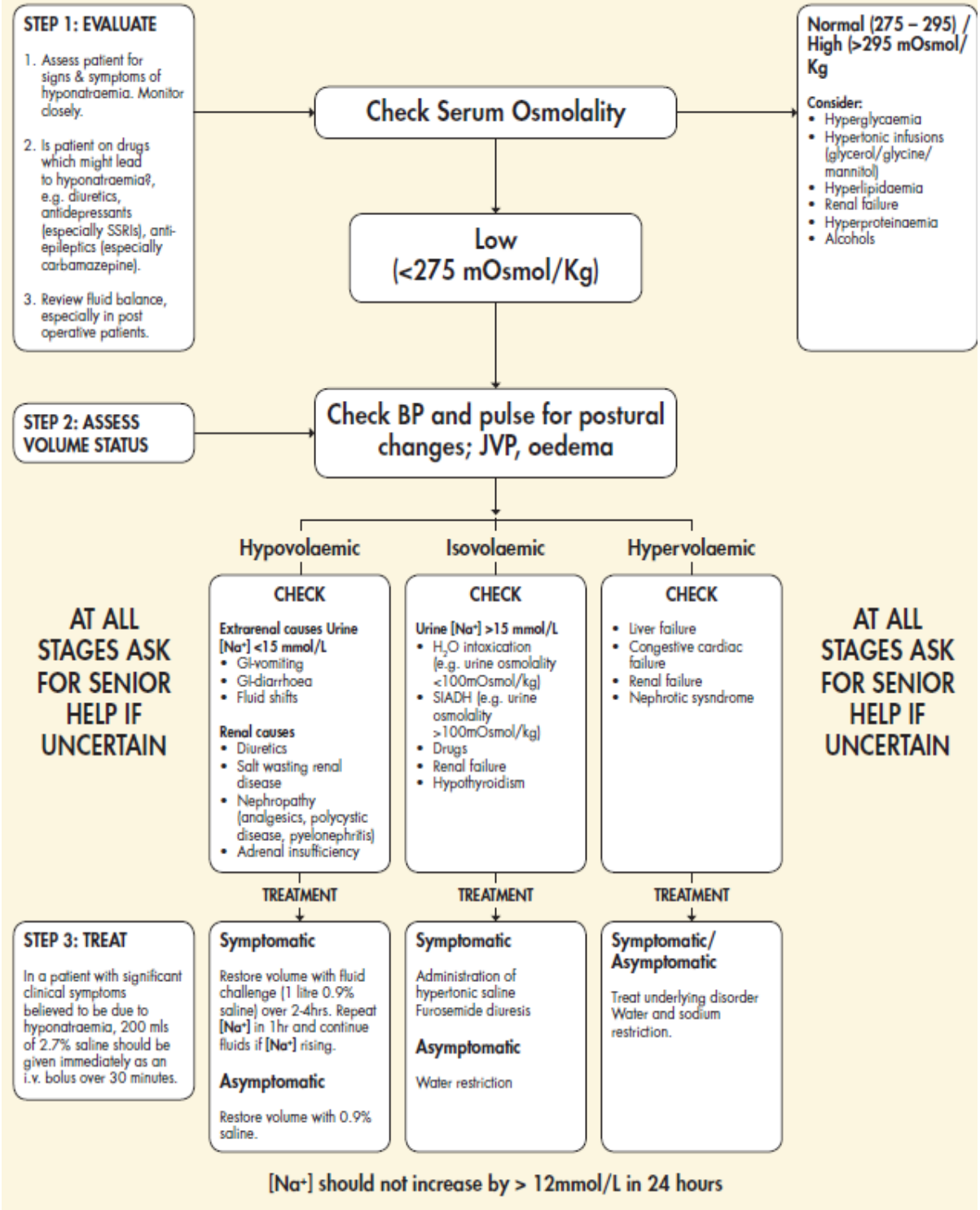
Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

This involves correction of the underlying cause and abnormal sodium concentrations.

Significant acute hyponatremia with seizures or coma – immediately seek specialist advice from clinical biochemistry.
In **chronic hyponatraemia** correction should be gradual to avoid fluid overload and central pontine myelinolysis. Aim for a rise in sodium concentration of **5-10mmol/24 hours.**

Medications must be reviewed.
See GAIN guidelines for relevant investigations and treatment dependant on fluid status. Advice can be obtained from clinical biochemistry.

HYPONATRAEMIA IN ADULTS (ON OR AFTER 16TH BIRTHDAY) – A DISORDER OF WATER BALANCE WHICH IS POTENTIALLY FATAL



GAIN
GUIDELINES AND AUDIT IMPLEMENTATION NETWORK

Subsequent management options

In patients with SIADH where fluid restriction ineffective consider:

- Demeclocycline (600mg -1200mg daily) in order to create a drug induced nephrogenic diabetes insipidus. It may take up to 2 weeks to be effective.
- Tolvaptan – an orally active ADH antagonist is sometimes considered – discuss with endocrinology team.

Reference

Adapted from Gain Guidelines Hyponatremia in adults (on or after 16th Birthday 2010) (Currently under review)(found on www.rqia.org.uk)

Gain Guidelines - Hyponatremia in Adults

Lymphangitis Carcinomatosis

- The lungs are a common site for metastatic disease. This is commonly nodular but occasionally can present as lymphangitis carcinomatosis.
- Most often associated with adenocarcinomas – breast, stomach and lung.
- Refers to diffuse infiltration of lymphatic channels by tumour, resulting in obstruction and interstitial oedema.
- Symptoms often appear disproportionate to physical signs or x-ray findings.

Symptoms and signs

Symptoms: Can include dyspnoea, dry cough, fever, night sweats and chest pain.

Signs: Can include increased respiratory rate, fine crepitations on chest auscultation.

Investigations

Chest x-ray	May be normal. Changes can include reticular/reticulonodular shadowing, septal lines and peribronchial cuffing.
High resolution CT chest	Changes can include interlobular septal thickening, thickening of the fissures and peribronchovascular thickening. May be unilateral/bilateral, focal/diffuse. Mediastinal lymphadenopathy and pleural effusions may be associated.
Further tests e.g. blood tests and ECG may be helpful when considering other differentials including infection and pulmonary oedema.	

Management

Refer to local Acute Oncology Service

Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

1. Exclude infection, particularly atypical infections such as pneumocystic jiroveci pneumonia especially if patient has had previous immunosuppressive treatments or lung radiotherapy
2. Symptomatic treatment of dyspnoea and cough.
3. Steroids may offer relief e.g. Dexamethasone 8mg PO BD (am and lunchtime) with PPI cover

   Trial for 1 week. If helpful then titrate down to lowest effective dose.

   If no symptomatic improvement stop.
4. Systemic treatment e.g. chemotherapy or hormone therapy may be helpful if disease remains responsive to treatment.

Prognosis

Prognosis is poor and often limited to weeks or short months. It is however dependent on the underlying disease and response to treatment. Patients should be considered for specialist palliative care input.

Malignant Bowel Obstruction

Bowel obstruction can occur in patients with metastatic cancer from almost any diagnosis but occurs most commonly in patients with metastatic gynaecological, bowel or stomach cancer. This guideline is **not applicable** to patients presenting for the **first time with bowel (colon) cancer** even in the presence of metastatic disease. Those patients should be immediately discussed with the surgical team regarding surgery. Patients may be still potentially curable even if both colon and subsequent liver resection is required.

Obstruction can be

- **Malignancy related** (small or large bowel) – average life expectancy is normally less than 3 months but this can be significantly improved if systemic treatment is appropriately administered following resolution of the acute episode.
- **Non-malignancy related** – e.g. secondary to adhesions or post-operative complications.

Symptoms and signs

Symptoms: Abdominal pain, colic, nausea, heartburn/reflux symptoms, vomiting, constipation**.**

Signs: Hydration status, abdomen – ascites, palpable masses, bowel sounds, succession splash, PR examination.

Investigations

Bloods	Renal function and electrolytes (hypercalcaemia, hypokalemia, hypomagnesaemia)
Abdominal x-ray +/- erect chest x-ray	Can assess bowel lumen diameter and presence of air below the diaphragm to rule out perforation.
Further investigations if appropriate e.g. CT abdomen/pelvis or small bowel series may assist diagnosis of remediable causes.	

Management

Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

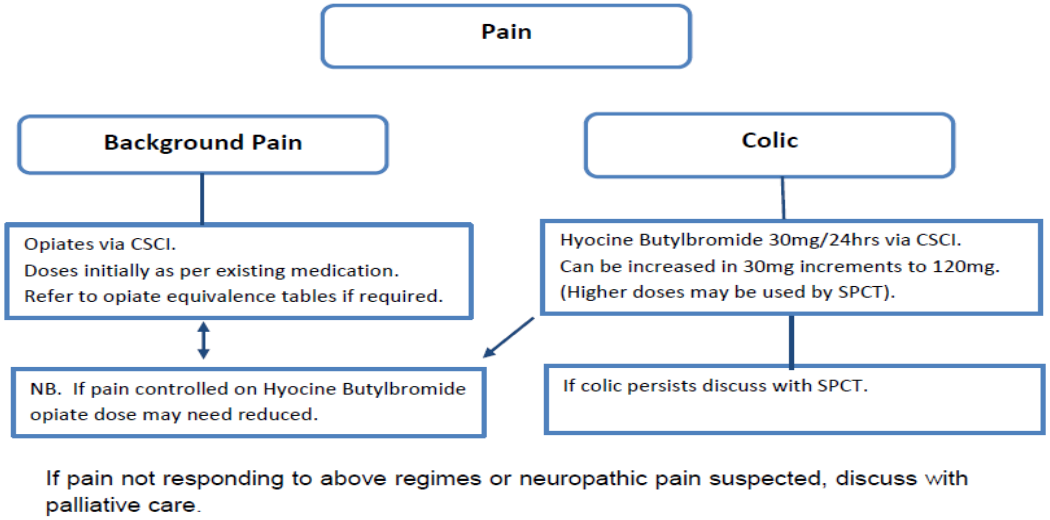
Management depends on a number of factors including the prognosis of the underlying cancer, performance status and severity of the obstruction (complete/partial, single point/multiple points of obstruction).

Initial management considerations should include:

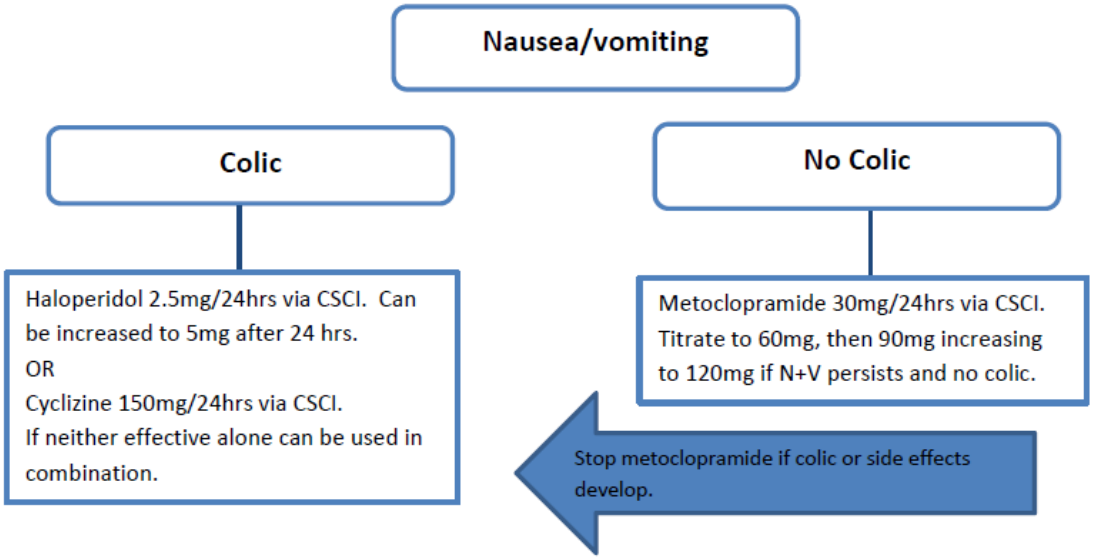
- Diet - The patient should normally be fasted for the first 24 hours. After this, sips of fluid may be introduced as tolerated for the next 48 hours, with light diet thereafter.
- IV fluids – with correction of any electrolyte imbalances.
- Monitor volume of vomitus.
- Mouthcare.
- Consider Nasogastric tube for symptomatic relief.

- Surgery is only indicated in a small select number of patients and referral should be made consultant-to-consultant. Initial referral to the surgical team by junior medical staff should only be made if there are signs of peritonism.

Symptom management - Suggestions for managing pain, nausea and vomiting can be found below. Seek advice from specialist palliative care (SPCT) early.



If pain not responding to above regimes or neuropathic pain suspected, discuss with palliative care.



Second line management options:

- Regardless of presence/absence of colic Levomepromazine 5mg/24hrs via CSCI, with 5mg doses SC on a prn basis. The CSCI dose can be titrated upwards in 5mg increments to 25mg as tolerated.
- If vomiting not settling after 72 hours despite the above, consider trial of high dose dexamethasone (e.g. 8mg IV OD (am) x5 days with IV PPI cover) provided no contraindications.

  If no benefit - stop. If beneficial consider down titrating over next 2 weeks. Review dose in setting of extreme hunger/hyperglycaemia/agitation.
- Persisting nausea consider Ondansetron 8mg/24hrs via CSCI. Can be uptitrated in 8mg doses to maximum of 32mg/24hrs.
- Persisting vomiting consider Octreotide 300micrograms/24hrs via CSCI. Can be uptitrated in 300mcg doses to 1200mcg.
- If control of vomiting remains difficult consider NG tube or venting gastrostomy after discussion with consultant.

Heartburn

Consider IV PPI e.g. omeprazole 40mg OD.

Constipation

PR examination should be performed as part of initial assessment.
If faeces in rectum, 2 glycerine suppositories should be inserted against side wall of rectum.
All laxatives should be stopped first 48 hours.
After this consider adding Docusate 100mg BD for patients with partial obstruction, which may be subsequently increased to 200mg BD.

Subsequent management

- Aim of chronic management is **symptom control**.
- Level of intervention dictated by multiple factors, chiefly performance status and patient preference.

- Will include a combination of pharmacological management, diet as tolerated, parenteral fluids where appropriate, mouthcare and venting gastrostomy or colonic stenting in selected cases.
- **Nutrition**: In the vast majority of cases, patients will have rapidly progressive disease, other organ dysfunction and poor performance status; hence nutritional considerations are not relevant. In highly selected cases where life expectancy is estimated to be longer and patient is otherwise 'well', a discussion led by the consultant regarding TPN may be appropriate.

Reference

Adapted from Northern Ireland Cancer Centre Clinical Recommendations for the Management of Malignant Bowel Obstruction in Advanced Ovarian Cancer

Malignant Pericardial Effusion

Malignant pericardial effusions occur in up to 20% of patients with advanced cancer, however do not usually require treatment unless there are increasing symptoms and/or haemodynamic compromise. Pericardial effusions are most likely to be seen in breast, lung, oesophageal cancer and also lymphoma. Most effusions are due to direct infiltration of the pericardium, however rarely thoracic radiotherapy and some chemotherapy agents can also cause pericarditis and a pericardial effusion.

Signs and Symptoms

- Patients with mild-moderate effusions may be asymptomatic.
- Fatigue, dyspnoea, chest pain
- Signs of cardiac compromise requiring urgent treatment include: Raised JVP, muffled heart sounds, tachycardia and hypotension.

Investigations

Chest X-ray	Cardiomegaly
ECG	Low voltage QRS complexes in all leads, rarely electrical alternans
Transthoracic ECHO ideally using Point-of Care Echo (PoCUS)	Establishes presence and volume of pericardial effusion, presence or likelihood of cardiac tamponade, and ideal window to insert a drain if required. degree of cardiac dysfunction, detect structural heart disease or pericardial pathology

Management

Refer immediately to local cardiology and acute oncology teams

Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

Management will depend upon symptoms, anticipated prognosis, and responsiveness of underlying cancer to systemic anti-cancer therapy

- Asymptomatic / minimally symptomatic – conservative management with echocardiogram monitoring, treatment of the underlying disease
- Symptomatic – patients with haemodynamic compromise require urgent pericardiocentesis by local cardiology teams.
- Recurrent pericardial effusions –seen in up to 60% of cases, discuss with cardiology/ cardiothoracic teams - consider prolonged catheter drainage or surgical pericardiotomy (window).

References

Problem Solving in Acute Oncology, second edition, Atlas publishing Ltd 2020

Malignant Pleural Effusion

Malignant pleural effusion is associated with a poor prognosis with median survivals of 3-12 months. Cancers most often associated with pleural effusions include breast and lung cancer (50-65%), ovarian and upper GI cancers

Signs and Symptoms

Shortness of breath, chest pain, fatigue, cough.

Investigations

The pathway for patients will differ depending on whether this is a new presentation with cancer or whether there is an established cancer diagnosis. Investigations to consider include:

History & examination	Typically fluid accumulations of >500mls detected clinically
Chest X-Ray	Typically fluid accumulations of >300mls detected, assess for other causes of symptoms
CT chest/abdomen	In newly diagnosed patients, or those with a long disease-free interval for staging – discuss with AOS
Cytology	Required to establish diagnosis in patients with no previous cancer diagnosis / long disease-free interval
Lung Point-of-Care Ultrasound (PoCUS)	For assessment of extent of effusion. For procedural guidance during drainage (as per NICE guidance)

Management

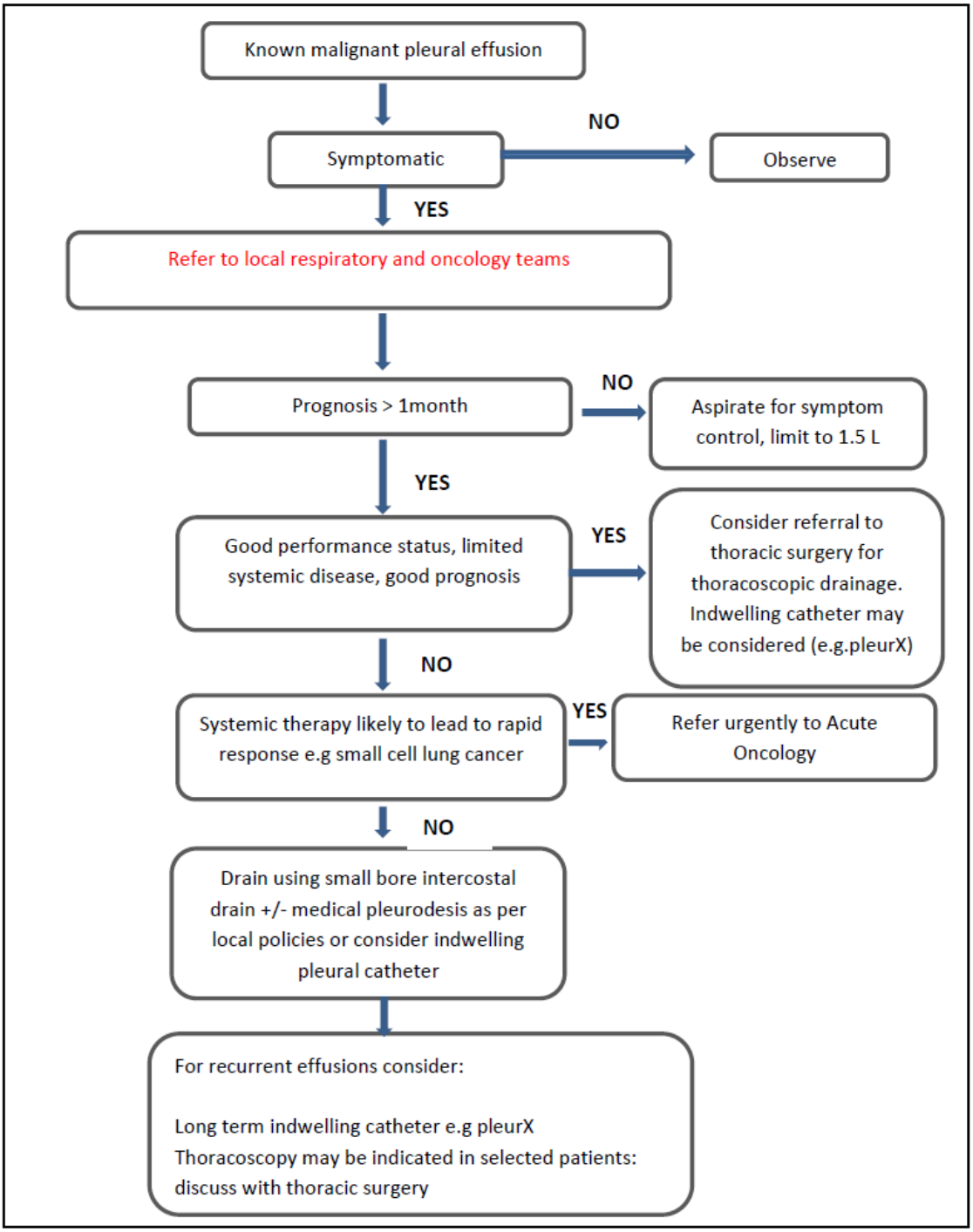
Refer to local Respiratory and Acute Oncology Service

Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

Assess

- Symptoms
- Performance status
- First or subsequent presentation
- Prognosis
- Histology / responsiveness of tumour to systemic anti-cancer treatment / prior treatments / disease burden
- **NB** Withhold any anticoagulants and antiplatelet agents prior to intervention if it is clinically appropriate to do so

Flowchart for management of malignant pleural effusions



References
British Thoracic Society Pleural disease Guideline 2010
UKONS Acute Oncology Management Guidelines 2013

Metastatic Spinal Cord Compression

Due to metastatic spread or direct extension of malignancy causing compression of the spinal cord or cauda equina by direct pressure and/or vertebral instability or collapse, and so threatening or causing neurological disability.

Can occur in almost all malignancies, but myeloma, lung, prostate and breast cancers are the most common types.

Patients with a history of bone metastases in the vertebral column are at higher potential risk and should be educated to urgently report suggestive symptoms. Patients who have an existing cancer diagnosis can also develop MSCC if there is cancer progression. In approximately 20% of patients the patient has MSCC as the initial cancer presentation.

Urgent assessment, imaging and management is essential to ensure the best neurological and functional outcomes.

Signs and Symptoms

- New, progressive or severe pain in the spine (including nocturnal pain disturbing sleep), which may be aggravated by straining
- Radicular pain (pain "radiating" along the dermatome of a nerve due to inflammation or irritation of the nerve root at its connection to the spinal column)
- Any limb weakness or difficulty in walking
- Sensory loss or bladder or bowel dysfunction
- Localised spinal tenderness
- Neurological signs of spinal cord or cauda equina compression.

Investigations

Urgent MRI of whole spine (if contraindicated,spinal CT may be considered)	This should be done **within 24 hours** in the case of spinal pain suggestive of spinal metastases and neurological symptoms or signs suggestive of MSCC. MRI may occasionally be needed **more urgently** if there is a pressing clinical need for emergency surgery e.g. significant and rapid neurological deterioration
CT chest, abdomen (+/-pelvis)	Consider after discussion with specialist teams if patient has a new cancer diagnosis or if re-staging required in an existing cancer patient

Other investigations may also be required if a new cancer diagnosis.

Routine bloods including calcium and coagulation/group and hold if surgical option or biopsy being considered.

Management

Refer urgently to local acute oncology team, or radiation oncology on-call registrar (NICC or NWCC) or on-call Spinal Registrar, BHSCT (if surgery to be considered).

Aim is to start definitive treatment, if appropriate, before any further neurological deterioration and ideally within 24 hours of the confirmed diagnosis of MSCC

- **If suspected MSCC, commence patient immediately on high dose steroids (Dexamethasone with a loading dose of 16mg or 8mg BD PO/IV (unless contraindicated)) with PPI, before diagnosis is confirmed.**
- Organise urgent MRI of whole spine. **Investigation must not be delayed.**
- Discuss results once available urgently with local acute oncology team (in hours), or on call registrar for radiation oncology NICC/NWCC via hospital switchboard or on-call Spinal Registrar, BHSCT (if surgery to be considered).

A definitive treatment plan must be established ASAP and will take into consideration the cancer diagnosis, characteristics of the MSCC, functional level of the patient (neurological and performance status), overall disease status and likely prognosis.

The diagnosis and proposed treatment plan should be discussed with the patient and their family.

Management Options

1. **Spinal surgery** may be more effective than radiotherapy at maintaining mobility in a subset of patients.

Surgery is particularly indicated for fit patients with a short history of neurological symptoms, when there is no previous histological diagnosis of malignancy (e.g. new cancer presentation with MSCC), vertebral instability or displacement with bone impingement on spinal cord, if there is worsening of symptoms during or soon after previous spinal radiotherapy, and if patient has a reasonable prognosis (e.g. >3 months). Radiotherapy can be given post-operatively (usually a number of weeks later once wound well healed) and cases should be discussed on an individual basis.

2. If patient is not suitable for surgery, urgent **radiotherapy** to the spine is the usual treatment and is organized by the oncology on-call team at the Cancer Centre.

Options may include 1 or 5 fractions of radiotherapy. If a bed is not available in the cancer centre arrangements should be made for daily transfer from the local hospital with the patient accompanied by a member of nursing staff.

3. Patients of poor performance status or completely paraplegic or tetraplegic for more than 24 hours, should be discussed urgently before any imaging or hospital transfer.

Best supportive care may be appropriate for patients unable to tolerate treatment or who have established paralysis in the absence of pain. They should be promptly referred to palliative care.

4. **Chemotherapy** rarely indicated for treatment of MSCC but may be considered in very chemosensitive tumours e.g. germ cell tumours, lymphoma, myeloma.

Identifying Spinal instability

Spinal instability is thought to account for pain in **approximately 10%** of patients with vertebral metastases and is characterised clinically by severe pain at the site of the lesion on attempted movement. Instability may be present if the patient has any of the following are present:

1. Severe pain at site of lesion, increasing on movement.
2. Worsening neurology (increasing pins and needles and/or weakness)
3. Involved vertebral bodies have collapsed to less than 50% of their original height.
4. The odontoid process has been destroyed, leading to possible atlanto-axial subluxation. Patients may complain of severe pain

****Clinical features of pain and neurology are the best indicators of instability****

Moving and Handling

Moving and handling recommendations need to be made for each patient with MSCC. Alongside radiological findings consider the following moving and handling options and then **select one option** for the patient's care team. For patients at end of life, be aware of the implications of recommendations on quality of life. Discuss with oncology/surgical team to decide the most appropriate option.

Recommendations for patients include -

Bed rest & log roll If patient has increasing pain and worsening neurology on movement consider recommending bed rest and log roll. Review recommendations daily.

Monitored graduated sit-up and mobilise as pain and neurology allows If patient has manageable pain, stable neurology and walking prior to diagnosis consider recommending graduated sit up and progress to mobilise as pain and neurology allows. Bracing may also be appropriate - liaise with physiotherapists.

Mobilise as pain and neurology allows If patient has minimal pain, neurology and is independently mobile consider recommending mobilise as pain and neurology allows.

Subsequent Management

Consideration should also be made for the following management steps

- Adequate analgesia
- Rehabilitation – prompt referral to physiotherapy (within 24 hours) and occupational therapy.
- Venous thromboembolism prophylaxis
- Bowel management
- Catheterisation if bladder function affected
- Ensure a plan for weaning steroids is in place

Recurrent MSCC – treatment options may include surgery, re-irradiation, supportive care and symptom relief.

Prognosis

The strongest predictor of post treatment neurological function and survival is pre-treatment neurological function.

Reference

Metastatic Spinal Cord Compression: Diagnosis and management of adults at risk of and with metastatic spinal cord compression. (NICE, 2008) Available from http://www.nice.org.uk/guidance/cg75

Guidelines for the Rehabilitation of Patients with Metastatic Spinal Cord Compression (MSCC), Assessment and Care Provision by Occupational Therapists and Physiotherapists in the Acute Sector Guidelines for the Rehabilitation of Patients with MSCC

(found on www.rqia.org.uk)

Treatment Related Nausea and Vomiting

- SACT and radiotherapy induced nausea and vomiting is one of the most commonly encountered side effects of these treatments.
- It is easy to assume the nausea and vomiting is the result of the patient's treatment but other common causes in cancer patients should be assessed for.
- These include other medications (e.g. opioids), constipation, infection, anxiety, metabolic abnormalities (e.g. renal failure, hypercalcaemia), peptic ulcer disease, bowel obstruction and brain metastases / raised intra-cranial pressure.

Symptoms and signs

Symptoms: A detailed history is essential. It is important to assess the timing of symptoms, oral intake, amount of vomit, and presence of any haematemesis or coffee-ground vomit. Also check for bowel movements, reflux/gastritis and abdominal pain as well as a detailed medication history.

Signs: Check for signs of dehydration, abdominal distension/tenderness, abnormal or absent bowel sounds.

CTCAE v5.0 Grading of Nausea and Vomiting

	Grade 1	Grade 2	Grade 3	Grade 4
Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition	Inadequate oral caloric intake; tube feeding, TPN or hospitalisation indicated	
Vomiting	Intervention not indicated	Outpatient intravenous hydration; medical intervention indicated.	Tube feeding, TPN, or hospitalization indicated.	Life threatening consequences

Investigations

Bloods	Consider FBP, U&E, Bone profile, LFTs, CRP
Abdominal x-ray	If concerns regarding obstruction.
Other investigations as indicated e.g. CT brain if brain metastases is a differential diagnosis.	

General Management Principles

Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

- Investigate and treat for any **non – SACT / radiotherapy related causes**.
- Assess need for **rehydration**. Ensure adequate IV fluids, especially if patient is hypotensive, tachycardic or oliguric.
- Stop any **causative drugs**. NB. If patient is on opioids do **NOT** stop these abruptly but add in anti-emetic treatment.
- Advise patient to eat small, frequent meals (if bowel obstruction excluded).

- **Anti-emetics**:

  - Anti-emetics with different modes of action should be combined.

  - Consider an appropriate route of administration – IV/SC routes may be required initially but these must be regularly reviewed.

  - Note that some drug combinations are inappropriate e.g. prokinetic drugs (e.g. metoclopramide) are antagonised by anticholinergic drugs (e.g. cyclizine).

- Domperidone is recommended in younger patients as metoclopramide is associated with an increased risk of dystonic reactions in this patient group.
- Seek specialist palliative care advice if nausea and vomiting remains difficult to control.

SACT induced nausea and vomiting

SACT induced nausea and vomiting is normally defined accordingly -

Acute	N&V during the first 24hrs after SACT.
Delayed	>24 hours after SACT and may continue for up to 6-7 days after SACT.
Anticipatory	N&V prior to the beginning of a new cycle of SACT.
Breakthrough	N&V despite standard anti-emetics, which require extra treatment.
Refractory	Patients who have failed both standard and rescue medication.

- Patients often develop anxiety about the symptoms recurring in the future. Optimal control is required in the acute phase to prevent nausea and vomiting in the delayed phase and reduce the chances of anticipatory vomiting developing.
- Patients will receive different combinations of anti-emetics pre chemotherapy and to take at home depending on the potential for the different agents to cause nausea and vomiting.
- If possible establish what ant-emetic regimen has been prescribed by the oncology team. The patients treating cancer unit should be able to help you with this information which will be documented on the SACT prescription chart.
- Check whether the patient has been taking these anti-emetics correctly and regularly – educating patients and carers is essential to optimise compliance.

The following table is helpful for guiding breakthrough antiemetic choices.

SACT antiemetic schedule	**Breakthrough**
No anti-emetics pre SACT Metoclopramide prn as take home	If not taking regular anti-emetics Metoclopramide 10mg orally/parenterally TID for 5 days or Domperidone 10mg PO TID for 5 days. If taking regular anti-emetics Substitute Metoclopramide/Domperidone with Levomepromazine 6mg (unlicensed) orally at night initially increasing to BD if necessary (more sedating) or Cyclizine 50mg orally/parenterally TID.

Dexamethasone pre SACT Dexamethasone as take home Metoclopramide as take home	Substitute Metoclopramide/Domperidone with Levomepromazine 6mg (unlicensed) orally at night initially increasing to BD if necessary (more sedating) or Cyclizine 50mg orally/parenterally TID.
Ondansetron pre SACT Dexamethasone pre SACT Dexamethasone as take home Metoclopramide as take home	Ondansetron 8mg orally/ parenterally twice a day Or Substitute Metoclopramide/Domperidone with Haloperidol 1-2mg orally/parenterally OD/BD Or Levomepromazine 6 mg (unlicensed) orally up to TID or 5-10 mg continuous subcutaneous infusion over 24 hours Or Cyclizine 50mg orally/ parenterally TID Or Cyclizine 150mg continuous subcutaneous infusion over 24 hours
Ondansetron pre SACT Dexamethasone (20mg) pre SACT Ondansetron as take home Dexamethasone as take home Metoclopramide as take home	Substitute Metoclopramide/Domperidone with Haloperidol 1-2mg orally/parenterally OD/BD Or Levomepromazine 6 mg (unlicensed) orally up to TID or 5-10mg continuous subcutaneous infusion over 24 hours Or Cyclizine 50mg orally/ parenterally TID Or Cyclizine 150mg continuous subcutaneous infusion over 24 hours.
Ondansetron pre SACT Dexamethasone (12mg) pre SACT Aprepitant pre SACT Dexamethasone as take home Aprepitant as take home Metoclopramide as take home	Ondansetron 8mg orally/ parenterally Or Substitute Metoclopramide/Domperidone with Haloperidol 1-2mg orally/ parenterally OD/BD Or Levomepromazine 6 mg (unlicensed) orally up to TID or 5-10mg continuous subcutaneous infusion over 24 hours Or Cyclizine 50mg orally/ parenterally TID Or Cyclizine 150mg continuous subcutaneous infusion over 24 hours

The patient's oncology team will then make changes to the patient's anti-emetics for their next cycle of SACT. For anticipatory nausea and vomiting Lorazepam 1mg orally or sublingually 30 minutes before SACT, or even the night before/on the morning of SACT might be helpful.

Radiation induced nausea and vomiting

Is an acute radiotherapy side effect characterized by a latent asymptomatic period 1-2 hours after treatment, followed by sudden nausea and vomiting that can last for 6-8 hours. It may occur periodically or persistently during radiotherapy treatment, typically resolving within a short time of treatment ending.

Again the aim of anti-emetic therapy is to prevent nausea and vomiting with prophylactic anti-emetics prescribed by the treating oncology team.

The risk of radiation induced nausea and vomiting depends on the area being treated, doses being delivered and if concurrent chemotherapy is being given.

The following table is helpful for selecting additional ant-emetics.

Area receiving radiotherapy	**Antiemetic prophylaxis**	**Rescue antiemetic (one off dose**	**Subsequent fractions (radiotherapy treatments)**
Extremities Breast	No routine antiemetics usually necessary, Consider: Cyclizine 50mg orally three TID when required	If not taking regular anti-emetics Cyclizine 50mg orally/parenterally	If not taking regular anti-emetics Metoclopramide 10mg orally TID
		If taking regular anti-emetics Substitute cyclizine with ondansetron 8mg orally/parenterally	If taking regular anti-emetics Substitute metoclopramide with: Ondansetron 8mg orally BD
Cranium Head and neck Lower thorax region Pelvis	Cyclizine 50mg orally three times a day Consider: Ondansetron 8mg orally BD	If taking cyclizine add in ondansetron 8mg orally/parenterally If taking ondansetron add in dexamethasone 4mg orally/parenterally	Ondansetron 8mg orally BD Consider Dexamethasone 4mg orally in the morning
Upper abdomen Hemibody Abdominal-pelvic Mantle Craniospinal	Ondansetron 8mg orally BD	Dexamethasone 4mg orally/parenterally Consider Levomepromazine 6 (unlicensed) orally up to TID	Ondansetron 8mg orally twice a day And consider Dexamethasone 4mg orally in the morning and/or Levomepromazine 6 mg (unlicensed) orally up to three times a day
Total body irradiation Total nodal irradiation	Ondansetron 8mg orally BD for at least 24 hours after completion of radiotherapy And Dexamethasone 4mg orally BD.	Levomepromazine 6 (unlicensed) orally up to TID. 5 to 10 mg continuous subcutaneous infusion over 24 hours	Ondansetron 8mg orally BD and Dexamethasone 10mg orally in the morning and Levomepromazine 6 mg (unlicensed) orally up to TID or 5 to 10 mg continuous subcutaneous infusion over 24 hours

PPI is standardly prescribed in radiotherapy when steroid therapy is initiated.

Reference

Adapted from M. McGrady et al Regional Antiemetic Guidelines for Adult Patients Receiving Systemic Anti-Cancer Treatment and /or Radiotherapy, January 2021. For further details see NICaN SACT CMG SharePoint site.

Neutropenic Sepsis

- Systemic infection in neutropenic patients is potentially life threatening. Left unchecked it can prove rapidly fatal. Simple, timely intervention can be lifesaving.
- The most predictable cause of neutropenia is systemic anti-cancer therapy (SACT), which can result in myelosuppression and immunosuppression.
- Other causes: aplastic anaemia, haematological malignancies, hereditary conditions, radiation exposure, vitamin deficiencies and autoimmune conditions.

Neutropenia: An absolute neutrophil count (ANC) of $<1.0 \times 10^9$/L regardless of the overall white cell count.

Severe Neutropenia: ANC of $<0.5 \times 10^9$/L.

- Neutropenic sepsis (NS) is a time-critical condition. The goal is a 'door to needle' time of **<60 minutes** for administration of first dose intravenous antibiotics.
- Early recognition of a patient's potential to have NS at triage is crucial. All patients within 6 weeks of SACT presenting as an emergency must be assumed to have NS until proven otherwise.

DO NOT DELAY treatment to wait for an ANC result if there are any signs of sepsis.

Symptoms and signs

Classical signs and symptoms of infection may be absent. A careful history and examination should aim to identify potential sources of infection.

Organ dysfunction can be represented by an increase in the Sequential Organ Failure Assessment (SOFA) score of 2 points or more, which is associated with an in-hospital mortality greater than 10%

If any of the clinical signs below are present, assume early sepsis including:

- Temp >38.0C or <36.0C
- Pulse >90 bpm
- RR >22 breaths/minute
- Altered mental state

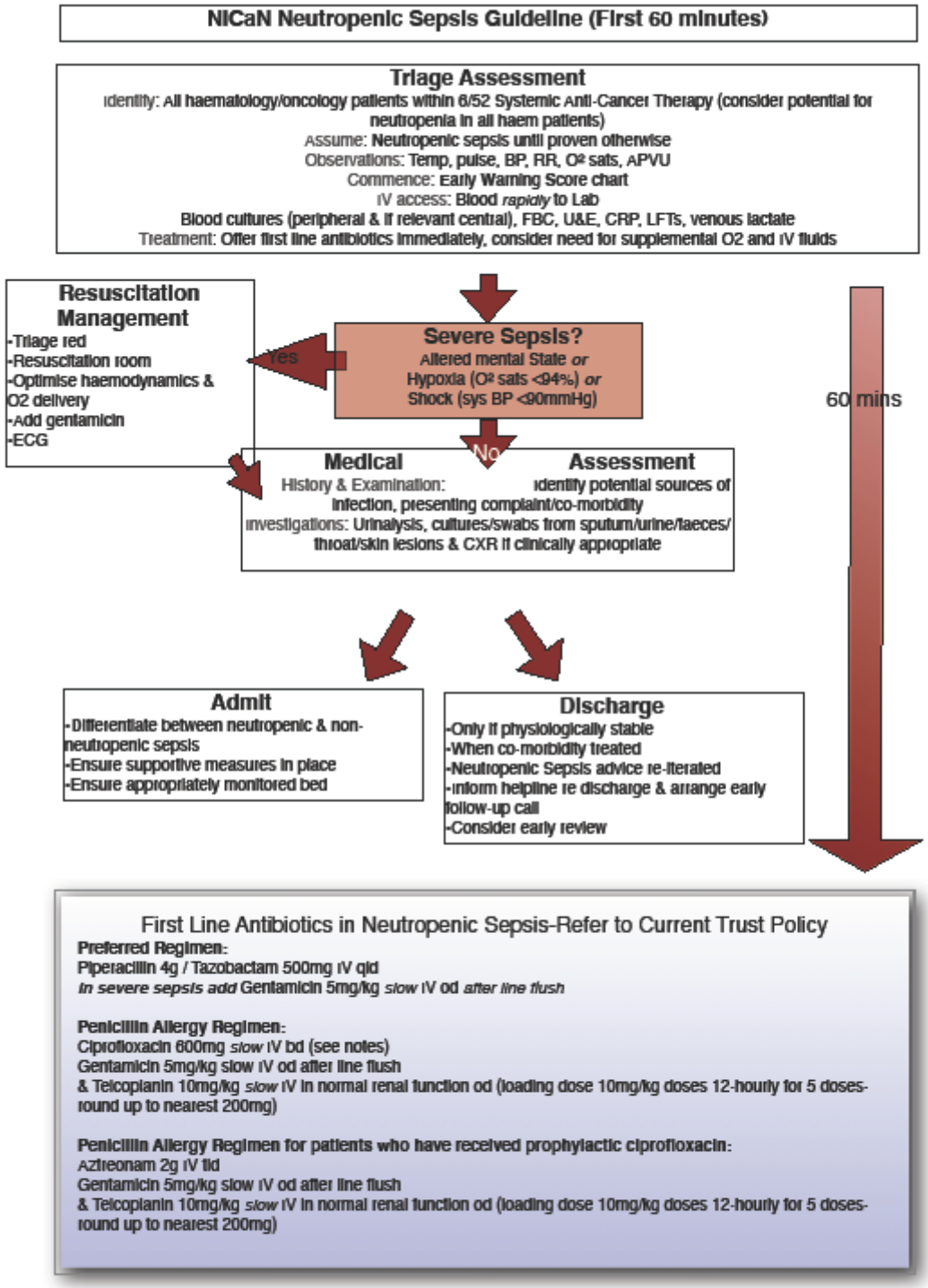
- Hypoxia (O2 saturations <94%)
- Shock (sys BP <100mmHg)

Please note the UKONS Triage tool indicates a temperature > 37.5^{0}C, this is a trigger for assessment. In all cases clinical judgement should be used, some patients who do not have a temperature of >38C but who have other clinical features of NS should be treated as having NS.

Investigations

Bloods	FBP, U&E, CRP, LFTs, venous lactate and blood cultures (peripheral and if relevant central) ASAP.
Urinalysis, cultures/swabs from sputum/faeces/throat/skin lesions and chest x-ray if clinically appropriate.	

Initial Management – First 60 minutes



***see local trust antimicrobial guidelines for recommendations for loading doses, adjustments for renal impairment and advice regarding therapeutic drug monitoring for Teicoplanin, Gentamicin, Amikacin.**

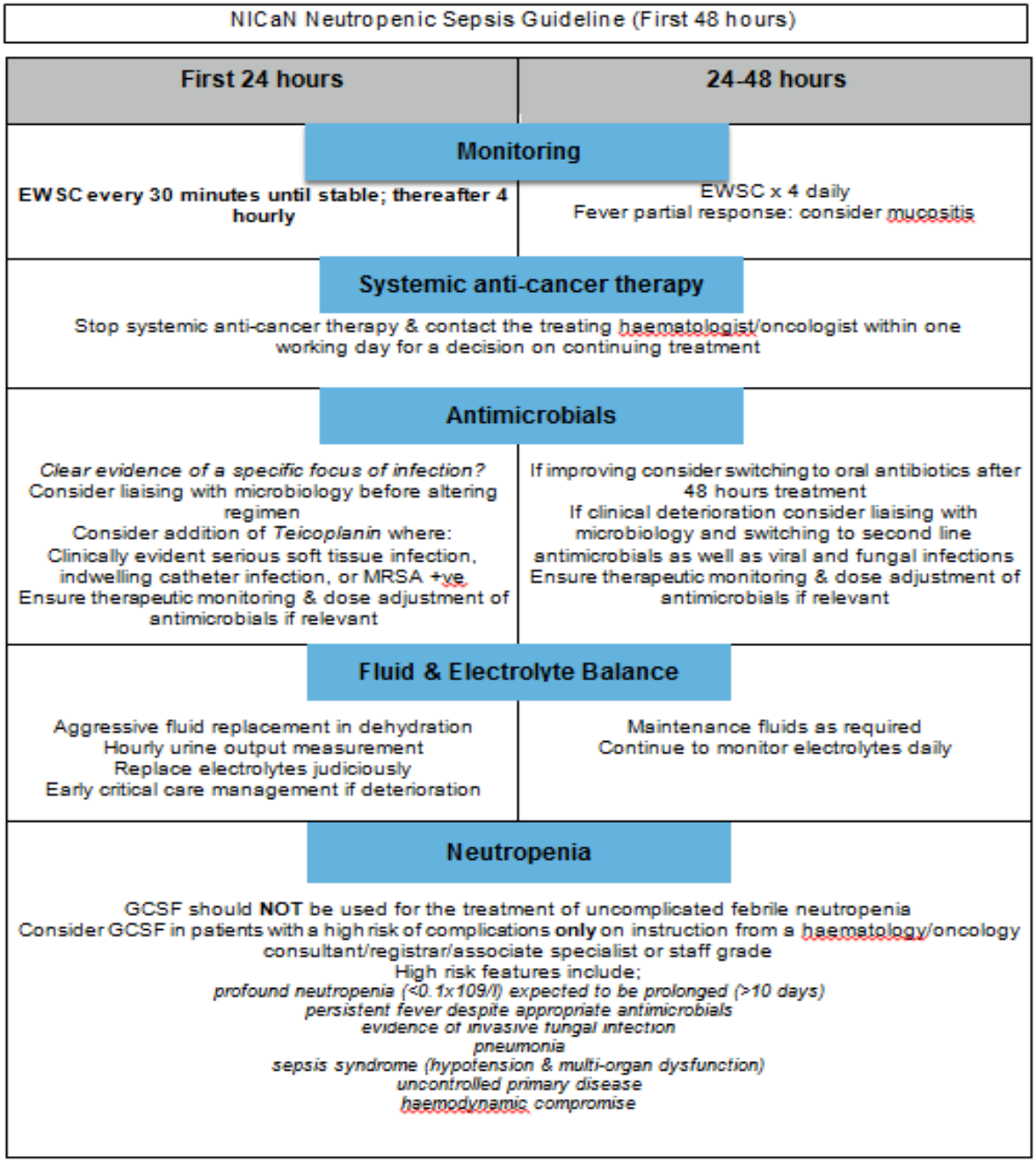
If neutropenia is excluded an alternative management plan can be made.

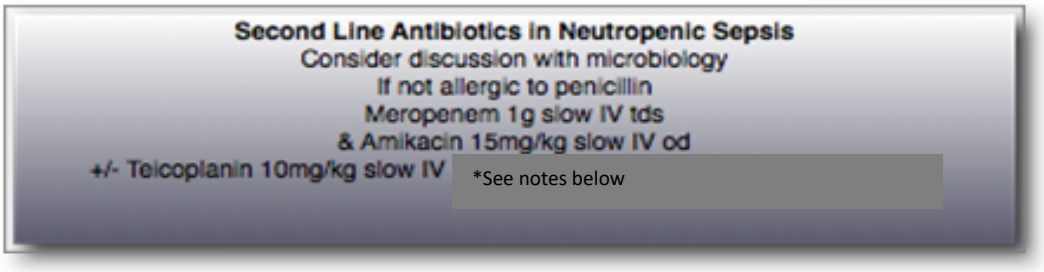
Care should be taken with neutropenic patients who do not meet sepsis definition criteria but have low grade pyrexia. They should have follow up and may require admission for monitoring as they could deteriorate.

Subsequent Management – First 48 hours

Refer to local Acute Oncology Service

Interrupt any systemic anti-cancer therapy including oral drugs until discussed with the Acute Oncology Team.
Ongoing management of the neutropenic sepsis patient should be in a Cancer Unit or Centre.





***see local trust antimicrobial guidelines for recommendations for loading doses, adjustments for renal impairment and advice regarding therapeutic drug monitoring for Teicoplanin, Gentamicin, Amikacin.**

- Do not switch initial empiric antibiotics in patients with unresponsive fever unless there is a clinical deterioration or a microbiological indication.

- Some antimicrobial doses must be adjusted in the elderly and where there is renal impairment, notably Gentamicin, Teicoplanin and Amikacin. Pre-dose levels need monitored and appropriate dose adjustments made.
- When GCSF is appropriate (see previous) make sure the patient has not already received pegfilgastrim in which case GCSF should NOT be given.
  Use standard (i.e.nonpegylated) GCSF as a daily subcutaneous injection. Discontinue after 2 consecutive days of ANC >1x10^9/L.

Reference

- *Adapted from Scullin P et al. Guidelines for the management of oncology/haematology adult patients (>18 years) with neutropenic sepsis (NICaN guidelines, 2013).*
- *United Kingdom Oncology Nursing Society (UKONS) (2016) Oncology/Haematology 24-hour Triage, Rapid assessment and Access toolkit. Information and instruction manual. Available at: https://www.ukons.org/site/assets/files/1134/oncology_haematology_24_hour_triage.pdf*

Mucositis

- Mucositis is a general term for erythematous, erosive, inflammatory and ulcerative lesions that can occur in the mucosal lining of the mouth, pharynx, oesophagus or entire gastrointestinal tract secondary to cytotoxic treatment.
- It is a commonly encountered acute side effect of both SACT and radiotherapy treatment which can be very distressing for patients.
- Particularly at risk patients include those receiving high dose chemotherapy (e.g. for leukaemia or lymphoma) and those receiving radiotherapy +/- chemotherapy for head, neck and oral cancers.

Symptoms and signs

Symptoms: Check for pain, oral intake and swallow. Also check smoking and alcohol consumption.

Signs: Check for signs of dehydration and perform careful oral assessment. Assess lips, gums, teeth, tongue and mucus membranes. Check for presence of candida and for evidence of complicating bacterial or viral infection.

CTCAE v 5.0 Grading of Oral mucositis

Grade	**1**	**2**	**3**	**4**
Symptoms / signs	Asymptomatic or mild symptoms; intervention not indicated.	Moderate pain or ulcer that does not interfere with oral intake; modified diet indicated	Severe pain; interfering with oral intake	Life threatening consequences; urgent intervention indicated

Investigations

Bloods	Update FBP, U&E and CRP if concerns regarding dehydration or infection
Microbiology	Send oral swabs if evidence of bacterial, fungal or viral infection.

General Management Principles

➢ **Basic mouthcare regimen**

- Mouthwashes - 0.9% saline mouthwash QID and at bedtime.
- Biotene mouthwash 15mls QID can help moisten mouth.
- Brush teeth twice daily using soft toothbrush with fluoride toothpaste.

Interrupt any systemic anti-cancer therapy including oral drugs until discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team
Admission to the Cancer Centre is preferable if the patient is still on radiotherapy treatment

- Rinse toothbrush well in saline after use.
- If dentures are worn – remove from mouth clean with toothpaste and soak in suitable solution overnight.

- Chlorhexidine mouthwash not recommended if patient has or is recovering from cytotoxic induced mucositis as can inhibit mucosal regrowth.
- Increase frequency of basic mouth care regimen if severe mucositis.

➢ **Mucosal protection**

- Gelclair x1 sachet TID.
- Tea tree essential oil mouthwash 2-4 drops in 10-50ml used QID (unlicensed) is also an option for mucositis.

➢ **Pain**

Use liquid/soluble formulations and titrate up as required. Options include:

- Paracetamol 1g QID (effervescent/suspension)
- Co-codamol 8/500 or 30/500 (effervescent tablets, up to QID)
- NSAIDS to be used in caution with SACT patients
- Oramorph 10mg/5ml liquid or Oxycodone liquid (oxynorm)
- Aspirin mouthwash 300mg dissolvable up to QID.
- Difflam mouthwash (Benzydamine 0.15%) – Difflam contains alcohol and can cause stinging. If used should be diluted to reduce irritation e.g. 10mls diluted in 10ml of water repeated as required.
- If unresponsive to above measures consider syringe driver. Ensure constipation assessed for and laxatives prescribed.

➢ Encourage smoking and alcohol cessation.

➢ **Dietician** referral if eating and drinking affected. Assess for IV fluids if severe mucositis.

➢ Any concerns regarding dysphagia refer to **Speech and Language Team**

➢ Consider referral to Respiratory Physiotherapy if patient has difficulty clearing respiratory tract secretions and/or if there is suspicion of aspiration.

➢ Introduce treatments for specific problems as necessary. See following table.

➢ An oesophageal stricture may be a late side effect (usually >90 days) after an acute radiation oesophagitis - consider OGD if symptoms are prolonged and persist despite treatment

Mouth Ulcers Bonjela Hydrocortisone 2.5mg mucoadhesive buccal tablets' or 'hydrocortisone 2.5mg oromuscoal tablets 1 tablet placed on ulcer up to QID after meals and allowed to dissolve in close contact with the ulcer.	**Oesophagitis** Sucralfate 1g (in 5mls) up to QID 30 minutes before meals and bedtime Oxetacaine with antacid 10mls TID 30 minutes pre meals . (Both often only available from hospital pharmacies). Proton pump inhibitor
Neutropenic sepsis If neutropenic and signs of infection treat according to neutropenic sepsis guidelines.	**Fungal infection (Candidiasis)** Nystatin oral suspension – 1ml to be held in mouth for at least a minute before swallowing, QID after food or Fluconazole 50mgs OD for 7 days. IV treatment if required.
Viral infection Consider topical aciclovir 5% for local infection in low risk patients. Aciclovir can also be given orally or as an IV infusion for higher risk patients.	**Dry mouth** Frequent sips of water Sugar free chewing gum Sucking crushed ice or fresh pineapple although if patient has already developed ulceration may cause further discomfort.
Dry lips Yellow/white soft paraffin at night or aqueous or diprobase cream. Sugar free chewing gum Oral balance dry mouth gel applied as required.	**Coated tongue** Toothbrush/sponge dipped in saline Vitamin C effervescent ¼ of a 1g tablet – dissolve on tongue TID.
Sputum viscosity Fizzy drinks Saline nebulisers Carbocisteine (Mucodyne)	**Bleeding from the mouth** 500mg tranexamic acid injection added to 5ml sterile water and used as a mouthwash 4 hourly.

Reference UK Oral Mucositis and Cancer Group; Mouth Care Guidance and Support in Cancer and Palliative Care (2015)

Radiotherapy

What is Radiotherapy?

- Radical radiotherapy is second only to surgery in achieving cancer cures, and is one of the major curative options of treatment in head and neck, lung, prostate, bladder, cervix and anal cancers in particular.
- Radical radiotherapy is given alone or sometimes with concurrent chemotherapy.
- Adjuvant radiotherapy is given in some cancers after surgery e.g. breast cancer and head and neck cancer.
- The majority of radiotherapy is given with palliative intent, often to help cancer-related local symptoms or complications.
- Patients are currently only treated with radiotherapy at the Radiotherapy Departments at the NICC and NWCC. .
- Radiotherapy generally involves a planning phase (which often includes a planning CT scan) followed by a treatment course.
- Treatment usually uses X-rays (photons) and occasionally electrons (for superficial e.g. skin treatment), and the radiotherapy is delivered by a linear accelerator treatment machine.
- Each treatment is known as a fraction.
- The radiotherapy course is usually short for palliative treatments (e.g. 1-10 fractions) and longer (e.g. 20-30 fractions over 4-6 weeks) for radical treatments although there are a few exceptions (e.g. Stereotactic Ablative Body Radiotherapy (SABR) for Stage 1 lung cancer where the treatment is curative but the high dose is given over a small number of treatments e.g. 3-5 fractions over 1-2 weeks).
- The side effects of radiotherapy are generally related to the area which is being irradiated, with the main general side effect of treatment being fatigue.
- Side effects generally build up during the course of radiotherapy and can last after treatment ends.
- Acute side effects are defined as occurring within 90 days of the end of radiotherapy treatment and late effects are defined as occurring more than 90 days after the end of radiotherapy treatment.

- If a patient develops complications of radiotherapy during the period of treatment it is important to notify the Acute Oncology Team and / or the patient's oncology team or the NICC or NWCC clinical oncology on-call team, as the patient may need to be admitted to avoid any interruption in radiotherapy treatment.
- If a patient develops complications of radiotherapy after treatment is completed, please also notify the oncology team.

Radiation Associated Neurotoxicity

- Radiation associated neurotoxicity of the brain or spinal cord can develop as an early or late side effect of radiotherapy treatment, and the most commonly seen side effect is acute cerebral oedema after cranial irradiation.
- The effect of radiation on the nervous system cell depends on both radiation and host factors. The area and volume of radiotherapy treatment, total dose, the dose per fraction, and the energy of radiation are important factors. Concurrent disease and previous treatment e.g. chemotherapy, may influence the nervous system response, and younger patients and males may be more affected.

Signs and Symptoms

Classification may be made according to the time of presentation.

Acute reactions	• Occurs during the course of treatment and symptoms include increased intracranial pressure or worsening of existing neurological symptoms. • Symptoms usually mild and transient and considered to be caused by radiation-induced oedema. • In cranial radiotherapy acute reactions also include skin reaction (see advice on radiation skin reactions) and scalp hair loss (temporary alopecia usually occurs approximately 2-3 weeks after treatment with anticipated hair re-growth beginning 2-3 months after treatment, and generally total scalp hair loss occurs if the whole brain has been irradiated).
Early delayed reactions	• Occur several weeks to months after finishing radiation treatment. • May also present with worsening symptoms or increasing somnolence and fatigue. • Somnolence syndrome is typically temporary and mild and is due to transient demyelination occurring approximately 4 weeks to 4 months after treatment; effect may be noted on imaging, especially MRI; usually self-limiting condition with most patients returning to baseline status but very occasionally there is a severe reaction requiring intensive medical support. • Careful consideration is needed to **avoid interpreting an early delayed reaction as a failure of treatment or progressive disease;** discuss with the treating neuro-oncology team.

Late delayed reactions	• May occur months to years after completion of radiation therapy. • The major type of late delayed reaction is radiation necrosis, which can mimic tumour recurrence as the necrosis can be progressive, irreversible, and fatal • Radiation necrosis is difficult to diagnose with imaging and may require biopsy. • Other late side radiation effects can include atrophy, haemorrhage, infarction, encephalopathy and neoplastic transformation.

Specific radiation associated neurotoxicity presentations may include:

Cerebral oedema	• Patients may experience an acute radiotherapy reaction during or just after cranial radiotherapy treatment with headache, nausea and rarely a seizure or additional neurological symptoms. • Generally self-limiting but steroids (or an increase in the dose of steroids) may be required to reduce the radiation-induced oedema or increase in intracranial pressure. • Contact oncology team for advice. ***Management principles*:** • Start steroids or increase dose if already prescribed. Steroids are usually only required for a temporary period and the dose is often tapered down. • Usual initial steroid dose is Dexamethasone 4-8mg BD PO/IV Maximum dose is usually Dexamethasone 16 mg/day. Add PPI. • Anti-epileptic medication may be required if seizures: specialist advice can be obtained from neurology. • Occasionally mannitol is used for patients not responding to dexamethasone after specialist advice. • If relevant, prescribe analgesia for headache and antiemetics for nausea.
Spinal cord myelopathy	• An early delayed transient myelopathy can occur after radiotherapy, particularly if treatment is in the cervical and thoracic spine regions. **Lhermitte's sign** may be detected: a shock-like sensation which radiates down the spine on neck flexion. Most patients improve over months up to one year. • Late effects are less common and more severe, and include radiotherapy myelopathy, a progressive syndrome with initial particle cord involvement and progression to a total transverse myelopathy. Investigation is generally required as differential diagnosis may include epidural spinal cord compression, intramedullary metastasis, and paraneoplastic necrotic myelopathy.
Brachial plexopathy	• An early or delayed syndrome occurring predominantly in patients who have undergone radiation therapy for Hodgkin's lymphoma and breast cancer. • Early brachial plexopathy may occur during or in the months after radiotherapy, may be painful at times with weakness and atrophy, and is usually reversible. • Delayed brachial plexopathy is more common, usually occurring months to years after radiotherapy treatment; pain is usually absent but sensory loss is almost always present, with or without weakness. The condition is usually not reversible. Differential diagnosis should include exclusion of recurrent tumour.

Investigations

Repeat imaging is generally not required if the presentation is consistent with radiation-induced oedema.

Consider repeat CT brain or MRI spine	Main indication is if a different diagnosis e.g. haemorrhage is suspected

Management

Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

See above for specific interventions.

Radiation Pneumonitis

- Radiation pneumonitis is inflammation of the lungs caused by radiotherapy and occurs in between 5-15% of patients who are treated with radiotherapy to the thorax. The risk is related to the volume of normal lung irradiated and the dose of radiotherapy delivered. It is most likely to occur with radical (potentially curative) treatments for lung cancer and less commonly oesophageal cancer, but can also occur occasionally after palliative thoracic radiotherapy treatment.
- Symptoms usually arise within the first 90 days of radiotherapy treatment (acute side effect) but can occur later and usually within 6 months of treatment. Lung fibrosis is the resulting chronic lung injury. The risk of radiation pneumonitis is increased by the concomitant use of chemotherapy and if patient has pre-existing lung disease e.g. COPD.

Signs and Symptoms

Symptoms may be minimal or can mimic a chest infection or the symptoms of lung cancer, but should be considered suspicious for radiation pneumonitis if onset of symptoms is <90 days after completion of thoracic radiotherapy.

- Cough (may be dry/non-productive or productive)
- Shortness of breath

- Chest pain
- Chest congestion
- Fatigue
- Low-grade fever
- Pleural friction rub (possible)

Investigations

Chest X-ray	Commonest finding is patchy opacification. Later changes can include fibrosis, volume loss and pleural thickening
CT or high resolution CT chest (or CTPA if needed to exclude pulmonary embolism)	May have ground glass changes, consolidation and volume loss

Tests (including those listed) may be needed to exclude other differential diagnoses e.g. infection (in particular Pneumocystis jirovecii pneumonia), pulmonary embolism, disease recurrence and lymphangitis carcinomatosis.

Management

Discuss management with acute oncology team and patient's consultant clinical oncologist

Treatment should be prompt if there is clinical suspicion, with introduction of oral steroids +/- antibiotics, and consideration of hospital admission if there are concerning clinical symptoms or signs. Management will depend upon severity of symptoms, and responsiveness to treatment.

Assessment of radiation pneumonitis:

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., tracheotomy or intubation)
5	Death

Source: Common Terminology Criteria for Adverse Events 4.0

Advice from respiratory team may be required particularly if >Grade 2 radiation pneumonitis

- If asymptomatic, no action may be required.
- If symptomatic, commence **Prednisolone** as per Lung clinical protocol with a slow tapering of dose: Prednisolone 60 mg/day x 3 weeks, 40mg/day for 2 weeks, 30mg/day x 2 weeks and 20mg/day for 2 weeks, then stop.

Consider course of **Clarithromycin** 500 mg BD. x 1 week (if no contraindication) also**.**

Simple linctus or **codeine linctus** may help cough.

- If severe radiation pneumonitis, patient may require hospital admission, oxygen therapy, and consideration of intensive care unit support if required. **IV Methylprednisolone** may be indicated if no clinical response to oral steroids. Active management is required, liaising with oncology, respiratory and intensive care teams.

Ensure appropriate oncology or respiratory follow-up after initial management.

Radiation Skin Reactions

- Radiation may cause a skin reaction dependent on extrinsic factors (treatment-related) including the site and volume of radiotherapy treatment, the dose given, and number of fractions (treatments).
- Intrinsic factors (patient factors) which affect skin reactions can include age, hormonal status, infection, obesity, diabetes and rare inherited conditions such as ataxia telangiectasia. Smokers are at a higher risk of a more acute and prolonged skin reaction.
- Acute skin reactions occur more commonly in head and neck treatment where the skin generally receives a high dose over the period of treatment (and as concurrent chemotherapy is often used), in breast cancer (over the surface of the breast and sometimes more pronounced in the inframammary fold), in other regions with skin folds e.g. the groins and perineal skin folds in anal cancer radiotherapy, and also in skin cancer superficial radiotherapy (using electrons).
- The acute skin reaction typically builds and develops during radiotherapy treatment, may peak 10 days after completing treatment and subsides within

approximately 4 weeks of completing treatment in most cases, though it rarely can take longer .

- Longer term side effects of a skin reaction may include hypopigmentation or hyperpigmentation, skin thickening or scarring, and rarely ulceration.
- Note that radiation recall reaction (so called “radiation recall dermatitis”, defined as the “recalling” by the skin of previous radiation exposure in response to the administration of certain response-inducing drugs) may rarely occur with the use of some chemotherapy drugs but also with other agents including statins and antibiotics. Please seek advice from the treating clinical oncology team if required.

Symptoms, Signs and Management

Discuss management with Acute Oncology Team, the patient’s treating oncology team or Cancer Centre oncology on-call team if any concerns about skin reaction and management.

Table 11: Adapted Radiation Therapy Oncology Group (RTOG) acute radiation dermatitis grading criteria

Grade 0	Grade 1	Grade 2a	Grade 2b	Grade 3
No visible change to the skin	Faint or dull erythema Mild tightness of the skin and mild itching may occur.	Tender or bright erythema Skin may feel tighter, itchy and/or sore.	Patchy moist desquamation Areas where skin has broken down can be seen. Yellow/pale green exudate may be visible on the surface. Soreness and oedema are evident.	Confluent moist desquamation More pronounced areas of broken skin can be seen. Yellow/pale green exudate are visible. Soreness and oedema are evident.
ASSESSMENTS				
Weekly assessments and RTOG score			Daily assessments and RTOG score	
AIMS OF CARE				
To promote hydrated skin and maintain skin integrity To promote comfort			To reduce risk of complications of further trauma and infection To promote comfort	
GUIDANCE				
MOISTURISE: Advise the patient to continue moisturising with preferred products. If the patient is not already using a moisturiser, advise them to start. ENCOURAGE SELF-CARE: Discuss self-care guidelines and ensure that the patient has sources of information to refer to, including 'Radiotherapy skin reactions - Information for patients'. STEROID OR CORTISONE CREAMS: Steroid or cortisone creams should only be used following advice from an independent prescriber or from staff qualified to dispense medication under patient group directions (PGDs). Contraindications for using these creams are broken skin or signs of infection. ANALGESIA: Ensure adequate analgesia is prescribed for the patient if needed. IF THE SKIN BREAKS: Patients should be advised to discontinue using any cream and should be advised on, or provided with, appropriate dressings. If there are signs of infection, undertake screening. Increase skin assessments to daily frequency. Seek further advice, if required, from a practitioner trained in radiotherapy induced skin reactions and wound care or tissue viability.			MOISTURISE: Continue to apply moisturiser to skin within the treatment field that is still intact. ENCOURAGE SELF-CARE: Discuss self-care guidelines and ensure that the patient has sources of information to refer to. Follow skin care guidelines and ensure patient has information sources to refer to. including 'Radiotherapy skin reactions - Information for patients'. DRESSINGS: Use appropriate dressings/products on broken skin, e.g. non-adhesive, silicone low adhesion. Do not use paraffin/petroleum jelly-based products or gentian violet. ANALGESIA: Ensure adequate analgesia is prescribed for the patient if needed. INFECTION SCREENING: Take a swab if there are signs of infection and arrange antibiotic treatment if infection is indicated.	
If you are unsure, seek advice from the wound care team, tissue viability specialists or dermatology.				

Source: The Society and College of Radiographers Practice Guideline Document - Radiation Dermatitis Guidelines for Radiotherapy Healthcare Professionals, Second revised edition, April 2020

Reference

The Society and College of Radiographers Practice Guideline Document - Radiation Dermatitis Guidelines for Radiotherapy Healthcare Professionals, Second revised edition, April 2020

Systemic anti-cancer therapy

There are a range of different classes of systemic anti-cancer therapies that patients are treated with. These include

- **Cytotoxic chemotherapy**
- **Immunotherapy**
- **Hormone therapies**
- **Bisphosphonates**
- **Biological therapies**

Biological therapies include a wide range of **cancer growth inhibitors**.

Examples include

- Gefitinib, Erlotinib, Afatinib, Crizotinib (non-small cell lung cancer)
- Sunitinib, Axitinib, Pazotinib Everolimus (renal cancer)
- Dabrafenib, Trametinib, Encorafenib, Binimetinib (melanoma)

These oral anti-cancer treatments have a range of unique toxicities, which are managed according to standard protocols.

Patients on these oral drugs should contact their oncology telephone helpline if they are experiencing troublesome side effects.
Patient management can also be discussed with the patient's treating oncology team, acute oncology team or Cancer Centre oncology on-call team

Biological therapies also include **monoclonal antibodies** e.g. Herceptin and Cetuximab and in particular immunotherapy drugs.

Immunotherapy

It is recommended that all patients who present with toxicity from immunotherapy have their management immediately discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

Immunotherapy is being increasingly utilised in a number of cancer sites including melanoma, lung, head and neck, gastrointestinal and genitourinary cancers.

Examples of immunotherapy include (list not exhaustive):

- Ipilimumab
- Pembrolizumab
- Nivolumab
- Pertuzimab
- Atezolizumab
- Durvalumab
- Avelumab
- Cemiplimab

These agents are generally well tolerated but can cause severe and potentially fatal immune mediated adverse reactions which can affect any organ system.

The most common immune mediated adverse reactions include

- Diarrhoea and Colitis
- Hepatitis
- Dermatitis
- Neuropathy
- Endocrinopathy (adrenal insufficiency, thyroid dysfunction and hyperglycaemia)
- Pneumonitis
- Nephritis

The majority of these immune mediated reactions initially occur during treatment however some may occur weeks to months after the course of immunotherapy has completed.

Patients who have received immunotherapy are entitled to use the oncology helpline for up to **12 months** (not the normal 6 weeks) after their last treatment.

Severe toxicities require patients to be managed with high dose steroids (prednisolone or methylprednisolone) after discussion with oncology and preferably in their treating unit. Please follow the specific regional NICaN immunotherapy guidelines which can be accessed on NICaN SharePoint Site.

SACT Skin Toxicity

Many systemic anti-cancer agents can cause skin toxicities including the oral EGFR inhibitors gefitinb, erlotinib, as well as the oral drugs capecitabine, sunitinib, and IV cetuximab. Involvement of the palms of the hands and soles of the feet only is called hand-foot syndrome and most commonly seen with capecitabine, sunitinb and liposomal doxorubicin. Radiation treatment and other supportive drugs such as steroids can also cause skin rashes. Skin toxicity from immunotherapy should be

managed as per the NICaN immunotherapy toxicity guidance available on NICaN SACT SharePoint.

Signs and Symptoms

- **Mild** - Dry skin or localised erythema +/- rash which is asymptomatic
- **Moderate** - Scattered rash or erythema with itch or other symptoms not interfering with function
- **Severe** - Exfoliative or ulcerative dermatitis or widespread skin changes with pain or other symptoms interfering with function
- **Hand-foot syndrome –** Tingling or burning, erythema, flaking, swelling, blistering palms / soles only

Investigations

Full blood count	Patients may be neutropenic and/or thrombocytopenic
U&E, LFTs	Exclude other metabolic causes of itch or rash e.g. renal or hepatic impairment
Blood cultures, septic screen, swab areas suspicious of secondary infection	Appropriate if patient is showing signs/symptoms of sepsis

Management

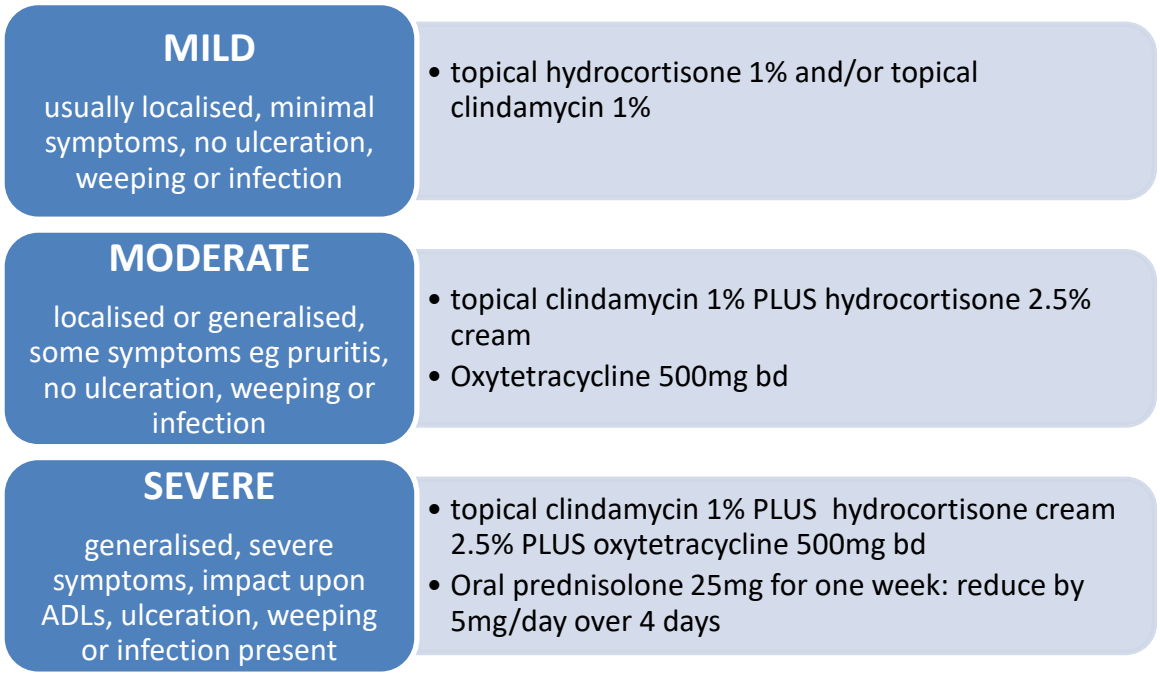
Refer immediately to local acute oncology teams and consider referral to dermatology

Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

General principles of management

- Treat any evidence of dehydration or sepsis according to neutropenic sepsis / local antibiotic guidelines
- Check platelet count – rash may be secondary to thrombocytopenia
- Full medication history including over the counter medications
- Topical emollients (alcohol free) to affected areas e.g. aqueous cream, diprobase, cream E45
- Topical emollients with high urea content in hand-foot syndrome e.g. Eucerin 10% urea, or cream E45 5% urea
- Consult dermatology for advice in *all* cases of severe skin toxicity and in those failing to respond to first line treatment

Treatment algorithm for management of EGFR induced skin rash



Reference- Expert consensus on the management of erlotinib-associated cutaneous toxicity in the U.K. The Oncologist, 2009: 14; 840-47 Thatcher N et al

SACT Hypersensitivity

While any SACT may cause a hypersensitivity reaction (HSR), some are much more commonly implicated than others.

- Paclitaxel, Docetaxel and Trastuzumab commonly cause HSR at cycle 1 or 2.
- Carboplatin, Oxaliplatin and Irinotecan commonly cause HSR but are rare at cycle 1 and become more common with increasing number of exposures to the drug.

Symptoms and signs

There are a wide spectrum of symptoms associated with HSRs. These include wheeze, dyspnoea, itch, urticarial rash, flushing, abdominal pain and collapse. A high index of suspicion should be maintained in all patients receiving SACT even when symptoms are atypical.

Severity of Reaction	Symptoms and Signs
Mild	Can include erythema/itch/rash

Moderate	As with mild but also angioedema (tongue/lip swelling), throat/chest tightness/pain, abdominal/back pain, nausea, vomiting
Severe	As with mild or moderate but with any life threatening features including: airway swelling/stridor/wheeze, hypoxia/respiratory distress, hypotension, collapse/loss of consciousness, persisting and escalating symptoms

Principles of management

Interrupt any systemic anti-cancer therapy including oral drugs and discuss management with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

In any patient suspected of having an HSR, the **infusion should be stopped immediately** but IV access maintained. Patients with respiratory symptoms should be given 100% Oxygen.

Mild/Moderate	Administer • **200mg Hydrocortisone IV slow bolus, 10mg Chlorphenamine IV slow bolus** (if this has not been given as a pre-medication). After 5 minutes, if symptoms have not completely settled they can be given a • further **100mg Hydrocortisone IV.** If the reaction has settled the patient should be observed for a period of 30minutes. If they remain asymptomatic, the infusion can be recommenced at 50% of the previous infusion rate for 30minutes. Thereafter the infusion rate can be increased to 100% if tolerated. If symptoms do not settle after 30 minutes admission should be considered.
Severe	Refer to local Trust anaphylaxis guidelines

Adrenaline (Epinephrine) 500micrograms (0.5ml 1:1000 by deep intra-muscular injection) should be used in first instance for life threatening hypersensitivity reactions.

- **Document name of agent and nature of reaction in notes and drug chart.**

Rechallenge

- All patients who have had a Grade 1 or Grade 2 reaction should be considered for re-challenge.

- Patients who have had a Grade 3 or Grade 4 HSR should not routinely be re-challenged. All should be discussed with the consultant

- If patients who have previously reacted are being re-challenged, this should be undertaken and completed between 9am and 5pm with easy access to emergency drugs. Emergency resuscitation equipment and personnel should be available during the re-challenge period.

- If the patient has had a previous hypersensitivity reaction maximal pre-medication should be administered and the rate of infusion adjusted (refer to the SPC of the particular agent). Patients should have medicines reconciled to highlight any concurrent medicines that may contribute to infusion related events or complicate the treatment of hypersensitivity. Refer to the full NICaN SACT Hypersensitivity Reactions - January 2024 guidance available on NICaN SharePoint.

Reference

L.McCann et al. NICaN Guidelines for the Management of Systemic Anti-cancer Treatment (SACT) Hypersensitivity Reactions (HSR) in Adults, October 2019

Steroid Induced Hyperglycaemia

Glucocorticoids may result in worsening of hyperglycaemia in patients with known diabetes and new onset hyperglycaemia in patients without previous diabetes. The hyperglycaemia is mainly postprandial with a relative lack of fasting hyperglycaemia. The risk of steroid induced hyperglycaemia is increased with high dose glucocorticoids.

Management

No known diabetes or diabetes controlled on diet or agents other than insulin or sulphonylurea:

- Check capillary blood glucose (CBG) before lunch and evening meal.
- If >7mmol/L stop high sugar food and drinks.

- CBG mostly <10mmol/l: Continue daily monitoring for 1 week, then reduce to once daily/stop.
- CBG mostly >10mmol/l: Increase frequency of CBGs to four times daily, check HbA1C and start treatment as below.

If CBG remains mostly >10mmol/L, titrate Gliclazide every 48 hours to a maximum dose of 160mg BD.

- If CBG remains mostly >10mmol/L on maximum dose Gliclazide after 48 hours see below

10 – 12.9 mmol/L	Gliclazide 40mg BD breakfast and lunch
13 – 14.9 mmol/L	Gliclazide 80mg BD breakfast and lunch
15 – 19.9 mmol /L	Gliclazide 120mg BD breakfast and lunch

>20 mmol/L	Gliclazide 160mg twice daily breakfast and lunch AND Humalog mix 25 or Novomix 30 10 units at breakfast. Isophane insulin may be used as an alternative particularly for patients with poor oral intake. Consider additional insulin at lunch if pre tea and bedtime CBGS still mostly >10mmol/L and titrate.

Type 2 diabetes on sub-maximal dose sulphonylurea:
Check HbA1C; Check CBG 4 times daily.
CBG mostly < 10mmol/L continue routine treatment.
CBG mostly >10mmol/L, optimise sulphonylurea first (as detailed above). If required, start premixed insulin as described below.

Type 1 diabetes, type 2 diabetes on insulin or maximal dose sulphonylurea
Check HbA1C; CBG 4 times daily.
CBG mostly <10mmol/L, continue routine treatment.
CBG mostly > 10mmol/L, add or adjust insulin as below depending on usual diabetes treatment.

Basal insulin only	Add 6-8 units bolus insulin with meals and adjust according to CBG.
Basal Bolus insulin	Increase bolus insulin by 25-50% and adjust according to CBGs. Do not change basal insulin dose unless advised by diabetes team.
Premixed insulin	Increase morning dose by 25% and extra 25% morning dose pre-lunch. Evening insulin as before. For initiation of insulin start Humalog mix 25 or Novomix 30 10 units at breakfast and consider additional insulin at lunch if pre-tea and bed time CBG still >10 mmol/L. Adjust according to CBGs. Ispohane may be used as an alternative, particularly for patients with poor oral intake.

- See BNF for cautions and contraindications.

- Refer to diabetes team as many will require home glucose monitoring, education and follow up.
- If approaching end of life, avoidance of symptomatic hyperglycaemia rather than tight glycaemic control is appropriate.
- Additional glucose lowering treatment should be reduced when steroid dose is reduced to avoid hypoglycaemia. If steroid treatment stops, revert to diabetes treatment prior to steroid use unless glucose control was poor in which case additional treatment can be reduced and closely monitored.

Discuss management with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team if any concerns

Further advice regarding end of life diabetes care including medicines management, treating hypoglycaemia and managing glucose control on steroids is available from Diabetes UK in their End of Life Diabetes Care guidance - https://www.diabetes.org.uk/upload/Position%20statements/End-of-life-Supplement111113.pdf

Reference

Adapted from Nugent, A G. Guidelines for management of steroid induced hyperglycaemia for adult patients (BHSCT 2017)

Superior Vena Cava Obstruction

- SVCO is usually associated with lung cancer (80%) but can occur with other cancers including lymphoma, breast or mediastinal germ cell tumours.
- Most commonly occurs in patients with known cancer diagnosis but can be a presenting feature of a new diagnosis.

Symptoms and signs

Symptoms: Acuteness of presentation dependent upon rate SVC obstruction occurs compared to recruitment of venous collaterals.

Symptoms are often worse first thing in the morning and exacerbated by bending or lying down.

Can include neck, face or arm swelling, dyspnoea, cough, headache, dysphagia, visual disturbance and hoarseness.

Signs: Although the signs are characteristic they may be absent and an index of suspicion is required based on tumour type and symptoms.

Can include fixed engorgement of external and internal jugular veins, collateral veins over the chest wall, facial/conjunctival or arm oedema, facial plethora or cyanosis.

Observations including oxygen saturations required.

Investigations

Bloods	FBP, U&E, LFTs and coagulation (in case interventional procedure required)
Imaging	Chest x-ray Urgent contrast CT chest
Biopsy	In the absence of a known malignancy biopsy is preferable prior to commencing steroids

Initial Management

Refer to local Acute Oncology Service

Interrupt any systemic anti-cancer therapy including oral drugs until management discussed with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team

Most patients present with symptoms of insidious onset and there is time to establish a histological diagnosis and extent of disease if not known prior to commencing treatment.

Unrelieved SVCO is generally not life threatening except if there is cerebral dysfunction, decreased cardiac output or upper airways obstruction.

- Sit the patient up.
- Consider oxygen and analgesia.
- If dyspnoeic oramorph 2.5-5mg PO 4 hourly is usually helpful.

Steroids

- **First presentation** of suspected cancer – hold off steroids, unless the patient has respiratory compromise, as they may compromise interpretation of biopsies.
- Already confirmed cancer diagnosis – Dexamethasone 8mg BD PO/IV (am and lunchtime) with PPI cover. NB. PO steroids preferred unless highly symptomatic/unable to swallow.

Anticoagulation

- High incidence of thrombus with intravascular stents and therefore prophylactic anticoagulation or antiplatelets may be considered although their exact role has yet to be confirmed.
- Full anticoagulation should be given, where appropriate if evidence of thrombus.

Subsequent Management

Treatment options include:

1. Stent insertion

- Insertion of an expandable metal stent into the SVC at the point of stricture can offer quick symptomatic relief and restoration of the normal pattern of flow.
- Treatment of choice for severe symptoms or recurrent SVCO in a previously irradiated field.
- Used less frequently in potentially curable patients where stents may migrate if there is a significant response to treatment.
- Discuss the case with interventional radiology.

2. Chemotherapy

- Urgent chemotherapy often treatment of choice for patients with chemo-sensitive disease such as small cell lung cancer, lymphomas or mediastinal germ cell tumours.

3. Radiotherapy

- May be recommended depending on underlying histology, particularly if non chemo-sensitive disease or occlusion not amendable to stent placement.
- May make subsequent histology difficult to obtain.
- Does not provide immediate symptomatic benefit, response rates vary according to underlying disease and anticipated life expectancy must be weeks to see full benefit.
- Radiotherapy schedule depends on volume of disease and performance status of patient.

Following initial medical management, consider referral to Physiotherapy and/or Occupational Therapy if patient has on-going symptoms of dyspnoea and/or impaired physical functioning.

Venous Thromboembolism

VTE Prophylaxis

- VTE risk assessment should be completed on the drug kardex and thromboprophylaxis prescribed accordingly.
- Once daily enoxaparin is the anticoagulant of choice for pharmacological thromboprophylaxis.
- Prophylactic dose of enoxaparin can be used when platelet count >75 x 10^9/L.
- When platelet count <75 x 10^9/L prophylactic LMWH should be omitted or considered on a case-by-case basis only.
- In patients with severe renal failure (creatinine clearance< 30 mL/min) the dose of enoxaparin should be reduced to 20mg OD.

VTE Treatment

- LMWH (Enoxaparin 1.5mg/kg once daily) or direct oral anticoagulant (DOAC) is recommended for the initial treatment, early maintenance treatment (10 days to 3 months) and long-term treatment (beyond 3 months) of VTE in cancer patients. A 25% dose reduction if using LMWH may be considered after the initial 8 weeks of therapy, particularly in those patients with a perceived greater bleeding risk.
- In the presence of severe renal failure (creatinine clearance < 30 mL/min) LMWH heparin doses can be commenced at 1mg/kg once daily and optimized based on anti-Xa level.
- DOACs can be used for cancer patients with an acute diagnosis of VTE, a low risk of bleeding, and no drug–drug interactions with current systemic therapy. LMWHs constitute an acceptable alternative
- If treatment with a DOAC is used for initial anticoagulation, consider whether a lead in time with LMWH is required as well as patient's renal function. Consult BNF for

all dosing schedules. An individualised approach should be taken following shared decision making with the patient.

- There is an increase in major bleeding risk with DOACs. LMWH is recommended for cancer patients with an acute diagnosis of VTE and a high risk of bleeding, including patients with luminal gastrointestinal cancers with an intact primary, patients with cancers at risk of bleeding from the genitourinary tract, bladder, or nephrostomy tubes, or patients with active gastrointestinal mucosal abnormalities such as duodenal ulcers, gastritis, esophagitis, or colitis.
- After 3–6 months the benefits and risks of continued anticoagulation should be assessed. This should take into account patients' tolerability, cancer activity and other VTE risk factors. For long-term anticoagulation, LMWH, or DOAC for at least 6 months are recommended due to improved efficacy over vitamin K antagonists.
- Anticoagulation beyond the initial 6 months should be offered to select patients with active cancer, such as those with metastatic disease or those receiving chemotherapy. Anticoagulation beyond 6 months should be reassessed on a regular basis to ensure a continued risk-benefit profile.
- A brain tumour alone is not a contraindication for anticoagulation.

LMWH dosing for VTE in the presence of thrombocytopenia:

Platelet count should be closely monitored if further decline anticipated or platelet count nadir has not yet been reached.

Platelet count >50 x 10^9/L	Full therapeutic dose LMWH
Platelet count 25-50 x 10^9/L	Prophylactic dose once daily LMWH*
Platelet count <25 x 10^9/L	Omit anticoagulation *or* use prophylactic dose unfractionated heparin TID*

*(Individual bleeding risk should be considered)

Central Venous Access Device (CVAD) related

- Diagnosis of CVAD related thrombosis requires radiological evidence. If a CVAD related thrombosis is suspected an ultrasound scan should be performed. If the ultrasound result is normal in the presence of clinical suspicion of a CVAD related thrombosis then further imaging with MRI or CT scan can be considered.
- For a confirmed CVAD related thrombosis the CVAD does not necessarily have to be removed if it remains functional and the venous access is still required.

- LMWH (Enoxaparin 1.5mg/kg once daily) is the anticoagulant treatment of choice. Anticoagulation should be given for a minimum of 3 months. If the CVAD is not removed then anticoagulation should continue for as long as the CVAD remains in situ and for at least 3 months.
- The efficacy of DOACs have not been established in CVAD associated thrombosis and LMWH remains the treatment of choice.

Recurrent VTE on Treatment

- In the event of VTE recurrence whilst on warfarin or a DOAC it is advised to switch to therapeutic weight-adjusted dose LMWH.
- For VTE recurrence whilst on LMWH which is at less than the therapeutic weight-adjusted dose then the dose of LMWH should be increased to the therapeutic weight-adjusted level.
- For VTE recurrence whilst on therapeutic weight-adjusted dose LMWH then the dose should be increased by approximately 25%.
- If the patient has symptoms from the VTE recurrence which have not improved 5-7 days after the dose increase then the peak anti-Xa level should be checked to guide any further increase in dose.

Inferior Vena cava (IVC) filters

- Should be considered in the treatment of acute VTE when anticoagulation is **absolutely** contraindicated. The presence of contraindications to anticoagulation should be regularly reassessed. Anticoagulation should be commenced and the retrievable IVC filter removed when the contraindication has resolved.
- Not recommended for primary VTE prophylaxis in cancer patients.
- Absolutely indicated in major or life-threatening haemorrhage which requires interruption of anticoagulation in the presence of acute VTE. Once bleeding resolves the retrievable IVC filter should be removed and anticoagulation recommended.

Discuss management with the Acute Oncology Team, the patient's treating oncology team or Cancer Centre oncology on-call team or local haematology team if any concerns

Reference

Venous thromboembolic diseases: diagnosis, management and thrombophilia testing NICE guideline [NG158] Published: 26 March 2020

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Abbreviations

Blood tests

ANC	Absolute neutrophil count
cCa	Corrected Calcium
Coag	Coagulation Screen
CRP	C reactive protein
FBP	Full blood picture
K	Potassium
U&E	Urea and electrolytes
LFT	Liver function tests
Mg	Magnesium
PTH	Parathyroid hormone

Medication related

OD	Once daily
BD	Twice daily
TID	Three times daily
QID	Four times daily
IV	Intravenous
PO	Orally
Prn	When required
SC	Subcutaneous

Other

ADL	Activities of daily living
CBG	Capillary blood glucose
CSCI	Continuous subcutaneous infusion
CTCAE	Common Toxicity Criteria for Adverse Events
CVAD	Central Venous Access Device
DOAC	Direct-acting Oral Anticoagulants
DVA	Driver and Vehicle Agency
GCSF	Granulocyte Colony Stimulating Factor
HSR	Hypersensitivity reaction
LMWH	Low molecular weight heparin
MSCC	Metastatic Spinal Cord Compression
NSAIDs	Non-steroidal anti-inflammatory drugs
NS	Neutropenic Sepsis
PICCs	Peripherally Inserted Central Catheters
PPI	Proton Pump Inhibitor
SACT	Systemic Anti-Cancer Therapy
SPCT	Specialist Palliative Care Team
SVCO	Superior Vena Cava Obstruction
TPN	Total Parenteral Nutrition
VTE	Venous Thromboembolism